ABSTRACTS

This section of the Annals is published in collaboration with the two abstracting Journals, Abstracts of World Medicine, and Abstracts of World Surgery, Obstetrics and Gynaecology, published by the British Medical Association.

The abstracts selected for this Journal are divided into the following sections: Acute Rheumatism; Chronic Articular Rheumatism (Rheumatoid Arthritis, Osteo-Arthritis, Spondylitis, Miscellaneous); Sciatica; 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 new section "ACTH, Cortisone, and other Steroids", which appears in the present issue, includes certain abstracts and titles of articles dealing with steroid research, which although not directly concerned with the rheumatic diseases, may make an important contribution to the general study of the scope and modus operandi of steroid therapy.

Acute Rheumatism


A group of children who had suffered from rheumatic fever and who received 50,000 units of oral penicillin thrice daily for 2 years was compared with a control group of 38 similar children as regards (1) the occurrence of β-haemolytic streptococci in repeated throat cultures; (2) the number of upper respiratory infections; (3) recurrence of rheumatism. The groups were made as similar as possible as regards sex, age, and duration of illness. Blood penicillin levels in ten children after a single 50,000-unit dose averaged 11 units per ml. after one hour, 0.035 unit per ml. after 2 hours, and 0.025 unit after 3 hours.

During the 2 years of the trial, 52 throat swabs out of 576 in the control group grew β-haemolytic streptococci, but only three out of 570 in the penicillin-treated group grew the organism. The authors conclude from this that haemolytic streptococci can be largely eliminated from the throat by the above dosage, and that this would be a useful safeguard in a community of children during an epidemic. There was no epidemic during the trial. A gradual increase in the number of positive cultures occurred in the autumn and early winter, reaching a peak in March. There were 158 colds in the control series and 151 in the treated group.

There were six cases of rheumatic recurrence in the control group, including two patients with streptococci in their throat and five with a raised antistreptolysin titre. In the treated group, among the three patients with recurrence none had haemolytic streptococci in the throat but all three had a raised antistreptolysin titre. The numbers were not large enough to draw clear-cut conclusions, but there was suggestive evidence that the recurrence rate is reduced by giving penicillin. There were no cases of a rash or allergic reaction in the series. R. Hodgkinson.


The author describes the use of troches containing 5,000 units of penicillin in a small group of children with rheumatism (63) or with congenital heart disease (23). Of the former 33 and of the latter thirteen were given penicillin troches to suck three times daily from September to June, the remainder acting as controls. The bacteriological results are given with such conciseness that they are difficult to comprehend. It would seem, however, that β-haemolytic streptococci were infrequently present, whereas Staphylococcus aureus was isolated from "95 per cent. of all the cultures taken". In the control group there were two recurrences and in the treated group none. The author concludes [somewhat naïvely] that "this study confirms a previous opinion that 5,000 unit penicillin throat troches are of value in temporarily eliminating S. haemolyticus from the throats of rheumatic children". The condition of the staphylococci in regard to their resistance to penicillin before, during, and after the treatment does not appear to have been studied.

[This paper has no value as a contribution to the study of the prevention of recurrences of rheumatic fever.]

T. Anderson.


Working in Pawtucket, U.S.A., the authors have investigated the effects of salicylate and succinate on hyaluronidase activity in normal and rheumatic subjects (four showing signs of active disease and eighteen convalescent from acute rheumatism). As controls they used 22 children recovered from primary tuberculosis. The hyaluronidase was a highly purified extract of bovine testicular origin which produced no inflammation on injection. The indicator dye used was Evans blue.


Chronic Articular Rheumatism

(Rheumatoid Arthritis)


Evidence of the effect of intravenous iron in the hypochromic anaemia of infection, particularly that associated with rheumatoid arthritis, is conflicting. The present authors have recently made an intensive study of fourteen cases. They conclude that despite the large doses given and a rise in serum iron level immediately following treatment, in no instance where the associated illness persisted following therapy was the hypoferremia permanently corrected. In no case was there a reticuloctosis or haemoglobin rise comparable to that found in patients with a straightforward iron deficiency. In three cases urinary iron was estimated, and in one the iron in a purulent exudate: loss of iron by these routes was not significant. In two patients who subsequently died analysis of viscera showed that an amount corresponding to 46 to 88 per cent. of the administered iron was recoverable in the liver and spleen. The reason for this diversion of iron to the tissues remains obscure. The authors suggest that since the satisfactory response obtained by Sinclair and Duthie (Lancet, 1949, 2, 646; Brit. med. J., 1950, 2, 1257) was associated with a fall in erythroocyte sedimentation rate, there was possibly an equal improvement in the clinical condition of the patient, and therefore in the anaemia, which was not due to iron therapy. JANET VAUGHAN.
The Manubrio-sternal Joint in Rheumatoid Arthritis.


In the report is presented from the Westminster Hospital Rheumatism Unit, of five cases of involvement of the cartilaginous manubrosternal joint in rheumatoid arthritis. Pain, swelling, and tenderness at the joint site were noted, and were aggravated by respiratory movements—particularly coughing, sneezing, and yawning. Differential diagnosis had to be made from angina in one case in which the pain was particularly aggravated by the deeper inspirations resulting from exertion. In one case the affection of this joint was the first manifestation of rheumatoid arthritis. Radiological changes are best seen in coned lateral views (of which four examples are reproduced) and occur later; they may include irregularity and narrowing of the joint space, erosion of the articular surfaces, and irregular expansion of the articulating bone ends. Progression to bony ankylosis was not observed in these cases. Harry Coke.

Objective Assessment of Improvement in Rheumatoid Arthritis.


The introduction of the potent antirheumatic agents, cortisone and adrenocorticotropic (ACTH) has underlined the need for reliable objective tests of improvement in rheumatoid arthritis, sensitive and accurate enough to demonstrate a response to single injections of cortisone or ACTH, which would be used in estimating dosage and in comparing the effects of unknown substances, standard active preparations, and inert controls in the same patient, and which would eliminate the psychological factors involved in any subjective or clinical assessment. By measurements of joint tenderness, strength of grip, articular blood flow, finger-tip temperature, and number of circulating eosinophils in cases of rheumatoid arthritis under standard conditions, the author claims to have evolved a reliable method of objective assessment responsive to the effects of single doses of cortisone and ACTH. A new method for measuring joint tenderness in the fingers is described, and both this measurement and the measurement of grip are reproducible within a narrow range. Blood flow in involved knee-joints is measured by plethysmography, and skin temperature by thermocouples on the finger-tips. Daily measurements were carried out on patients at rest under basic conditions and those in which all readings showed steady improvement, indicating that they were going into remission on rest alone, were eliminated, only those patients whose measurements were largely unchanged over a period of several days being selected for study of the effects of treatment. After an injection of 25 mg. ACTH a lessening of joint tenderness and an increase in strength of grip, maximal between 6 and 8 hours, and a fall in the number of circulating eosinophils were demonstrated. Knee blood flow showed a biphasic response, a variable initial increase at 6 hours being followed by a rapid decrease between 8 and 12 hours after the injection. Skin temperature was unchanged. The responses to a single injection of 200 mg. cortisone were similar but slower, except that there was not the early increase in knee blood flows which was produced by ACTH. In view of this variability in response, it was decided that the measurement of knee blood flow was not suitable for inclusion in the test.

Clinical Assessment of Rapidly Acting Agents in Rheumatoid Arthritis.


This interesting investigation seems to prove that the intramuscular injection of deoxycortone acetate followed immediately by intramuscular injection of ascorbic acid has no specific, objectively demonstrable, therapeutic effect on out-patients suffering from rheumatoid arthritis. Injection of any substance, even of no therapeutic value whatever, may produce a transient subjective improvement in about two-thirds of cases of rheumatoid arthritis treated.

It has long been known that subjective improvement of this sort is to be anticipated in certain cases when a new treatment is undertaken, but that this will occur in as much as 58 per cent. of cases is of interest. Such a result emphasizes the fact that the strictest control methods are necessary to demonstrate that improvement of this sort is not in fact due to the test substance used. The authors were able to do this by proper randomization of the control injections together with certain other precautions. No significant difference could be detected after careful observation when the results of objective tests with control injections were compared with those in which the test substance was used. [Future investigators will do well to follow the criteria indicated in this well-planned investigation.]

W. S. C. Copeman.

Insulin and E.C.T. in Treatment of Rheumatoid Arthritis.


Insulin hypoglycaemia provokes the liberation of adrenaline, and thereby may stimulate the adrenal cortex. It is possible that this also explains the effect of electric convulsion therapy. It was decided to treat two series of cases of rheumatoid arthritis by these two methods.

Fourty cases of active rheumatoid arthritis were treated five times weekly for 3 or 4 weeks by induction of hypoglycaemia with insulin. In 22 cases there was marked improvement, and in ten this was maintained for 6 weeks after completion of treatment. All the patients gained weight, but there was no significant change in the erythrocyte sedimentation rate. In 24 cases the eosinophil count fell 4 hours after maximal hypoglycaemia, but there was no apparent correlation between the degree of hypoglycaemia, eosinopenia, and recovery. Neither was there an apparent correlation between the degree of recovery and the depression of eosinophil count provoked by adrenaline or adrenocorticotropic.

Eleven cases were treated by electric convulsion

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In a number of experiments, single injections of ACTH (in three different test doses), of cortisone, and of ACTH peptide produced regular and statistically significant deviations in eosinophil count, pain threshold for joints, and strength of grip, whereas no such deviations were seen after the administration of various other drugs which have been claimed to be effective in rheumatoid arthritis, or after injections of inert substances. It was noted, however, that of ten patients tested there appeared to be some response to aspirin in three, in all of whom the drug produced eosinopenia; the eosinophil count was unchanged in the remaining seven cases. Ellis Dressner.
therapy, an average of five shocks being given. Three cases were markedly improved.

It is stressed that further control and follow-up is needed before results of these two forms of treatment can be assessed.

D. P. Nicholson.


It was reported by Rose and others (Proc. Soc. exp. Biol., N. Y., 1948, 68, 1) that serum from cases of rheumatoid arthritis agglutinated sensitized sheep erythrocytes in high dilutions, whereas normal sheep cells were agglutinated only in low dilutions. The author demonstrates that the factor responsible for agglutination in sensitized sheep erythrocytes is not the heterophil antibody, but must be an entirely different and hitherto unrecognized substance. He standardizes the duration of the test and points out that the rabbit anti-sheep-erythrocyte serum used for the sensitization of the sheep cells may not always contain equal proportions of haemolysin and of agglutinin. With a sufficiently wide margin between agglutinin and haemolysin titres, the original technique of standardizing the sensitizing serum on the basis of its haemolysin content is satisfactory, but in rare cases the agglutinin titre of the rabbit serum may be so high as to cause spontaneous agglutination of the sensitized cells. The author therefore checks the haemolysin content against a human serum of which the agglutinin titre for sensitized cells is known.

Out of 286 cases diagnosed clinically as of rheumatoid arthritis, the serum in 49 per cent. contained the factor, and in 51 per cent. it was negative. The test was negative in 97·6 per cent. of 85 cases of ankylosing spondylitis, in 98·3 per cent. of 107 cases of osteo-arthritis, and in 94·2 per cent. of 120 cases of arthritis of other types. Of 79 patients attending a rheumatism clinic suffering from indeterminate painful states such as fibrositis, all but one gave a negative reaction, while 100 per cent. negative reactions were obtained in nine cases of rheumatic fever, eight cases of acute or subacute rheumatism, and 134 cases of various non-arthritic diseases. Of 67 medical and surgical patients chosen at random, only one gave a positive reaction.

The author concludes that the factor in human serum which agglutinates sensitized sheep erythrocytes and is distinct from heterophil antibody is of considerable serological interest. It seems to be present in relatively small amounts in the sera of some apparently healthy persons as well as in various diseases, but in a proportion of cases of rheumatoid arthritis the concentration of the factor is greatly increased, with the result that the agglutination of sensitized cells may be evident when the serum is diluted a thousand times or more. He suggests that this factor may possibly be related to the disease process of rheumatoid arthritis.

From the clinical trials it is concluded that the test offers the advantage of considerable specificity, as 91·5 per cent. of the cases in which positive results were obtained had been diagnosed clinically as of rheumatoid arthritis. Further, five out of thirteen false-positive results occurred in patients with arthritic disease which might easily have been labelled "rheumatoid arthritis". The author points out that—rheumatoid arthritis being an ill-defined clinical syndrome which merges with various arthritic, peripheral vascular, and other diseases—any test which facilitates the delineation of a single clinical group might be of value in the study of rheumatoid disease.

H. Lehmann.

Assessment of Adrenal Cortical Activity in Cases of Chronic Rheumatism after the Intravenous Administration of Large Doses of Sodium Glycerophosphate. (Esame della funzionalità cortico-surrenale in "rheumatic" cronici dopo somministrazione endovenosa di glicerofosfato di sodio ad alte dosi.) NATALE, P., and PALA, A. (1950). Policlinico (prat.), 57, 1365. 20 refs.

After a brief review of the theories of the pathogenesis of chronic rheumatic disorders Selye's general adaptation syndrome in response to stress, and the alarm reaction, are discussed as being concerned with upsetting the balance of the diencephalic-pituitary-adrenocortical system, thus leading to chronic disorder of the joints. An attempt was made to determine whether the good results of large doses of sodium glycerophosphate are due to its activation of a "stress" mechanism, thereby stimulating the output of cortisone and/or adrenocorticotrophic hormone (ACTH).

Six patients with rheumatoid arthritis and two normal controls were given 10 ml. sodium glycerophosphate (2·5 g. in a 25 per cent. solution) intravenously for three consecutive days. Three days before, and for 3 days after, the injection, Thorn's test was carried out to see if there was any marked drop in the number of the eosinophils in the blood or an increase of the uric acid/creatinine ratio in the urine, indicating an excess of ACTH and/or cortisone. The results showed a complete irregularity before and after the experiment, and have to be regarded as negative. Lucherini's view that the beneficial effect of large doses of sodium glycerophosphate is perhaps due to their influence on the acid-base balance is thought to be nearer the mark.

[A study of the tabulated results of these carefully performed experiments is of much interest. The great variation in the findings even before the injections, and in the controls, should be a warning against wishful thinking and exaggerated hypotheses in connexion with indirect biochemical and biological assays of cortisone and ACTH.]

V. C. Medevi.


In view of the established observation that the favourable effects of adrenocorticotrophin (ACTH) treatment in rheumatoid arthritis rapidly disappear when it is discontinued, and that with prolonged administration untoward side-effects tend to occur, the authors of this paper set out to find some method of combining a minimal maintenance dose of this material with one of the approved medical remedies in the hope that a remission might be induced and that no relapse would then occur after the discontinuation of ACTH injections.

With this end in view, they treated five patients with rheumatoid arthritis and one with ankylosing spondylitis with small doses of ACTH over periods of 2 to 6 months. In four of these cases there was a completely favourable reaction, which it was found possible to maintain with six intramuscular injections of 2 mg. ACTH daily.
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An attempt was then made to maintain this improved condition with injections of gold salts. Although this procedure would appear to be a reasonable one the authors were unable to decide whether it was successful in their cases, and they state that more experience with the combined treatment will be necessary before conclusions can be drawn.

W. S. C. Copeman.


The authors give a general survey of the action of adrenocorticotropic (ACTH) in rheumatoid arthritis, and then describe in detail fourteen cases treated with nitrogen mustard. Pain and joint inflammation lessened considerably, mobility increased, and temperature returned to normal. The original dosage employed (five injections of 0.5 mg. per kg. body weight) was found to be excessive, causing anaemia, leucopenia, and in one case thrombocytopenia—all successfully treated by blood transfusion. It was later found that results as good could be obtained with a total of three doses of 4 mg. each, given on alternate days. With this dosage no haematological complications ensued.

The mechanism of action of nitrogen mustard is obscure, but is related to that of ACTH, in that the former is also antimitotic, produces lympholysis, and causes a lowering of the blood eosinophil count and an increase in the urinary excretion of 17-ketosteroids. In spite of this, the authors do not consider that nitrogen mustard acts by excitation of the adrenal cortex, but that it more likely has a direct action on mesenchymal structures and "defence organs". If Sabin's view that antibodies are formed by lymphocytes and released by lympholysis is correct, then another possible mode of action of nitrogen mustard related to its lympholytic effect must be considered.

René Méndez.


This study of copper therapy in rheumatoid arthritis was undertaken because of Forester’s favourable report published in 1946. First, twenty patients with severe rheumatoid arthritis, in which gold therapy had been either ineffective or toxic, were treated by intravenous injections of "cupra len," an organic copper salt,

\[
\text{COONa} \quad \text{NH}-\text{C}-\text{N}-\text{CH}_2\text{CH}_2: \text{CH}_3 \\
\text{S}-\text{Cu}
\]

receiving an initial dose of 100 mg., followed by 250 mg. twice weekly until a total of 4 g. had been given. This is the dosage recommended by Forester. No toxic effects of importance were observed. In only two cases was the condition improved.

Higher doses were used in a second course. The same patients were given 500-mg. doses once or twice a week, and seven more, with disease of less than one year’s duration, after preliminary 100- and 250-mg. doses, were given the same amount, in most cases up to a total of 10 g. The results were equally disappointing, but toxic effects were very definite. The more serious of these were nausea, vomiting, and rigors coming on in from 1 to 8 hours after an injection, and severe, rapidly developing anaemia. The authors conclude that cupra len is of no value in the treatment of rheumatoid arthritis.

Kenneth Stone.


A 62-year-old woman with rheumatoid arthritis and anaemia (haemoglobin value 50 per cent.) was treated with adrenocorticophrin for two periods of 31 and 20 days respectively. Serial blood counts and examinations of sternal marrow were made. During treatment, there was a slight increase in erythrocyte count and haemoglobin value with a sharp rise in serum iron level. There was also a granulocytosis, with the expected fall in eosinophil count. The bone marrow changes were not remarkable.

P. C. Reynell.


Complement-fixation and precipitin tests were carried out to test the hypothesis either that connective tissue in cases of rheumatoid arthritis has become antigenic and had provoked immune body formation, or that normal connective tissues are being attacked by abnormal immune bodies. Tissues—subcutaneous nodules and joint tissues—removed from six patients with rheumatoid arthritis were used as test antigens; details of preparation are given. Control antigens were prepared from tissues removed from patients without arthritis. In general, both sera from patients with rheumatoid arthritis and controls when tested with the two types of antigen gave negative complement-fixation reactions. On the other hand, a number of precipitin reactions were obtained between sera from patients with rheumatoid arthritis and antigens from such patients and from controls, control sera giving only one doubtful reaction. The negative complement-fixation reactions make it unlikely that this is a true antigen-antibody reaction; its significance is unknown.

Kenneth Stone.


Considerable evidence is available that abnormal metabolism of amino-acids is a frequent accompaniment of rheumatoid arthritis. The investigation reported by the authors was undertaken in order to determine whether a difference exists in the plasma content of free amino-acids as between normal individuals and patients with
rheumatoid arthritis. The levels of free arginine, glycine, histidine, lysine, phenylalanine, serine, and threonine in the plasma of groups of 21 to 46 normal subjects and of 25 to 61 patients are reported upon. Since it is generally agreed that plasma values for these amino-acids are normally relatively constant, it would be reasonable to suppose that any significant change observed in an adequate series would be worthy of further consideration. It was found that the mean values for arginine, histidine, and threonine in the rheumatoid arthritic patients were very significantly lower than those obtained in the normal groups. The values for glycine, lysine, phenylalanine and serine were not significantly different in the two groups.

W. S. C. Copeman.


The urinary excretion of free threonine, lysine, tyrosine, and arginine was estimated in 41 patients suffering with rheumatoid arthritis before and during treatment with adrenocorticotrophin (ACTH) or cortisone (on which they all subsequently improved to a varying extent), the excretion values during the control periods being compared with the average and maximum values during treatment. The authors were able to show a highly significant increase in urinary excretion of free threonine, lysine, and tyrosine in patients treated with ACTH, as calculated both from the average and maximum 24-hour excretion. Patients treated with cortisone excreted a highly significantly increased amount of threonine and tyrosine, but not of lysine, at the maximum. Arginine excretion was not increased by either drug. The cause of this increase in urinary excretion of the amino-acids under study is not known, but may possibly be associated with the metabolic changes brought about by the remission of rheumatoid arthritis.

W. S. C. Copeman.


The continued administration of adrenocorticotrophin (ACTH) may be harmful, as it may over-stimulate the adrenal glands, while that of synthetic cortisone may, on the other hand, result in some degree of adrenal atrophy (as in certain examples of Cushings’s syndrome where one cortex is hyperplastic and the other hypoplastic). In view of these facts it seemed worth while to treat a series of cases of active rheumatoid arthritis with a course of ACTH, followed after an interval by a course of cortisone. During the interval, injections of prenenelone acetate, deoxycorticosterone acetate and ascorbic acid, sodium, or salicylic acid were given. Only ACTH and cortisone produced any beneficial effect.

There is no evidence that the fundamental disease process of rheumatoid arthritis is cured by this treatment, but the course of the disease is favourably influenced and all the patients treated obtained temporary remission. The authors suggest that the aim should be to treat each relapse with the minimum amount of hormone required to establish a remission, possibly using ACTH and cortisone alternately.

D. P. Nicholson.


The investigation here reported was undertaken to ascertain whether or not there was any abnormality in the lipid content of the plasma post partum which might account for the fact (Granirer, 7th internat. Congr. Rheum. Dis., New York, 1949), that a sustained remission could be produced in rheumatoid arthritis by the administration of suitable amounts of pooled post-partum plasma. The mechanism of this effect has not yet been elucidated, but the evidence suggests that it is not due solely to steroidal factors. The subjects of the investigation were parturient patients, with no evidence of liver disease, in the obstetrical wards of the Queens General Hospital, Jamaica, Long Island. All patients were maintained on an ordinary diet and blood obtained 48 to 72 hours after delivery was pooled so that each plasma specimen represented the blood of ten mothers. Lipid estimations were determined according to the method described by Bloor.

In a group of eighty subjects the average plasma level of total lipids was 465 mg. per 100 ml. of fatty acids 355 mg. per 100 ml., and of phospholipids 8-2 mg. per 100 ml. In 250 patients the average plasma total cholesterol content was 119 mg. per 100 ml. and that of cholesterol esters 68 mg. per 100 ml. It is concluded that there is a decrease in the plasma cholesterol after delivery, which may be a reflexion of pituitary adrenocortico-trophic activity.

Lilian Raffery.


The authors report their observations on the use of cortisone in two cases of rheumatoid arthritis and one of acute rheumatic fever. The dosage used was 200 mg. on the first day, with 100 mg. on subsequent days, given intramuscularly. In the cases of rheumatoid arthritis there was dramatic relief of pain, with return of movement and function in the affected joints, within 4 hours of the first injection. In the case of rheumatic fever, which had not responded to salicylates, there was a marked improvement on giving cortisone. In each case there was the usual return to the former state after treatment was stopped.

Cortisone produced in all three cases a slight polymorphonuclear leucocytosis, eosinopenia, slight hypertension, a rise in the blood sugar level of 20 to 30 mg. per 100 ml., and an increase in the urinary excretion of 11-oxysteroids, 17-ketosteroids, and of acid. These changes are listed in detail day by day in all three cases before, during, and after treatment. A warning of the possible ill-effects of cortisone is given.

G. S. Crockett.


In an investigation carried out at the University of Illinois, Chicago, the potential difference between the
The Treatment of Chronic Rheumatoid Arthritis. (Considérations sur le traitement de la polyarthrite rhumatismale chronique.) Bickel, G. (1951). **Pr. méd.,** 59, 59. 15 refs.


Deoxycortone Acetate and Ascorbic Acid in Rheumatoid Arthritis. MacLean, K. S. (1951). **Lancet,** 1, 444. 10 refs.


The Tuberculin Reaction in Different Parts of the Skin and the Sensitivity in Rheumatoid Arthritis. With Special Reference to the Technical Error in the Mantoux Reaction. [In English.] Wasz-Höckert, O. (1950). **Acta paediatr. Stockh.,** Suppl. 79. 2 figs, bibl.


The relationship between spinal osteo-arthritis and rheumatism has not been yet fully explained. Osteo-arthritic changes occur in the vertebrae not only in man but also in erect animals (baboon, kangaroo), and represent not inflammatory but degenerative changes. Inflammatory changes occur in the soft tissue surrounding the vertebral column, and usually follow a throat infection.

The author has studied radiography of the vertebrae of 1,017 patients. They reveal an increased incidence of osteo-arthritic changes in older patients, this increase being related to the age (in the 2nd decade, 3 per cent.; in the 5th decade, 55 per cent.; in the 8th decade, 95 per cent.).

The operation of joint debridement described by the author is essentially one of synovectomy, with, in addition, the removal of osteophytes. The articular cartilage is smoothed where degenerate; the menisci are preserved if they appear healthy. A total of 35 operations are reviewed after periods of 1 to 9 years. The striking results were the relief of pain (28 knees) and the restoration of movement (full extension in 25 knees, and flexion to or beyond a right angle in 27 knees).

[This valuable procedure is one which should be more often used for the osteo-arthritic knee which resists conservative treatment.]


The author records his experience of the use of oxidized cellulose and instillation of cortisone in the prevention of excessive bone and scar tissue formation after orthopaedic procedures. Oxidized cellulose was used in 22 cases of arthroplasty of the hip, knee, elbow, or hallux. The range of movement in these cases was greater than that achieved when oxidized cellulose was not used. There was little or no new bone formation, but fibrous-tissue formation proceeded normally, or was even accelerated. Accordingly the effect of cortisone, which is known to inhibit wound healing by suppressing the growth of connective tissue, was studied in experimental arthroplasty in dogs. Post-mortem examination of the joints in which cortisone was used revealed a reduction in fibrous-tissue formation. The author suggests that in clinical practice fibrous-tissue formation after arthroplasty could be controlled by the use of cortisone.

(In the discussion it was suggested that although cortisone might reduce fibrous-tissue formation around joints after arthroplasty, there was a risk that it might inhibit the process of wound healing.) J. S. Batchelor.


The case is reported of a man, aged 20, who first came under treatment at the Boston City Hospital in 1944 with urethritis, conjunctivitis, and arthritis of the left knee. He was treated with sulphanilamide, apparently with success. Later that year the urethral discharge, conjunctivitis, and arthritis recurred and he was again admitted to hospital. Investigation showed a leucocyteosis of 12,000 per c.mm., but the condition responded to sulphanilamide as before. He was admitted for a third time in 1946 with urethritis and a swollen left knee and, shortly afterwards, the conjunctivitis again became evident. This time he was treated with penicillin and was discharged from hospital 13 days later. The condition recurred, however, after 2 months, with urethritis, conjunctivitis, and a swollen left heel. He was then treated with aureomycin, 100 mg. per kg. body weight being given in the first 24 hours, followed by 75 mg. per kg. daily for one week, after which time the daily dose was reduced to 50 mg. per kg. [Total dose not stated]. Improvement was immediate and the urethral, eye, and joint symptoms cleared by the third day. When seen 25 days later he was apparently well.

It is claimed that this is the first recorded case of Reiter’s disease to be treated with aureomycin. [No investigations for pleuro-pneumonia-like organisms are reported as having been undertaken either in the patient or his consort(s).]

[Reiter’s disease is attracting increasing attention in the U.S.A. at a considerable interval after similar interest was aroused in Great Britain. It is noteworthy also that in the U.S.A. non-specific urethritis is regarded as much less of a problem than it is in Britain.]

R. R. Willecox.


Since Reiter’s description (in 1916) of the syndrome which bears his name, its boundaries have remained ill-defined. This emphasis on the triad of urethritis, conjunctivitis, and arthritis. All but one of the cases reported hitherto have been in young adult males. The causation of the disease remains in doubt. Some workers have recovered pleuropneumonia-like organisms from the genito-urinary tract and joint fluid (though they were unable to reproduce the disease experimentally); others have suggested that the syndrome is similar to dysenteric polyarthritis with toxic manifestations.

The present authors describe the effect of pituitary adrenocorticotrophic hormone (ACTH) and cortisone in the syndrome in three cases, inert injections being given both before and after the above preparations, so that the patients were unaware of any change in treatment. The patients, whose case-histories are given, were all males, aged 29, 35, and 24 respectively. The first patient was treated with ACTH in doses of 25 mg., given intramuscularly every 6 hours for 12 days; the second with 10 mg. 4-hourly for 14 days, and the third with 25 mg. 6-hourly for 14 days. Response to ACTH was dramatic (within a few days) and relapse occurred 14 to 48 hours after discontinuing the treatment. In the third case, 8 days after withdrawal of ACTH, cortisone acetate was given intramuscularly in a dosage of 300 mg. daily for 3 days, 200 mg. for 10 days, and 150 mg. daily for 10 days, making a total of 4-4 g. The condition improved even more readily than with ACTH, and the subsequent relapse upon withdrawal was not so severe. A few weeks later cortisone was given by mouth at 12-hourly intervals, the dosage being 300 mg. daily for 3 days, 200 mg. daily for 10 days, and 150 mg. daily for 4 days, making a total of 3-5 g.; it was as effective as when given by injection and the relapse seemed even milder. Clinical impressions were fully supported by laboratory tests. The authors point to one significant and satisfactory feature. In spite of relapse on withdrawal of treatment, the course of the disease was materially shortened in the first two cases (in which the patients recovered completely) and probably shortened in the third.

A case which presented all the signs and symptoms of Reiter’s syndrome (the only unusual feature being that the patient was a young woman) was demonstrated at the January (1951) meeting of the Heberden Society; cortisone administration was without effect, the disease actually progressing while it was being given.

D. Preiskel.


The authors of this article describe a number of cases of neurofibromatosis, scleroderma, spinal osteomalacia, and chronic back pain due to spondylitis in which removal of the parathyroid gland on one side gave relief—in one case in which the operation was performed under local anaesthesia the pain vanished as the gland was removed. [They do not distinguish between osteoporosis and osteomalacia and the rationale of the operation is not discussed.] Three conditions which must be fulfilled to obtain success in cases of chronic rheumatism are that the tissue removed be shown to be parathyroid by histological examination, that there be hypercalcemia, and that the rheumatism be confined to the spine.

G. S. Crockett.


After a review of the literature on the shoulder-hand syndrome, four cases observed by the authors are described. Three of the patients developed the typical signs and symptoms of the syndrome after an attack of myocardial infarction, and the fourth had syphilitic aortitis with severe retrosternal pain and dyspnoea. This last patient died and necropsy revealed, in addition to the cardiac and aortic changes, microscopic lesions of a proliferative type in the region of the last two cervical and first dorsal nerve roots, with some degenerative changes in the corresponding spinal ganglia.
ANNALS OF THE RHEUMATIC DISEASES

After describing the general course, progress, radiological appearances, and treatment of the condition, the authors discuss its aetiology in some detail. It is considered that the most probable cause is reflex sympathetic inhibition affecting the upper dorsal and stellate ganglia and that this is confirmed to some extent by the post-mortem findings. Kathleen M. Lawther.

Accessory Sacroiliac Articulations with Arthritic Changes.


Accessory articulations may frequently be demonstrated between the ilium and the posterior surface of the sacrum. These joints may show arthritic changes of lesser or greater degree, and ankylosis may occur. Many of the patients complain of low backache, and some of tenderness when pressure is applied over the accessory joint. Photographs of two osteological specimens and radiographs of six patients with accessory sacro-iliac articulations are reproduced, illustrating asymptomatic, arthritic, and ankylosed joints.

A. Orly.


This work was undertaken in an attempt to facilitate the differentiation between dermatomyositis and acute disseminated lupus erythematosus, which is sometimes difficult in the early stages of these diseases. Muscle biopsies were performed in eight cases of dermatomyositis, eleven cases of acute disseminated lupus erythematosus, six cases of subacute lupus erythematosus, and one case of chronic discoid lupus erythematosus.

Some degree of nodular myositis was found in all cases of dermatomyositis, but this change was also found in those cases of disseminated lupus erythematosus in which joint or muscle pains occurred. It is concluded that although muscle biopsy may help in the diagnosis of dermatomyositis it does not provide a means of differentiation when this is difficult clinically. On the other hand, the finding of the L.E. cell in bone-marrow preparations is diagnostic of acute disseminated lupus erythematosus, although it is not present in every case and is more easily found in the acute and early stages of the disease than later on. It was not found in any case of dermatomyositis or of subacute or chronic discoid lupus erythematosus.

H. R. Vickers.


Results to be Expected from Crenotherapy in Rheumatic Disease. (Ce que l’on peut attendre de la creno-thérapie des affections rhumatismales.) JUSTIN-BESANÇON, J., and RUBENS-DUVAL, A. (1950). *Concours méd.,* 72, 3317.


The Use of Physostigmine and Foreign Protein Therapy in Arthritis and Related Conditions. STAHMER, A. H. (1950). *Wis. med. J.,* 49, 1020. 2 figs, 10 refs.


ABSTRACTS


Sciatica

Anomalies of the Lumbosacral Vertebrae in Five Hundred and Fifty Individuals without Symptoms Referable to the Low Back. SOUTHWORTH, J. D., and BERSACK, S. R. (1950). Amer. J. Roentgenol., 64, 624. 3 figs, 13 refs.

The authors review the radiological findings in the lumbar spine of 550 patients referred for barium-meal examination at the Mt. Alto Veterans’ Hospital, Washington, D.C., in order to assess the clinical significance of the common variations found in this region.

The length and width of the transverse processes of the lower lumbar vertebrae were measured. The maximum width for those of L4 and L5 were found to be 14 and 19 mm. respectively, values exceeding 19 mm. for L5 being considered to indicate an attempt at sacralization. L4 could be identified by the fact that its transverse processes were smaller and more sharply angulated upward than those of L3. Asymmetry of the planes of the posterior articular facets between L4 and L5 and L5 and S1 was found in 36% per cent. of subjects. As none of these complained of symptoms it is concluded that such asymmetry, though mechanically undesirable, is not necessarily significant.

Some degree of spina bifida occulta occurred in 18-2 per cent. of subjects, but the incidence of scoliosis was no higher in these cases than in the rest of the series. In 6-4 per cent. of subjects there was evidence of sacralization of L5 in the form of grossly overdeveloped and wing-shaped transverse processes. Lumbarization of S1 was found in 2 per cent., and first lumbar ribs in 11-3 per cent. The incidence of osteo-arthritis appeared to be mainly related to age, but was slightly more frequent in patients with scoliosis. It was found rather often between the contiguous margins of the sacrum and sacralized transverse processes of L5. Otherwise the condition did not appear to be associated with congenital anomalies.

J. A. Shiers.


The authors examined the spinal column in 99 cadavers and found protrusion of intervertebral disks in 63. Cervical protrusion was seen twice as often as lumbar, which, in turn, was seen four times as often as thoracic protrusion. The commonest sites were the 4th, 5th, and 6th cervical disks and the 4th and 5th lumbar disks. In nearly half the specimens there were multiple lesions. Many protrusions showed no rupture of the annulus, which was merely bulged. It is suggested that certain cord changes may result from compression or occlusion of spinal branches of the vertebral artery or aorta as a result of disk protrusion, and that there is no simple rule whereby the degree of neural damage may be assessed from the size, site, or nature of a disk lesion.

[The cadavers studied were dissecting-room subjects whose ages are not stated, nor are the methods and time of preservation mentioned; measurements, which are recorded in millimetres, would thus appear to be liable to wide limits of error.]

Lambert Rogers.


Gout


Adrenocorticotrophin (ACTH), given in doses small enough to be free from undesirable effects, will end almost all acute attacks of gout within 24 hours. When the hormone is withdrawn some patients relapse within a few days, but this is found to be prevented by the simultaneous administration of colchicine. In this study three preparations of ACTH were used: (1) aqueous ACTH; (2) a long-acting preparation of ACTH adsorbed on colloidal aluminium phosphate; (3) a new long-acting preparation named “polyvinyl-adactar” (ACTH adsorbed on aluminium phosphate in polyvinylpyrrolidone).

Patients treated with the first two preparations received an initial dose of 50 mg. which was repeated at 6-hour intervals until 75 to 90 per cent. improvement was observed. Administration of colchicine was started at the same time in a dose of 1-75 mg. (0-65 mg.) four times daily, which was continued until diarrhoea occurred, when it was stopped; with recovery from the diarrhoea it was resumed at a lower dosage, the process being repeated until the maximum daily dose which was well tolerated was ascertained, and this was continued for at least 2 weeks after all residual joint soreness had disappeared. The results of eosinophil counts in the peripheral blood, taken before, and 4 hours after, each dose of ACTH, and determinations of the urine urate/creatinine ratio, in 1-hour urine samples taken before, and during the 4th hour after, each dose suggest that a good therapeutic response is not obtained until ACTH evokes a good increase in adrenal function. Clinically, little change is noted for 2 to 3 hours after the initial 50-mg. dose of ACTH. Then, in patients who respond well, subsidence is rapid. In other cases there may be no change until the second or third dose is given, when there may be either the same rapid improvement or a more gradual recession. The emotional state which commonly precedes and accompanies acute gout is dissipated as rapidly as the joint symptoms. In a series of 38 attacks treated by the authors 75 to 90 per cent. improvement was generally obtained within 24 hours.

Patients treated with polyvinyl-adactar were given an initial dose of 100 mg., which was repeated at 24-hour intervals until 75 to 90 per cent. improvement was noted. This preparation appears to be active up to 48 hours after a single dose. Colchicine was given simultaneously in the manner already described. Of thirteen attacks
treated (five not previously treated with colchicine, eight colchicine-resistant attacks), all but one were terminated by a single injection of the ACTH preparation, and in eleven of the attacks 75 per cent. improvement was apparent after 12 hours. Kenneth Stone.


This survey is based on a study of five patients with gout and one patient aged 83 without clinical gout in whose kidneys urate deposits were found at necropsy. The authors believe that urates are first precipitated in the tubules, and that subsequent necrosis and fibrosis of the tubular wall may confuse the picture; this would account for previous reports of interstitial deposits. In three of their six cases there was pyelonephritis, and the lesions were most definite in relation to urate deposits blocking the tubules. It is suggested that associated pyelonephritis, as well as vascular degeneration, may play a part in the genesis of renal failure in gouty persons.

D. A. K. Black.


Non-Articular Rheumatism


A case of Weber-Christian disease is recorded. This is an uncommon syndrome characterized by successive crops of nodules in the subcutaneous (and sometimes internal) fatty tissue, as well as with fever. As long as there are nodules present, fever persists. The nodules, single or in clusters and mainly on the thighs, are caused by a focal inflammatory process. Histologically, the early changes are oedema, congestion, infiltration with segmented cells and lymphocytes, necrosis of fat, and phagocytosis of fat droplets by large histiocytes; later there is replacement by collagen, and ultimately fibrosis. The overlying skin is at first red and raised; with involution of the nodule it becomes pigmented and depressed.

The case reported occurred in a woman aged 29, who was admitted to the City Hospital, Quincy, Massachusetts, with migratory joint pain and fever, and gave a past history of rheumatic fever. The author suggests that Weber-Christian disease is not a disease entity, but an allergic reaction with local manifestations in the subcutaneous or intra-peritoneal fat, and that it is allied to the group of collagen diseases.

Kenneth Stone.


Dermatomyositis is a well-recognized condition, but reports in the literature on pure myositis are infrequent. The author describes six cases of the latter.

Family histories were negative in all cases, two of which were in males and four in females. Symptoms had been present for 6 months to 10 years—in a boy of 9 since birth. The main complaints were of pain, weakness, and tenderness of muscles, with predominant involvement of the limbs and back. Rarely the facial, oculomotor, and pharyngeal muscles were affected. Atrophy of muscles was common but pseudohypertrophy was seen in two cases.

Muscle biopsy examination was performed in all cases, with the finding of fibrillary atrophy, lymphocytic infiltration (frequently perivascular), and a less marked cellular exudate of mononuclears, polymorphonuclear, or eosinophil cells. In two cases biopsy was repeated after a course of streptomycin and the cellular infiltration was then found to be much reduced. In four of the cases streptomycin led to improvement and to a fall in the erythrocyte sedimentation rate.

Proximal muscles were mainly affected, as in a dystrophy, and in three cases a clinical distinction from muscle dystrophy was impossible; the electromyographic findings were also compatible with a dystrophy. In two cases the initial biopsy diagnosis was myositis, but re-examination of a specimen after an interval showed the picture of a dystrophy.

In myositis, streptomycin may lead to improvement or complete remission. Some cases of muscular dystrophy may be the late result of an attack of myositis.

[From the clinical and microscopical descriptions given, the abstracter finds it difficult to withhold the diagnosis of muscular dystrophy in some of these cases.] D. P. Jones.


An outline of the features of panniculitis, and of the 34 cases described in the literature, is given, three personal cases being reported. The first patient was a woman with a history of tender tumours on arms and legs for 9 years. After x-ray treatment for menorrhagia she became ill and the fatty tumours broke down and discharged pus. New lesions appeared and became necrotic: she became progressively weaker and eventually died. The other two cases were both of fat necrosis of the new-born. The first child had a fatty tumour of the back which had almost disappeared at 3 months. The other had firm nodular bluish masses on the shoulders, which from time to time turned yellowish and became less firm. They gradually disappeared. All cases were associated with pyrexia. In all cases, microscopy showed necrosis of tissue fat and foreign-body cell reaction. It is noted that one child was born to a diabetic mother, while the other mother died of fat embolism a few days after delivery. The hypothesis that changed fat metabolism causes foreign-body reaction is discussed.

E. H. Johnson.


General Pathology


The uroprecipitation reaction was studied in 123 cases of rheumatism. Positive results were obtained in 54 cases. Both auto- and iso-uroprecipitation have been observed by other workers in a variety of diseases (pneumonia, jaundice, typhoid fever, typhus) but in low titre (1 in 2, 1 in 4, occasionally 1 in 8), whereas in cases of rheumatic disease the titre was usually 1 in 32 to 1 in 64.

The authors recommend for the test 0·2 ml. inactivated serum from the patient, superimposed on 0·5 ml. boiled and filtered urine. After this combination has been incubated at 37°C. for 18 hours, the results are read in an agglutinoscope. Controls include saline and serum, and saline and urine.

J. W. Czkalowski.


The authors made a comparative study of the antibodies liberated in the body as a result of haemolytic streptococcal infection. Quantitative tests for the presence of these antibodies in the blood were made in the following groups: (1) patients with, and convalescent from, acute β-haemolytic streptococcal infections; (2) patients with active rheumatic fever; (3) patients with inactive rheumatic fever; (4) patients with rheumatoid arthritis; (5) patients with non-rheumatoid forms of arthritis; (6) normal subjects. The anti-bodies studied were: (a) antistreptolysin "O"; (b) antistreptokinase; (c) antihyaluronidase; (d) agglutinins to auto-claved streptococci.

A rise in titre was observed for all the antibodies in patients suffering and convalescent from haemolytic streptococcal infection and active rheumatic fever. Those with rheumatoid arthritis only showed a significant rise in the agglutinin titre, and those with non-rheumatoid forms of arthritis showed no consistent change in antibody titre as compared with normal subjects. It is suggested that these differences in antibody pattern are indicative of fundamental differences between the diseases, and might be used as the basis of a test for the diagnosis of acute rheumatism, provided recent infection with haemolytic streptococci is excluded. S. Karani.


ACTH, Cortisone, and Other Steroids


A series of fourteen patients with disseminated lupus erythematosus were treated with cortisone and adrenocorticotrophin (ACTH). On the whole, ACTH was quicker in its action but its effect terminated very abruptly when it was withheld. All fourteen showed dramatic improvement in the characteristic clinical features of the disease, namely, fever, weakness, joint pains, characteristic eruption, and cardiovascular changes. There was, however, little change in the biochemical findings in the patients under treatment, the effect apparently being a matter of simple clinical improvement without arrest of the essential disease processes. All fourteen patients had some oedema, hypertension, heart failure, and either depression or euphoria. Of the fourteen patients, one died in convulsions under treatment, one died from an intercurrent unrelated malady, and in one diabetes mellitus developed. Treatment was continued for several months but all the patients who survived promptly relapsed when the treatment was stopped. It is quite clear that considerable further study of this clinical enterprise is needed. G. F. Walker.


The authors describe their experience with adrenocorticotrophic hormone (ACTH) in eight patients suffering from disseminated lupus erythematosus. The initial daily dose was 100 mg., reduced gradually to 20 or 10 mg., and the period of treatment was 15 to 68 days. To four other patients suffering from the same condition the authors gave cortisone in initial doses of 200 to 400 mg., reduced gradually and continued for 11 to 18 days. The patients had had the disease for periods varying from 1 month to 8 years, with an average of 2 years. In all cases there were systemic features as well as skin lesions. All the patients responded immediately and dramatically to administration of ACTH or cortisone, the temperature became normal and the joint pains disappearing within 24 hours. An increased sense of well-being, loss of fatigue, and increase in appetite were noted, together with recession of skin lesions, absorption of pleural and pericardial effusions, and subsidence of palpable lymph nodes. Temporary relapse occurred in five cases, with recrudescence of fever and of skin and joint lesions, when the dose of ACTH was reduced to less than 40 mg. daily. This "rebound
phenomenon subsided spontaneously in 7 to 15 days. Up to the time of the present report five patients had had remissions lasting from 3 to 11 months. In five there was a relapse of varying severity from 7 days to 4 months after treatment; two of these patients had a further course of treatment, which was followed by a relapse after 7 days in one case and a remission lasting 6 months in the other. There were two deaths, one from empyema, the other from renal insufficiency.

In five other patients (four of whom received ACTH and one cortisone) with predominant skin manifestations and no significant systemic involvement the response was less satisfactory. There was some 40 to 50 per cent improvement in chronic lesions, but relapse occurred soon after treatment was discontinued.

Neutrophilia and lymphopenia followed administration of ACTH or cortisone, but eosinophils were already greatly reduced in number or absent before treatment was begun in most cases and therefore did not form a satisfactory index of response. The erythrocyte sedimentation rate fell to normal in seven cases and was unchanged in 10, there being a quantitative relation with the degree of clinical response and the duration of remission. Hargreaves's "L.E." cells were reduced in the peripheral blood during treatment, and serum gamma-globulin concentration fell strikingly.

One case of periarteritis nodosa is also reported in which recurrent episodes of the disease each responded in turn to three separate courses of ACTH, as shown both clinically and by muscle biopsy.

Robert de Mowbray.


This paper by workers from the Presbyterian Hospital, New York, describes studies undertaken on a patient who had had hypertension, mild diabetes mellitus, and rheumatoid arthritis, and who had more recently developed Addison's disease. Throughout the studies sufficient salt was given to maintain normal sodium values in the serum.

A dose of 25 mg. cortisone daily was sufficient to improve the arthritis without causing hypertension. With a constant sodium chloride intake, increase of the dose of cortisone or addition of deoxycortone acetate (DCA) caused haemodilution and hypertension, which subsided on withdrawal of the hormones. During the intervals between hormone therapy a rise in sodium chloride intake was accompanied by haemodilution but not by hypertension. When, however, the patient was given 1 mg. DCA daily, increase in the salt intake was accompanied by both haemodilution and hypertension. It is suggested that the action of sodium chloride on blood pressure is mediated by the adrenals.

G. Ansell.


The duration and intensity of fever induced by intravenous injection of killed typhoid bacilli were studied in two cases of chronic rheumatoid arthritis at the City Hospital, Boston. Pretreatment with a few doses of adrenocorticotropic hormone (ACTH, 12.5 to 50.0 mg.) resulted in a diminished response as measured in "fever units," one fever unit being defined as a rise of 1°F. (0-56°C), over 100°F. (37.8°C), maintained for one hour. A similar effect was observed in rabbits in the response to injections of typhoid bacilli or influenza virus.

The authors conclude from their experiments that in some patients the administration of ACTH will result in reduction in fever, but no alteration in the fundamental pathological process of the illness which is being treated. [The original article should be consulted for full details.]

R. N. W. Taylor.


An investigation is reported of the serum cholesterol level in a number of patients undergoing treatment with cortisone or adrenocorticotropic (ACTH) for a wide variety of diseases. Total and esterified cholesterol was determined by the method of Sperry and Schoenheimer.

Of 26 courses of cortisone acetate administered to 22 subjects, 21 were accompanied by high cholesterol levels, both total and esterified. Elevation of serum cholesterol also occurred in fifteen out of 21 courses of ACTH therapy. Of eight patients who received hormone treatment for longer than 60 days, seven developed hypercholesterolaemia (over 280 mg. per 100 ml); the incidence was much lower in those patients on shorter courses. If hormone therapy was reduced for terminated the serum cholesterol level often fell with the recurrence of symptoms, and on resuming treatment the amelioration of symptoms was usually accompanied by elevation of the cholesterol level. Consistent parallelism between the serum phospholipid and cholesterol levels was observed. Cortisone appeared to be more effective than ACTH in producing sustained hypercholesterolaemia. Investigation of the families of some of the patients concerned showed that hereditary hypercholesterolaemia was present in only two of the eight subjects undergoing prolonged hormone treatment.

It has now been demonstrated that prolonged administration of adrenal cortical agents (cortisone and ACTH) can produce sustained hypercholesterolaemia, as can suppression of normal thyroid function. Abnormal distribution of body fat and elevation of serum cholesterol level, characteristics of Cushing's syndrome, are frequently observed in patients undergoing long courses of treatment. Moreover, premature atherosclerosis (associated with hypercholesterolaemia), often observed in Cushing's syndrome, may be induced by such treatment. Animal experiments to test this possibility are in progress.

Nancy Gough.


The authors present a preliminary report on the effect of adrenocorticotropic hormone (ACTH) and cortisone...

The effects of adrenocorticotropic hormone (ACTH) and cortisone in 23 cases of asthma, five of serum sickness due to penicillin, two of sympathetic ophthalmia, and two of urticaria and angioneurotic oedema were studied. The ACTH was given daily in divided doses, except in two cases. The cortisone was given in one case on the first day only.

In the treatment of peptic ulcer. The effect of this hormone was tested on twelve dogs in whom experimental ulcers had been produced by the Mann-Williamson operative technique and on eleven control animals. 10 mg. cortisone acetate was given subcutaneously or intramuscularly twice daily throughout the life of the animal and this treatment started 13 to 30 days after operation. The dosage of ACTH used was 5 to 7.5 mg. by either route twice daily and was commenced 8 to 35 days after operation.

It was found that the dogs treated with cortisone lived, on an average, twice as long as the control animals. Those treated with ACTH lived longer than the controls, but not so long as the cortisone-treated animals. The treated animals as a group were in a good state of nutrition and vigour as compared with the untreated ones. Similar results were obtained in Mann-Williamson dogs treated with an extract made from pregnant mare's urine ("wroanthelone", "kutrol") which indicates that this effect of cortisone and ACTH is not specific.

The urinary excretion of 11-oxy-corticosteroids and 17-ketosteroids was studied in 31 normal subjects and fourteen patients suffering from duodenal ulcer. In twelve of the latter steroid excretion was studied during an attack and repeated during a remission of symptoms. Those with active duodenal ulcer showed a statistically significant diminution of urinary excretion of 11-oxy-corticosteroids as compared with normal subjects, and as compared with their excretion during a symptom-free period. This finding indicates that there is diminished adrenal activity during the active phase in duodenal ulcer.

Treatment of active duodenal ulcer with these hormones was carried out on four patients, two of whom received 1,300 mg. cortisone over a period of 11 days. One failed to respond, but the other became symptom-free with marked feelings of well-being, which continued up to 9 months after treatment. In both cases there was a decided response to the cortisone as shown by increased steroid excretion and fall in the eosinophil count.

In treating two patients with ACTH the first received 100 mg. per day (33-3 mg. 8-hourly by intramuscular injection). On the 4th day of treatment the symptoms became worse and by the 9th day had reached the stage of impending perforation; hormone treatment was then stopped. The second patient was given a dosage of 15 mg. 6-hourly for 4 days, 20 mg. 4-hourly for 4 days, 25 mg. 4-hourly for 2 days, and finally 33-3 mg. 8-hourly for 6 days. Symptoms abated on the 5th day and after the 12th day the patient became symptom-free. A few days after discharge from hospital the symptoms recurred. The response to the administration of ACTH was marked by an increased urinary excretion of steroids and a lowering of the eosinophil count.

From the material available the authors are of the opinion that, in peptic ulcer, cortisone by injection or pregnant mare's urine given orally might be of value before resorting to surgical measures, but that pituitary adrenocorticotrophic hormone should be used guardedly, if at all.

M. Beaton.


Five patients who were penicillin-sensitive (manifested by urticaria and angioneurotic oedema and, in two of the patients, by fever and arthritis) responded dramatically to the administration of 50 to 100 mg. daily for from 3 to 9 days of adrenocorticotrophic hormone (ACTH). Improvement was noted within a few hours and was complete in 1 to 3 days. Response was slower and less complete in another patient given 200 mg. of cortisone daily for 4 days. In four of the six patients minor relapses occurred 5 to 14 days after treatment was stopped. In one of the patients receiving ACTH there was only a minimal reaction to a further injection of penicillin.

ACTH, 100 mg. daily, was given to a patient who was sensitive to iodine (high fever, angioneurotic oedema, buccal ulceration, and exfoliative dermatitis). He responded within 48 hours, resolution being complete within 4 days. Although treatment was continued for 8 days, the condition relapsed 6 days later; it again responded to ACTH, this time permanently.

In two patients who reacted to local application of atropine to the eye (oedema of the eyelids and cornea, and dermatitis of the face) there was a rapid response to ACTH, 100 mg. daily; sensitivity to atropine was abolished, as shown by the patch test. One patient in whom there was an acute reaction to 3-hydroxy-2-phenylcinnamic acid (HPC), given in the treatment of...
chronic lupus erythematosus, received 200 mg. ACTH; resolution was rapid and there was no reaction to a further dose of HPC. An asthmatic patient who was sensitive to aspirin reacted only mildly to 130 mg. of aspirin during treatment with 140 mg. of ACTH daily and did not react to 80 mg. of aspirin after ACTH was discontinued. In two cases of hypersensitivity to sulphonamides (generalized skin eruption, stomal ulceration, and agranulocytosis) the leucocyte count returned to normal and there was some improvement in the skin condition. One of the patients, however, a man of 55, was receiving penicillin and aureomycin at the same time; the dosage of ACTH was inadequate and he subsequently died in uraemia.

Robert de Mowbray.

Skin Complications of Cortisone and ACTH Therapy.


The case histories of patients of the Mount Sinai Hospital, New York, are recorded in order to illustrate cutaneous complications seen there in patients under treatment with adrenocorticotropic (ACTH) and cortisone. Three of the cases were of acute disseminated lupus erythematosus and had been treated with ACTH in doses of 80 mg. or more, over periods of 26 to 42 days. The other patient, who had a type of recurrent erythema multiforme, had received 1.5 g. ACTH in 13 days. The skin manifestations seen were hyperpigmentation, acneiform eruptions, hirsuitism, rounding of the face (moon face), striae atrophicae, delayed wound healing, and flattening of keloid scars. Cutaneous manifestations previously reported in the literature are briefly reviewed.

N. R. W. Taylor.


Changes have been noted in the tissues of the upper air passages under adrenal cortical stimulation by ACTH and following the administration of cortisone. During administration of ACTH the nasal mucous membranes lose their swelling, develop a slate-pink colour and are covered with a thin layer of clear mucus. Polyps lose their translucence, become pink and begin to shrink, in many cases disappearing completely. Such changes seem to be correlated with the initial eosinopenia developing under ACTH therapy. Changes have also been observed in the nasopharyngeal lymphoid tissue. It becomes clearly outlined from its surrounding structures, developing an orange-pink colour. Discharge around it clears up and the crypts become more prominent. Microscopic studies show demonstrable change in such lymphoid tissue or in the nasal polyps.

The changes in the nose and nasopharynx regress after discontinuing therapy. Within a few days the nasal mucosa loses its dusky appearance, and the lymphoid tissue returns to its former state. Nasal polyps return in from 2 weeks to 2 months.

Cortisone therapy has very much the same effect on the mucous membranes of the upper respiratory tract, except that no marked colour change was noted in the nasal mucosa or in the nasopharyngeal lymphoid tissue in the patients under such treatment. Nasal sprays of cortisone have resulted in a slow but definite regression of nasal polyps.—[Author's summary.]


Three patients with pneumococcal and one with viral pneumonia were treated with varying amounts of adrenocorticotropic (ACTH); in another patient with viral pneumonia the administration of ACTH seems to have coincided with the beginning of natural recovery. These studies, made by the authors at the Boston City General Hospital, do not suggest any superiority of ACTH over the sulphonamides or penicillin in the treatment of pneumonia.

The details given suggest that full clinical control of the disease is obtained more slowly, an impression supported by the persistence of irregular fever for 8 to 12 days in two of the three pneumococcal cases and by a severe recurdescence in the 3rd, in which empyema also developed after 4 weeks, by the absence of any demonstrable effect of ACTH on the pneumococci, and by the persistence of rusty sputum or bacteriemia despite clinical improvement. On the other hand, ACTH seems to have induced remarkable crises on the 4th day in two patients with pneumococcal pneumonia, and a sharp lysis on the 4th day in the other. Symptomatic relief, as shown by disappearance of pain, lessening of toxaemia and headache, and general subjective improvement, was notable. The appearance of antipneumococcal antibodies and cold agglutinins was neither delayed nor accelerated. Two patients developed glycosuria and two facial oedema. There was some evidence to support an antipyretic action of ACTH. MAXWELL TELLING.


Adrenocorticotropic hormone (ACTH) was given to a series of patients of both sexes and practically all age groups who were suffering from a variety of conditions including acute and chronic rheumatism, leucoderma, scleroderma, disseminated lupus erythematosus, and Boeck's sarcoid. The ACTH was from four different batches and the dose was usually between 30 and 100 mg. daily, given in three or four divided doses. The treatment was continued for periods ranging between 4 and 125 days. Urine was collected in 24-hour lots and was assayed for 17-ketosteroids, corticoids, and occasionally glucocorticoids. Ten patients showed a normal response: the urinary excretion of steroids increased on the first day of treatment and continued to increase progressively to reach a maximum on the 3rd to 5th days, then remaining fairly constantly elevated; the excretion of corticoids generally reached a maximum before that of 17-ketosteroids, and the relative increase in the excretion of corticoids was generally greater than that of 17-ketosteroids. In four other cases there was a poor response similar to that observed in Addison's disease, but none of these patients had any symptoms of Addison's disease.

A further series of five patients were given larger doses of ACTH, varying between 980 and 2,700 mg. daily,
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during periods ranging between 14 and 23 days. The excretion of urinary steroids was at a high level, but after 9 or 10 days the excretion of corticoids decreased, suggesting an adequate adrenal cortical reserve. One of these patients, however, although given the high dosage, had only a very poor response throughout the period of treatment. Finally, five patients were treated for longer periods varying between 26 and 125 days. In only two was there some evidence suggesting that a refractory state developed after about 40 and 70 days respectively.

From the available data it is concluded that the minimum effective daily dose of ACTH required to produce an increased corticoid output is about 5 to 6 mg. in children and about 12 mg. in adults. The corresponding dosage required to produce an increased 17-ketosteroid output is about 12 mg. in children and 14 mg. in adults. A. C. Crooke.


In these studies the Scarborough negative-pressure method of determining capillary resistance was used throughout. The apparatus and technique are described. The effects of heat, cold, ultraviolet radiation, x rays, nitrogen mustard, histamine, and T.A.B. vaccine on capillary resistance are briefly reviewed. The authors observed a rise in capillary resistance after a dose of adrenaline or insulin.

In six patients with rheumatoid arthritis, a single dose of 25 mg. adrenocorticotrophin (ACTH) caused a significant rise in resistance in 4 hours, with a delayed response in one case. With doses of 25 mg. every 8 hours capillary resistance reached a maximum in 72 hours and continued at this level until administration stopped. The resistance then fell at varying speeds, generally returning to basal levels in 10 to 14 days. The extent and speed of the rise, however, did not always coincide exactly with the percentage fall in eosinophils in the blood. In two cases of spondylitis ankylopoietica and in one out of two cases of disseminated lupus erythematosus, resistance also increased after ACTH therapy. Definite clinical remission on three occasions followed the use of ACTH in two cases of idiopathic thrombocytopenic purpura. It is suggested that the rise in capillary resistance might be due to adrenocortical stimulation by endogenous adrenaline or some similar mechanism, and that capillary resistance estimations may be used as a measure of the response of the adrenal cortex to stimulation. N. R. W. Taylor.


Pregnenolone (the 3-hydroxy derivative of progesterone) was prepared in the laboratory in 1934 and isolated from hog testis in 1943. In experimental animals it favours spermatogenesis without affecting the interstitial cells of the testis, and protects the testes against the damaging action of oestrogen. Unfortunately the effect on spermatogenesis is a maintaining and not a curative one—it prevents the loss of spermatogenes after hypophysectomy, but will not restore it once it is lost. In doses usual for steroids it has no oestrogenic, androgenic, or adrenal-cortical activity, but all these activities can be demonstrated with massive doses in particular types of experimental situations. The latter activity; mice survive single doses of 5 g. per kg. body weight without any ill effect, and very large doses can be repeatedly given during long periods without affecting their growth or fertility, or altering the blood picture.

The clinical application of pregnenolone has so far been empirical. It was first given to volunteers subjected to fatigue in experimental conditions under which the urinary 17-ketosteroid excretion is increased. This increase and other objective signs of fatigue were lessened by giving 50 mg. of pregnenolone daily by mouth. This effect has not been generally confirmed—the drug is apparently only of benefit in fatigue associated with an element of urgency or anxiety. The 17-ketosteroid excretion is increased in ankylosing spondylarthitis and can be reduced to normal by giving 50 to 150 mg. of pregnenolone daily by injection; the treatment reduces pain and muscle spasm and extends the limits of movement. In rheumatoid arthritis the 17-ketosteroid excretion is normal, but the fatigue incident to the condition suggested that the steroid might be of some benefit. Conflicting clinical reports of its effect are summarized, some of which claim relief of pain, lessening of fatigue, and in some cases measurable reduction in swelling. High dosage seems to be necessary and daily doses of 1 g. by mouth or 600 mg. by injection have been given for long periods without any side-effects being noted. Further investigation is warranted, but definite benefit has not yet been proved. The compound has no significant effect on oligosperma.

The authors point out that until a normal physiological role has been assigned to the steroid its use will remain empirical, which the remarkable absence of effects on the rest of the endocrine system makes relatively harmless. Peter C. Williams.


The effects of cortisone acetate alone and in combination with Desoxycorticosterone (DCA) was investigated on the cardiovascular-renal system and plasma electrolyte balance of Sherman albino rats weighing 60 to 70 g. Eight animals were used in each of the control and test groups. Cortisone acetate was given in daily injections of 2-0 mg. per animal. DCA was given as subcutaneous implants weighing approximately 19 mg. Two implants were inserted on the 1st day, and one on the 4th, 8th, and 12th days of the experiment. The experiment was continued for 20 days; blood for electrolyte analysis was taken by intracardiac puncture without anaesthesia and then the animals were killed. Blood pressure was estimated by a modified tail plethysmographic method. In all animals receiving cortisone growth was completely suppressed, an effect which was not antagonized by DCA. The blood pressure on the last 7 days of the experiment was raised in the animals receiving DCA, while cortisone appeared to inhibit the rise. The authors did not consider cortisone to be completely antagonistic to DCA as regards effects of the latter on the cardiovascular-renal system, because it failed to prevent the increase in weight of heart and kidneys produced by DCA although the blood pressure failed to rise when both
Effects of 17-Hydroxy-cortisterone (" Compound F ")


Work with adrenocorticotrophic hormone (ACTH) has suggested that the adrenal cortex produces three types of hormone, one affecting carbohydrate metabolism (" sugar " or " S " hormone), one affecting Na and K metabolism (" Na " hormone) and one with somatotropic and androgenic properties (" nitrogen " or " androgenic " hormone). Earlier work by the present authors indicated a possibility that " S " hormone could influence K balance and hence Na balance, so that the postulation of a separate " Na " hormone in response to ACTH stimulation is unnecessary. This paper describes the investigation on the possibility by the use of a pure " S "-hormone-like substance, 17-hydroxycortisterone or compound F.

Compound F (50 mg.) was administered to a normal man in four doses on each of two separate days, and its effects were studied on the ensuing three days as compared with three corresponding control days, the diet being identical on all the days. The urinary excretion of nitrogen, potassium, sodium chloride, phosphorus, calcium, magnesium, and 17-ketosteroids was determined, and also the blood sugar and eosinophil levels. Glycosuria occurred after compound F on both occasions, but without a raised blood sugar level, indicating a lowered renal threshold. A fall in eosinophil count followed the injections and there was a slight loss of nitrogen, as expected. The effect on the excretion of K was more marked than on any of the other electrolytes; K loss began soon after injection, and 20 mEq. was lost before large dietary intake restored the balance. Some water and salt retention occurred, but the observations were difficult to interpret. Changes in phosphorus, calcium, and magnesium output were not significant: 17-ketosteroid excretion was slightly reduced.

The authors conclude that since compound F, with " S "-hormone-like action, reproduces the changes in K, Na, and Cl balance characteristic of ACTH, there is no need to postulate that a separate " Na " hormone is secreted when the adrenals are stimulated by ACTH.

Nancy Gough.

The in vitro Production of Cortisone by Mammalian Cells.


Adrenal tissue was incubated at 37° C. in a complex nutrient medium with deoxycorticosterone, and the formation of corticosterone determined by extraction and examination by paper chromatography. The addition of vitamins C, B1, B2, and B6, nicotinic acid, and insulin gave the best results, omission of any or all of these materials giving lower yields of cortisone. Addition of glutathione to this optimum medium gave completely negative results. The highest positive results were given by the adrenals of the cat and man (one case) followed by the dog, rat, and guinea-pig, those of the chicken being negative. Liver, testis, kidney, and ovary gave a few positive results.

F. W. Chattachway.


An investigation into the urinary excretion of neutral 17-ketosteroids was carried out in the Clinical Endocrinology Research Unit (M.R.C.) at the University of Edinburgh, on two women, aged 48 and 39 respectively, before and after undergoing sympathectomy for hypertension. Bilateral splanchnicectomy was performed in both cases, the greater splanchnic nerve being divided, the sympathetic chain removed from T8 to L3, and all communications to the coeliac ganglion from the spinal nerves divided just short of the ganglion. In one patient the right adrenal gland was also removed. The operation was performed in two stages with an interval of more than 10 days: repeated estimations were made of 17-ketosteroids excretion over a control period before operation (15 weeks in one case and 2 weeks in the other), during the interval between the two stages of the operation, and for 4 to 8 weeks subsequently. Fluctuations in 17-ketosteroid excretion which usually occur after operation or trauma were thus allowed for.

Forbes and others (J. clin. Endocrinol., 1947, 7, 264) observed an initial rise in 17-ketosteroid excretion after various forms of trauma, followed by a fall and return to normal within 10 days, but this was not found in the two cases reported here. Although there was considerable day-to-day fluctuation in 17-ketosteroid excretion (mainly between 4 and 12 mg. daily in one patient and between 3 and 6 mg. daily in the other), the operation had no significant over-all effect on the level of excretion. Since the operations involved complete division of the nerve-supply to the adrenals in both cases, and in one case the removal of one adrenal as well, it would appear that the excretion of 17-ketosteroids is not under nervous control, and that when one adrenal is removed the other can compensate for it adequately. Robert de Mowbray.


From the results obtained in a series of 23 control subjects and six patients with Addison's disease who were given subcutaneous injections of 0.3 to 0.5 mg. adrenaline, it was concluded that the changes in the number of circulating eosinophil cells and in the concentration of uric acid 4 hours afterwards were too variable to serve as a useful clinical test of adrenal cortical function.

A. C. Crooke.

Guinea-pigs were used throughout this study. The number of eosinophils in the blood of males was significantly lower than that in females. Cortisone reduced the number of eosinophils in the blood of males and females. ACTH produced a pronounced eosinopenia in males and nonpregnant females. Pregnancy abolished the eosinopenic effect of ACTH. Neither cortisone nor ACTH had any effect upon the degree of anaphylactic shock produced in guinea-pigs by the intravenous injection of the agent to which the animals had been sensitized. — [Authors' summary.]


Preliminary Observations on Patients Treated with Cortisone at the Rheumatic Clinic of the Cochín Hospital. (Premières observations de malades traités par la cortisone à la clinique rhumatologique de l'hôpital Cochin.) COSTE, F., DELBARRE, F., LAURENT, F., and LACHRONIQUE, F. (1951). Gaz. méd. France, 58, 11. 10 figs, 1 ref.


General Subjects


