
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.

急性风湿热

心力衰竭在具有活性风湿热性心内膜炎中的儿童。


在加拿大红十字会纪念医院的泰普洛，巴克斯，有证据表明，在风湿热性心内膜炎儿童中，异常的体征被归因于心力衰竭，但这通常不常见，而是由于心包积液。尽管显微镜下可以检测到，但影响良好，因此在所有病例中均具有心包积液。由于该条件在本例中未被报告到数字化。尽管其中4例已经死亡，但是心力衰竭的预后被认为更好。

其他七例心力衰竭的儿童，均为发热，但并未发烧。死亡出现于疾病过程中的存在，即为在发病期和第二次发病期中。在所有病例中，存在肝性水肿，尤其是血容量性肿胀，以及在左心室的异常体征，或被归因于胸膜性积液。由于该条件在本例中未被报告到数字化。尽管其中4例已经死亡，但是心力衰竭的预后被认为更好。

残余性心内膜炎的危险。


作者认为，早期和大量治疗与皮质醇在剂量调整后的影响可能预防心包性损伤。在支持本文的模型中，他们报告了在1971年及1975年期间治疗的32例儿童中，存在于第一攻击性风湿热性心内膜炎的患者。心包积液和皮质醇的剂量为200和300 mg.，分四次口服。该给药方式为2周或更长时间，然而在疾病过程中出现的皮质醇被抑制。剂量后6个月，死亡后6周。所有病例被仔细观察，并进行血清学和实验室检查。

这些作者未能发现皮质醇在治疗中残留性心内膜炎的危险。

[作者的结论是“我们的经验也表明，皮质醇在适当剂量下可能更为有效，在控制性心包性炎性关节炎中，它已被广泛使用。”] R. S. Ilingworth.

类风湿性关节炎的预防。

上呼吸道感染与类风湿性关节炎


由于长期的皮质醇治疗，尽管有可能被错误的疾病，以及控制性病理学和类风湿性关节炎的治疗，但皮质醇治疗的评估是必要的。
of penicillin as a prophylactic against streptococcal infection of the upper respiratory tract is considered essential in the management of patients with cardiac disease or a history of rheumatic fever. All subjects with active infection are possible future victims of rheumatic fever, and since carriers of the streptococcus may endanger the health of contacts, family prophylaxis has been recommended.

At the out-patient clinic of the Children’s Orthopaedic Hospital, Seattle, a single daily dose of a slowly-excreted penicillin, “bicillin” (dibenzylethylendiamine dipenicillin G), was given by mouth to 57 children and two adults for periods ranging from 3 to 10 months. Of the 59 patients, 25 were ill at the beginning of the treatment, and among the remainder were eight with congenital heart disease and thirteen with a history of rheumatic fever. All the patients were given one tablet (containing 200,000 units of bicillin) daily. In spite of a fairly constant exposure to infection, throat cultures examined monthly remained consistently negative for β-haemolytic streptococcus, except in two cases. There was no recurrence of rheumatic fever in the affected patients and no evidence of bacterial endocarditis in those with congenital or rheumatic heart disease. Time lost from school was reduced by over 80 per cent. compared with the time lost by the same group in the year preceding the start of prophylactic treatment. The author concludes that a single daily dose of bicillin is effective in eliminating the haemolytic streptococcus from the pharynx, and preventing a recurrence of rheumatic fever.

No results are reported for a similar group not receiving penicillin prophylaxis. The efficacy of the drug in preventing recurrences of rheumatic fever is scarcely proven by these observations. Kenneth Stone.


There is a growing conviction that the haemolytic streptococcus is the cause of rheumatic fever, presumably acting through some antigen–antibody mechanism. An investigation was carried out at Pennsylvania Hospital, Philadelphia, to determine whether streptolysin-S is the streptococcal component responsible for rheumatic fever. Serum from healthy subjects and from hospital patients, both children and adults (illness not specified), was analysed for its phospholipid content and for the inhibitor of streptolysin-S, the method of Youngburg and Youngburg being used for estimation of phospholipid. Streptolysin-S inhibitor was measured, normal human erythrocytes being used, against serum-extracted haemolysin contained in the supernatant of broth serum cultures of a strain of streptococcus which produced streptolysin-S but no streptolysin-O. This supernatant, being unstable, was preserved at -16°C. or lyophilized, remaining potent at a titre up to 1 : 320 or 1 : 640 for at least 2 years. A haemolysin titration against a dilution of standard human serum and erythrocytes was made as a preliminary to each test in order to determine the combining dilution of haemolysin for each particular batch of erythrocytes.

The results showed that there was no real change with postprandial increase in serum phospholipid content; a low serum phospholipid level was found in association with a very weak streptolysin-S inhibitor, but with medium and high phospholipid levels the correlation was less definite.

Since it has been shown that the serum phospholipid level tends to be below normal in individuals who are susceptible to rheumatic fever, the authors consider that their findings lend support to the view that streptolysin-S may be the cause of this disease, and that susceptibility to it may vary inversely with the strength of the natural serum inhibitor of streptolysin-S. E. G. L. Bywaters.

The object of the investigation described in this paper from the United Bristol Hospitals (University of Bristol) was to determine the value of benzathine penicillin (N,N'-dibenzy lethylendiamine penicillin G) in the prophylaxis of streptococcal infection in patients who had had rheumatic fever. To 22 rheumatic children, fifteen of whom had been persistent carriers of Group-A haemolytic streptococci for 4 to 9 weeks, the antibiotic was given intramuscularly at monthly intervals in doses of 1·5 mega units each; one child received five doses, seven received four doses, six received three doses, five received two doses, and three received only one dose. The serum penicillin level was estimated 4, 11, 18, and 25 days after the injection. Most of the injections caused local tenderness for 24 to 48 hrs, and in eighteen out of 67 instances slight fever was noted on the day after injection. On the 4th day the serum concentration of the drug ranged from 0·24 to 0·025 unit per ml. (average 0·08); on the 11th it ranged from 0·14 to 0 unit per ml. (average 0·043); on the 18th day from 0·1 to 0 unit per ml. (average 0·029); and on the 25th day from 0·07 to 0 unit per ml. (average 0·012).

Within 4 days Group-A streptococci were eliminated from the throats of all except one of the fifteen persistent carriers. New infections were almost, though not completely, prevented.

R. S. Illingworth.


At the University Medical Clinic, Bologna, skin tests were performed with a commercial product, used for the estimation of serum antistreptolysin, which contains a known amount of streptolysin-O and small amounts of other streptococcal products. In this method the amount of streptolysin is expressed in terms of a “combining unit”, which is defined as the maximum quantity of toxin which, in the presence of a unit of antistreptolysin, does not produce haemolysis of 0·5 ml. rabbit erythrocytes in 5 per cent. isotonic solution. A quantity ranging from 0·1 to 0·15 ml. of a solution of this lyophilized, standardized, and sterilized streptolysin containing one combining unit in 1,000 or 2,000 ml. was injected into the flexor surface of the forearm. [No control injections were apparently given, except as stated below.] The reaction was regarded as positive when there was a fairly intense, clearly demarcated oedema and erythema, reaching its maximum after 20 to 30 hrs and then gradually but completely disappearing. Results were read at 24 hrs; reactions less than 10 mm. in diameter were ignored, and larger positive reactions were graded according to degree. The test was performed on 152 “normal” subjects (that is, patients considered free from streptococcal infection), 136 patients with upper respiratory infections, and 108 with rheumatic disease. In addition, 94 “normal” subjects were similarly tested with a suspension of a 24-hr culture containing 5,000,000 haemolytic streptococci per ml.

In the normal subjects the proportion of positive reactions to streptolysin-O averaged 9·8 per cent., and to the streptococcal suspension 30·8 per cent. In patients with acute infections of the upper respiratory tract positive reactions to streptolysin occurred in 52·9 per cent., and in those with chronic infections in 92·1 per cent. No constant correlation with organisms found in the throat was established, and no definitive explanation of the findings is offered. Of 23 patients with articular rheumatism also tested, 22 gave positive results, while of 85 patients with rheumatic cardiac lesions but no articular lesions a positive result was obtained in 56 cases. The occurrence of positive reactions coincided with clinical and pathological indications of activity. The authors suggest that cardiac lesions only become evident when activity is diminishing, and hence positive results of this test are accordingly less frequent.

W. A. Bourne.


The comparative effects of aspirin, ACTH, and cortisone on the serum antistreptolysin-O titre and γ globulin concentration in rheumatic fever was studied at a U.S. Air Force Base Hospital in Wyoming. A total of 144 young adult males were divided by random selection into three groups, receiving respectively aspirin, ACTH, and cortisone. The drugs were given in a diminishing dosage for 6 weeks in all except eight cases, these requiring a further 4 weeks' treatment because of continued rheumatic activity. An intramuscular injection of 600,000 units of penicillin was given on the day of admission and then every 3 days for four injections; thereafter each patient received 1 g. sulphadiazine by mouth daily.

The antistreptolysin-O titre and the γ globulin concentration were estimated weekly in half the patients and at 10-day intervals in the remainder. The average values week by week for each of the three treatment groups are plotted on graphs. These show that both values fell most rapidly in the group receiving ACTH and least rapidly in the group receiving aspirin. It is stated (though the evidence is not given) that at the end of treatment the values were significantly lower in the ACTH group than in either of the other two groups, and that the difference between the values in the cortisone-treated group and those in the group receiving aspirin was not statistically significant. After treatment ceased there was a slight increase in the average γ globulin concentration in all three groups, coincident with a slight "rebound", which was noted clinically in some cases. Thereafter, there was a continued fall, and 14 months after the start of treatment the average γ globulin concentration was the same in both the ACTH- and cortisone-treated groups, the concentration in the aspirin-treated group being slightly higher.

The authors suggest that the difference between the

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effect of ACTH and that of cortisone may have been related to the dosage of each drug, the patients receiving cortisone showing fewer signs of hyperadrenalinism.

B. E. W. Mace.

Results of Hormone Therapy in Acute Rheumatic Carditis.


The authors give an interim report on the treatment with steroid hormones of 267 cases of rheumatic fever associated with carditis, some of which have been observed for more than 2 years. The results have varied; in most cases, however, the treatment was rapidly successful in reducing the activity of recurrent attacks, and this has led them to adopt steroid therapy as the basal treatment for this disease. They consider that it should be employed early in all cases of acute rheumatism, whether accompanied by carditis or not. They also give salicylates, and regard the use of antibiotics in addition as helpful in certain cases, as tending to prevent the occurrence of bacterial endocarditis on the site of an old valvular lesion.

W. S. C. Copeman.


It is pointed out that the effect of pregnancy on patients with mitral stenosis is to accentuate the natural features of the disease. The risk to life arises from acute pulmonary oedema and, to a lesser extent, from congestive heart failure. Early recognition of pulmonary hypertension and the efficient treatment of acute pulmonary oedema will contribute to a reduction in maternal mortality.

The author, writing from Aberdeen University, discusses his findings in one hundred cases of rheumatic heart disease in pregnancy, in 83 of which there was mitral disease and in seventeen mitral disease with aortic incompetence. Symptoms were classed as mild in 28 cases, moderate in sixty, and severe in twelve. Pregnancy was terminated in six of the patients with moderately severe symptoms and in six with severe symptoms. In the series as a whole there were three neonatal deaths and one stillbirth, but no maternal deaths. None of the patients was subjected to valvotomy. [This paper is of value because it indicates the results to be expected in these cases with expert obstetrical management in the absence of cardiac surgery.] T. Semple.


The authors, from the Queen Elizabeth Hospital, Birmingham, describe a technique for measuring changes in venous and arterial blood oxygen saturation, and thus in cardiac output, during 5 minutes' exercise and subsequent recovery in patients with rheumatic heart disease. The errors of the method, which are discussed, were found not to be of significant importance. In over half of the cases studied a steady state—that is, no important change or trend—in oxygen uptake, arteriovenous oxygen difference, or cardiac output was observed after 2 or 3 minutes; in severe cases in which the cardiac output was not raised on exercise and there was an abnormally high arterio-venous oxygen difference a longer time was required to reach equilibrium. There appeared to be no correlation between the degree of dyspnoea and the ventilation, the level of mixed venous oxygen saturation, cardiac output, pulmonary arterial pressure, or pulmonary capillary pressure.

J. Shillingford.


Side-Effects, Complications, and Results of Hormone Treatment in Rheumatic Fever with Carditis. (Incidents, accidents et résultats du traitement hormonal de la maladie de Bouillaud.) D'OELSINITZ, M., GIOANNI, T., and DESESTRES, —. (1954). Pediatric, 9, 705. 27 refs.


Chronic Articular Rheumatism
(Rheumatoid Arthritis)


Nitrogen mustard has been shown to inhibit a number of hypersensitivity phenomena; it suppresses local tissue reactivity, inhibits antibody formation, and blocks antigen-antibody combinations. These findings suggested to the authors the use of nitrogen mustard in the treatment of rheumatoid arthritis.

At the hospital of the State University of Iowa College of Medicine, seventeen patients with severe, active, deforming rheumatoid arthritis of long duration were studied for 8 months. The study was divided into four periods of 2 months each, 2 weeks of each period being spent in hospital and the remaining 6 weeks at home. During each period in hospital an extensive laboratory investigation was conducted in a metabolic ward, and the patient's clinical condition and particularly range of joint movement were assessed. For the first 4 months of the trial (that is, the first two periods) the patients were treated only by physical therapy and aspirin, but during the third period in hospital, nitrogen mustard was given in a dose of 0-1 mg./kg. body weight daily for 4 days. To reduce the incidence of vomiting, pentobarbitone and pethidine were administered beforehand. In the majority of patients, subjective improvement in joint pain began after the second dose of nitrogen mustard. In two cases in which the arthritis was accompanied by marked oedema of the lower extremities and severe joint effusion, treatment with nitrogen mustard resulted in a prompt diuresis, followed by disappearance of the oedema and marked reduction of the effusions. All but one of the patients showed an increase in joint mobility after treatment, in spite of the fact that the improvement due to the previous forms of treatment had reached its maximum after 4 months. The subsequent improvement in joint mobility was fairly well maintained for 12 weeks.

Laboratory studies carried out after the administration of nitrogen mustard showed the following results. There was a slight decrease in the erythrocyte count and haemoglobin level, and the leucocyte count decreased, reaching its lowest level about one week after completion of treatment, and then slowly returned to normal; the erythrocyte sedimentation rate was unchanged. The urinary excretion of 17-ketosteroids, and their ratio to creatinine, were normal and were not changed by treatment. The number of eosinophil leucocytes remained unchanged despite the temporary leucopenia, so that a relative eosinophilia existed for a few days. The glucose tolerance curves had shown a slight impairment of carbohydrate utilization and this was unchanged after treatment. The "bromsulphalein" test of liver function and the protein-bound iodine content of the plasma were normal before and after therapy. Electrophoretic analysis of the plasma proteins revealed abnormalities characteristic of rheumatoid arthritis, but after treatment with nitrogen mustard the various fractions tended to shift towards the normal. During and after treatment there was marked improvement in calcium balance. During therapy, heavy losses of nitrogen and phosphorus occurred, but this was due in part to decreased intake, and was followed by a gradual return to pre-treatment levels. The changes in the eosinophil and erythrocyte counts, sedimentation rate, 17-ketosteroid excretion, glucose tolerance, and calcium excretion, and the absence of hirsutism, elevation of the blood pressure, oedema, acne, or "moonface", suggest that the action of nitrogen mustard is not similar to that of cortisone and ACTH. A. Swan.


The blood pressure readings of 320 patients with rheumatoid arthritis of at least 9 months' duration, admitted to Temple University Hospital, Philadelphia, were compared with the values in the published results for a series of 5,540 presumably normal subjects; in the case of the patients the pressure was determined on admission to hospital, in order to discount the hypotensive effect of subsequent bed rest.

The results showed that the average blood pressure (by decades) in the arthritic group was significantly lower than in the control group, ranging from 115/74 to 127/75 mm. Hg in the former, and from 120/77 to 166/92 mm. Hg in the latter. The average diastolic pressure of the arthritic patients remained virtually unchanged through all age decades from 20 to 70 years at about 75 mm. Hg, whereas that in the normal group rose with age; the differences in the systolic pressures were less striking. Only 5 per cent. of the rheumatic cases were considered to be hypertensive.

The authors conclude that hypotension [sic] is a constant feature of rheumatoid arthritis. They discuss at some length what they consider to be the aetiological implications of their observations, in the light of reports that the use of hypotensive drugs (particularly hydralazine) may precipitate clinical syndromes resembling rheumatoid arthritis, disseminated lupus erythematosus, and scleroderma. Kathleen M. Lawther.

The colloidal preparations of gold salts have never proved satisfactory in the treatment of rheumatoid arthritis mainly owing to their low content of metallic salts. A new preparation has, however, recently been introduced in the form of colloidal gold sulphide ("auroul-sulfide"), which contains a higher proportion of active gold. This preparation has been found by the authors to be highly effective and in their experience has been better tolerated by the patients than are the "classic gold preparations".

Of 23 patients with chronic rheumatoid arthritis, eleven responded in an extremely satisfactory fashion, seven received appreciable benefit, and only five showed no improvement. In all the cases which benefited the erythrocyte sedimentation rate diminished pari passu with the clinical improvement. The authors consider this new preparation of gold to represent an advance in chrysotherapy.

W. S. C. Copeman.


An investigation was undertaken at Staincliffe General Hospital, Dewsbury, Yorkshire, to compare the effects on rheumatoid arthritis of transfusions of blood from pregnant women and of similar transfusions from men and non-pregnant women. Transfusions of 300 ml. were given weekly and the cases followed up for 6 to 18 months.

Of the 53 cases given blood from pregnant donors 19 per cent. are stated to have shown marked subjective and objective improvement, as compared with 13 per cent. of 45 cases receiving blood from men and non-pregnant women.

The author concludes that in rheumatoid arthritis transfusion of blood from pregnant donors produces improvement similar to that resulting from transfusion of blood from non-pregnant donors, but does not produce remissions comparable to those observed during pregnancy.

H. F. Turney.


Methods of preventing or correcting deformities due to rheumatoid polyarthritis, so that the patient does not become fixed in an armchair posture, are discussed. Flexion of the knee should be prevented by application of a weight-bearing caliper, by quadriiceps exercises, and by daily walking. If necessary the joint is manipulated under anaesthesia, the aim being to straighten the knee and to keep the patient walking. As regards hand deformities, a small hand plaster to immobilize only the metacarpophalangeal joints is recommended. For inflamed wrist-joints a wrist plaster which allows free finger movements is advocated. It is stated that ankylosis does not develop with this method of treatment.

In the author's view it is a mistake to move a painful joint through a full range of movements daily; moreover, immobilization of a joint for a few weeks does not result in ankylosis. The patient should walk each day and should not be allowed to become bed-ridden.

J. B. Millard.


The authors have compared the effects of cortisone acetate and of cortisol (hydrocortisone "free alcohol") in 22 cases of rheumatoid arthritis under treatment at the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases. These patients, who had previously received a long-term programme of cortisone acetate treatment, were transferred to cortisol treatment and observed for 3 months. The results were assessed on the basis of physical ability, strength of grip, and erythrocyte sedimentation rate. The authors conclude that cortisol is more potent as an antirheumatic agent than cortisone acetate, but that on the other hand it is more prone to produce undesirable side-effects.

Oswald Savage.


In an investigation carried out at six centres in England and Scotland, 61 patients suffering from rheumatoid arthritis and who had developed the disease not more than 9 or less than 3 months previously were treated at random with adequate doses of either cortisone or aspirin. The patients were admitted to hospital for a minimum of 4 weeks, when treatment was initiated. Those treated with cortisone, which was labelled "Tab. (or Mist.) Rheumatic A" and given by mouth, received 300 mg. on the first day; the dose was gradually reduced until the 3rd week, after which "the minimum dosage that would restore maximal functional efficiency without producing serious side-effects" was employed. Patients given aspirin, which was labelled "Tab. Rheumatic C", were started on 6 g. daily, and this too was cut down to a minimum satisfactory dose when possible. At the 12th week drug treatment was gradually withdrawn, and during the 13th week no cortisone or aspirin was given and the patients were observed and investigated. If symptoms recurred the 12 weeks' course of the standard dose was resumed.

Patients were assessed before and at regular intervals during treatment, the assessment including judgment of the patient's functional capacity and of the activity of the disease. Strength of grip, dexterity, joint tenderness, and range of movement were also assessed. Complications, side-effects, and further involvement of new joints were noted and haemoglobin value and erythrocyte sedimentation rate regularly estimated.

Of the 61 patients originally admitted to the trial, three who were being treated with aspirin defaulted, and
two of these cases were regarded as failures of treatment. Of the remaining 38 patients, thirty received cortisone and 28 aspirin. At the end of a year the results were analysed, and it was found that as regards joint tenderness both treatments had had equal effects. The results in regard to range of movement and strength of grip showed that both treatments were about equal in producing an increase of 20 to 30 per cent. of movement and one of 40 to 50 per cent. in strength of grip. Similarly, both treatment groups showed equal improvement in dexterity, but in respect of haemoglobin level and erythrocyte sedimentation rate there was a significantly greater improvement in the group treated with cortisone. Clinical assessment showed a remarkable similarity between the two treatment groups; minor complications of treatment were also equally distributed between the two groups.

It is envisaged that the trial will continue into a second and third year.

[It is important to realize that this investigation covers only one aspect of the comparison between the efficacy of cortisone and of aspirin in rheumatoid arthritis. The study was not of a wide series of patients suffering from rheumatoid arthritis at all stages, but was confined to a small group of sufferers in the early stages of the disease.]

W. Tegner.


The authors, working at the Hôpital Beaugrenelle, Paris, treat rheumatoid arthritis by multiple intra-articular injections of hydrocortisone acetate under general anaesthesia. Depending on the size of the joint, 10 to 100 mg. of hydrocortisone is injected into each of the affected joints at one session. The total dose of several hundred mg. given has not produced any of the side-effects associated with systemic therapy with adrenal hormones. Depending on the result, the treatment may be repeated two or three times at weekly intervals; there has been no apparent loss of effect with repeated injections, and improvement has been maintained for periods varying from a few weeks to several months. The authors prefer this method to daily injections of two or three joints under local analgesia as it saves time and is considered to be less disagreeable to the patient.

Of seven cases of advanced rheumatoid arthritis treated by this method after failure to respond to other therapy, including administration of cortisone and ACTH, three showed marked improvement, three were moderately improved, and one did not respond; the cause of failure in this last case was considered to be insufficient dosage. In view of the absence of side-effects and the encouraging results obtained, the authors consider this to be one of the best methods of treatment of rheumatoid arthritis so far available.

[Seven cases is too small a series upon which to base any assumption, but further work is continuing.]

F. Clifford Rose.


The incidence and significance of amyloid changes in rheumatoid arthritis was investigated at the University Institute of Pathological Anatomy, Copenhagen. Using methyl violet as a stain for sections of tissue obtained at necropsy in 28 cases of rheumatoid arthritis, the authors found amyloid deposits in seventeen, the amyloidosis being moderately severe or severe in ten. The deposits were most pronounced in the kidneys, spleen, and adrenal glands, but were also found in the liver, myocardium, and intestine. Vessel walls were frequently involved. Albuminuria was present in thirteen of the seventeen cases in which amyloidosis was found, and uremia was the cause of death in seven of the 28 cases. Amyloidosis was diagnosed clinically in only one case, and only in two was the condition recognized macroscopically at necropsy.

A. Wynn Williams.


The authors maintain that gold still plays a valuable role in the treatment of rheumatoid arthritis and that there is room for new preparations of low toxicity. They have recently observed at the University Medical Clinic, Graz, Austria, the effects of a complex preparation, "aurubin", containing gold salts among a number of other constituents and which can be taken by mouth, in the treatment of various rheumatic conditions, mostly rheumatoid arthritis. In this disease its effects were less obvious in cases of recent onset than in more chronic cases; in eleven out of 35 of the latter with sufficient follow-up improvement was noted within 4 to 7 days. Side-effects (mainly nausea and diarrhoea) were encountered in eight cases, but there was no occurrence of leucopenia, albuminuria, or haematuria. Excretion of 17-ketosteroids was unaffected and no change was observed in the number of circulating eosinophil leucocytes. It is assumed that gold is the active principle in this complex preparation, but its mode of action has yet to be elucidated and further studies are in progress.

D. Preiskel.


(Osteo-Arthritis)


The authors point out that in articles and textbooks dealing with the treatment of osteo-arthritis the value of rest is nearly always emphasized but its hazards are rarely mentioned. They agree that excessive use of an affected joint will produce a sharp reaction within 24 to 48 hours, but hold that immobilization may produce much more prolonged disability. When elderly patients are rested in bed as part of the treatment of cardiac decompensation, bronchitis, pneumonia, bleeding peptic ulcer, or other diseases, they may develop for the first time joint symptoms associated with osteo-arthritis, or existing symptoms of osteo-arthritis of the hips or knees may be severely aggravated. The histories of four such patients admitted to St. Stephen's Hospital, London, are described to illustrate this point.

Harrison and others (J. Bone Jt Surg., 1953, 35B, 598) have emphasized “the necessity for use and compression of cartilage in order to maintain its continued health”, while Lloyd-Roberts (J. Bone Jt Surg., 1953, 35B, 627) has pointed out the effect of fibrosis and shortening of the capsule in the production of symptoms in osteo-arthritis of the hip. Those two findings together help to explain the deterioration which occurs in a patient’s weight-bearing joints during a period of complete rest in bed, when there is a tendency for the hip to be held in flexion and lateral rotation, while the knee is also flexed. In order to prevent the adverse changes which follow long-continued maintenance of this position the authors suggest that patients should spend part of the day lying flat, and selected patients with flexion deformities already present should be induced to spend periods in the prone position. Exercise of the hips, knees, and ankles should be undertaken as soon as possible. Analgesics should be used freely if pain prevents proper co-operation in the performance of these exercises, while the injection of a local analgesic into ligamentous attachments or the intra-articular injection of hydrocortisone may be useful in helping to mobilize stiff and painful knees.

C. E. Quin.


Sudden and slight tendency of uveitis; posterior synechiae, iris, and affection of the retina. The symptoms of uveitis are generally confined to the uvea. The reported incidence of uveitis has varied widely. In the authors' series of 200 cases of ankylosing spondylitis uveitis was seen in seventeen cases (8.5 per cent.); in this group no other eye affection, such as the Gougerot-Sjögren syndrome, was observed. They point to the great rarity of uveitis in rheumatoid arthritis, and are convinced that uveitis and spondylitis are manifestations of the same morbid process.

The symptomatology of uveitis is discussed. Attacks may be repeated at intervals for some years before the appearance of the first somatic symptoms of spondylitis, and they often occur in the early pre-ankylosis phase of the disease. It is particularly important, therefore, when confronted with a case of uveitis in a young man, even if it is accompanied only by vague "rheumatic" pains, to remember this possibility and investigate the radiological appearances of the sacral-iliac joints. The clinical forms of uveitis, which vary in severity and gravity, are fully described. The benign form is liable to be mistaken for conjunctivitis; it manifests itself by slight symptoms and signs or iritis, very slight pain, some photophobia and lachrymation, and a sluggish pupil reaction, but usually abates spontaneously in 8 to 10 days. In more marked attacks there is some pericorneal injection, and some fragile synechiae may form. More severe is the typical form, an acute diffuse uveitis, of sudden onset. Here there is marked photophobia, with the usual signs of inflammation of the iris, but only a slight tendency to the formation of posterior synechiae. These attacks also generally subside fairly quickly, leaving no residual signs, but in rare cases may progress to a more severe form resulting in total uveitis, with severe pain, marked signs of iritis, and affection of the vitreous. During the following 6 to 8 weeks the condition slowly abates, although some posterior synechiae persist. Much more severe are the granulomatous forms of uveitis; these follow recurrences of simple iritis, are characterized by a tendency to form tough posterior synechiae, and nodules may be observed in the iris. The most serious of all, however, is torpid uveitis, which begins quietly, with mild symptoms, and progresses chronically and insidiously over months or years, with the formation of very strong synechiae, which by occluding the pupil may lead to total blindness.

The treatment is discussed. In the authors' practice, to obtain and maintain pupillary dilatation, atropine is always combined with repetitive instillations of cortisone. If this fails, subconjunctival injections of cortisone and adrenaline are tried; in still more resistant cases hyaluronidase is given in addition. In severely painful attacks the authors advise the early retrobulbar injection of 1 to 2 ml. 40 per cent. alcohol. Kenneth Stone.


(Miscellaneous)


The occurrence of pain and limitation of movement in the shoulder in patients suffering from coronary ischaemia is well recognized. In this paper from the University Medical Clinic, Modena, the authors describe six typical cases to illustrate the clinical features and report an attempt to determine whether patients complaining primarily of symptoms of scapulo-humeral peri-arthritis present any evidence of coronary insufficiency.

In a series of 48 such patients, ranging in age from 27 to 68, electrocardiography showed that nine had definite evidence of coronary insufficiency, while a further ten suffered from lesser degrees of myocardial damage. Few of these patients had symptoms referable to the cardiovascular system, but since the electrocardiogram was abnormal in nearly 40 per cent. of them it is suggested that the heart should be carefully investigated in all such cases. Two reasons are given for the association of these lesions:

1. the similarity of the sympathetic nerve supply to the shoulder and the heart;
2. the fact that the connective tissue and vascular structures in the myocardium, shoulder, thyroid gland, and gall-bladder have a common developmental origin.

As might be expected, therefore, periartthritis of the shoulder is also often associated with thyrotoxicosis and cholecystitis.

[Unfortunately, no comparable electrocardiographic findings are given for a group of patients of the same age distribution not suffering from scapulo-humeral peri-arthritis.] A. Paton.


After a brief review of the literature the authors, from Stanford University School of Medicine, San Francisco, report six cases of scleroderma in which, in addition to the well-recognized oesophageal lesions, there were widespread lesions of the intestinal tract. These involved the duodenum, jejunum, and ileum, and their presence was suggested clinically by anorexia, abdominal pain, and loss of weight. Radiological examination revealed alteration in the calibre (dilatation), tone, peristalsis, and motility of the affected bowel. The cases are illustrated by excellent reproductions of radiographs and of photomicrographs of post-mortem material.

In three of the six cases the course was rapidly progressive, death occurring within 2 years of the onset of symptoms. The characteristic finding at necropsy in
these cases was loss of muscle fibres in the muscularis without appreciable replacement by fibrous tissue.

Treatment with cortisone or corticotrophin produced a temporary remission in two other cases, and in the remaining case resection of the oesophagus and gastroenterostomy were performed for the relief of dysphagia.

Nigel Compston.


Writing from the Rheumatological Clinic, Faculty of Medicine, Paris, the authors describe a method for the measurement of synovial exchange in which, after injecting radioactive sodium (24Na) in an isotonic solution intra-articularly, they record its disappearance from the joint by means of a Geiger-Müller counter to which is attached a graphic recorder; this method has the advantage over those used previously in that the injection does not interfere with normal metabolism. It was found that in animals of the same species and age, the graph obtained obeyed constant laws.

Sodium permeability depends upon two factors—the state of the connective tissues and the blood supply—and one or other of these was varied in the study here reported of synovial exchange in the knee-joint of the rabbit. The connective-tissue barrier was altered by injections of testicular hyaluronidase, and as expected, the clearance of 24Na was more rapid. The blood supply was altered either by femoral arteriotomy, when the clearance was less, even after the injection of hyaluronidase; or by the injection of vasodilator substances when, however, the results were equivocal after administration of acetyl-β-methylcholine, and no alteration in synovial clearance was found when sodium nicotinate was given.

The synovial exchange was also measured after inflammation in the joint had been produced by repeated intra-articular injections of ethanamine oleate, the effect of steroids on the exchange taking place in the inflamed joint being then ascertained. It was found that systemic administration of cortisone or intra-articular injection of deoxycorticosterone acetate or hydrocortisone slowed down exchange when this was initially rapid, and increased it when it was initially slow. The authors stress that since the experimentally induced inflammatory reaction altered the basic structure of synovial connective tissue, the results obtained in this study are not necessarily applicable to inflamed joint conditions in the human patient.

F. Clifford Rose.


The author describes the treatment of a series of 466 consecutive cases of chronic arthritis (excluding 150 in which the course was not completed) with “nyloxin”, a preparation containing cobra venom, formic acid, and silicic acid, given by subcutaneous injection in doses increasing from 1 to 3 ml. Treatment was usually given at weekly intervals at first, then less frequently as control of symptoms was obtained, until eventually in most cases the patient received only a maintenance injection every 3 months. The patients are classified in three broad diagnostic groups—osteo-arthritis, rheumatoid arthritis, and mixed types—the numbers in these groups being 344, 74, and 48 respectively. The results as assessed by the physician after consideration of all the relevant factors were “satisfactory” in 426 cases (91·4 per cent.) and “unsatisfactory” in forty (8·6 per cent.). The patients’ own opinions on their condition before, during, and after treatment are analysed separately and here again the results show a high proportion of successes; for instance, of 94 patients reporting 6 months to 5 years after cessation of treatment, 88 (93·6 per cent.) said that their condition remained satisfactory. The author also notes that the patients’ general health was improved, often with a rise in the haemoglobin level, and that hypertension, where present, was reduced.

[It is unfortunate that insufficient clinical details are given in this paper to enable the reader to assess the value of this treatment.] K. C. Robinson.


An investigation was carried out at the Maryland General Hospital, Baltimore, into the claims of Bryson (see Abstract on this page) that a mixture of cobra venom and silicic and formic acids was effective in the treatment of chronic arthritis. Three solutions were prepared for subcutaneous injection:

(A) containing formic acid only;
(B) containing all three ingredients in the proportions used by Bryson;
(C) a mixture of formic and silicic acids.

The patients, who were classified as having either rheumatoid or hypertrophic arthritis (the latter predominating), were given weekly injections of one or other of these preparations in increasing doses, the interval being later extended gradually as described by Bryson.

The results were as follows:
Ten patients had Solution A, and one responded;
61 had Solution B, and 52 responded;
Ten had Solution C, and eight responded (though the degree of improvement was thought to be less than with Solution B).

A response was defined as the subsidence or cessation of pain, swelling and stiffness in the affected joints, and improvement in general health. The authors conclude that Bryson’s treatment gives substantial relief of symptoms in more than 80 per cent. of cases of chronic arthritis.

K. C. Robinson.


The investigation described in this paper from the Middlesex Hospital, London, was undertaken to determine whether the beneficial effect of mepacrine in chronic
lupus erythematosus is the result of an increase in tolerance to light. Patients with chronic lupus erythematosus received up to 100 mg. mepacrine twice a day, and the sensitivity of the skin to light was tested monthly. A commercial "sun lamp" with a filter of cellulose acetate was used to test light sensitivity, a photometer being employed to ensure accuracy of dosage. The minimum erythema dose (M.E.D.) was measured on the skin of the abdomen.

The average M.E.D. in untreated patients with lupus erythematosus was about half the normal. In patients receiving mepacrine the increase in light tolerance was very gradual but the clinical effect on the lesions of lupus erythematosus was more rapid. The authors believe the results indicate that "mepacrine has another action which exerts a more immediate effect on the disease itself than simply by increasing tolerance to sunlight".

[The conclusions reached would be more impressive if the findings were considered statistically. Averaged results from five control subjects and nine patients with lupus erythematosus after one-half or one-quarter minute's exposure cannot be assessed satisfactorily in any other way.]

S. T. Anning.


The literature on the metabolic functions of pantothenic acid and vitamin E (α tocopherol) is reviewed at length, and the results of the use of these compounds in the treatment of lupus erythematosus are summarized. The author believes that many of the failures have been due either to the fact that these vitamins were administered individually instead of in combination, or to inadequate dosage.

To 67 patients suffering from lupus erythematosus massive doses of pantothenic acid combined with α tocopherol were given, the treatment schedule being 10 to 15 g. calcium pantothenate daily, 10 to 15 g. pantothenyl alcohol daily, and 5 to 10 g. sodium pantothenate daily, combined with 3 to 6 g. daily of a mixture of three tocopherols. In a group of 36 patients with chronic discoid lupus erythematosus objective improvement was observed in 4 to 6 months; in half the patients the condition had cleared completely and in the remainder it was much improved at the time of reporting. Similar results were obtained in a group of seventeen patients with disseminated discoid lupus erythematosus, improvement being noted after 2 months, and in eleven with the subacute disseminated form of the disease, the response in this group being rapid, usually after one month. In three cases of acute disseminated lupus erythematosus treatment was started while the acute phase was being brought under control with steroid hormones; by administration of pantothenic acid and tocopherol the patients were maintained without relapse for 7, 11, and 19 months respectively. In general, it was noted that the more hypertrophic and infiltrated the process the slower the response. Apart from transient nausea and gastric distress there were no complications, and there were no abnormal findings in the blood or urine of patients treated for 1 to 3 years.

Discussing the results, the author suggests that as α tocopherol may be metabolized in the body to furnish precursor "cortisone-like materials", and pantothenic acid is related to the secretion and formation of steroid hormones—a theory supported by the functional inadequacy of the adrenal cortex in pantothenate deficiency—massive doses of pantothenic acid with α tocopherol enables the body slowly to synthesize a cortisone-like compound. Benjamin Schwartz.


Following claims that nitrogen mustard is of value in the treatment of glomerulonephritis and also in that of systemic lupus erythematosus with renal involvement, the author studied the effect of this form of therapy and of treatment with triethylene melamine in twenty cases of the latter disease.

None of the patients was treated until the maximum possible benefit had been obtained with cortisone, and this steroid was administered throughout the trial. No improvement was noticed in five patients suffering from active disease without apparent renal involvement, nor in four with or without overt renal disease in whom there was established hypertension. Considerable improvement was observed, however, in the group of patients suffering from "nephrotic nephropathy". The greater the degree of oedema and albuminuria, the greater was the response to treatment. All twenty patients were given nitrogen mustard intravenously in a single dose of 20 mg. in a dextrose infusion. In successful cases a diuresis occurred within 3 to 14 days. No serious toxic effects were observed.

Triethylene melamine was given to five of the patients in a total dose of 10 to 15 mg. over a 2- to 3-day period. In one of them agranulocytosis developed and in another a fatal aplastic anaemia. It was not used further because of its unpredictable behaviour in this disease.

Nigel Compston.


Reports of the successful treatment of lupus erythematosus with the synthetic antimalarial compound mepacline, and later with the less toxic compound chlorquine, prompted a trial of the latter drug in rheumatoid arthritis. The authors find that a dose of 100 to 200 mg. chloroquine per day produces only minimal toxicity, causing at most slight nausea, loss of appetite, or tinnitus. With a dose of 300 to 450 mg. daily, however, intolerance is more common.

In 46 cases of rheumatoid arthritis the drug had a beneficial effect, which was in marked contrast to the absence of any effect in 25 control cases of radicular pain.
and nineteen of osteo-arthritis, improvement, apparent on the 15th day, being noted in approximately two-thirds of the former group. The erythrocyte sedimentation rate also fell, but not in proportion to clinical improvement.

The average dose was 100 to 150 mg. each morning for the first 3 to 10 days, after which a second dose of 100 to 150 mg. was added in the evening. If well tolerated, this dosage was continued for 4 to 6 weeks, but if symptoms of intolerance—loss of appetite, nausea, vertigo, tinnitus, or paralysis of accommodation—appeared, it was reduced to 100 mg. daily and continued for 2 to 3 months. Kenneth Stone.


Since it was first observed in 1951 that associated joint symptoms improved during the treatment of lupus erythematosus with mepacrine, several observers have reported improvement in cases of rheumatoid arthritis as a result of treatment with either mepacrine or chloroquine. The present authors have used both substances, but find that tolerance to chloroquine is decidedly greater than to mepacrine. Only three of eleven patients given mepacrine failed to show symptoms of intolerance, whereas of seventeen patients given chloroquine, only one had to stop taking the drug because of digestive disturbance. As the effect of the two drugs on the rheumatic condition appeared the same, the use of mepacrine has therefore been abandoned.

The dosage used in either case was 0-1 g. twice daily for 20 days in each month for periods varying from 1 to 6 months. Of eleven cases of rheumatoid arthritis treated with mepacrine and seventeen with chloroquine, about one-half showed improvement, with reduction in pain and joint swelling, increased activity, and often a fall in the erythrocyte sedimentation rate. But only one of three patients with ankylosing spondylitis appeared to derive benefit. Kenneth Stone.


The work described in these three papers was aimed at assessing the value of hydrocortisone in the treatment of the condition known as tennis elbow. There are numerous references to the literature concerning the histopathology of the syndrome, and some emphasis is laid upon the ineffectiveness of the many methods of treatment hitherto employed, with the single exception of surgery, which, though effective, is a rather major undertaking for a relatively minor complaint that in any case spontaneously recovers in due course. Quin and Binks present the results in 31 cases, with much clinical information. They were not convinced that trauma was a significant aetiological factor, and were impressed with the fact that there was often a history of "aches and pains in other parts of the body", suggesting that the condition is a manifestation of a more generalized disturbance. Pain is aggravated by gripping and dorsiflexion of the wrist. Murley notes that the condition commonly affects those over 30 years of age who undertake unaccustomed activities involving repeated pronation and supination while the hand is gripping.

The authors of all three papers compare the effect of hydrocortisone with that of procaine, another commonly used method of treatment. Quin and Binks injected procaine at the maximum point of tenderness and then injected varying amounts of hydrocortisone into the identical spot. The authors of the other two papers injected 25 mg. hydrocortisone alone into the area of maximum tenderness; or, in their control series, 1 ml. 2 or 5 per cent. procaine respectively. Results were assessed at definite intervals afterwards. Quin and Binks recorded 26 successful results from a single injection (combined procaine and hydrocortisone). Of the five cases in which this treatment was a failure two responded after a second injection. Various reactions are described. Murley records fourteen successful results and five failures out of nineteen cases. Subsequent relapses were common, but responded to further injections; no patient was made worse. Of the eighteen patients treated with procaine alone as a control "a few found their symptoms improved but most were unrelied". Freeland and Gribble, on the basis of sixteen injections in fourteen cases, conclude that "the local injection of hydrocortisone . . . was no more or less effective in curing tennis-elbow than a similar injection of 5 per cent. procaine". They express surprise that procaine, being only a short-lasting local analgesic, produced such a clear and long-lasting improvement at all. Such a view overlooks the other pharmacological actions of this substance. There is perhaps some doubt about the advisability of using procaine as a control injection in such cases as these, as it is known to have some degree of effectiveness in the treatment of this condition.]

The only deduction to be made from consideration of the three papers together is that Freeman and Gribble obtained equally effective results from hydrocortisone and 5 per cent. procaine, while Murley, using only 2 per cent. procaine, failed to observe any effective response in the patients so treated, which seems to indicate that procaine may be as effective as hydrocortisone provided it is used in sufficient concentration. Harry Cote.


After discussing briefly the information that may be obtained by joint puncture and examination of the punctate as an aid to diagnosis in arthritic conditions, the author describes his experience in private practice with the intra-articular injection of hydrocortisone acetate. A dose of 25 mg. (or 10 mg. for the smaller joints) for
ABSTRACTS

five to ten injections per case produced satisfactory results, as judged 4 weeks after completion of treatment, in 75 per cent. of 160 patients with various forms of rheumatic joint disease. Improvement was judged by lessening of the pain, stiffness, and inflammation, which was generally accompanied by simultaneous improvement in the condition of the punctate. The response was better in osteo-arthritis conditions (60 per cent.) of patients improved) than in rheumatoid arthritis; in humero-scapular periartthritis, however, the results were generally inferior to those obtained by intravenous infusion of ACTH. The best results were seen in monarthritic conditions and in cases in which one or two joints in polyarthritis proved resistant to systemic treatment with gold or cortisol. The technique of injection of the joints presented no particular difficulties.

R. Crawford.


At the Manchester Royal Infirmary the effect of cortisone was compared with that of an inert substance in treating 32 cases of periartitis of the shoulder. The patients, all between 20 and 70 years of age, had periartitis of one or both shoulders without radiological evidence of bone or joint disease and in all of them the erythrocyte sedimentation rate was normal; those with symptoms or signs of generalized arthritis were excluded. Half the patients were given a suspension of cortisone by mouth for 4 weeks and the other half received an inert suspension in the same amount, the latter being indistinguishable in both appearance and taste from the cortisone suspension.

All patients were instructed in shoulder exercises, and at the end of 4 weeks the shoulders of those who had not progressed satisfactorily were manipulated under general anaesthesia. It was found that although some of the patients receiving cortisone had less pain before and after manipulation than the control group and fewer required restoration of movement under anaesthesia, some patients were not helped by the hormone. No statistical difference was observed between the results in the two groups.

Oswald Savage.


The Bottyán test is of great value in the diagnosis of dental foci of infection in ocular disease. The Bottyán antigen does not contain bacteria and is not toxic. In eye diseases caused by syphilis or tuberculosis the test is negative. Where there is a positive Bottyán test a rheumatic aetiology must be considered even when there is not rheumatic illness and no history of rheumatic illness.

Official Abs. (abridged).


A 67-year-old woman had suffered from severe arthritis for 17 years. Besides the stigmata of severe arthritis, she showed dry corneae, conjunctiva, mouth, and throat, and a depression at the angle of the jaw, corresponding to the region of parotid glands. A sialogram of the right parotid gland presented a picture suggestive of parenchymal atrophy. Gastric anacidity was reduced. She was anaemic and one test showed L.E. cells in the peripheral blood.

C. McCulloch.


Case report of a 35-year-old man who had two onsets of Reiter's syndrome with a 15-year interval. The aetiology could not be determined. He was given post-insulin light hypoglycaemic "states" with good results.

W. H. Melanowski.


The patient, shortly after his marriage, developed urethritis, arthritis, and conjunctivitis. "Pleuroneuromenia-like-organisms" were cultured from the urethra.

C. McCulloch.


Disk Syndrome

Gout

The authors report upon the use of phenylbutazone in the treatment of ten patients with acute gouty arthritis and sixteen cases of chronic gout at the Veterans Administration Hospital, San Francisco. The drug was given either by intramuscular injection in 20 per cent. aqueous solution, or by mouth in enteric-coated capsules. The daily dose in the acute cases was 0.8 to 1 g., but varied in the chronic cases from 0.4 to 1 g. Subjective relief was obtained in nineteen out of twenty attacks of acute gout, and the number of exacerbations was effectively reduced in the chronic cases. Toxic symptoms, however, occurred in nine of the sixteen cases of chronic gout. The majority of these occurred during the first few weeks of treatment, but the fact that some occurred later suggests that the drug should not be used as a routine in chronic gout unless all other forms of treatment have failed.

The exact mode of action of the drug is not known; it lowers the blood uric acid level and also diminishes urinary excretion of uric acid, 17-hydroxycorticoids, and sodium. The authors do not advocate the routine use of phenylbutazone in the treatment of gout; they merely indicate its therapeutic effect and recommend consideration of its use in cases of gout resistant to other established forms of treatment.

R. E. Tunbridge.


The author, from the General Hospital, Newcastle upon Tyne, describes the results obtained with 3-hydroxy-2-phenyl-4 cinchoninic acid (HPC), a derivative of cinchophen, in the treatment of ten cases of gout, and briefly records two further cases. The dosage was 1 to 2 g. daily for an initial period, usually a few days, then 0.5 to 1 g. daily.

Satisfactory results were obtained in acute gout, apparently quite as good as some obtained with colchicine. The drug was also effective in the chronic type of gouty arthritis, but in these cases more prolonged treatment was necessary. Administration of the drug had often to be interrupted, however, because of troublesome skin reactions; erythema was a frequent early reaction and vesiculation was observed later in six cases. Nevertheless, the drug was persevered with, in some cases for
long periods; one patient received a total of 210 g. HPC within a trial period of 9 months. No serious toxic effects were observed; nausea and diarrhoea, which occurred in some cases, could usually be prevented by giving the drug in small doses after the main meals with an equal amount of sodium bicarbonate. In the author's view HPC should be reserved for short-duration treatment of acute gout or for prophylactic treatment of patients with premonitory symptoms. Joseph Parness.


General Pathology


The authors have determined at the Institutes of Hydrology and Climatology, of Paris and Aix-les-Bains, the serum protein levels in 97 cases of inflammatory rheumatism, comprising 62 cases of rheumatoid arthritis, eight of Still's disease, 24 of ankylosing spondylitis, and three of gout. The serum protein level was below normal in only eight of the cases, and was generally raised, being higher in men than in women. Except in cases of ankylosing spondylitis, in which the serum protein level was always raised, the degree of hyperproteinæmia was roughly proportional to the activity of the disease and to the erythrocyte sedimentation rate.

Paper electrophoresis of serum from patients with rheumatoid arthritis showed that the albumin fraction decreased and the globulin fraction increased as the disease became more active. Variations in the globulin fraction were found to be related to the type of arthritis. In early cases the alpha-2 globulin value was raised, whereas in more advanced cases showing fibrous or ankylosing changes, the gamma globulin value also rose. The electrophoretogram in long-standing cases showed an increase in alpha-1 globulin if the disease was active, but this value was within normal limits in quiescent cases. The beta globulin value was slightly raised in one-fifth of cases. The changes in protein fractions in cases of Still's disease were similar to those in the adult type of rheumatoid arthritis. In the cases of ankylosing spondylitis the changes in the globulin fractions were less marked, and the authors believe this was associated with the less intense activity of the disease. In two of the three cases of gout there was a rise in gamma globulin level, but in the third case there was no change even during an acute attack.

It is concluded that these findings are not specific for the diseases discussed, but may be of help in assessing prognosis and confirming the diagnosis of the type of lesion present. F. Clifford Rose.


In a further investigation carried out at the Karolinska Hospital, Stockholm, of the factor present in the serum of patients with rheumatoid arthritis which agglutinates sensitized sheep erythrocytes, inactivated serum was treated with sheep cells to remove heterophile antibody, diluted with 14 vol. water, and kept at 4°C. for 48 hours; the precipitate which formed was separated by centrifugation and redissolved in saline. This solution was found to contain a haemagglutinin for sensitized sheep erythrocytes which was specific to serum from rheumatoid arthritic patients. A factor with similar properties could be produced in vitro by growing bacteria isolated from the throat of patients with rheumatoid arthritis on a medium containing bovine or human collagen tissue. D. J. Bauer.


The serum of patients affected by various types of chronic inflammatory rheumatism have been titrated at the Pasteur Institute, Paris, for antistreptolysin-O (by the method of Todd and Kalbak) and the results compared with those obtained in normal subjects and in patients suffering from acute articular rheumatism. Although a titre of 200 units is generally taken as the upper limit of normal in Europe, a titre between 200 and 400 units was found in 7.8 per cent. of a control series of 115 normal subjects aged 20 to 60 years, the corresponding figure given in reports from different European countries varying from 6 to 26 per cent.

Of 393 cases of rheumatoid arthritis in adults, a raised titre was found in 52.6 per cent., the titre being 800 units
or more in 11-8 per cent. The proportions of men and women with high titres were much the same, but a higher proportion of increased titres was found among patients with a history of infection of any sort preceding the onset of the disease or of an exacerbation than among those with no such history. A high titre was found less often when the erythrocyte sedimentation rate (E.S.R.) was below 20 mm./hr, and more often in patients with marked constitutional symptoms. In four out of five cases of rheumatoid arthritis in children the titre was more than 200 units. A high titre was found in 61-2 per cent. of 96 cases of ankylosing spondylitis. This proportion is similar to that found in rheumatoid arthritis, but included a greater number of cases in which the E.S.R. was normal or only slightly raised. In spondylitis, however, the E.S.R. is often not in harmony with the clinical signs of activity. A titre of between 200 and 800 units was found in fourteen out of 21 cases of chronic gouty polyarthritis, and in twelve out of nineteen cases of psoriatic rheumatism. Repeated examinations carried out on 77 of these patients over periods up to 2 years showed a variation in titre in only nineteen per cent. of cases.

The proportion of cases of acute articular rheumatism in which an increased antistreptolysin titre has been reported by previous writers has varied from 69 to 100 per cent. Among twenty such cases the present authors found seven with a titre between 200 and 800 units, and eleven with a titre above 800 units. In the absence of a large series of cases of rheumatoid arthritis in children, however, a comparison between the findings in rheumatoid arthritis and rheumatic fever cannot strictly be made.

Kenneth Stone.


In a study carried out at the Institute of Rheumatology, Dresden, the following serological tests were carried out on 228 rheumatic patients:

1. determination of antistreptolysin titres;
2. Rose agglutination test, using sensitized sheep erythrocytes;
3. Paul-Bunnell test, using fresh, untreated sheep erythrocytes;
4. Svirz and Schlossmann agglutination test, using absorbed serum and sensitized sheep cells;
5. I-agglutination test, based on the agglutinable antigen of ß-haemolytic streptococci (method of Nicholls and Stainsby).

From the results of these tests the authors conclude that high titres in Tests 2 and 5, together with low titres in Tests 1 (antistreptolysin), 3, and 4 are serologically diagnostic of rheumatoid arthritis. In cases of ankylosing spondylitis, antistreptolysin titres were particularly high and all the other tests gave low readings. It is claimed that serological tests are of practical value in rheumatoid arthritis, since by their use a diagnosis can frequently be made before the appearance of the characteristic clinical changes and of the accelerated erythrocyte sedimentation rate.

[The original paper should be consulted for the various serological techniques which are given in some detail.]

D. Preiksel.


Studies have been made in an effort to gain some understanding of the reason for the difference in anti-arthritic effect of intra-articular injections of cortisone and hydrocortisone. The results are as follows:

1. The rates of decrease in concentration of 17-hydroxycorticoids in the joint fluid during the first few hours after intra-articular injections of hydrocortisone, hydrocortisone acetate and cortisone acetate are approximately the same, the effect of differences between some clinical subjects being greater than that of differences between compounds.
2. The hydrolysed forms of both hydrocortisone acetate and cortisone acetate were present in greater proportions in the fluid than in the cells.
3. The proportion of 17-hydroxycorticoids present in the cells after injection of cortisone acetate is greater than after the injection of the free form of hydrocortisone, but less than after the injection of hydrocortisone acetate.

These data do not afford an explanation for the difference in anti-arthritic effect between hydrocortisone and cortisone. Further studies are in progress.

[Authors' summary.]


The hearts of 32 patients dying of rheumatic carditis (of which seventeen form the basis of this study) were examined at the University of Bristol in order to determine whether necrosis of muscle fibres occurs in rheumatic carditis and whether Aschoff bodies originate from damaged muscle cells or from connective-tissue cells—two questions which have been much disputed.

As a result of his study the author is led to the conclusion that the characteristic cells are not of muscular origin. He noted that there was a more intimate relationship between the Aschoff bodies and myocardial cells in cases with a brief clinical history. He concludes that the underlying lesion is a fibrinoid necrosis of the interstitial connective tissue which also involves the thin sarcolemma of the muscle fibres, and that this is sometimes accompanied by secondary damage to the muscle cells.

A. C. Lendrum.

Changes in Complement and its Fractions in Rheumatoid Arthritis and its Relation with the Haemagglutinating Factor. (Sul comportamento del complemento e delle sue frazioni nell'artrite reumatoide e sui suoi rapporti con fattore emoagglutinante.) CASTELLI, D., and DANEO, V. (1954). Reumatismo, 6, 346. 1 fig., 20 refs.


ACTH, Cortisone, and Other Steroids


The authors’ experience at Guy’s Hospital, London, during a 21-year period in the treatment of various diseases with cortisone and ACTH is briefly reviewed. Patients receiving these drugs for the first time were treated for about 3 weeks according to one of the following dosage schedules:

1. 20 to 40 mg. ACTH daily by slow intravenous infusion for a minimum of 8 and occasionally up to 16 hrs;
2. 20 to 40 mg. ACTH gel daily by a single intramuscular injection;
3. 100 to 200 mg. cortisone by mouth daily in four divided doses;
4. 100 to 150 mg. cortisone daily in a single intramuscular injection.

When it was apparent that the disease was controlled, usually in 7 to 14 days, the daily dose of cortisone was reduced or ACTH was administered on alternate days. Serum sodium and potassium levels were estimated initially, such estimation being repeated only if intensive treatment was continued for more than 2 weeks or the patients’ condition required it. When the drugs were given daily, fluid intake was restricted in apyrexial patients to 50 to 60 oz. (1·4 to 1·7 l.) a day. No additional sodium chloride was permitted, but up to 4 g. potassium chloride was given daily.

The disease conditions in 185 patients are tabulated. Complications included gastro-intestinal perforation in three cases (the classic early symptoms being masked by the drugs), with two deaths; acute psychosis in three cases; and steroid diabetes in one case.

The results of long-term out-patient treatment in 44 cases are discussed. Of these 44 patients, eighteen had Addison’s disease or pituitary dysfunction, three polyarteritis nodosa, two disseminated lupus erythematosus, one subacute collagen disease, five scleroderma, one rheumatoid arthritis, six pemphigus, two exfoliative psoriasis (response poor), and six eye diseases. The results were highly satisfactory; in many of the cases the disease underwent remission so that treatment could be stopped, at any rate for a time.

Norval Taylor.


Using the granuloma-pouch technique, it was shown that, depending upon circumstances, systemic stress can either inhibit or aggravate the topical damage caused by exposure of a limited tissue area to a pathogen—for example, a chemical irritant, such as croton oil.

The antiphlogistic effect of stress is not merely due to increased secretion of cortisol-like hormones, since it is also observed in adrenalectomized animals maintained on (in themselves inactive) threshold doses of injected cortisol. The aggravation of topical tissue injury by systemic stress also depends in part upon endogenously produced adrenal hormones; it is abolished by complete adrenalectomy, but not if suitable substitution therapy with antiphlogistic corticoids (cortisone, cortisol) is given. Both these effects of systemic stress upon topical tissue reactions can be delayed, becoming manifest only after the systemic stressor has ceased to act.

The interrelation between systemic and local manifestations of disease in general are discussed in the light of these findings.—[Author’s summary.]


It has been suggested that salicylates act in rheumatic diseases by stimulating the adrenal cortex via the anterior pituitary to produce adrenocortical steroids, which are considered to be the active therapeutic agents. Some of the evidence supporting this hypothesis and some conflicting with it is here cited.
ANNALS OF THE RHEUMATIC DISEASES

In the present study, carried out at King's College Hospital Medical School, London, the authors investigated the urinary excretion of adrenocortical steroids in five patients receiving salicylates, a paper-chromatographic method which allows separate assay of cortisone, 17-hydroxycorticosterone, and tetrahydrocortisone being employed.

The patients investigated included three women with rheumatic fever and one woman and one man with rheumatoid arthritis. All patients received 4-hrly doses of sodium salicylate totalling 150 to 200 gr. (10 to 13 g.) daily, and the excretion of adrenocortical steroids in 24-hr specimens of urine and the plasma salicylate levels were determined.

In no case did salicylate administration affect the urinary adrenocortical steroid excretion, even when, as in one instance, the dosage of salicylate reached a toxic level. Subsequent administration of corticotrophin to two of the patients was followed by a large increase in steroid output. It is clear, therefore, that these results do not support the hypothesis that the therapeutic activity of salicylate depends on the intermediary production of corticotrophin.

Nancy Gough.

SALICYLATES AND THE PLASMA LEVEL OF ADRENAL STEROIDS.


This paper from the Postgraduate Medical School of London reports a study of the plasma level of adrenocortical steroids during salicylate therapy which was undertaken as a direct approach to the problem of whether or not salicylates stimulate the pituitary–adrenal system. Observations were made on eleven patients with either rheumatic fever or rheumatoid arthritis. The plasma levels of 17-hydroxycorticosteroids (cortisone and hydrocortisone) were measured by the authors' modification of the method of Nelson and Samuels (J. clin. Endocr., 1952, 12, 519) and the plasma salicylate level by the method of Brodie and others. Seven of the patients received prolonged treatment with salicylates in a dosage of 0-75 to 1-75 g. 4-hrly, and four were given a single dose of 3-3 to 5-3 g., which is sufficient to raise the plasma salicylate concentration to 20 mg. or more per 100 ml.

In no case was there any significant effect on the level of circulating adrenocortical steroids. Hence the authors conclude that salicylates in clinical dosage do not stimulate the pituitary–adrenal system. They add that toxic doses of salicylate may increase the blood level of adrenocortical hormones, but this is merely the normal response to any non-specific poison.

Nancy Gough.

EFFECT OF ACTH ON THE ADRENALS IN THE NEPHROTIC SYNDROME AND RHEUMATIC FEVER.


In a study carried out at the Children's Medical Center (Harvard Medical School), Boston, the adrenal glands of three untreated patients with the nephrotic syndrome due to chronic glomerulonephritis were smaller in weight and had a higher fat content than the glands from patients with untreated rheumatic fever. Administration of ACTH (corticotrophin) to the nephrotic patients produced an increase in zone thickness and cell size in all three zones of the adrenal cortex, these values returning to normal on withdrawal of the hormone. In the patients with rheumatic fever, ACTH provoked a greater response in the zona fasciculata than in the zona reticularis.

F. W. Chattaway.

EFFECT OF ADRENOACTHROPIC HORMONE AND CORTISONE ACETATE ON THE URINARY AND BLOOD LEVELS OF ASCORBIC ACID IN MAN.


At McGill University Clinic, Royal Victoria Hospital, Montreal, the authors have studied the effect of ACTH and cortisone acetate on the blood and urinary ascorbic acid levels of 32 chronically diseased patients receiving supplements of 250 or 1,000 mg. ascorbic acid, or on a normal diet containing from 15 to 90 mg. ascorbic acid per day.

Of 27 patients receiving ACTH, 21 showed an increased urinary excretion of ascorbic acid extending over the first 24 to 48 hrs of hormone administration, and a reduction of excretion on withdrawal of the hormone. Of nine patients receiving cortisone acetate intramuscularly, three showed similar changes in ascorbic acid excretion; in six cases there was no response, possibly owing to slow absorption of the cortisone, since three patients receiving cortisone by mouth all showed increased excretion of ascorbic acid. The dietary level of ascorbic acid did not appear to affect the type of response observed. Two scurvy infants also showed increased urinary ascorbic acid excretion after injection of ACTH, together with an increase in the urinary content of formaldehydegenic corticoids, accompanied by clinical improvement.

In general the blood levels of ascorbic acid rose along with the urinary levels. The possible sources of the increased ascorbic acid output and the endocrinological implications of the results are discussed. It is suggested that increased glomerular filtration rate, lowered tubular reabsorptive capacity, and release of ascorbic acid from the adrenal cortex may all play a part.

F. W. Chattaway.

EFFECTS OF HYDROCORTISONE ACETATE IN NON-ARTICULAR RHumatism.


This article from the Institute of Rheumatology, Lisbon, records the results of treatment of various soft-tissue lesions with local injections of hydrocortisone in doses of 25 to 75 mg. The lesions included bursitis, pruritis, epicondylitis, tennisovinitis, periartritis of the shoulder, and sciatica. More than 200 injections were made into 85 patients.

No untoward reactions were experienced, and nearly 100 per cent. of cures were reported in epicondylitis and "tendoperiostitis", with less dramatic results in the other
lesions. No beneficial effect was produced in cases of Dupuytren's contracture or psoriasis.

W. S. C. Copeman.


The results of treatment with Compound E (17-hydroxy-11-dehydrocorticosterone), Compound F (17-hydroxycorticosterone), and ACTH in idiopathic thrombocytopenic purpura are reported in this paper from the Temple University School of Medicine, Philadelphia. All cases in which an allergic or drug reaction appeared to be aetologically significant were excluded. The L.E.-cell test was performed in all the eleven cases studied to exclude a diagnosis of systemic lupus erythematosus. The reaction to the Coombs test was positive in three cases, and in two there were positive reactions to repeated serological tests for syphilis. These last reactions were proved to be false by the treponemal immobilization test, and the authors emphasize the value of this test in excluding spirochaetal infection.

As a result of treatment, haemorrhage was arrested in all cases; this was associated with an increase in capillary resistance. However, there was not always a comparable remission in the thrombocytopenia. In three cases in which the rise in the platelet count was negligible, splenectomy was performed, with apparent cure in one, a partial improvement in one, and temporary improvement only in one. In a further case an increase in the platelet count was observed at first, but this was not maintained even during treatment. In the remaining seven cases there was adequate haematological remission. The authors consider that two of these seven patients were cured after one course of steroid; the condition of two others was satisfactory at the time of the report. In three cases the platelet count increased with each course of treatment but gradually fell thereafter. There did not appear to be any difference between the response to oral administration of Compound E or Compound F, and of ACTH, but in one case Compound F given parenterally was ineffective although there was a response when the drug was later given by mouth. *Nigel Compston.*


The authors present a concise review of the present position in regard to assays for corticotrophin in human blood, and discuss the merits and demerits of various techniques that have been developed, particularly at the Mayo Laboratories, Rochester, Minn., since the earlier report by Taylor and others (Endocrinology, 1949, 45, 335; *Abstracts of World Medicine*, 1950, 7, 294).

They consider that the method of Sayers and others (Endocrinology, 1948, 42, 379), which depends on the measurement of adrenal ascorbic-acid depletion in hypophysectomized rats, is still on the whole the most reliable, though in their experience it has some limitations: for example, the assay rat must be completely hypophysectomized, and the method cannot be depended on for quantitative measurement of ACTH activity, the results obtained having tended to be capricious. Another reliable method, although it requires comparatively larger amounts of blood, is that employed by Sydor and Sayers (Proc. Soc. exp. Biol. (N.Y.), 1952, 79, 432) who used extracts of blood prepared by the oxycellose process of Astwood and colleagues. By both these methods corticotrophic activity has been demonstrated in Addison's disease, the adrenogenital syndrome and in a few miscellaneous conditions, whereas no activity could be detected in normal persons or in patients with Cushing's disease or febrile miliary tuberculosis. A number of other workers have claimed to have found high corticotrophic activity in normal serum, but their results have so far been too contradictory to be relied on. *Richard de Alarcón.*


The authors have conducted experiments at the University of Utah College of Medicine, Salt Lake City, to examine the claim of Strauss and Brokaw (New Engl. J. Med., 1951, 245, 798) that there is "functional adrenocortical insufficiency" in certain cases of pernicious anaemia in relapse.

Estimation of the plasma 17-hydroxycorticosteroid level in 8 cases of pernicious anaemia revealed normal values in all but one patient who was critically ill. After the oral administration of adrenal steroids (ACTH or hydrocortisone) there was a more rapid and sustained rise in the plasma level of 17-hydroxycorticosteroids than normal, but after intravenous injection the "clearance" of these steroids was unimpaired. The plasma level of 17-hydroxycorticosteroids rose normally in patients with pernicious anaemia after giving ACTH. In one patient with gastric achylia but without pernicious anaemia the level of 17-hydroxycorticosteroids was similar to that found in the plasma in cases of pernicious anaemia after the administration of adrenal corticoids by mouth. In patients with pernicious anaemia the administration of gastric juice along with adrenal steroids produced levels nearer to the normal.

The authors therefore conclude that there is no evidence of adrenal insufficiency accompanying pernicious anaemia, but that the changes they observed following the oral administration of adrenal corticoids to achyllic patients were probably due to the absence of gastric juice, since normally a large fraction of the dose of corticosteroids is destroyed in the gastrointestinal tract before absorption can take place. *Nigel Compston.*


After reviewing the literature on the treatment of ulcerative colitis with cortisone or ACTH and on the
complications encountered, the authors report an uncontrolled therapeutic trial of ACTH in fourteen cases of this condition seen at Addenbrooke’s Hospital, Cambridge. The hormone was given initially in a dosage of 15 mg, 6-hrly by intramuscular injection or 20 mg, daily in the form of a gel, this dosage being gradually increased until improvement, as judged by gain in weight and fall in temperature, was observed. The maximum effective dosage was continued for 2 to 5 weeks, and then gradually reduced. Details of the results and the duration of the follow-up are given in a comprehensive table, and certain cases are discussed.

In seven of the fourteen cases there was complete remission and in four some maintained improvement. The authors conclude that ACTH has a place in the management of cases of ulcerative colitis, particularly in acute and severe cases of recent onset. J. Naish.


A “blind” therapeutic trial of cortisone in ulcerative colitis was carried out at the Radcliffe Infirmary, Oxford, in conjunction with similar trials at hospitals in North-west London, Edinburgh, Leeds, and Birmingham, a total of 213 patients being treated. The dosage of cortisone was 100 mg a day for the first 3 weeks, followed by smaller doses in the next 3 weeks. Approximately half of the patients received a placebo, but the physician in charge did not know whether the patient was receiving this or cortisone.

The results obtained in first attacks and in relapses are considered separately, the patient’s condition being assessed as “clinical remission”, “improved”, and “no change or worse”. At the end of 6 weeks, in the series as a whole significantly more treated patients than controls were in clinical remission. Of the patients given cortisone during a first attack, 42 per cent. were in remission, 36 per cent. were improved, and only 22 per cent. showed no change or were worse. Of the patients given cortisone during second or subsequent attacks, the percentage in remission was slightly lower and the percentage improved was substantially lower than was the case in the patients treated during a first attack. The number of patients subjected to ileostomy and the number of deaths were higher in the controls than in the treated group. X-ray examination and sigmoidoscopy were not carried out in all cases, but such data as were available confirmed the general clinical assessment. A few patients had a relapse soon after cessation of cortisone therapy.

It is concluded that cortisone is beneficial in the treatment of an acute attack of ulcerative colitis. J. Naish.


At the University of Maryland School of Medicine, Baltimore, local application of hydrocortisone acetate in the form of a lotion or ointment in a strength of 0-5 per cent., 1 per cent., and 2-5 per cent. was tried in the treatment of 418 patients suffering from a variety of dermatoses. It was found that in a strength of 0-5 per cent. both lotion and ointment were relatively ineffective, and that in general an oily base was the most suitable vehicle. Hydrocortisone was of value in atopic dermatitis, neurodermatitis, seborrhoeic dermatitis, contact dermatitis, pruritus ani, and pruritus vulvae, but was ineffective in alopecia areata, psoriasis, pityriasis rosea, acne vulgaris, lupus erythematosus, and lichen planus. In patients with acne vulgaris the condition became worse (probably as a result of direct hormonal effect), but other untoward reactions in the series were due to sensitivity to the vehicle. In patients with chronic dermatoses there was a tendency to relapse when the hydrocortisone was discontinued: nevertheless, it is considered that the drug has an important place in the treatment of skin conditions.

H. R. Vickers.


A clinical and laboratory investigation of fifteen cases of severe pellagra at the Dermatological Clinic of the University of Skopje, Yugoslavia, suggested a relationship between the manifestations of the disease and adrenal dysfunction. Five severe cases were therefore treated with injections of 25 mg ACTH (corticotrophin) daily for 16 to 20 days without any other medication or change of diet. Improvement in the mental state, the condition of the skin, and the gastrointestinal symptoms was manifest in every case after six doses, and after ten doses the patients were normal in every respect except for some residual skin lesions. After 400 to 500 mg ACTH had been given the patients were discharged cured, the only remaining sign of the disease being slight depigmentation of the skin in the areas which had been most severely affected. James Marshall.


An interim report is presented from Dumfries and Galloway Sanatorium on the results of administration of cortisone to nine patients (six males, average age 45, and three females, average age 33) with pulmonary tuberculosis who had previously received streptomycin with PAS and/or isoniazid, the choice as regards the last two drugs depending on individual drug resistance, if any. Four of the patients had a positive sputum and moderate or advanced disease, four having bilateral lesions with cavitation. Streptomycin with PAS and/or isoniazid was known to be relatively ineffective in at least two of the patients.

Cortisone was given cautiously, the first patient receiving 12-5 mg., the second and third 25 mg., and the others 50 to 100 mg. daily, for 2 months. The other
chemotherapeutic drugs were given at the same time and were continued for at least another 2 months after administration of cortisone ceased.

In all these patients there was initial symptomatic improvement, which was maintained in most of them. One patient died (the influence of cortisone in this case was uncertain); in the others an increase in weight, diminished cough, and an improvement in general condition and well-being were observed. A fall in the erythrocyte sedimentation rate was noted in seventeen patients, but in most of them the rate promptly returned to the original level when cortisone was withdrawn.

In four patients the radiological improvement was greater than could be expected from standard chemotherapy. With the possible exception of the fatal case, no adverse results of any consequence attributable to cortisone were observed. The author considers that the results warrant an extended trial of this form of treatment. The cases are reported in detail. [The author's conclusion seems justified.]

R. J. Matthews.

**ABSTRACTS**


In the hope that it might improve the distribution of streptomycin in the cerebrospinal fluid (C.S.F.) in cases of tuberculous meningitis with signs of intrathecal block, the authors used cortisone in the treatment of thirty such cases in patients varying in age from 1 1/2 to 41 years at the paediatric and other clinics of the University of Florence. Five of the patients were suffering from optic atrophy, and cortisone was given in the hope of improving the vision of these patients. The remaining 25 patients showed evidence of obstruction to the flow of C.S.F. The authors emphasize that treatment was begun at varying times in the course of the disease and that different doses of the drug were given for varying lengths of time. They cannot therefore make an accurate assessment of the results.

Of the first five cases mentioned above, there was slight visual improvement in three and none in two. Of the other 25 patients, eight received cortisone or hydrocortisone by mouth only. In two of these cases the treatment was started fairly soon after signs of blockage appeared and resulted in a great improvement in the flow of fluid. In the other six cases cortisone was given at a much later stage and little benefit resulted. The remaining seventeen patients received cortisone both by mouth and intrathecally. There was no improvement in five cases and the results were only mediocre in two, but a "good" result was obtained in two others and a "very good" result in eight. The earliest day of the disease on which cortisone therapy was started in this group was the 38th, while even in one case first treated on the 263rd day some improvement still occurred.

The authors consider that in sixteen of the 25 cases there was evidence that the block was relieved as a result of cortisone therapy, and on these grounds they are convinced of its value. J. G. Jamieson.


The authors report from the University Medical Clinic, Geneva, a study of the action of the new corticoid, aldosterone, in two cases of Addison's disease. Both patients also received deoxycortone acetate under similar conditions, and the clinical and metabolic effects were compared.

One hour after the injection of aldosterone the symptoms of adrenal insufficiency had disappeared completely, this beneficial effect lasting for 6 or 7 hours. After a few days of treatment the pigment of the skin cleared in a striking and unexpected way. In one case, treatment with aldosterone for 6 days had more effect on the pigmentation than several months' treatment with cortisone. The changes in the electrolyte balance were similar to those obtained with deoxycortone acetate, that is, there was retention of sodium and chloride and increased potassium excretion, without, however, affecting the water balance or producing a pathological retention of water. The corticoid had no effect on the blood pressure, although haemodilution tests showed an increase in blood volume. The typical flattened glucose tolerance curve seen in adrenal insufficiency, with a marked secondary hypoglycaemia, reverted to normal after administration of aldosterone, but this effect on carbohydrate metabolism was not obtained with deoxycortone acetate.

Aldosterone is an extremely active hormone, and the authors found the effective dose in Addison's disease to be about 2.5 to 3.3 μg per kg. body weight. It is thus some twenty to thirty times more active than deoxycortone acetate. Its action in Addison's disease is similar to that of cortisone in so far as it acts on the pigmentation and carbohydrate metabolism, but it has no effect on the leucocytes, particularly eosinophils, nor on nitrogen and water metabolism. Richard de Marcón.


The authors here summarize their experience during the period 1950-53 in 83 cases of overwhelmingly severe infection which were considered likely to prove fatal if treated by "standard" methods, and which were treated with corticotrophin (ACTH), cortisone, or hydrocortisone in addition to antibiotics. A short, intensive course of hormone treatment was given, only the most severely ill patients receiving it for as long as 7 days. Antibiotic therapy was always continued for at least 3 days after the discontinuance of hormone administration. The conditions treated included meningococcal
infection (fourteen cases), pneumonia (six cases), peritonitis (twenty cases), and miscellaneous infections such as tetanus, diphtheritic myocarditis, hepatitis, botulism, poliomyelitis, and post-infectious encephalomyelitis.

It is argued that the effect of the hormones in reducing inflammation will in many cases prevent irreversible damage to the infected tissues and even (as in mumps orchitis) the complete destruction of an organ. The concomitant danger of dissemination of the infection is minimized by giving the hormones for only a limited period and by adequate antibiotic therapy.

Of the 83 patients treated, only 29 died, and the authors are convinced that the hormones were responsible for rapid and striking clinical improvement in the majority of cases. They advocate that as a general rule the use of ACTH and cortisone with antibiotics should be restricted to those non-surgical conditions which do not appear to be responding (or likely to respond) to antibiotic treatment alone, and to surgical conditions in which operative treatment is intended in the immediate future. They make an exception to this rule in the case of meningococcal meningitis, advocating hormonal therapy in every case. They also advocate the combined treatment in cases of acute hepatitis and mumps orchitis, despite the lack of effect of antibiotics on the viruses concerned.

R. S. Illingworth.


Arch. intern. Med., 93, 850. 4 figs, 27 refs.

In a series of experiments carried out at the University of California School of Medicine, San Francisco, it was found that in two subacute bacterial infections induced in mice very small amounts of cortisone markedly interfered with the therapeutic efficacy of antibiotics. The organisms employed were *Klebsiella pneumoniae* and *Streptococcus pyogenes*, and the antibiotics were crystalline preparations of potassium benzylpenicillin, streptomycin sulphate, and chlorotetracycline hydrochloride.

The usual dose of cortisone was 0.75 mg. in 5 days (approximately 8 to 10 mg./kg. body weight per day); the total dose never exceeded 1 mg.

Cortisone in well-tolerated amounts lessened the therapeutic efficacy of antibiotics in lethal and sublethal infections in mice, this phenomenon being observed not only when the animals were given cortisone before infection, but also when administration of both cortisone and antibiotic was started several hours after infection. The effect varied with the size of the inoculum and the total dose of the antibiotic; it was greatest when the antimicrobial therapy was subcurative; when the dose of antibiotic was well in excess of the curative dose the reduction of its therapeutic efficacy by cortisone was no longer evident.

Cortisone interfered much more with the action of the predominantly bacteriostatic chlorotetracycline than with the action of the bactericidal penicillin or streptomycin. This suggests that the effect of cortisone is mediated through host-defence mechanisms, and that bactericidal antibiotics in curative doses do not depend to so great an extent on host mechanisms and are thus less influenced by cortisone.

Cortisone in concentrations up to 2 mg./ml. had no direct effect on micro-organisms or antimicrobial drugs in vitro. Moreover, the drug was without effect on the total leucocyte count, the morphological differences in the tissue response to infection, and the viable bacterial counts in the tissues of experimental or control animals. The precise site and mechanism of action of cortisone are therefore undetermined.

A. W. H. Foxell.


In this study carried out at the Hôpital de la Charité, Paris, the adrenal areas of 96 rats were subjected to X irradiation at 130 kV, H.V.L. 7-4 mm. Al, through a 6-cm. layer of rice to correspond to the lumbar tissue in man (giving about 24 per cent. transmission), doses of 25, 50, or 75 r being delivered at the upper surface of the rice. The effects were assessed by changes in the weight of the glands, of the blood sugar level, and the urinary nitrogen excretion, the last two being known to be controlled by 11-oxysteroids.

The results showed that gland weight was increased, even after as short a period of irradiation as 45 minutes, increases in gland weight of up to 107 per cent. being found, as compared with controls. Blood sugar levels showed an early rise, which was maximal in about one week. Urinary nitrogen excretion was also increased for about 18 days, as compared with no significant increase in adrenalectomized controls. A dose of 75 r seemed to give the maximum effect possible. The main effects are attributed to the action on the cortex, since (a) stimulation of the medulla results in only a short period of hyperglycaemia followed by a later glycosuria, whereas the glycosuria in these experiments appeared before the maximal hyperglycaemia; and (b) similar findings to the above were obtained with ACTH and cortisone. The mechanism is thought to be by inhibition of utilization of glucose by 11-oxysteroids, accompanied by secondary gluconeogenesis, as shown by the increased nitrogen excretion.

In further experiments on five human subjects in which 100 r was delivered to the adrenal areas, increased excretion of urinary 17-ketosteroids occurred, which was maximal in 3 to 4 days.

J. Walter.


The authors describe experiments carried out at the Presbyterian Hospital and Columbia University, New York, which confirmed that hydrocortisone when added in a concentration of 200 µg./ml. to chick embryo tissue cultures in a medium composed of chicken plasma and amniotic fluid consistently inhibited the growth of fibroblasts. This effect could be partially antagonized by the addition of embryonic extract. The growth of gastric and intestinal epithelium was not inhibited by
hydrocortisone. In heart-tissue cultures the fibroblasts whose growth had been inhibited, grew normally when the hydrocortisone was removed. Aqueous soluble deoxycorticosterone produced similar effects to those of hydrocortisone. Minimal inhibition of growth was also seen when cholesterol in suspension was added.

Similarities and differences between these findings and those usually seen in vivo are indicated and discussed. The cause of the inhibitory action of embryonic extract is not clear. Norval Taylor.

**ABSTRACTS**


At the Rigshospital, Copenhagen, the authors have studied the effect of calcium, vitamin D, and methyl- androstenediol on the calcium metabolism of a man aged 24 who was bedridden with severe spondylitis anklylopoietica and calcification of the spinal ligaments. The patient was maintained on a low-calcium diet containing 160 mg. calcium daily. Vitamin D (5,000 i.u.), cortisone, methylandrostenediol, and extra calcium were administered in varying combinations and amounts for periods of 2 to 3 weeks at a time.

On this low calcium intake the negative calcium balance was further depressed by cortisone. When the intake of calcium was raised by giving calcium phosphate and vitamin D, however, the calcium balance became positive in spite of the continued administration of cortisone; calcium retention was still further increased during a 21-day period during which methylandrostenediol was given, excretion of calcium in both the urine and faeces being reduced by the hormone. It is therefore suggested that to counteract the danger of osteoporosis in patients with Cushing’s syndrome or those receiving prolonged treatment with ACTH or cortisone, calcium and vitamin D should be given freely, with, in addition, occasional short courses of methyl- androstenediol. C. L. Cope.


At the National Institute for Medical Research, London, the biological activity of the compound 9α-chloro-17α-hydroxycorticosterone (9α-chloro-hydrocorti- sone) acetate was compared in several tests with that of cortisone acetate and hydrocortisone acetate. In a toxicity test on adult mice, in which each steroid was injected daily in doses of 50 mg./kg. body weight for 10 days, the chloro-steroid killed seven of ten mice and cortisone acetate killed three of ten mice. Atrophy of the thymus, spleen, and adrenal cortex was maximal in both groups so that the activity of the steroids could not be compared by this method. Both steroids in doses of 2.5 and 1.25 mg./kg. inhibited the growth of nesting rats to comparable degree but the chloro-steroid proved to be 3.4 times more active than cortisone acetate in causing atrophy of the thymus and 4.76 times more active in causing hypertrophy of the liver. Comparison between the chlorosteroid and hydrocortisone acetate showed that chlorine substitution increased the thymus-involving activity of the latter 1.42 times. The chloro-steroid was about 5 times more effective than cortisone acetate in depressing sensitivity to tuberculin in guinea-pigs infected with B.C.G.

C. L. Cope.


For the purposes of a search for derivatives of cortisone with prolonged action when given parenterally, routine tests were adopted which permitted both the therapeutic effect and the general effects of the substance under consideration to be gauged. Of the latter the effect on the body weight and the weight of the adrenal glands appeared to be of most importance, while a modification of the “granuloma test” was used to determine the therapeutic effect. These tests permit the assessment not only of the duration of action of the substance, but also of its intensity.

The procedure employed was as follows. Male rats of 100 to 110 g. were given a single injection of 150 mg. of the substance to be investigated per kg. body weight. On the day of the injection and on the 2nd, 4th, 8th, and 16th days thereafter, a group of rats were anaesthetized and pressed raw cotton wool pads were implanted bilaterally in the back, the animals being killed and a post-mortem examination carried out after a further 7 days. The granulomata thus produced were weighed when fresh and in a dry condition, as were also the adrenal glands.

With all compounds tested the loss of weight of the granulomata in treated animals was significantly greater than in control animals. Cortisone acetate exerted its maximum effect on granulomata induced on the day of injection, and the weight of granulomata induced on the 4th day was only slightly less than in the controls. The effect of cortisone trimethylacetate was also noticeable on granulomata induced on the day of injection, but the maximum effect was on those induced on the 2nd day, when the effect of cortisone acetate was already waning, while its effect on granulomata induced 16 days after the injection was equal to that of cortisone acetate 4 days after injection. A similar difference was evident on comparing the increase of body weight and the weight of the adrenal glands in animals treated with these two preparations. Besides permitting assessment of the length and intensity of action of the test substances, the experiment also confirms that at a given intensity and duration of the effect there is only one crystal form of the seroid hormone ester which will guarantee the optimum action without side-effects. V. C. Medvei.

**Apparent Exophthalmos in the Rat following Cortisone Treatment or Thyroidectomy.** BOAS, N. F., and SCOW, R. O. (1954). *Endocrinology*, 55, 148. 3 tables, 3 figs.

Exophthalmos in rats following cortisone treatment or thyroidectomy has been recently reported. As such
treatment retards growth generally and the exophthalmos is found only in young retarded animals, such experiments were repeated and the eyes and orbital contents weighed after apparent exophthalmos had appeared. The results clearly show that the weight of the orbital contents actually decreased in the operated animals and that the exophthalmos was only an indication of the normal growth rate of the eyeball in the presence of marked inhibition of head and body growth.

E. S. Perkins.


An interesting case report of Basedow's disease with slight exophthalmos in a 14-year-old girl. An acute hyperpyretic episode with rheumatism and an increase of the goitre and exophthalmos responded within a few days to ACTH injections.

S. Vallon.


In 23 cases of perennial severe asthma of undetermined aetiology seen at Massachusetts General Hospital, the symptoms were brought under control by the parenteral or oral administration of cortisone in high doses. Then the dosage was gradually decreased until symptoms reappeared, so enabling a maintenance dose to be established at a slightly higher level. In twelve of these patients the maintenance dose was 62.5 or 75 mg., while in the others it varied between 50 and 150 mg.

In this way many of these patients have been maintained without symptoms for 3 years. All of them developed some minor side-effects such as "moon face", facial hair, or acne, and all but one gained weight, some of them considerably, but diabetes, oedema, hypertension, and potassium deficiency did not occur. One patient developed marked hypercalcuria and showed evidence of osteoporosis, calcium output falling to normal when cortisone was stopped and rising again when it was resumed. In five other cases a high urinary calcium content was repeatedly found, but there was no evidence of osteoporosis.

H. Hersheimer.


Hydrocortisone was given by mouth at the Mayo Clinic to thirteen patients suffering from ragweed hay-fever (seven of whom also had asthma) who had not benefited from desensitization. The daily dose varied initially from 30 to 160 mg., average 80 mg., and after a few days this was reduced to 30 to 40 mg. The duration of the course varied from 2 to 14 days. All the patients benefited from the treatment, the relief obtained being described as either "good" or "excellent". In some cases the relief lasted for the remainder of the pollen season although treatment was discontinued and the pollen count remained high. This symptomatic treatment is, in the opinion of the authors, justified only in certain carefully selected cases. H. Hersheimer.


The author describes a case of diffuse endarteritis, seen at the Frederiksborg Hospital, Copenhagen. The patient was a 69-year-old diabetic woman, in whom the diabetes was satisfactorily controlled by insulin. Two days after the completion of a 4-day course of benzylpenicillin—administered for an indefinite illness manifested by general weakness, nausea, and pain in the chest—she developed pain in both hands, which was followed by oedema and cyanosis. Eventually gangrene of several finger-tips developed, leading to loss of one distal phalanx. Petechial haemorrhages, epistaxis, haematuria, and deterioration of a previously noted diabetic retinopathy completed the picture. Skin biopsy showed obliteration or narrowing of the smaller vessels and degeneration of the endothelium.

The patient was treated with ACTH, 60 mg. daily in divided doses being given initially and then in gradually diminishing doses, for 20 days. A course of di-penicillin for hyposystic pneumonia led to no complications, but a further course given for suppuration in a gangrenous finger caused pruritus, sneezing, and conjunctival inflammation. The progress of the endarteritis was arrested, however, and the diabetes, control of which had become unbalanced during ACTH therapy, returned to its former state.

H. F. Reichenfeld.


The dermatological indications for cortisone therapy can be divided broadly into two groups:

(1) as a short-term measure in certain acute but ordinarily self-limited eruptions, such as widespread eczematous dermatitis, acute urticaria, angioneurotic oedema, and certain drug reactions;

(2) for long-term use in:

(a) certain chronic, not ordinarily fatal, but severely incapacitating dermatoses, such as atopic dermatitis, exfoliative erythrodermia, or exudative discoid and lichenoid chronic dermatosis,

(b) ordinarily fatal but chronic conditions such as pemphigus and acute disseminated lupus erythematosus.

When cortisone has to be given daily in doses of 75 mg. or more for months or even years special problems arise and the authors discuss these on the basis of some 4 years' experience. They first emphasize the need before treatment to exclude the presence or history of cardiac, renal or pulmonary disease, gastric or duodenal ulcer, tuberculosis, diabetes, thrombo-embolic diseases, and psychiatric disturbances. This is always desirable even when
short-term administration only is contemplated, and is imperative whenever a patient is expected to have to take cortisone for a prolonged period.

The results of the treatment with cortisone of 35 patients with a variety of dermatoses (including fifteen cases of atopic dermatitis) for periods ranging from 2 months to several years are given in tabular form, and were almost universally good. The initial dosage varied from 300 to 1,000 mg. daily in the "fatal" conditions, whereas many of the non-fatal skin diseases could be brought under control by doses of 100 to 300 mg. a day. Otherwise healthy persons were given an initial dosage sufficiently large to allay the signs and symptoms rapidly, the dosage then being reduced as rapidly as possible to the lowest effective maintenance level. In general it was found inadvisable to attempt to relieve the signs and symptoms completely, adverse effects being better avoided by giving doses just short of the amount required to achieve this. Such adverse reactions rarely occurred except when doses of more than 100 to 125 mg. were given daily for a protracted period. As precautionary measures the blood pressure and weight were recorded frequently, the urine tested for sugar, and a salt-poor diet given together with a daily supplement of 3 g. potassium chloride in several doses.

The authors stress the need for the regular and frequent supervision of ambulatory patients and emphasize that cortisone may mask the signs of active infection, render painless the perforation of a vescus, reduce fever, and maintain a feeling of well-being in the face of serious infection and destruction of tissue. The most encouraging experience in the prolonged administration of cortisone was that in almost all cases the dosage could be reduced, often to a fraction of that originally required, and in a few cases discontinued altogether without a recurrence of the disease. There were no instances of acquired drug resistance or of addiction.

E. E. Prosser Thomas.

Treatment of Chronic Joint Diseases with Cortisone and ACTH on the Basis of Personal Experience. (Lěčenі chronických chorob kloubnich cortisonom a adreno- kortikotropinum hormonem na podkládě vlastních zkušeností.) LENOCHE, F., and KNOBOVA, J. (1954). Čas. Lék. Čes., 93, 1121. 7 figs, 21 refs.


Other General Subjects


The authors report from the Oxford United Hospitals a clinical survey of 37 men suffering from Raynaud's phenomenon, the diagnosis of which was made on the history alone. The condition was found to be present in 29 out of 31 men using a pneumatic hammer delivering 2,300 blows per minute, and in eight out of 9 men using a trip hammer [the frequency of which is not stated]. Sensory loss in the affected fingers was estimated by:

(a) the assessment of the sense of light touch made with graded nylon threads and by the response to pinprick, using a standard needle variously weighted;

(b) from the time of onset of numbness due to ischaemia after application of a sphygmomanometer cuff.

In addition, four men were examined by means of a nerve clamp which rendered a segment of the ulnar nerve in the upper arm ischaemic.

There are two views of the causation of Raynaud's phenomenon, one being that it is due to a local fault in the condition of the digital arteries, the other that over-activity of the vasomotor nerves is the primary cause. From the fact that in the cases examined a permanent sensory deficit was common in association with Raynaud's phenomenon, the present authors conclude that lesions in the peripheral nerves are the probable cause. Motor weakness was also elicited in the adductor digit minimi in ten cases, in the first dorsal interosseous muscle in four cases, and in the long flexors of the fingers in four cases. Owing to the nature of the job, the left hand only was affected in the majority of the men using the pneumatic hammer, the condition starting in the terminal phalanx of the little finger; in the men using the trip-hammer both hands were affected. The condition caused little disability and the use of the pneumatic hammer was not a precipitating factor, for if an attack was present it soon passed off when the men started work. Attacks were not particularly related to cold, many of the men developing attacks when their hands were warm. The condition commonly developed from 3 months to 2 years after starting this type of work and was not cured by removing the men from it. From their experimental observations the authors conclude that there are disturbances in the peripheral nerves and that these may be the main cause of the simultaneous blanching of the fingers and the motor and sensory changes.

[The incidence of Raynaud's phenomenon observed at this factory appears to be much higher than that recorded by other workers.] L. G. NORMAN.
Raynaud's Phenomenon in Workers with Vibratory Tools.


An investigation was carried out at the Royal Infirmary, Manchester, to determine whether patients suffering from Raynaud's phenomenon as the result of using vibratory tools can be distinguished from normal subjects and from those in whom the condition is due to some other cause. The 34 patients examined were employed in a wide variety of occupations involving vibration. The onset of the condition followed a symptomless period of work with a pneumatic tool which ranged from one month to 20 years. Not all exposed workers developed Raynaud's phenomenon, but some, such as flangers and clinchers in the motor industry and shoe pounders, were particularly liable, symptoms often being noted within the first year. The fingers first affected were those most exposed to vibration. The symptoms appeared to reach a peak in their severity; thereafter they did not progress but persisted unchanged, even if the patient left the industry concerned. X-ray examination revealed carpal or metacarpal cysts in only four of the 34 patients. In all the patients there was a normal reaction to the hyperaemia test; fourteen developed white "dead" fingers when the hands were immersed in a water bath at 15°C. for 15 minutes. The response to the heat-flow test, carried out with a copper-tellurium heat-flow disk, was normal in thirteen out of 24 of the patients, compared with eight out of 29 healthy controls.

The author concludes that the diagnosis of Raynaud's phenomenon caused by vibratory tools must at present be made on clinical grounds. John Pemberton.


Robert Burns, the eldest of the seven children of William Burns [sic] and his wife, Agnes Broun, was born in January, 1759. Throughout his later childhood and adolescence the family went through difficult economic times; young Robert was assisting at the threshing when 13, and at 15 he was the principal labourer on the small family farm. During this period of overworked adolescence he suffered from numerous bouts of nervous depression, nocturnal headaches, and cardiac palpitation associated with feelings of faintness and suffocation. From this early strain he never really recovered, and in later life was seldom free from illness.

In 1784 Burns had a severe physical breakdown with alarming symptoms, and for this his physician, Dr. John Mackenzie of Mauchline, actually prescribed cold baths and continued farm work. During his visits to Edinburgh later on he had numerous riding accidents, and once was thrown from a coach and sustained a severely strained knee which laid him up for several weeks. This joint injury never healed satisfactorily in spite of the devoted ministrations of the celebrated Drs. James Gregory and Alexander ("Lang Sandy") Wood of Edinburgh.

Leaving the capital, where he realized his dazzling popularity would not last, Burns, in 1788, married Jean Armour and rented a small farm near Dumfries. At the same time he applied for a post with the Excise, hoping to combine the activities of farmer and exciseman. In spite of hard work the farm proved a failure, and in 1791, after ridding himself of the lease, Burns moved with his wife and family into Dumfries, where as exciseman his salary enabled them to live in some comfort. He did not regard himself as an invalid, but as a result of his frequent feverish illnesses and numerous accidents his activities were limited and he rested a great deal. In 1795 he was seriously ill with an arthritis and fever which his physicians called "flying gout". For this he was recommended sea-bathing and country life, and so poor Burns betook himself to Brow on the Solway. Writing from there to a friend, he describes himself as "pale, emaciated and so feeble as occasionally to need help from my chair—my spirits fled!" Returning shortly afterwards to Dumfries all the worse for his sea-bathing, he felt himself so near death that he wrote to his father-in-law asking Mrs. Armour to come immediately to look after Jean, who was expecting another child. Three days later, on July 21, 1796, Burns was dead.

The author of this article considers that there is no evidence to support the assertion of Dr. Currie, the poet's first biographer, that Burns died from alcoholic excess and venereal disease; rather is the evidence in favour of the diagnosis of rheumatic endocarditis as suggested by the late Sir James Crichton-Browne and others.

H. P. Tait.


The authors report a preliminary study of the mode of action of gold therapy in chronic articular rheumatism using a preparation containing radioactive gold (197Au). It was found that whereas radioactive iodine (131I) injected into an arthritic joint in three cases had disappeared completely within an hour, 197Au injected intra-articularly could still be detected up to 10 days later. In a fourth case 197Au was injected intramuscularly and was found to accumulate steadily in an arthritic knee-joint, little or none being found in the opposite knee, for at least 5 days after injection.

No definite conclusions can be drawn from such small numbers, but the authors suggest that further systematic work on these lines might increase our knowledge of the role of gold salts in rheumatic therapy.

W. S. C. Copeman.

