ABSTRACTS

This section of the ANNALS is published in collaboration with the two abstracting Journals, ABSTRACTS OF WORLD MEDICINE, and OPHTHALMIC LITERATURE, published by the British Medical Association.

The abstracts selected for this Journal are divided into the following sections: Acute Rheumatism; Chronic Articular Rheumatism (Rheumatoid Arthritis, Osteo-Arthritis, Spondylitis, Miscellaneous); Disk Syndrome; Gout; Non-Articular Rheumatism; General Pathology; ACTH, Cortisone, and other Steroids; Other General Subjects. At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.

The section "ACTH, Cortisone, and other Steroids" includes abstracts and titles of articles dealing with steroid research which, although not directly concerned with the rheumatic diseases, may make an important contribution to knowledge of the scope and modus operandi of steroid therapy.

Acute Rheumatism


The authors compare the results of treatment at the Clinique Médicale Infantile, Toulouse, of 28 children with acute juvenile rheumatic carditis, of whom thirteen were given salicylates and fifteen ACTH (corticotrophin) or cortisone. Details of dosage, types of cases, and follow-up results are given. In the authors' opinion acute attacks of carditis, unless very severe, can generally be treated successfully by the usual salicylate therapy, but recurrences are not infrequent and valvular lesions often persist. Of those treated with the hormones, three, all severe cases, died, but the other twelve responded favourably, although no change was seen in established valvular lesions. It is concluded that treatment with ACTH or cortisone is preferable to that with salicylates, particularly in severe attacks of rheumatic carditis, but that it must be started early in the disease if it is to be effective; if this can be done, permanent cardiac damage may be avoided. Hormone therapy is not advised for patients with chronic valvular lesions, nor as interval treatment between attacks. Kathleen M. Lawther.


The combination of salicylates with cortisone or ACTH (corticotrophin) in the treatment of rheumatic fever allows the use of smaller doses of each substance; it seems probable also from experimental evidence that the two drugs enhance one another's action, and that their use together may prevent the development of adrenal atrophy.

At the Paediatric Institute of the University of Pisa, thirteen children with rheumatic fever or chorea have been treated in this way, eight during their first attack. Doses of 25 mg. ACTH or 50 mg. cortisone were given daily for 3 weeks, and the dose was then halved for a further 3 weeks. Simultaneously, 4 to 6 g. sodium salicylate was administered daily, this dose also being halved later. In addition, penicillin and streptomycin were given during the whole period of treatment, partly because of a belief in the initial infective nature of the disease and partly to combat any increased risk of infection resulting from the hormone therapy. A low-salt diet with added ascorbic acid was given, and the usual measures for the relief of cardiac failure were instituted when necessary.

All the patients improved rapidly, the most striking effect being noted on the extracardiac manifestations of the disease: one patient with chorea, for instance, lost his symptoms altogether within 10 days. No danger was encountered from fluid retention, and three patients in heart failure—one seriously ill—all responded satisfactorily. The effect of the combined therapy on the cardiac lesions was much more difficult to assess: although the signs of endocardial involvement did not progress, in only two patients did they entirely disappear, and this during their first attack. As might be expected, myocarditis and pericarditis appeared to be more susceptible to treatment than endocarditis, but the electrocardiogram was of little help as a guide to improvement because of the changes produced by the electrolyte disturbances accompanying treatment.

The authors conclude that while the course of the disease was much shortened and, although several were extremely ill initially, no patient in this series died, it cannot yet be said that a form of treatment has been found which materially alters the results of cardiac involvement in rheumatic fever. A. Paton.

Non-Specific Myocarditis in Acute Rheumatic Fever.


Doubting the role attributed to the Aschoff bodies in the aetiology of myocarditis and in the causation of myocardial failure in acute rheumatic fever, the authors, working at the (U.S.) Armed Forces Institute of Pathology, Washington, D.C., studied microscopically the
myocardium in 22 cases in which death was due to acute rheumatic disease and in which there was clinical evidence of myocarditis. Electrocardiographic records were available for twelve of the cases. Only cases were examined in which typical Aschoff bodies were present in the interstitial tissue; in all cases interstitial lymphocytic infiltrations were also found, both in association with and apart from the Aschoff bodies. In eighteen cases there were in addition circumscribed foci of myonecrosis which, when cellular reaction had occurred, resembled Aschoff bodies. It is suggested that these appearances may explain the recent revival of the theory that the Aschoff body arises from damaged muscle. The authors regard these necrotic foci as due to a non-specific myocarditis and relate the changes in the electrocardiogram to its occurrence.

A. C. Lendrum.


The significance of the presence of Aschoff bodies in the auricular appendage of forty rheumatic hearts was studied post mortem at Bellevue Hospital (Columbia University), New York. In five of the cases commissurotomy had been performed for mitral stenosis. It is suggested that if Aschoff bodies are present in the appendage there are likely to be signs of activity elsewhere in the heart, and that the absence of Aschoff bodies from the appendage does not exclude the possibility of signs of activity elsewhere. Of the eighteen hearts with appendicular thrombus, seventeen were from cases of auricular fibrillation, and fourteen of them on histological examination showed no signs of activity in the form of Aschoff bodies, auriculitis, or acute verrucous endocarditis, singly or in combination.

A. C. Lendrum.


The authors draw attention to a syndrome that they have noted as a sequel to mitral valvotomy. The symptoms, mainly precordial pain and fever, have been noted in 43 out of 179 cases of mitral stenosis treated by commissurotomy (24 per cent.) and are regarded as something separate from the ordinary complications that may arise in the course of any thoracic operation. In 24 additional cases the patient complained of pain, coming on after discharge from hospital, which was of a similar nature but unaccompanied by fever.

The onset of pain is sudden and may take place anything from 10 days to a month after operation. It is gripping and vice-like over the pericardium, radiates over a wide field, may last several weeks, and may recur. Associated with the pain is a variable degree of fever, which is accompanied by toxaemia, weakness, and sweating. Other features, such as psychosis, heart failure, and arthritis, may be added to the picture, the cardiac symptoms being the most important. The most likely explanation is that there has been a reactivation of the rheumatic process; the 179 cases included in this study formed part of a consecutive series of 183, four having been excluded because the operation was followed immediately by acute rheumatic fever. Biopsy of the left atrial appendage was taken at operation in 37 of the 43 cases in which the syndrome subsequently developed. Aschoff bodies were identified microscopically in fifteen (40.5 per cent.) of these, but also in a practically identical percentage of cases in which the syndrome did not occur.

The fate of the 43 patients who developed the syndrome was varied: three died, two developed hemiplegia, three became psychotic, and five went into permanent auricular fibrillation. Of the remaining 29, the majority require as much medical attention as they did before the operation, or more.

The authors do not discuss the implication of these findings for the selection of patients for operation beyond insisting on the desirability of excluding patients with clinically active rheumatism and commenting on the difficulty of recognizing this condition.

T. Holmes Sellors.


The histological examination at the Thorndike Memorial Laboratory (Harvard Medical School) of biopsy specimens from the auricles of 183 patients undergoing operation for mitral stenosis at Boston City Hospital showed that 45.4 per cent. contained typical Aschoff bodies, although all patients had been carefully selected as showing no clinical evidence of rheumatic activity. The incidence of Aschoff bodies declined with age, 73 per cent. of patients aged 20 to 30 years showing the bodies as contrasted with only 8 per cent. of those over 50. It was also found that Aschoff bodies were much less frequent when auricular fibrillation was present (17 per cent. of cases) than when the heart rhythm was normal (76 per cent.). This difference was independent of the age of the patient and the duration of the disease. The results of clinical tests for rheumatic activity or active carditis, such as estimation of the erythrocyte sedimentation rate and antistreptolysin titre, and electrocardiography could not be correlated with the incidence of Aschoff bodies.

The authors suggest that although their results do not disprove the generally accepted view that the presence of Aschoff bodies indicates a state of rheumatic activity, it must be concluded, if this view is correct, that the current clinical tests for rheumatic activity are too crude to detect a smouldering rheumatic carditis.

H. F. Turney.


Recent evidence seems to show that the increased susceptibility of some patients to rheumatic fever may
be related to the immunological status of the blood. In this study, carried out at the Children's Hospital, Iowa City (State University of Iowa College of Medicine), the authors investigated by electrophoresis the changes in serum and plasma protein levels of 77 children with “definite rheumatic fever” treated by “standard non-specific methods of therapy”, and five patients with chorea but without other manifestations of rheumatic fever. The plasma or serum, diluted with 3 volumes of a barbiturate buffer (pH 8.6, ionic strength 0.1), was dialyzed in the cold for 3 days, and electrophoresis was carried out in the Longsworth modification of the Tiselius apparatus.

The results were considered in nineteen separate groups or subgroups, according to the stage of the disease, the presence of decompensation, and the presence of mild intercurrent infections or exacerbations at the time the serum sample was obtained. [The criteria by which these patients were assigned to the various groups are not further specified.] Patients with a remittent type of disease and those with chorea alone formed two separate subgroups, but any one patient might appear more than once in any particular group or once in each of several groups; thus, the study was based on 205 separate samples of serum or plasma, each patient being counted a mean of 2.2 times. The results of the estimation of the total protein content and the percentage composition of the various components are given, standard deviations being shown for each group. Some over-all clinical data for the various groups are also included, for example the percentage of patients with fever, or with signs of active carditis, the mean and range of the erythrocyte sedimentation rate, and the mean and range of the interval from onset of the disease, these values being compared with those in a group of 31 normal children as reported by Knapp and Routh (Pediatrics, 1949, 4, 508).

Briefly, it was found that during recovery there was a progressive increase towards normal in the proportion of albumin, a marked decrease towards normal in the proportion of alpha-2 globulin, fibrinogen, and gamma globulin, a less marked fall in alpha-1 globulin and gamma’ globulin, but no significant change in beta globulin. There was good correlation of the erythrocyte sedimentation rate (Westergren) with the values of albumin (correlation coefficient \( r = -0.55 \)), and of alpha-1 and alpha-2 globulin, fibrinogen, and gamma globulin \( r = +0.43 \) to 0.56 but no correlation with beta globulin \( r = +0.04 \).

In cases with decompensation there was a tendency to elevation of the alpha-2 globulin and a decrease in beta globulin values compared with those in patients in the same clinical stage but without decompensation. In those with chorea but with a normal sedimentation rate, there was a significant departure from normal values of the albumin, alpha-2 globulin, and to a lesser extent, gamma globulin levels. It is thought that the changes in the serum albumin level may be compensatory to the changes in globulin level, while the change in the values of alpha-1 globulin may be related to the increase in C-reactive protein and of the alpha-2 globulin to increase in serum mucoprotein. The obscuring of the true gamma’ globulin values by the incorporation of gamma’ globulin in the fibrinogen peak is discussed.

[As the groups differed in composition, except for the occasional presence of certain individuals, they are not strictly comparable, especially as some subjects furnished two or more samples of serum for inclusion in the same group.]

E. G. L. Bywaters.

Aureomycin in the Prophylaxis of Rheumatic Fever


Aureomycin was given prophylactically to 23 patients who had had rheumatic fever, twelve similar patients serving as controls. Of the treated group eighteen (average age 17 years) had had an attack of rheumatic fever in the preceding 5 years, as compared with eight (average age 16 years) of the control group. A dose of 250 mg. aureomycin was given 30 minutes or one hour before breakfast and again 2 hours after the evening meal. The period of observation ranged from 2 to 20 months, averaging 9 months in the treated group and 11 months in the control group. Rheumatic fever recurred in one of the 23 treated patients and in four of the twelve controls during the investigation. A reduction in the incidence of respiratory infections of approximately 50 per cent. was observed in the treated group.

Side-effects of the antibiotic were minimal.

This series is too small and the observation period too short for firm conclusions to be drawn. The patients were mostly from an older age group, in which recurrences are normally less frequent than in young children. Penicillin is less expensive than aureomycin and should therefore be used as a routine until some other drug is shown to be more effective in preventing a recurrence.

R. S. Illingworth.

Chorea Minor. Preliminary Report on Six Patients treated with Combined ACTH and Cortisone


This is a preliminary report on the simultaneous use of ACTH and cortisone in the treatment of chorea minor.

The trial was carried out at the Flower and Fifth Avenue Hospitals and the Metropolitan Hospital, New York, in six cases of the disease in children between 6 and 11 years old. The combined therapy was continued until symptoms disappeared, which occurred in from 8 to 48 days. As regards side-effects, moon-face was noted in all cases, and hypertension in three. When untoward symptoms appeared the dosage of the hormones was at once reduced. There was an absence of rebound phenomena at the end of treatment. In three cases latent urinary infection with positive urine cultures was discovered leading the authors to suggest that the renal tissues of growing children may be vulnerable to the action of these hormones.

In view of the small number of cases in this series the conclusions drawn are cautious and tentative, but the authors, comparing their own results with those of others who have used one or other of these hormones, not in combination, consider that the combined administration...
of ACTH and cortisone has given “rather better” results. At this stage of the study it is not claimed that “hormone therapy is the preferred and acceptable one for this condition”, and it is admitted that further study and investigation are required.

Charles McNeil.


Chronic Articular Rheumatism

(Osteoarthrosis)

Cortisone and Rheumatoid Disease. West, H. F., and Newns, G. R. (1953). Lancet, 2, 1123. 6 refs. It is known that cortisone in a daily dosage of 100 mg. or more has a profound effect on the symptoms and signs of rheumatoid disease, but unfortunately doses greater than 75 mg. a day can rarely be maintained for many months without serious complications. The present investigation was undertaken at the Centre for the Investigation and Treatment of Rheumatic Diseases, Sheffield, to provide a definite answer to the question whether the oral administration of cortisone acetate in doses of 50 to 75 mg. per day over a long period favourably affects the course of the disease.

To this end 27 patients were given cortisone acetate in the above dosage for an average of 19 months, and the results compared with those in a similar group of 27 patients who did not receive cortisone. (A further three patients treated with the hormone died after 9 to 13 months and were excluded from the study.) The effects on the fundamental disease process were assessed by objective determination on six points: stiffness of joints after rest; need for analgesics; physical abilities; erythrocyte sedimentation rate; anaemia and plasma protein level; and the radiographic changes. In addition, observations on weight, strength of grip, and blood pressure, as well as the results of various laboratory investigations, are recorded. It is pointed out that an over-all average leucocytosis, with a stable lymphocyte count, is a feature to be taken into account when considering whether the treatment given had been physiologically or not.

Of the three deaths, two could not be ascribed to the cortisone treatment, but may have been hastened thereby, while the third patient died from haemorrhage from an internal lesion of polyarteritis nodosa.

The conclusion is reached that long-continued cortisone therapy for rheumatic disease is not to be recommended. The observations were not, however, considered necessarily to exclude the possibility that corticosteroids play an important part in the pathogenesis of rheumatoid disease, or that prolonged administration of cortisone may be of benefit in certain types of the disease. It is, however, considered that there is no theoretical reason why this hormone should have any curative effect in this disease [as distinct from the peripheral blocking of symptoms], and that long-continued suppression of adrenal production of hydrocortisone constitutes a real danger to the subsequent effectiveness of the defence mechanisms against normal and abnormal stresses.

Harry Coke.

Observations on the Use of Cortisone and ACTH in Rheumatoid Arthritis. Clark, W. S., Tonning, H. O., Kukla, J. P., and Bauer, W. (1953). New Engl. J. Med., 249, 635. 8 figs, 13 refs. Observations are reported from the Massachusetts General Hospital, Boston, on the treatment with cortisone or ACTH (corticotrophin) of 52 patients ranging in age from 21 to 62 years suffering from rheumatoid arthritis of 1 to 29 years' duration. A number of patients received both drugs, but at different times. A total of 42 courses of cortisone were administered, with major subjective improvement in 31 (74 per cent.) and major objective improvement in 16 (38 per cent.). Similar degrees of improvement occurred in 11 (60 per cent.) and 4 (22 per cent.) of the eighteen courses of ACTH given. In addition to the hormones, the patients also received basic treatment consisting of rest, aspirin, hydrotherapy, and active exercises. No prolonged remission of the disease was observed after withdrawal of the hormones, and relapse was rapid in most cases. Histological examinations of tissue made during treat-
ment showed a decrease in oedema and inflammatory cellular infiltration, with some reduction in fixed cellular hypertrophy and hyperplasia.

The most serious side-effects encountered were psychosis, for which cortisone treatment had to be stopped in eight cases and ACTH treatment in six, oedema, and severe potassium loss. The authors found that the effective use of the hormones in this series was limited by the hazards of hypercorticism, and emphasize that no precautionary measure is known which will obviate the need for constant observation. In their view the most valuable effect of the drugs is to decrease pain and stiffness, with consequent improvement in function.

Oswald Savage.

A New Form of ACTH Therapy for Rheumatoid Arthritis.

The effect of an intravenous drip infusion containing both ACTH (corticotrophin) and insulin was studied at the University Medical Clinic, Munich, on eleven patients suffering from polyarthritis of varying degree and was found to equal that of a much higher intramuscular dose of ACTH alone; further, only small doses of ACTH were found to be necessary to prevent relapses once maximum improvement had occurred. It was also observed that many of the frequently described symptoms following withdrawal of ACTH therapy, such as severe exacerbation of the arthritis and mental depression, did not occur after treatment with ACTH combined with insulin.

Hypoglycaemia due to the insulin was a side-effect difficult to control; the addition of glucose to the infusion to counteract this also seemed to increase the beneficial effects of the therapy. One patient who continued to complain of pain despite the administration of large amounts of ACTH was relieved of symptoms by the addition of insulin and glucose. Although the urine was regularly tested for sugar and frequent blood sugar estimations were performed, in most patients no marked changes were found, most of the glucose added to the infusion being completely absorbed, and only after a large amount had been given did traces appear in the urine.

The levels of corticosteroids in the urine paralleled the clinical improvement, and in most patients the levels were as high with ACTH and insulin as they were with much larger doses of ACTH alone. Insulin alone or small doses of ACTH alone did not always lead to a rise in urinary steroid level, and Ringer's solution given intravenously as a control produced no alteration in the steroid excretion. The possibility of insulin acting as a stimulator of the synthesis of biologically active hormones from the adrenal glands is discussed.

Robert Hodgkinson.


In an attempt to determine the factors of possible prognostic value in the treatment of the anaemia which often accompanies rheumatoid arthritis, a course of iron was given intravenously to each of fifty patients with rheumatoid arthritis, in this investigation reported from the Rheumatism Research Unit, Bath. The total dose of iron given was calculated (on the basis that each 100 mg. iron raises the haemoglobin level by 4 per cent.) to be more than adequate to raise the haemoglobin to 100 per cent. (14.8 g./100 ml.). In fifteen patients the haemoglobin level became normal, in 22 it was improved, and in the remaining thirteen it was unchanged.

The results of the determination of various blood components in these three groups of patients were then analysed to determine if there were any prognostic factors which might be of use in forecasting the response to intravenous iron therapy. It was observed that a normal haemoglobin level was always achieved if the erythrocytosis and sedimentation rate was below 30 mm./hr, or if microcytosis, gross hypochromasia, or a raised total iron binding capacity of the serum was present. But the haemoglobin level also became normal in some cases in which none of these features was present. The degree of activity of the rheumatoid arthritis, or the levels of plasma iron, serum protein, and the free erythrocyte protoporphyrin were therefore concluded to be of no prognostic value.

K. C. Robinson.

Diagnosis and Treatment of Still's Disease. DIMSON, S. B. (1954). Rheumatism, 10, 18. 1 fig., 27 refs.


Rheumatoid Arthritis after the Age of 55. (La polyartritis crónica que se produce a partir de los 55 años.) ISÈNE, L., and REDON, M. (1953). Rev. Rhum., 20, 877.

(Osteo-Arthritis)


As osteo-arthritis of the scapulo-humeral joint is relatively uncommon—in two series quoted, only 12 instances were found in 763 cases of painful shoulder—the authors give a short clinical account of the condition. It is found chiefly in elderly subjects, and is usually secondary to a congenital malformation of the humeral head, to an old osteochondritis, or to severe trauma. The clinical features, namely, dull pain in the shoulder, atrophy of the deltoid and supra- and infra-spinatus,
muscles, with restriction of movement, are similar to those observed in the late stages of the more common scapulohumeral periarthritis, in the slowly progressive shoulder stiffness of senile tuberculosis of the joint, in rheumatoid arthritis, and in the arthritis of ankylosing spondylitis.

The differential diagnosis is discussed, and the several varieties of the condition are illustrated by typical radiographs. The treatment recommended is the administration of vitamins, calcium, or compounds of iodine and sulphur, and in some cases mud packs and radiotherapy have proved useful. Mobilization of the shoulder is considered to be dangerous (but the reasons for this are not stated).

Kenneth Stone.


In a previous paper (Brit. med. J., 1952, 2, 1295) the author suggested that an alteration in the collagen: chondroitin-sulphate ratio in cartilage occurred in the weight-bearing joints, the decrease in the ratio being due to an increase in chondroitin-sulphate which is a measure of the protecting matrix. In the present paper, from the Canadian Red Cross Memorial Hospital, Taplow, Bucks., he describes an investigation of damaged fibritration cartilage and healthy cartilage in the knee-joint and patellar surface of the femur. The collagen: chondroitin-sulphate ratio was higher in fibrillar (degeneration) cartilage than in healthy cartilage. The author interprets this finding as indicating a slower rate of loss of collagen as compared with matrix substance, the loss or absence of matrix substance rendering the cartilage liable to greater damage and fissuring.

The paper certainly opens up a chemical approach to the problem of osteo-arthritis. R. E. Tunbridge.


The author reviews the literature of the treatment of osteo-arthritis by intra-articular injection of lactic acid. In his own study, carried out at the Rheumatism Research Centre, University of Manchester, he treated one hundred patients by standard methods of physiotherapy, but fifty of these received in addition intra-articular injections of lactic acid combined with procaine. The two groups were considered to be of similar severity, and assessment of the results was made after 3 and 6 months.

It was found that subjective and objective improvement occurred in equal numbers in both groups. The psychological effect of the injections did not seem to affect the results in the group receiving lactic acid. Similarly, the number of patients who were able to return to work was the same in both groups.

The author therefore concludes that the intra-articular injection of lactic acid is of no therapeutic value in osteo-arthritis.

W. Tegner.


Radiotherapy in Osteo-Arthritis. (Röntgen-therapie der Arthritis deformans.) Pannewitz, G. Von (1953). Strahlentherapie, 92, 375. 4 refs.


(Spondylitis)


While it is generally agreed that typical changes in the sacro-iliac joints are found in all but very early cases of ankylosing spondylitis, opinions differ as to whether such changes are associated with this disorder alone, some authors alleging that they occur in a certain percentage of cases of rheumatoid arthritis, and that ankylosing spondylitis is not a separate entity but merely a particular manifestation of rheumatoid arthritis.

In the study here reported from the Maggiore Hospital, Turin, the pupils of 71 female and 29 male patients aged from under 20 to 70 years, with rheumatoid arthritis, were examined radiologically. In 76 cases the sacro-iliac joint was judged to be normal. In the remaining 24 cases the joint showed various changes, consisting in most cases in marginal sclerosis and a narrowed and indistinct joint space. Exceptionally, the joint margins were irregular and the joint space was interrupted by bony bridges, but none showed complete disappearance of the joint line. The changes were not related to the duration of the disease, to the number of other joints involved, or to the involvement or not of the hip-joints, but there appeared to be some relationship with involvement of the lumbar spine. In no case did the changes correspond to the typical evolutionary phases of ankylosing spondylitis, the changes in the sacro-iliac joint of most of the patients being unilateral, a finding considered rare in ankylosing spondylitis. Other workers have reported similar changes in the sacro-iliac joints of non-arthritic subjects, particularly women who have had multiple pregnancies; also such changes are not uncommon in elderly subjects, in whom they are due to degeneration.

The authors conclude from their study that the radiological changes observed in the sacro-iliac joints of rheumatoid arthritic patients are not significant, as they do not vary substantially from those in non-arthritic subjects of the same age and sex, and also do not present the characteristics generally considered typical of ankylosing spondylitis. They maintain, therefore, that the two diseases are distinct entities.

W. D. Nichol.

(Miscellaneous)


This paper describes an empirical method of treatment of chronic arthritis which the author has found “very valuable”. It consists in the application of deep x rays to the cervical and lumbo-sacral regions for arthritis of the upper and lower limbs respectively. For the upper limb a surface dose of 75 to 80 r, gradually reduced to 55 or 60 r, is given to the back of the neck at 200 kV, with F.S.D. of 40 cm., a Thoraæus filter, and a field of 15 x 15 cm. For the lower limb, a field of 20 x 15 or 20 x 12 cm. is used, extending from D 12 to S 3, at 50 cm. F.S.D., the dose given being 80 to 100 r, reduced gradually to 65 or 70 r. The addition of small doses to the affected joints seems to be of value—a depth dose of 60 r, reducing to 45 r, being advised. Treatment is given weekly (though this may not be the optimum interval) and most patients experience an increase of pain after 12 to 48 hrs. The course is continued for 12 to 16 weeks, or until reaction ceases; results are better in the presence of reactions. Courses can be repeated two or three times, as the skin doses are so low. If there is no response after six doses, treatment is discontinued. A few cases in which striking results were obtained, including disappearance of gross synovial thickening of the knee joints, are quoted [but no attempt is made at a statistical evaluation of results]. The mode of action is not understood, though it has been attributed (without supporting evidence) to some effect on the sympathetic nerves or ganglia with consequent changes in blood supply to the joints.

J. Walter.


An investigation previously carried out at the University of Würzburg into the action of “Venostasin” (an extract of horse-chestnut containing glycosides of the flavone group) suggested that the drug inhibits hyaluronidase in vivo. It therefore seemed likely that it would be found useful in the treatment of cases of arthritis in which the viscosity of the synovial fluid is increased, since it has been suggested that the beneficial effects of ACTH are largely due to its power of inhibiting hyaluronidase. Moreover, in rheumatic fever the blood has been found to contain increased quantities of non-specific inhibitors of hyaluronidase as well as specific antibody.

The results are now reported of the treatment of eleven cases of chronic arthritis with daily intravenous injections of 10 ml. Venostasin for 12 days. Most of the cases treated were of rheumatoid arthritis which had proved resistant to other forms of therapy. There were no unpleasant side-effects. All the patients benefited to a greater or lesser extent, although the erythrocyte sedimentation rate appeared to be uninfluenced. In every case capillary permeability, as estimated by Landis’s method, was diminished and capillary resistance, as estimated by Hecht’s method, was increased, and this phenomenon was in direct relation to the amount of clinical improvement obtained. The beneficial effect of the drug on the capillaries is ascribed to its inhibition of hyaluronidase.

D. Preiskel.


The natural history of dermamyositis and the value in treatment of the administration of endocrines are discussed with reference to 26 cases seen at the Children’s Medical Center and Massachusetts General Hospital, Boston, between 1916 and 1952. The ages of the patients ranged from 2 to 11 years. At the time of the report sixteen of the patients were still alive; seven of the ten who died had had the disease for less than 2 years. The diagnosis was confirmed by biopsy in 23 cases; no other diagnostic aid was of any value. Generally the onset was insidious, with weakness and tiredness as the predominant symptoms. In 23 cases the face was involved.

The authors point out that vigorous physiotherapy and orthopaedic treatment, to prevent crippling contractures and deformities and to correct them once they occur, are the only effective measures available at the present time. Corticotrophin (ACTH) or cortisone by intramuscular injection was tried in the acute stage of the disease and appeared to be of some value; testosterone was then given sublingually, in the hope that the improvement would be maintained. Symptomatic benefit was observed in all the thirteen so treated. The authors recommend a full dose of ACTH or cortisone at the beginning of treatment, the patient being placed on a low-sodium diet supplemented with potassium. This is continued for 2 to 3 weeks, when the dose of hormone is gradually reduced; testosterone is then administered and continued for several months. Wilfrid Gaisford.


Mepacrine was tried in the treatment of patients with lupus erythematosus at the Royal Infirmary, Glasgow, the series comprising twenty patients who had not previously been treated for the condition and 42 who had failed to respond to other therapeutic measures. Only twelve of the patients in the first group responded satisfactorily, while in 25 of the patients in the second group the response was considered good. In nearly all the patients, however, there was a relapse after withdrawal of the drug, a much higher relapse rate than that observed with bismuth and oxophenarsine hydrochloride (Mapharside). A good temporary response was also obtained in
three patients with subacute and one patient with acute lupus erythematosus. Exfoliative dermatitis developed in one patient, lichenoid dermatitis in three patients, and hyperkeratosis of palms and soles in two. Proguanil hydrochloride (Paludrine) and chloroquine were each given to ten patients. The former was without effect, but the response in two of the patients given chloroquine was excellent, although one of these subsequently relapsed.

The percentage of satisfactory results in this series was 59-7, as compared with 73.5 in a series of 117 cases treated with bismuth and 66-2 in a series of 56 treated with oxophenarsine.


It is first pointed out that there are several syndromes which are now generally regarded as unusual manifestations of erythema multiforme, first described by Hebra in 1866; these include the so-called Stevens-Johnson syndrome, the eczodermosis erosiva pluriorificialis of Rendu, dermatostomatitis as described by Baader, the mucosal respiratory syndrome of Stanyon and Warner, Behcet's syndrome, ulcer vulvae acutum of Lipschutz, and Reiter's syndrome. No single specific cause of erythema multiforme is known; it appears likely that it is an allergic manifestation to a number of different agents.

The authors, after briefly reviewing the literature on the relationship of erythema multiforme to virus infections, report a case seen at the Vanderbilt University Hospital, Nashville, Tennessee, in which the virus of herpes simplex was isolated. The patient, a 19-year-old white woman, developed generalized lesions of herpes simplex infection which at one stage were indistinguishable from the lesions of erythema multiforme. In spite of intensive treatment over a period of 44 days in hospital the patient died from the disease.

In the authors' view sufficient evidence is available to indicate that the virus of herpes simplex is concerned in the pathogenesis of at least some cases of erythema multiforme.

H. R. Vickers.


A previous report from the Postgraduate Medical School of London (Edholm and others, Clin. Sci., 1945, 5, 249) described the investigation of cardiac function in a case of osteitis deformans, in which the signs of a hyperkinetic circulation with a greatly increased cardiac output were found. In the present paper the findings are reported in thirteen further cases. Cardiac output was measured by right-heart catheterization and was found to be above normal limits, ranging from 7.2 to 13.3 litres per minute in the five patients with the most active and extensive osteitis. Cardiac output was normal in all cases in which skeletal involvement was less than 35 per cent. and the plasma alkaline-phosphatase level less than 45 units per 100 ml. The extent to which the skeleton is involved by active disease, it is suggested, may be of greater significance than the plasma alkaline-phosphatase level in this connexion. In one case of Paget's disease in which the previous history suggested a high cardiac output the result during an inactive phase was normal.

(Details of the method used for assessing the volume of bone involved relative to that of the whole skeleton are given in an appendix.)

G. W. Csonka.


Studies of the peripheral circulation were carried out at the Postgraduate Medical School of London on eighteen patients with active osteitis deformans (Paget's disease). The peripheral blood flow, measured with the venous occlusion plethysmograph, was found to be increased in 21 out of 23 limbs in which the underlying bone was affected, whereas in nineteen limbs in which the underlying bone was radiologically normal the blood flow was within normal limits. In six cases of active Paget's disease measurement of the blood flow through the humerus by a method previously described (Edholm and others, Clin. Sci., 1945, 5, 249) gave higher values than those recorded in normal control subjects and in a case of inactive Paget's disease. In two cases in which the bone marrow was presumed to be highly active there was also an increase in bone blood flow. The skin temperature was raised in areas directly overlying bones with active disease. In tests on two patients an intravenous injection of adrenaline was found to decrease the blood flow in the affected limbs, whereas the flow was increased in normal limbs, this being attributed by the authors to construction of the blood vessels of the diseased bone.

Bone biopsy and dissection of affected limbs at necropsy confirmed the increase in vascularity of bone in the active phase of osteitis deformans and its absence in the inactive phase and, together with the radiographic appearances, suggested that the greater part of the increased blood supply passes through the periosteal plexus rather than the nutrient artery. G. W. Csonka.


The authors report their observations on 103 consecutive cases of acute pyogenic osteitis and four of primary chronic osteitis of the long bones seen in children admitted to the Royal Victoria Infirmary, Newcastle-upon-Tyne, since June, 1948. A simple classification based on the clinical picture is proposed.

In older children a severe clinical condition was found to be accompanied by marked radiological changes, but in clinically mild cases it was unusual to see any bone destruction, even when treatment was started late. In the severe acute cases the radiological changes were of no practical help in diagnosis as they appeared too late; the time of first appearance of these changes was unaffected either by the stage at which penicillin treatment was started or by the dosage of the antibiotic. In the
mild cases, however, the x-ray changes were of considerable value, as in these cases it was often impossible to be certain of the diagnosis on clinical grounds alone. In newborn and very young infants the clinical diagnosis may be delayed or difficult in both the mild and severe types; in the authors’ cases bone changes were already present in the initial radiograph in eleven out of thirteen cases. In primary chronic osteitis, radiological changes were of course always present when the patient was first seen, and the problem was usually one of differential diagnosis. Of the four cases of secondary chronic osteitis, only one showed definite radiological evidence of persistent or renewed infection; in this respect clinical evidence was regarded as being more reliable.

In deciding on the best management of these cases the authors found that the radiological information was valuable in all cases, and in their 65 severe cases of acute osteitis it was a vital factor. Although the time to stop the administration of penicillin was always decided on clinical grounds, the radiological findings were of the greatest value in deciding when extensive surgery was necessary and the important question of when to allow unrestricted movement of the affected limb. The criterion for the latter was the first appearance of recalcification in areas previously showing progressive decalcification.

In the radiological diagnosis of osteitis in the newborn the problem of the double contour arises; this is briefly discussed and the authors agree that this appearance has a physiological cause and is not a manifestation of disease. The problem of deciding when to allow unrestricted movement is complicated by the decalcification resulting from disuse. For this reason the period during which a limb was splinted was kept to the minimum in this series. 

John H. L. Conway-Hughes.


In this investigation of the cause of loss of height in old persons, carried out at Crumpsall Hospital, Manchester, the authors made a radiological and anthropometrical study of 340 subjects (152 men and 188 women) whose average age was 68. (They [rightly] point out that as most of the subjects were chronic invalids, the results cannot be applied to old people in the general population.) In all subjects the “pelvi-costal ratio” was determined, this being defined as the ratio of the distance between the subcostal and supra-iliac lines to the subject’s total length. In 54 patients (22 men and 32 women) there was an abnormally low pelvi-costal ratio (less than 1 to 100), in four of these the ratio actually being negative, that is, the subcostal line was lower than the supra-iliac line.

This group of 54 was therefore compared with a similar number, comparable as to age and sex, selected at random from the remaining 286 subjects, and subjected to a full radiological examination of the lumbar and dorsal spine, the following measurements being particularly considered:

1. the angle between the lower ribs and the anterior border of the lower dorsal spine,
2. the degree of lumbar lordosis expressed as an angular measurement,
3. the length of the lumbar spine,
4. the portion of the lumbar spine occupied by the intervertebral disks, and
5. the degree of spinal osteoporosis.

Radiologically, the ratio of the minimum height of a single accurately-centred vertebral body to the average of its anterior and posterior heights, was taken as a better index of the presence and degree of spinal osteoporosis than the radiological density, which may be considerably affected by other factors.

The authors conclude that the main factor involved in shortening of the costo-pelvic distance is the increased obliquity of the ribs, which is secondary, at least in part, to senile kyphosis; and further, that spinal osteoporosis is almost universal amongst elderly chronic invalids, and is severe when the pelvicostral ratio is less than 1 per cent. of the total body length. 

P. D. Bedford.


It is first pointed out that the diagnosis of osteogenic sarcoma depends upon clinical, radiological, and pathological evidence, each of which is of fundamental importance, and that mistakes may occur if the diagnosis is based on only one of these.

As regards radiological examination, the author emphasizes the need for multiple films, taken with varying degrees of rotation of the limb, and for films taken with different penetration to show the soft tissues in addition to bone detail. Serial films should be obtained with the same technique after an interval of some weeks or months. He analyses twenty cases of osteogenic sarcoma selected from the Bristol Bone Tumour Registry. In fifteen of these the clinical, radiological, and pathological findings were typical. Of the five patients with atypical signs and symptoms, three survived for a long time after treatment, one of them being free from any sign of recurrence for 6 years, when metastases developed in the lung.

The author suggests that the prognosis is best in cases which are typical histologically, but atypical clinically and radiologically. The tumour in these cases is probably of low malignancy, and a relatively long survival time is to be expected, whatever the treatment. In prognosis in these cases serial radiographs are of more help than histology.

D. E. Fletcher.


In this paper from St. Thomas’s Hospital, London, the author briefly discusses the different methods used in the last 50 years in the treatment of Dupuytren’s contracture, particularly radiotherapy, and describes the results obtained in 25 cases by this means.

In Dupuytren’s contracture pathological changes occur not only in the palmar fascia but also in the interstitial
connective tissue, where there is a lymphocytic infiltration and an increase in the number of capillaries. This is followed by absorption of fat and the formation of new connective tissue, leading, in advanced cases, to subcutaneous fibrosis. The characteristic change in the palmar fascia is a proliferation of the fibroblasts in the nodules of the contracture. Subsequently there occur deposition of collagen fibres, contracture of the collagen, and compression of the fibroblasts, producing an avascular contracted scar. The similarity of these changes to keloid formation is discussed.

As regards surgical treatment, the author states that the operation most widely employed today is radical removal of the palmar aponeurosis, but an examination of the literature shows a recurrence rate following this procedure of 15 to 35 per cent. In his series of 25 cases given radiotherapy a radium mould was applied for 8 hours a day for 8 days, and a dose of 3,000 r was delivered during this time to the affected tissues. Subjective improvement was observed during the first month, and objective improvement was noted at about 2 months, becoming maximum at 6 months. The patients were followed up for 2 to 10 years. There was full functional recovery in eight patients, partial recovery in seven, and limited improvement in four; in six patients the condition was unchanged. In no case did the condition become worse or the contracture increase after treatment. The best results were obtained in early cases.

It is suggested that radiotherapy, alone or as a pre-operative measure in late cases, should be given in cases of Dupuytren's contracture. 

**R. D. S. Rhys-Lewis.**

**Arthrography of the Knee.** (L'arthrographie du genou.)

**ARCHIBAUD, J. (1953).** J. Radiol. Électrol., 34, 623. 22 figs., 4 refs.

After trying various methods of arthrography of the knee-joint, employing air, contrast media, or double contrast, the author has come to the conclusion that simple arthrography, with air only, gives all the necessary information. In the method used at the Hôpital Saint-Luc, Lyons, 2 or 3 ml of 1 per cent. solution of procaine is injected in the depression behind the outer border of the patella almost as deep as the capsule. Through a small intravenous needle, inserted until it almost touches the articular surface of the patella, any effusion which may be present is completely aspirated. Some 80 to 100 ml. of air is then introduced, slight flexing movements being made to help dispersion while this is being done, and the suprapatellar pouch being palpated to make certain that the air is actually entering the joint space. Contrary to the practice of most workers, no Esmarch bandage is placed over the suprapatellar pouch. The patient is then turned on his face, and asked to flex and extend the joint several times. It is important for the centre of the x-ray beam to pass through the line of articulation; this is situated 4 cm. below the popliteal fold and this point should be marked with a skin pencil. The knee-joint is now flexed through 10° by allowing the leg to rest on the dorsal surface of the big toe. In order to bring the menisci into view, a valgus displacement must be made to expose the internal meniscus and a varus displacement for the external; three tangential views are taken for each meniscus. The intercondylar notch is examined by flexing the knee through 80° and using a ray tangential to the upper end of the tibia. When arthrography is completed the air is aspirated as completely as possible; any remaining air is absorbed within a few days, during which time the patient is advised to rest.

A persistent synovitis seldom results from arthrography, and indeed some hyaluratheses disappear rapidly after the examination. No case of purulent arthritis was encountered in the author's series of 400 cases.

The normal and pathological appearances to be expected in the joint are discussed in detail. The 400 cases are divided into two series: in the first (125 cases), 52 were operated on and there were six radiological diagnostic errors; in the second (275 cases), 68 were operated on and there were two radiological errors. In three cases, joints which were operated on in spite of normal radiological appearances were all found to be normal.

**John H. L. Conway-Hughes.**

**Horizontal Tomogram in Rheumatology. Studies of the Knee in Anatomical Preparations and Normal Subjects.**

(Le tomogramme horizontal en rhumatologie. Études sur le genou: pièces anatomiques et sujet normal.)


The authors describe an experimental study of the possibilities of horizontal tomography as applied to bones and joints, with particular reference to rheumatic conditions. The technique employed resembles that of Vallebona, but the authors use a tube with a very fine focus (0·3 mm.), and the importance of using such a tube for obtaining clear images is strongly stressed.

They then go on to describe and illustrate in detail the results of examinations of a number of anatomical specimens of the knee, the lower femur, and the upper tibia and fibula. They have also applied the experience gained in their anatomical studies to the examination of the normal knee-joint in the living subject and of a grafted double fracture of the tibia and fibula. They claim that the method should have wide application particularly, for example, for the precise location of pathological areas in bone and in the demonstration of articular displacements.

[The importance of this paper is that it gives a fair idea of the degree of radiographic definition which may be obtained by this method of examination.]

**G. H. du Boulay.**

**Case of Reiter's Syndrome treated with Chloramphenicol.**


**Side-Effects of "Irgapyrin".** (Uber Nebenwirkungen des Irgapyrins.)

**SCHNITZER, A. (1954). Int. Arch. Allergy. 5, 47. 2 figs., 3 refs.**

**Dermatological Side-Effects of Irgapyrin.** (Haut-Nebenerscheinungen nach Irgapyrin-meditationen.)


Diagnostic Arthrography in Painful Conditions of the Shoulder. (L’artrografia opaca quale messo diagnostico nelle affezioni dolorose croniche della spalla.) CASTAGNOLI, M. (1954). Reumatismo, 6, 30. 6 figs, 31 refs.

Pulmonary Silicosis with Rheumatism or the Syndrome of Colinet and Caplan. (Silicose pulmonaire et rhumatisme ou syndrome de Colinet-Caplan.) CLERENS, J. (1953). Arch. belges Méd. soc., 11, 336. 3 figs, 44 refs.


Gout


It has been claimed that spontaneous attacks of gout are preceded by a diuresis of sodium and chloride, and that this is evidence of decreased activity of the adrenal cortex. The authors of this paper, who had previously failed to find diminished glucocorticoid excretion before attacks of gout, studied the electrolyte metabolism in two patients with gout at the Veterans Administration Center, Los Angeles. No evidence of diminished mineralocorticoid activity was found; “of the nine spontaneous gouty attacks studied none was associated with electrolyte or other changes indicative of decreased adrenal cortical function”. Administration of mercurial diuretics resulted in a marked increase in sodium chloride diuresis, but did not induce an attack of gout. The response to ACTH was normal, but after the drug was withdrawn attacks of gout were observed, although there was no evidence of abnormal “rebound” in the patients so far as mineralocorticoid function was concerned.

Disorders


Cervical spondylisis is a more common cause of dysphagia than is generally recognized. After a short review of the literature, the author describes six cases of dysphagia due to cervical spondylisis in patients over the age of 50, and discusses the radiographs, which are reproduced. In the acute stage of the disease osteophytes on the anterior aspect of the cervical vertebral bodies give rise to oedema of the prevertebral tissues. This causes dysphagia from interference with the normal distension of the pharynx and oesophagus during the passage of a bolus. Later, parapharyngitis and paraoesophagitis result in fixation of the pharynx and gullet walls, preventing the normal gliding movement of the pharynx and interfering with the peristaltic wave of the pharyngeal constrictors. The recurrent laryngeal nerves may be involved in the inflammatory process, causing cord paralysis. The author emphasizes that oesophagoscopy is necessary to exclude the presence of carcinoma. Treatment consists in dilatation and a diet of soft foods, coupled with a reassurance of the patient that the condition is benign. The disease tends to spontaneous arrest.

H. D. Brown Kelly.


Management of Sciatica by Vertebral Traction by means of Mechanical Table. NEUWIRTH, E. (1954). Rheumatism, 10, 12. 4 figs, 6 refs.

cine administration was associated with some retention of sodium and chloride.

The general conclusion seems to be that spontaneous changes in sodium, chloride, and potassium balance occur in patients with gout as they do in normal subjects, and they are not related to the attacks of gout.

D. A. K. Black.

General Pathology


The pathology of Dupuytren's contracture was studied in 77 specimens of involved palmar fascia obtained from 65 patients under the care of the Department of Veterans' Affairs, Toronto. More than half the patients were under 50 years of age, and only two were female. Plantar fascia and other sites were sometimes affected. The palmar fibrosis was insidious in onset, starting as a thickening and nodularity of the palmar fascia and spreading to involve skin, intersosseous fascia, tendon sheaths, and joint capsule. It was bilateral in forty cases. Subcutaneous fatty tissue was replaced by infiltration by two histologically distinct forms of fibrous tissue. Microscopically, remaining islets of fat were seen. The sweat glands were surrounded and there was considerable capillary vascularity. In the author's view the process is that of benign neoplasia. W. Skyrme Rees.

Urinary Steroid Excretion after Total Adrenalectomy.

Prompted by the work of Groen and others (New Engl. J. Med., 1951, 244, 471; J. Clin. Invest., 1952, 31, 87; Abstracts of World Medicine, 1951, 10, 188, and 1952, 12, 149) the authors have studied at the Institute of Cancer Research, Columbia University, New York, the effect of glycyrrhizinic acid in two post-menopausal women with cancer of the breast and one castrated man with prostatic cancer who had already undergone bilateral total adrenalectomy. After the operation the patients were satisfactorily maintained on 25 mg. cortisone acetate given twice daily by mouth. Later this dosage was reduced and supplemented with, and eventually replaced by, 4 g. daily ammoniated glycyrrhizin (U.S.P.), the liquorice extract with a deoxycortone-like action.

In all three patients the excretion of urinary 17-ketosteroids was reduced step-wise with each reduction of the dose of cortisone, the daily excretion being 3-6 mg. with 50 mg. cortisone daily, 1-99 to 2-5 mg. with 25 mg. daily, 1-3 mg. with 10 mg. daily, and 0-9 to 1-0 mg. with 5 mg. daily. These rates were unaffected by the addition of glycyrrhizin, and 17-ketosteroid excretion was virtually nil when the latter substance alone was given. The results do not entirely preclude the conversion of glycyrrhizin to steroidal substances, since atypical and unidentified chromogens were excreted in all patients and varied with the dose of cortisone. Peter C. Williams.

Serum Copper, Serum Iron, and Total Iron-Binding Capacity of Serum in Patients with Chronic Rheumatoid Arthritis. [In English.] BRENDSTRUP, P. (1953). Acta med. scand., 146, 384. 3 figs, 13 refs.

The serum iron and copper levels and the total iron-binding capacity of the serum were determined in patients with chronic rheumatoid arthritis at the Gigtanatorium, Skelskor, Denmark. These levels were examined in relation to disease activity, those included in the "active" group being female patients with an erythrocyte sedimentation rate over 10, and male patients with a sedimentation rate over 6 mm./hr [presumably by the Westergren method], unless these values were due to complicating disease, together with patients showing fever, anaemia, or particularly active joint lesions. Analysis was also made according to sex and to joint mobility, the latter being a numerical index obtained by calculating the sum of the mobilities of all joints of the extremities except the fingers and toes, according to Kalkbak's method, and expressing this as a fraction of the normal.

Serum iron showed a mean level of 68-6 μg./100 ml. in 85 active cases, there being no sex difference, as against 98 μg./100 ml. in 37 inactive cases, in which, as expected, women showed figures somewhat lower than the men, but both showed values above their respective "active" counterparts. The serum copper level was much higher in the "active" group (188 μg./100 ml. in 88 patients) than in the "inactive" group (132 μg./100 ml. in 45 patients). No sex difference was apparent in either group. Analysis according to duration of illness showed little difference between the inactive and active groups, but as followed from the method of selection the erythrocyte sedimentation rate was higher and the haemoglobin and mobility index considerably lower in the active group. The same tendency was seen for joint mobility as for activity, the serum iron level being lower and the copper level higher in the least mobile patients [no standard deviations are given]. The total iron-binding capacity, which was measured in nine patients with active rheumatoid arthritis and a high erythrocyte sedimentation rate, was found to be reduced below normal in all of them to a mean level of 183 μg./100 ml. The reduction from normal was, however, not as great as that of the serum iron levels. Three patients (two with disseminated lupus erythematosus and one with Reiter's syndrome) were treated with ACTH for periods ranging from 6 days to 3 weeks. Although the figures are incomplete, the serum iron values and the total iron binding capacity appeared to rise, and the serum copper level in one case was reduced.

The author concludes that the determination of the serum iron and serum copper values has no practical advantage over the determination of the erythrocyte sedimentation rate as a measure of disease activity.

E. G. L. Bywaters.


At the Oak Ridge Institute of Nuclear Studies, Tennessee, an attempt was made to determine the cause of
the fall in the number of circulating eosinophil granulo-
cytes which normally occurs after the administration of
ACTH (corticotrophin).

Specimens of blood and bone marrow were obtained
from twelve subjects before and after the intravenous or
intramuscular administration of 25 mg. ACTH, in each
case, the intravenous dose being infused over a period of
7 hrs. While there was the usual fall in the eosinophil
count in the peripheral blood (which was studied at
1- or 2-hr intervals) there was no significant change in the
number of eosinophils in the marrow (studied 4 hours
after the intramuscular injection and on conclusion of the
intravenous infusion of ACTH) at any stage in their
development, suggesting that ACTH caused no inter-
ference with the rate of their production. Nor was any
change observed in the number of mature eosinophils
in the marrow or evidence of eosinophil destruction there.

It is concluded that the bone marrow does not play an
important role in the phenomenon of eosinopenia after
the administration of ACTH.  
G. S. Crockett

Osteoblasts and Osteoclasts in Bone Marrow Aspiration.
Previously Undescribed Cell Findings in Paget’s Disease
(Osteitis Deformans).  RUBINSTEIN, M. A., SMELIN, A.,
92, 684.  10 figs, 20 refs.

Two new types of cell found in bone marrow aspirated
from patients with osteitis deformans are here described.
In the investigation of eight cases of osteitis deformans at
the Montefiore Hospital, New York, histological exami-
nations of bone marrow aspirated from the iliac
bone involved revealed large mononuclear cells and giant
multinucleated syncyntial forms.

The individual mononuclear cell is ovoid, measures
25 to 50µ at its greatest diameter, and has hazy cyto-
plasmic borders. The nucleus is round, with a diameter
of 12 to 16µ, is located eccentrically, and frequently
appears to have been partially excluded from the cyto-
plasm. These cells may occur singly or in clumps of
two or three, the total number varying inversely with the
haematopoietic activity of the marrow. They are not
found in bones in which there is no radiological evidence
of Paget’s disease.

The syncytial cell forms may be over 200µ in diameter
and contains as many as 100 nuclei, which are of uniform
size and are distributed haphazardly throughout the
syncytiulum. These cells were found in three of the eight
cases. It is presumed that the mononuclear cells corre-
spond to osteoblasts and the multinucleate forms to
osteoclasts.

The authors suggest that the finding of these cells may
be of help in the diagnosis of Paget’s disease.

[The article is well illustrated.]  
E. G. Rees

Diagnostic Tests for Acute Rheumatism.  (Maladie de
Bouillaud. Les tests d’identification.) LUTEMBACHER,

Bacteriologic Aspects of Rheumatic Disease.  SEVERNS,

Picture of the Bone Marrow in the Bone Marrow Disease.
(Obraz szpiku w chorobie gosciowej.) MACKIEWICZ, S.

Histochemical Studies on Cartilage and Bone.  III. Osteo-
Hopk. Hosp., 93, 386.  17 refs.

Researches into the Rate of Sedimentation of Erythrocytes
in Synovial Fluid.  (Ricerche sulla velocita di sedi-
mentazione dei globuli rossi nel liquido sinoviale.)
CARTESENGA, F., and DANEO, V. (1954).  Reumatismo,
6, 128.  14 refs.

A Study of the Adrenocortical Lipids in Various Experi-
mental Conditions.  I. The Action of Artificial Pyrexia.
(Studi dei lipidi corticosurrenalicic in diverse condizioni
sperimentali. I. Azione della piressa artificiale.)
SUMMA, C., and VOLPICELLI, M. (1953).  Reumatismo,
5, 358.  6 figs, bibl.

II. Action of Colchicine.  (II. Azione della colchicina.)
Reumatismo, 6, 12.  4 figs, 31 refs.

Agglutination of Sensitized Erythrocytes as a Serological
Diagnostic Test for Rheumatoid Arthritis.  I. Investi-
gation of Methods.  (Über die zur serologischen
Diagnose der chronischen Polyarthritis angewandte
Agglutinationsreaktion mit sensibilisierten Erythro-
cyten. I. Methodische Untersuchungen.) DICK-
122, 221.  28 refs.

Studies on Agglutination in Rheumatoid Arthritis.
Attempts to Purify the Factor causing Agglutination on
Sensitized Erythrocytes.  WAGER, O., and ALAMERI, E.
(1953).  Ann. med. exp. Biol. Fenn., 31, 361.  3 figs,
15 refs.

ACTH, Cortisone, and Other Steroids
ACTH in Reiter’s Syndrome; Four Cases with Review of
the Literature.  LARSON, E., and ZOECKLER, S. J.

Four cases of this syndrome are discussed, and as the
condition is self-limiting, the authors believe that the
primary objectives of treatment should be the shortening
of the illness and the prevention of permanent disability.
In this respect, antibiotics, sulpha drugs, antihistamines,
and TAB failed, whereas ACTH gave dramatic relief
from pain, stimulated appetite, and permitted vigorous
physio-therapeutic measures. The literature is fully
reviewed.

J. R. Hudson

Intra-Articular Hydrocortisone in the Treatment of
Med., 39, 735.  7 figs, 7 refs.

Intra-articular injection of hydrocortisone was tried
in the treatment of 852 patients with arthritis at the
Hospital of the University of Pennsylvania, Philadelphia,
a total of 8,693 injections being given into inflamed joints,
bursae, and tendon sheaths. Treatment was considered
to be successful if there was unequivocal improvement in
symptoms and signs in the affected joint for a minimum
of three days.
The best results were obtained from injection into the knee-joint, there being only 6 per cent. of failures in this group. In contrast, 52 per cent. of the injections into the hip-joint failed to give relief, this being attributed largely to technical difficulty. In acute subdeltoid bursitis the failure rate was 21 per cent. and in the chronic form it was 51 per cent. The author emphasizes the importance of injecting the hydrocortisone into the synovial space.

Of 547 patients followed up for at least one year, 106 obtained lasting relief of symptoms and signs of local inflammation for at least 12 months. This number included many patients with gout, traumatic arthritis, bursitis, and tenosynovitis, the exacerbations of which are, of course, self-limiting; it also included, however, 31 patients with osteo-arthritis and fourteen with rheumatoid arthritis. Although relief was temporary in 296 patients (54 per cent.) it was maintained by repeated injection for more than a year. Little or no benefit was obtained by eighty patients. The remaining 65 patients were lost to the long-term study.

Of 8,693 injections only 199 (2.3 per cent.) were followed by an untoward reaction, which, in the majority of cases, consisted in a temporary exacerbation of the joint inflammation, lasting a few hours to a few days, and often followed by improvement over the pre-treatment state. Other untoward reactions included local or general weakness, and hives at the site of injection. In only two instances did infection of the joint occur, and this was successfully treated with penicillin.

C. E. Quin.


The authors have noticed a pronounced tendency among patients treated with ACTH (corticoterph) in polyphloretin phosphate solutions to develop oedema, and have studied the problem, particularly in regard to electrolyte and fluid metabolism. Investigations were carried out at the Rigshospitalet, Copenhagen, over a period of 6 weeks on a young male patient suffering from anhydrous spondylitis associated with rheumatoid arthritis, who was treated successfully with polyphloretin phosphate alone (2 ml. daily for one week), ACTH alone (four doses of 20 units daily for one week), and ACTH dissolved in polyphloretin phosphate (one dose of 20 units daily for 2 weeks), with intervening control periods in which injections of saline were given. Nitrogen and electrolyte balances were determined throughout, but no significant difference was found between the period in which ACTH was given alone and that in which the composite dose was given; the blood chemistry and the urinary steroid output were also similar during the two periods. Water distribution was studied by the use of heavy water (Schloerb and others, J. clin. Invest., 1950, 29, 1296) and by the thyosulphate technique (Cardoza and Edelman, J. clin. Invest., 1952, 31, 280) and it was shown that during treatment with ACTH the extracellular space expands at the expense of the intracellular; but again no qualitative differences were observed between the two periods mentioned. Nor was the clinical state of the patient different, subjectively or objectively, whether the ACTH was given alone or with polyphloretin phosphate. Thus it would appear that polyphloretin phosphate has no metabolic or clinical activity per se, and that it does not alter qualitatively the effect of ACTH, but prolongs and intensifies its action, one dose of ACTH in polyphloretin phosphate being equivalent in this case to four doses of ACTH alone.

Nancy Gough.


The authors of this paper advocate the local injection of "hydrocortone" (Kendall's Compound F, 17-hydroxy-corticosterone) for the treatment of chronic inflammation of fibrous tissues resulting from trauma. [No case reports are quoted, however, and there are no references to the literature.] The authors have not found it helpful in the treatment of freezing arthritis (sic) of the shoulder, and consider that the indications for manipulation in such cases remain unaltered. They report that tennis elbow and other tendinous lesions respond particularly well to local injections of hydrocortone (hydrocortisone).

W. S. C. Copeman.


In view of the good results obtained with cortisone in some eye conditions and in certain types of lupus erythematosus, the effect of topically administered cortisone on experimentally-induced contact dermatitis was investigated at the City Infirmary Hospital (Washington University School of Medicine), St. Louis.

For 9 consecutive days, 375 mg. cortisone ointment was rubbed daily into an area of 40 sq. cm. on the left forearm of eleven subjects who had previously been sensitized to 2,4-dinitrochlorobenzene (DNCB); the right forearm in each case served as a control, ointment base only being applied. On the tenth day the skin was challenged with DNCB. Subsequently six patients continued inunction of cortisone daily for 8 days to both arms, the remaining five patients using ointment base only. The cortisone ointment in no way altered the development or course of the contact dermatitis.

A. W. Frankland.


Forty-two patients with atopic dermatitis, pruritus ani, pruritus vulvae, or discoid lupus erythematosus, were treated with topical applications of an ointment containing 2.5 per cent. hydrocortisone acetate. Twenty of 28 patients with atopic dermatitis showed definite improvement within 24 hrs. All patients had exacerbations when applications were discontinued. Five of eight patients with pruritus vulvae and one of three with pruritus ani improved as long as the ointment was kept applied but sustained flare-ups on withdrawal.

The results in discoid lupus erythematosus in this series
are such that further study is indicated, since other investigators do not agree as to its value.—[Author’s summary.]


Considerable visual improvement was seen in two cases after the administration of ACTH and cortisone: 4 days after operation in one case, and immediately after in the second. (ACTH 12.5 mg. four times daily for 20 days; cortisone 100 mg. once, then 25 mg. for 16 days.)

M. H. T. Yuille.


Atopic dermatitis in 35 children was treated with cortisone ointments containing between 3 and 25 mg. cortisone per gram of various ointment bases. Results from 68 treatment periods of at least one week’s duration were observed. Eczema was slightly improved in 31 (45·6 per cent.), was unimproved in 34 (50·0 per cent.) and became worse in three (4·4 per cent.). Relapses followed improvement in almost all cases after cessation of treatment.

Eosinophil responses to 21 treatments with topically applied cortisone in fifteen patients indicated little if any absorption of cortisone into the circulation. It is concluded that local absorption was also insufficient in the majority of cases. With the cortisone ointments used, an effective concentration of cortisone was probably not reached in the affected skin layers.

The therapeutic effect of cortisone ointment in eczema does not exceed the results obtained with conventional dermatologic treatment.—[Author’s summary.]


At the Institute of Allergy, Roosevelt Hospital, New York, twenty patients with ragweed hay fever, with or without asthma, were treated during the ragweed season with 40 units ACTH gel daily for periods varying from 2 to 19 days. There was marked improvement in all patients within 48 hrs, and the majority were symptom-free after four or five injections. Two patients with hay fever, who had become free of symptoms after two and three injections respectively during the height of the season, remained free during the remainder of the ragweed season without any further treatment.

H. H. HERXHEIMER.


In order to study the effects of corticosteroids and antidiuretic substances on diuresis in nephrotic children the presence and distribution of these substances was investigated at the Children’s Hospital, Havana, in four such children, two of whom were free from signs of glomerular involvement. One other child suffering from acute haemorrhagic glomerulonephritis without the nephrotic syndrome was included in the series so as to detect any possible difference that might be due to the nephrotic syndrome. Three further children recovering from other diseases and without any detectable sign of renal dysfunction served as controls. All five children with nephropathies had marked impairment of renal function as judged by the results of clearance tests. Clinical records included daily assessment of the physical status (oedema, weight, diuresis, blood pressure), diet, and liquid intake. The diet was calculated to contain 54 g. protein, 0·84 g. salt, 1,800 ml. water, and to supply about 1,000 to 1,250 Cal. per day. Determinations of the urinary volume, urinary protein content, and excretion levels of electrolytes and steroids were carried out daily, those of the blood chemical constituents and level of antidiuretic substance twice weekly, and clearance tests and urinary deposits were studied every 2 weeks for periods up to 2 months.

The results are shown in charts, tables, and graphs. Nephrotic children showed a low excretion of steroids during periods of spontaneous increase of diuresis and reduction of oedema, whereas in the child with glomerulonephritis there was increased steroid excretion during a similar event. A similar occurrence took place during the administration of ACTH (corticotrophin) or other concentrated human plasma albumin, but nothing similar was seen in the control patients. The urinary excretion of steroids in both the nephrotic and normal children was in relation to the tubular reabsorption function, as shown by the results of inulin and thiocyanate clearance tests, but in nephrotic children, after stimulation of the adrenal cortex by administration of ACTH, no proportional increase in urinary steroid excretion occurred, whereas the plasma steroid level increased during that period (except in one case). Plasma steroid concentration was influenced by adrenal and renal function and by the extent of diffusability of steroids into the interstitial fluid. There was some evidence of retention of steroids in ascitic fluid during oliguric periods. An antidiuretic substance was present in the globulin fraction of the plasma of nephrotic children, but it was not found in ascitic fluid, plasma filtrate, or in the plasma albumin fraction, as proved by the effect of intraperitoneal injection of these extracts into rats.

L. H. Worth.


The accumulation of oedematous fluid in nephrotic patients is probably due to a renal glomerular-tubular imbalance, of which a possible cause may be an excess in the secretion of adrenocortical salt-retaining hormone (electrocortin). This can be measured in terms of deoxycorticosterone by determining the sodium reten-
tion produced in adrenalectomized rats injected with radio-active sodium (\(^{44}\text{Na}\)). The method is applicable to extracts of urine.

At the Children's Memorial and Royal Victoria Hospitals (McGill University), Montreal, fourteen oedematous children with uncomplicated nephrosis were studied. Their urinary excretion of corticoids (chemically determined by formaldehyde formation during oxidation with periodic acid) was normal, but was increased during treatment with ACTH (corticotrophin).

When the excretion level reached 1 mg. daily or more (normal values 0.03 to 0.3 mg.) there was complete diuresis and remission. A second course of treatment with ACTH produced a greater effect, and diuresis was induced in three of the four cases which had not responded adequately to the first course. This relation between the level of corticoid excretion and diuresis was also shown to hold in two nephrotic patients in whom the excretion was increased by intercurrent infection; severe infection, however, produced a large increase in excretion and no diuresis. All but one of the nine patients examined during the accumulation of oedema showed an abnormally high urinary excretion of electrocortin, which was not evident in the same patients when their oedema was stabilized or was being reduced by treatment with ACTH. Symptoms recurred in 1 to 9 months in five patients, but two had no recurrence in periods of 14 and 24 months respectively. The time of recurrence bore no relation to the speed of the initial response.

The normal rate of corticoid excretion which was seen in these patients may have been due to an imbalance in the various excretion products as measured by the chemical method, and increased excretion of electrocortin may be accompanied by a decrease in that of carbohydrate-active steroids. Electrocorin secretion is not usually thought to be controlled by ACTH, and it may be that treatment with this substance corrects the imbalance by increasing secretion of the other adrenal steroids. It was noticeable that diuresis usually occurred after treatment was stopped, when total corticoid excretion fell to very low values.

**Peter C. Williams.**


In this paper the authors report from the University and Michael Reese Hospital, Chicago, their findings on the effects of cortisone and adrenaline on the level of circulating eosinophils in intact and adrenalectomized dogs, in one patient whose adrenal glands had been removed, and in another patient with Addison's disease. Cortisone in a dose of 1 to 3 mg./kg. body weight intramuscularly produced after 4 hrs a significant fall in the number of circulating eosinophils in the intact animals, but not in those which had been adrenalectomized. In these latter the injection of 0.3 mg. adrenaline 4 hrs after the cortisone resulted in a significant reduction of eosinophils in a further 2 hrs, whereas adrenaline without preceding cortisone caused a slight rise in eosinophil count. Similarly, when the patients, who were both being maintained on cortisone, were given 0.3 mg. of adrenaline subcutaneously, the eosinophil count fell by over 60 per cent by the end of 4 hrs.

The authors cite other work in agreement with these findings and conclude that adrenaline and the C-11 oxy steroids have a synergic action in producing eosinopenia. They also suggest that in the intact animal adrenaline may also produce an increased liberation of ACTH (corticotrophin) which may contribute towards the reduction in the number of eosinophils. *G. A. Smart.*


The effect of cortisone and ACTH in non-rheumatic diseases has been studied in 43 patients.

Fourteen patients with disorders of the blood have been observed. A favourable response occurred in three children with acute acquired haemolytic anaemia, and in thrombocytopenic purpura apparent clinical benefit resulted in the two patients treated. No effects were produced in aplastic anaemia, though one patient with acute agranulocytosis from thiouricil made a good response. The effect of ACTH in leukaemia was at best temporary. This small experience suggests that, apart from acquired haemolytic anaemia and some cases of purpura, cortisone and ACTH have little place in the treatment of blood disorders.

Sixteen patients with disorders of endocrine function have been studied. Of nine patients with exophthalmic ophthalmoplegia, only three responded well, the best results being obtained with ACTH in those examples of recent onset or rapid progression. Three patients with Simmond's disease have made a dramatic and sustained improvement on ACTH. Two patients showing the virilizing effects of adrenal hyperplasia have been treated by adrenalectomy and cortisone: in neither did the results obtained appear to justify the risks involved. 17-Keto steroid excretion was controlled in two pseudohermaphrodites by the use of cortisone.

The beneficial effect of cortisone and ACTH in asthma has been confirmed. The use of ACTH by intravenous drip and of cortisone by inhalation usually brought prompt improvement and was an important economy in prescribing. In two patients with nephrosis a considerable diuresis attended treatment, and in one of them the remission obtained has lasted more than a year. There is no evidence that ACTH influences portal hypertension accompanying cirrhosis, though apparent clinical benefit occurred in one patient.—[Authors' summary.]


The author has studied the adrenal glands of 190 patients who died at the Mayo Clinic of various diseases and who had received various doses of cortisone or
related hormones over periods of not less than 5 days ending up to 4½ months before death. In many cases where a total of more than 450 mg. cortisone had been given the weight of the adrenal glands was less than normal (6 to 8 g.) and deficient in lipids as shown histologically in sections stained with Sudan IV. These changes were, however, reversible, and normal glands were found in most cases where administration of cortisone had been discontinued more than 6 weeks before death. The whole pattern of adrenal changes appeared to be subject to considerable individual variation.

Mention is also made of unpublished studies by Kilby on the anterior lobe of the pituitary in 77 of the same cases. The basophil cells were affected to a greater or less extent in all cases. The earliest change was clumping of the granules, which later disappeared, with hyalinization and vacuolization of the cytoplasm. The severity of these changes could be correlated with the amount of hormone given, the duration of treatment, and the lapse of time between cessation of treatment and death. Corticotropin produced earlier and more severe changes than did cortisone. D. G. Adamson.


Since cortisone can suppress the function of the adrenal cortex, and since this effect may persist for some time after administration of the drug is stopped, there is a danger of acute adrenal insufficiency occurring after the stress of an operation in patients who have previously received cortisone therapy. The exact duration of the suppressive effect after the withdrawal of cortisone is unknown, but on the basis of available evidence the authors suggest that any patient who has received cortisone in significant amounts within 3 to 6 months of an operation should receive prophylactic treatment and that “any patient who has had extensive hypercortisonism within 1 to 1½ years of a proposed operation should, perhaps, be treated as though liable to acute adrenal insufficiency”.

From experience gained at the Mayo Clinic in the operative and post-operative care of patients with Addison’s disease the authors suggest that prophylactic cortisone treatment should consist in the administration of 200 mg. cortisone intramuscularly 48, 24, and 1 or 2 hrs before operation. Oral administration is not recommended. The administration of cortisone should usually be continued for 3 or 4 days post-operatively in reduced dosage. All patients who have received cortisone therapy before operation, whether or not they have been given prophylactic treatment, should be watched carefully during the first 24 hrs since this is the danger period. If acute adrenal insufficiency does develop the authors recommend the intravenous infusion of isotonic saline or 5 per cent. glucose solution combined with the intravenous injection of cortisone or hydrocortisone if suitable preparations are available. Otherwise, large quantities of aqueous adrenal extract should be given both intravenously and intramuscularly, while noradrenaline in doses of 4 mg. can with advantage be added to the saline; although no immediate effect can be expected, 200 mg. of cortisone should be injected intramuscularly or given by mouth if nausea and vomiting are absent. D. G. Adamson.


The difficulty experienced in estimating the small quantities of biologically active steroids present in the peripheral blood prompted the authors to study the steroid content of human ascitic fluid, this being obtainable in large quantities. Samples of 3 to 7 litres were obtained from “suitable patients”, extracted with chloroform, and the extract was then taken up successively in acetone (with magnesium chloride) and ethanol, re-dissolved in chloroform, and evaporated to dryness by a stream of nitrogen.

Extracts equivalent to 1,500 ml. asctic fluid were dissolved in propylene glycol and injected subcutaneously into adrenalectomized mice, and the fall in eosinophil count determined after 4 and 6 hrs, the greater fall being regarded as the significant value. The activity of the fluid was expressed in terms of the equivalent cortisone content, a calibration curve having been prepared by injecting cortisone acetate in various doses into adrenalectomized mice under identical conditions.

Of the ten samples of ascitic fluid examined in this way by the authors, five showed activity equivalent to more than 1·5 μg. cortisone per 100 ml. Three others gave equivocal results, the activity of samples removed from the same patient at different times varying, while the remaining two samples showed no activity at all. Equivalent activity did not exceed 5 μg./100 ml. in any sample. Analysis of four of the extracts demonstrated the presence of a substance behaving like 17-hydroxy-corticosterone, as shown by:

1. its rate of flow on paper chromatography; 2. its ability to reduce the blue tetrazolium reagent; and 3. its absorption of ultraviolet light at 240 μm.

It was possible to estimate the quantity of 17-hydroxy-corticosterone chemically in one extract. Cortisone was detected as a faint trace in only one of the extracts.

The authors tentatively suggest that the hormone content of ascitic fluid may be indicative of the content of extracellular fluid in general, and that their inability to demonstrate any hormonal action in two of the samples may indicate that under some conditions adrenal cortical hormone diffuses with difficulty from the blood into the extracellular fluid. This might possibly explain the response of the tissues and joints in rheumatoid arthritis to cortisone or 17-hydroxycorticosterone therapy, although adrenal cortical function appears to be normal in this disease. Robert de Mowbray.