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); Sciatica; Gout; Non-Articular Rheumatism; General Pathology; ACTH, Cortisone, and other Steroids; Other General Subjects. At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.

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

Acute Rheumatism

Rheumatic Fever in Young Adults. ZIMDAHL, W. T. (1952).
Brit. Heart J., 14, 70. 15 refs.

The authors present a study of 202 military patients between the ages of 17 and 39 suffering from rheumatic fever. Of these, 162 had the first attack of rheumatic fever after enlistment. The attack was preceded by an upper respiratory infection in 137 cases, and by scarlet fever in nineteen cases. Each case was investigated by all available means, and an elevated erythrocyte sedimentation rate (E.S.R.) was found to be the most valuable means of assessment of rheumatic activity. There was a possible correlation between a prolonged rise in E.S.R. and the development of carditis. Of the patients 95 (53 per cent.) developed murmurs during the period of observation: a presystolic murmur developed in seven cases and an aortic diastolic murmur in fifteen cases. Some account of other complications of rheumatic fever is given. Thus eight patients developed pericarditis and seven had nodules; pneumonitis was a rare finding. A prolonged P-R interval was the most frequent electrocardiographic abnormality. In thirteen cases a sinus bradycardia at a rate of 42 to 58 developed, and in half of these patients significant cardiac damage developed. In a few cases the clinical course was that of rheumatoid arthritis.

It is stressed that rheumatic fever is a clinical diagnosis, and active rheumatism may occur in the absence of pyrexia or a raised E.S.R. James W. Brown.


The results of the treatment of 21 cases of rheumatic fever with ACTH and of one with cortisone are given. All cases were in patients with objective evidence of carditis who had had rheumatic activity for over 3 months or who had severe pancarditis; their ages ranged from 3½ to 15 years. All had elevated erythrocyte sedimentation rates. Therapy was usually started with 80 mg. after 2 days, and most of the patients continued with the treatment for 4 to 6 weeks. In sixteen out of nineteen patients with a raised temperature before treatment the temperature returned to normal after ACTH was given. In one patient erythema marginatum developed during the course of treatment. Three patients had nodules, and in all three the nodules disappeared. The erythrocyte sedimentation rate fell to normal usually within 10 to 14 days. Aortic diastolic murmurs in some cases became more marked: in others there was a decrease in the intensity of the murmur. In seven out of ten cases with pericardial friction, the friction disappeared during treatment. In three out of thirteen cases with congestive failure there was aggravation of the signs of failure: in the others they disappeared. In three out of ten cases with a prolonged P-R interval the conduction time became normal. In almost all patients there was definite evidence of reactivation of the disease when the drug was withdrawn; five children died.

[It is unfortunate that there were no controls here. The paper gives suggestive evidence that ACTH may do something to reduce rheumatic activity, but it gives no evidence that the drug is in any way superior to salicylates in the treatment of rheumatic fever.]

R. S. Illingworth.


The evolution of histological changes in the small blood vessels of the heart valves in the course of acute rheumatism is described. In the acute stage there is swelling of the endothelial cells of capillaries and arterioles, sometimes accompanied by granulomatous changes in the media and adventitia. Later, in the subacute stage, the endothelial cells multiply, often diminishing the lumen of the vessel considerably and sometimes appearing to invade the media. Finally, interstitial "precollagenous argyrophil" fibres are laid down between the proliferated endothelial cells of the
intima, in the media, and particularly in the adventitia. The eventual result is hyalinization of the vessel wall.

The authors consider that these changes in the arterioles and venules are parallel with those recognized in larger arteries in rheumatism. They compare their findings with those which they have reported as occurring in the small cerebral vessels (Arch. Inst. Cardiol. Méx., 1947, 17, 488) and suggest that these changes are of a specific nature.

J. A. Cosh.


In previous experimental work the author found that the lesions of the Arthus and Shwartzman phenomena were due to occlusion of the capillaries and small veins by platelet thrombi, leading to the characteristic necrosis and haemorrhage. Since it has been suggested that rheumatic fever has a somewhat similar mechanism, search was made for these lesions in sections of heart muscle in five groups of cases at the Hospital of the Rockefeller Institute for Medical Research: six cases of acute rheumatic carditis and six of chronic carditis, fifteen cases of healed rheumatic heart disease, three cases of sub-acute bacterial endocarditis, and sixteen other cases without rheumatic carditis.

Platelet and leucocyte thrombi [which are well illustrated] were found in all cases in the acute group, in two of the six with chronic carditis, but in none of the remainder, excepting in two cases of subacute bacterial endocarditis. In each case these lesions were accompanied by Aschoff bodies, which were not found otherwise. Apart from the "granular plugged vessels" illustrated by Gross and others (Amer. J. Path., 1935, 11, 253) no mention of such lesions was found in the literature.

E. G. L. Bywaters.


The authors give a detailed account of eleven cases of acute rheumatic carditis treated by slow intravenous therapy with sodium salicylate (3 to 12 g. daily) or sodium gentisate (6 g. daily), with or without heparin, for periods of 3 to 9 days. The patients were young adults, acutely ill, some having had previous attacks of rheumatic fever. In most of the cases previous oral therapy with antipyrine or salicylates had given little or no relief.

One only case showed dramatic response to the intravenous therapy; eight others showed some improvement in the general condition but without any alteration in the heart condition. In two cases intravenous therapy had no effect whatever. It is concluded that intravenous therapy is not advantageous in the treatment of acute rheumatic carditis, and where salicylates have proved ineffective the authors prefer to use such other remedies as antipyrine, antibiotics, chryotherapy, or (in articular rheumatism) ACTH or cortisone. They again emphasize the absolute necessity of prolonged rest.

Kathleen M. Lawther.


Acute rheumatic fever cannot be regarded as a specific disease in the opinion of the author, since its cardiac manifestations for instance (including the Aschoff nodule and response to salicylates), may be mimicked by tuberculous endocarditis. He considers that in valvular disease of the heart the incidence of tuberculous infection in the patient or his relations is too great to be purely coincidental; he has observed ninety such cases during the last 20 years. The total number of cases of valvular disease from which these ninety cases are drawn is not stated.) Cardiac involvement need not be expected in florid tuberculosis—it is the hidden focus (possibly exerting its effect through allergy) which is more liable to cause trouble. Cutaneous sensitivity tests, both to tuberculin and to suspensions of tubercle bacilli, often give negative or inconclusive results but, the author argues, the sensitivity of the endocardium may be considerably greater than that of the skin so that until more delicate tests are available the evidence of tuberculous origin will mainly be found in a carefully recorded history.

[This paper is provocative, but unconvincing.]

D. Preiskel.


From a review of the literature the authors conclude that rheumatic carditis is due to sensitization of the arterial system following streptococcal infection, and describe the results of attempting desensitization in 82 cases. The method used was the injection of gradually increasing doses of "cardiostreptine" into the femoral artery. Technique and dosage are described in detail.

Reactions included mild temporary increase in temperature, dyspnoea, precordial or left chest pain, gallop rhythm, and an erythematous rash. Immediate results in 71 patients aged more than 16 years showed improvement in varying degree. Those with marked valvular involvement benefited least. In eleven children results were inconclusive, and two died during treatment. Of 42 patients followed up for 2 to 4 years, all maintained the initial improvement and had no relapse of the cardiac condition, although eighteen had experienced some joint pain of a temporary nature.

Kathleen M. Lawther.


Chronic Articular Rheumatism
(Rheumatoid Arthritis)

Short-Term Effect of Pitressin in Rheumatoid Arthritis.


In a previous paper the authors had suggested that a heightened adenosin-triphosphatase (ATP) activity was an underlying factor in rheumatoid arthritis. It was subsequently reported that “pitressin” reduced this activity. It was therefore deduced that pitressin should alleviate the symptoms of rheumatoid arthritis.

To test this theory, 4 units pitressin were given to eight patients with osteo-arthritis and trauma, and to eight patients with rheumatoid arthritis; in the latter marked improvement of symptoms occurred in the majority within half an hour, although the improvement was evanescent. In the osteo-arthritic and traumatic cases pitressin had no effect. Any possible ACTH-like action was ruled out, as an increase in the eosinophil count was found to occur. So far as they go the results support the original theory. It is emphasized that pitressin was used for research purposes and not as a form of therapy. H. F. Turney.

Hematologic Changes with ACTH and Cortisone Therapy of Rheumatoid Arthritis.


The haematological changes induced by treatment with ACTH and cortisone were observed in twenty patients with rheumatoid arthritis and other collagen diseases. A significant reticulocytosis occurred in every patient, the average peak being on the 9th day with ACTH and the 13th day with cortisone, its magnitude being unrelated to the initial degree of anaemia. In anaemic subjects the haematocrit and haemoglobin levels and erythrocyte count rose towards normal, but there was no change in these values in non-anaemic subjects or in those failing to show a clinical response to therapy. No patient became polycythaemic. Both hormones regularly caused a polymorphonuclear leucocytosis and eosinopenia, but lymphocytopenia was inconstant and not sustained. Apart from a reversion towards normal in the bone marrow of those patients who showed a moderate initial depression of erythropoiesis, there was no other change in the bone-marrow elements during or after therapy. Although the hormones had no effect on total blood volume, there was some degree of haemodilution during, and of haemoconcentration after, therapy, more marked with ACTH than with cortisone. Nevertheless, the most significant finding was a true average increase in erythrocyte mass of 18 per cent. at the end of treatment. This the authors believe to be a reflection of the control of the underlying disease rather than a primary effect on haematopoiesis. Ellis Dresner.


From the Hospital for Special Surgery and Cornell University Medical College, New York, the authors give an account of the results of cortisone therapy in 44 patients (25 women and nineteen men) suffering from rheumatoid arthritis. The patients received cortisone for periods ranging from 100 to 400 days. No attempt was made to produce a complete remission, because of the high dosage that would be required and the frequency of undesirable side-effects that this would entail. By using no more than 75 mg. cortisone daily, complications were readily corrected or controlled. In a few patients as little as 25 mg. daily produced a satisfactory response, but usually 50 mg. or more was required. Complications were considerably more frequent in female patients. Diabetes and hypertension did not develop gradually during prolonged treatment; if these complications occurred they did so in the early weeks of treatment. Treatment was discontinued in six patients because of complications: diabetes, 1; mental depression, 1; oedema and poor benefit, 2; massive gastro-intestinal haemorrhage, 2.

Cortisone was discontinued in 24 others for various reasons, and their withdrawal symptoms were studied. In only four patients was improvement maintained for longer than 60 days after cortisone was withdrawn. Relapse occurred as often in cases treated for long periods as in those treated for short periods. A severe “withdrawal syndrome” occurred in four women and one man. When cortisone treatment must be stopped, this should be done slowly, the authors consider, by gradual reduction of dosage.

They conclude that there is no evidence that the course of the arthritis is ultimately altered favourably by prolonged cortisone therapy as they used it. They do not consider that the administration of cortisone is practical as a routine treatment, nor that it is an adequate treatment in itself. They prefer to use it for a definite purpose, such as to check rapidly worsening disease or to facilitate physical therapy and rehabilitation. C. E. Quin.
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The authors report the results of prolonged cortisone administration in twenty cases of active rheumatoid arthritis at the West London Hospital.

On starting treatment ten of the patients were given 300 mg. cortisone on the first day, 200 mg. on the second, 150 mg. on the third, and then 100 mg. daily, whereas the other ten patients were given 100 mg. daily from the start; the authors prefer the latter dosage. When the disease process appeared to be satisfactorily under control, the daily dose was reduced by 12-5 mg. at a time until the minimum maintenance level was found. A reduction every 2 or 3 days was too rapid, and every 5 or 7 days was found to be a more satisfactory interval. The maintenance dose varied widely (between 37-5 mg. and 100 mg. daily) from case to case, but remained within a fairly narrow range for each individual.

Clinical results are reported as good in twelve and fair in five cases, these seventeen patients being able to resume their previous work. In three cases the results were poor: in one of these administration had to be stopped because of the development of Cushing's syndrome, while in the others the permanent joint damage was too severe for improvement. In all the cases side-effects were considered by the authors to be slight: injection abscess, 7; mild Cushing's syndrome, 5; fluid retention, 4. Haematological studies in three cases showed an increase in circulatory reticulocytes during the second week, followed by a rise in haemoglobin level and erythrocyte count to normal figures. A diminution in plasma control occurred in all three patients.

The authors' general conclusion is that when permanent joint damage is absent or slight, patients recover sufficiently under cortisone treatment to return to their work, but that the treatment has little effect when extensive joint damage is present. Administration has to be continued indefinitely although occasionally a long remission may follow its cessation. They consider that much significance need not be attached to mild side-effects.

Kenneth Stone.


The test for rheumatoid arthritis described in this paper involves the agglutination of sheep's erythrocytes sensitized with haemolytic serum. Horse serum was generally used for this purpose, but erythrocytes and serum from other species were found equally reliable.

Patients' serum in dilutions of 1 in 10 to 1 in 20 was added to the sensitized cells and the mixture incubated for 1 hour at 37°C. The end-point was taken as that serum dilution which gave agglutination just visible to the naked eye. Accepting a titre of 1 in 30 as normal, the titre in 85 per cent. of patients with rheumatoid arthritis, but in only 13 per cent. of patients with other diseases, was raised.

Destruction of the fourth component of the serum complement removed agglutinating activity from the serum.

G. Loewi.


The author, at the Canadian Red Cross Memorial Hospital, Taplow, Bucks, uses sheep's erythrocytes and rabbit anti-sheep serum in the differential agglutination test (D.A.T.) for rheumatoid arthritis. Two sets of inactivated serum dilutions are made from 1 in 4 to 1 in 2,048. Sensitized erythrocytes are added to one set and washed erythrocytes to the other. Tubes containing the suspension are placed in a water-bath for 1 hour at 37°C and left in a refrigerator overnight, results being read early the next morning. The result of the test is expressed as the ratio of the reciprocals of the titres of the two sets of readings; a titre of 1 in 16 or higher is considered positive.

Of 124 tests on patients with rheumatoid arthritis, the results in 60 per cent. were positive, but only 13-5 per cent. of those in cases of Still's disease were positive. No positive reactions were obtained from patients with rheumatic fever and heart disease. Of 34 cases of other types of arthritis, only one was positive. Positive results were obtained in two cases of disseminated lupus erythematosus and one of infective hepatitis, whereas serum from patients with a variety of other diseases and all healthy control subjects gave a negative reaction. A modification of the test, involving absorption of the serum, gave increased sensitivity, but a loss of specificity. No relationship could be established between the activity and duration of disease, or the age of the patient, and the level of the D.A.T.

The author concludes that the test has a definite place in the differential diagnosis of arthritis, but that a negative reaction does not necessarily exclude rheumatoid arthritis.

G. Loewi.


To test the assertion that focal collections of round cells in skeletal muscle and peripheral nerve are characteristic of rheumatoid arthritis, the author, at the University of Edinburgh, studied muscle from 93 cases of rheumatoid arthritis, 73 of other rheumatic disease, and 419 of non-rheumatic disease, and also nerves from similar groups of twenty, 21, and 120 cases respectively. Focal lesions were found in muscle in 45 per cent. of cases of rheumatoid arthritis, 44 per cent. of other rheumatic cases, and 14 per cent. of controls; the corresponding figures for nerves were 75 per cent., 57 per cent., and 17 per cent. The main lesion was a collection of lymphocytes, but slight variants from this were seen. There was no lesion characteristic of rheumatoid arthritis, though diagnostic lesions were observed in some cases of rheumatic fever, lupus erythematosus, and polyarthritis.
The author concludes that focal collections of round cells in muscle and nerve are non-specific.

C. V. Harrison.


Arthritis mutilans is a rare disease of which only a few cases have been published. It affects mainly the hands and feet, although any joint may be affected. The joint surfaces are destroyed and there is concentric atrophy and destruction of the diaphysis. The destruction is most frequently seen in rheumatoid arthritis, but similar destruction is found in psoriasis and leprosy. Of twenty skeletons found in an old leper cemetery in Denmark ten showed evidence of arthritis mutilans. Three new cases, all in patients with rheumatoid arthritis, are reported.

J. Agerholm.


The authors describe the case of a man of 58 who had the unusual combination of rheumatoid arthritis and Addison's disease. He had had recurrent attacks of polyarthritis for 15 years and then, after a tuberculous infection of the hips, developed excessive weakness, anorexia, loss of weight, and bouts of vomiting. He had typical Addisonian pigmentation of the skin and mouth, with a low serum sodium level and a very low 17-ketosteroid excretion. When seen by the authors he had had no attack of polyarthritis for 2 years, but a further acute attack occurred after 15 days' treatment with deoxycortone acetate (DCA), 10 mg. daily intramuscularly, and sodium chloride, 6 g. daily. In spite of this treatment he entered into a state of crisis, which responded to cortisone, 300 mg. intramuscularly followed by 100 mg. daily and later 50 mg. daily. Five days after treatment with cortisone was begun the joint swellings subsided completely.

Supplies of cortisone were intermittent and treatment with DCA and salt had to be resumed in the intervals. On three further occasions there was a relapse of the arthritis in 3 to 5 days of resuming treatment with DCA and salt, and on each occasion the joint condition again responded promptly to cortisone. Promethazine hydrochloride ("phenergan"), 1 mg., was given daily at the same time as the DCA and salt on one occasion, but this did not prevent a relapse of the arthritis.

The authors make the interesting comparison between the findings in this case and the work of Selye (Brit. med. J., 1949, 2, 1129), in which experimentally produced arthritis was aggravated by preliminary treatment with DCA and inhibited by cortisone. Robert de Mowbray.


The author reviews the clinical features of this disease, emphasizing the systemic elements which may accompany the arthritis, such as pericarditis and enlargement of the spleen and the lymph nodes. The disease appears to be more virulent when it occurs in the earlier years of childhood. Occasionally a monarticular form is encountered. The involvement of the cervical spine has been noted by the author and others.

Theories of aetiology are briefly dealt with. The morbid anatomy reveals a widespread disorder, granulomatous formations being characteristically present in muscle and subcutaneous structures. The incidence of organic heart disease has been placed at between 25 per cent. and 50 per cent. Joint changes consist primarily of a proliferation of the synovial membrane. This grows over and into the cartilage with erosion of the latter and eventually subchondral bone. Resolution may occur at any stage with fibrosis or ankylosis.

Radiologically the earliest change is a porosis of the subchondral bone. The author describes a magnification technique, which reveals the process of osteoporosis in this condition to be one of destruction or thinning of individual trabeculae.

Periostitis is not uncommonly seen as an early feature along the shaft of the bone associated with the affected joint. The joint space narrows as articular cartilage is destroyed. Changes in the bone structure are not reversible. Erosion of the joint surfaces may result in either subluxation or eventual bony ankylosis.

The effect of bone growth may be:
1. precocious development of epiphyseal centres;
2. premature fusion of epiphyses with stunting of growth;
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(3) deformities, sometimes gross, resulting from disparate development in bones such as the radius and ulna; (4) tapering of the shaft of the bone adjacent to the epiphyses.

Involvement of the cervical spine may reach such a degree as to show radiological evidence of ankylosis of the intervertebral joints. A. M. Rackow.


Gold Therapy in Rheumatoid Arthritis. Results in Patients followed up for more than Two Years. (Auroterapia en la artritis reumatoidea.) ARMAS CRUZ, R., MEREDITH, J., VALENZUELA, F., LACKINGTON, C., and CONTRERAS, V. (1951). Rev. med. Chile, 79, 675.

Fifteen Years of Chrysotherapy in Chronic Articular Rheumatism. (Quinze ans de chrysotherapie dans le rhumatisme articulaire chronique.) SIMONART, F. (1951). Rev. Rhum., 18, 569.


(OSTEO-ARTHRITIS)


In this paper the characteristics of mucous cysts of the fingers are described. According to the author there are three conditions in which there is a metaplasia of the connective tissue in the subcutaneous tissues of the fingers: (1) mucous cysts of the fingers; (2) ganglion; (3) periarticular fibrous nodules, called Heberden's nodes. The typical case of each of these conditions has such characteristics as to make them easily distinguishable.

Mucous cysts are usually situated on the dorsal aspect of the distal phalanx near the nail bed, and sometimes occur in several fingers and in association with ganglion and Heberden's nodes. Often they are symptom-free, but the patient may complain that they are unsightly or get in the way. Frequently they give an uncomfortable pricking or burning sensation and have a tendency to swell, especially at night, and there may be a mild tenderness. Females are affected in 75 per cent. of cases. The cysts occur especially in the long fingers, although even the thumb and toes may be involved as well. They vary in size from a pin's head to 1 cm. in diameter, and if near the nail bed may cause the formation of a groove in the nail. They may recur after local removal. In the well-established case there is a clearly defined wall lined by a modified connective tissue with a fluid content which blends with the collagenous wall.

A ganglion is usually a multilocular cyst lined by well-defined walls of synovial membrane, and often occurs in relation to the wrist-joint or tendon sheaths on the back of the wrist. If it occurs on the dorsal aspect of the distal phalanx it is more deeply situated than a mucous cyst. In a ganglion cellular activity is prominent and there is little mucoid change, whereas the opposite is the case with a mucous cyst.

As regards Heberden's nodes, Heberden himself described these as periarticular nodules composed of masses of fibrous connective tissue. They are situated subcutaneously near a joint, are firm and round, and are usually movable over deep structures. Necrotic changes and cystic areas appear as characteristic features. If the nodes appear on the surface they suggest a semi-solid structure.

There are apparently two conflicting views as to the formation of these three conditions: (1) that they are a degenerative process; (2) that the cells are actively proliferating and are synovial in origin, except that they have no connexion with the neighbouring joint.

W. E. Tucker.


The author reports his experience in the treatment of osteo-arthritis of the hip-joint with ultrasonic waves. He is inclined to compromise between the excessive optimism of some and the negative attitude of others in assessing the usefulness of this form of therapy in osteo-arthritis. The technique is useless in rheumatoid arthritis and of limited value in ankylosing spondylitis, in which condition deep x-ray therapy remains the treatment of choice.

In analysing the results of treatment he divides his 200 cases into three grades according to the extent of the radiological changes in the joint:

(1) Of early cases about one-third failed to respond; in another third marked lessening of pain and stiffness and increase in movement was observed, and in the remainder only partial improvement with a dulling of pain was obtained.

(2) In moderate cases nocturnal pain was usually suppressed after eight to ten treatments. Pain on weight bearing was usually more difficult to control. One advantage of ultrasonic over deep x-ray therapy is that treatment can be repeated as often as is necessary. There can be no standard technique for all cases; some may need as many as thirty treatments to be fully effective.
Favourable changes in x-ray appearances were observed in this group, such as disappearance of pseudo-cysts and healing of articular erosions, but the author admits that without examination of a control series these changes might well be regarded as fortuitous.

(3) In cases in which there are gross bony changes and dislocation, ultrasonic therapy was found to be of value only if the case was not suitable for surgery and had failed to respond to other forms of conservative treatment.

The generator used by the author is of the Siemens type (Sonastat) with a frequency of 800 kilocycles, a quartz surface of 10 sq. cm., and a maximum output of 50 watts (5 watts per sq. cm.). The treatment is given through three fields (anterior, lateral, and posterior) and the average intensity used for treatment of the hip-joint is 15 to 20 watts per sq. cm. Pain is avoided by using as low an effective intensity as possible. The total time for each treatment is about 30 minutes, treatment being given twice weekly. In advanced cases fifteen to thirty treatments are given. In successful cases treatment is repeated at yearly intervals starting 6 months after the first treatment, which is reported to keep symptoms in check. The author concludes that, compared with other types of conservative treatment, ultrasonic therapy is one of the best methods available to-day for the treatment of osteo-arthritis of the hip. M. H. L. Desmarais.


Of 118 operations for arthroplasty of the hip, vitallium cups were used in 65 and acrylic heads in 53. There were no operative deaths. For cup arthroplasty Smith-Petersen’s technique was followed; in acrylic-head arthroplasty an acrylic head with a broad cylindrical neck was used. The indications for these operations were: traumatic necrosis of the head of the femur, osteo-arthritis and subluxation, irreducible congenital dislocation, and osteomyelitic sequelae.

The technique employed varied. For necrosis of the head of the femur Heuter’s approach was used, with insertion of an acrylic head, transplantation of the greater trochanter, and suture of the capsule; a hip spica was applied with the hip in abduction and retained for a month. For osteo-arthritis of the hip when the acetabulum was apparently healthy the same simple procedure as above was adopted; but when there were changes in the acetabulum a Smith-Petersen approach was used and a cup inserted, except in cases with extensive and particularly cystic changes of the head, when an acrylic head was preferred. The post-operative treatment consisted in active exercises immediately and traction for 2 weeks—with weight-bearing after 1 month if the acetabulum was untouched at operation; otherwise no weight-bearing was allowed before the roof was solid, usually after 4 months.

The author examined 63 patients 6 months to 2½ years after operation with regard to pain, mobility, and gait. He found that on the whole arthroplasty proved an excellent pain-relieving operation. The majority of patients obtained an increased range of movement, but improvement in walking was less constant. In cases of post-traumatic necrosis of the head of the femur the best results were seen when the operation was done before absorption of the sump of the neck or changes in the acetabulum occurred; and in cases of osteoarthritis before muscles and periarticular tissue have deteriorated.

The author also reports on sixteen cases of unreduced dislocated hip in adults and nine cases with osteomyelitic sequelae, but operation in these cases was too recent for any certain conclusion to be drawn. J. Agerholm.


The authors describe the effects of cortisone therapy on eleven patients suffering from osteo-arthritis of the hip. The ages of the patients varied from 52 to 82 years. The dose of cortisone was 300 mg. on the first day, followed by 100 mg. daily for 5 to 17 days; and finally the patients received maintenance doses varying from 50 to 100 mg. three times a week. Very little improvement was noted in the first 4 days, but by the 7th day marked subjective improvement occurred in ten out of the eleven patients. In seven patients on whom measurements were made an increase in the range of movement of the affected hips was noted after treatment with cortisone. Of the patients, eight were followed up for 9 months, at which time five of them were still receiving cortisone therapy. In two patients the treatment was discontinued because of the appearance of congestive cardiac failure, and in one patient treatment was stopped because of an episode of enteritis. C. E. Quin.


In this paper is described the effects of cortisone treatment on eight patients with osteo-arthritis of the hips, six of whom were over 50 years of age. The dose used was thought to be sufficient to control a severe case of rheumatoid arthritis; an initial dose of 300 mg. was given, and this was then reduced to 200 mg., 100 mg., and finally to 75 mg. daily. In two cases there was subjective improvement, and also objective improvement as shown by an increase in hip movement; in the other six cases no improvement was noted.

The authors consider that on the basis of these results it is difficult to justify the use of cortisone in the treatment of osteo-arthritis with the known limitations and dangers of such treatment in patients in the older age groups. C. E. Quin.

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In view of the confusion caused by the American practice of including cases of ankylosing spondylitis in series of cases of rheumatoid arthritis subjected to clinical trials, the author studied the effect of treatment with ACTH (corticotrophin) on six selected cases of ankylosing spondylitis at the Westminster Hospital in order that the effect of the hormone on this disease entity could be estimated more clearly. He found that the early acute cases benefited most, although dosage was low and periods of administration were short. One case, which was of long standing, showed no improvement. In one case, treated during an acute episode, no rebound occurred after gradual withdrawal of the drug, and remission has now persisted for a period of 8 months.

The conclusion drawn by the author is that since ACTH is in short supply its use might reasonably be restricted in this disease to periods of painful exacerbation, to allow other, more slowly effective, methods of therapy to be instituted. He feels that the classical basic treatment of this disease remains unchanged by the advent of adrenal hormone therapy, although a potent short-term weapon is now available for use during the more acute episodes.

W. S. C. Copeman.


In four previous publications the authors have called attention to the osseous changes in the symphysis pubis in spondylarthritics ankylopoietica and have shown their polymorphism (proliferative osteitis, synostosis, coexisting often with a "spinosus" aspect of the pelvis). The present paper substantiates the radiological characteristics of such changes.

A typical case history is reported and eighteen further cases are described. These are related to the changes in the symphysis pubis and neighbouring regions seen in severe and old-standing forms of spondylarthritics ankylopoietica: spinous pelvis, proliferative osteitis, horizontal osseous tracts, osseous bridge, nail-scratch notches. Similarity is shown to exist between the symphysis and the intervertebral disk; the osseous proliferation is explained by the overworking of the abdominal muscles and the development of abdominal breathing. [Authors' summary.]


(Accessorios)


It is a matter of dispute whether acrosclerosis is a disease sui generis or a form of generalized scleroderma. It differs from generalized scleroderma in beginning with manifestations of Raynaud's phenomenon, which is much more common in women, and being frequently accompanied by visceral, especially oesophageal, lesions. Four patients, all women, with acrosclerosis are described. In all of them symptoms of Raynaud's phenomenon preceded the appearance of the skin changes. The oesophagus was affected in three of the patients, in one of whom also the heart may have been affected by the disease. Cervical sympathectomy does not relieve acrosclerosis. Changes in Raynaud's disease which suggest the presence of acrosclerosis are swelling of the fingers between attacks or after sympathetic blockage, changes in the face, pigmentation of the skin, and pain and stiffness of the joints without objective signs of arthritis and malaise.

E. Lipman Cohen.


Acrosclerosis is one of the conditions which have to be differentiated from Raynaud's disease. In the latter, the symptoms are intermittent and massive gangrene never occurs. Acrosclerosis usually occurs in women. It begins with pain in the fingers, which become stiff and often blue; when raised they become white. The symptoms are aggravated by cold. Later the skin begins to change, becoming waxy and shiny; small areas of gangrene appear and there may be chronic whitlows. The nail and finger-tip may slough away, and the phalanges gradually atrophy. Telangiectases appear on the face and there may be thick glossy areas of skin; the nose looks pinched and the lips thin. Areas of
pigmentation may appear anywhere and the body hair becomes scanty. Three cases, all in women, are described; two of the author's patients had had rheumatoid arthritis and two had rheumatic endocarditis. It is suggested that acrosclerosis is a disease of adaptation, and might respond to treatment with cortisone.

E. Lipman Cohen.


The authors report the occurrence of the syndrome of periodic arthralgia in 23 individuals in five generations of a family. This syndrome is characterized by regular attacks of arthritic pain, usually in one or both knees and often also in other joints of the limbs. There may be an associated stiffness of the joint and occasionally effusion. In some cases multiple petechiae in the skin are also present. The episodes recur at regular intervals of 7 to 21 days and last several days. There is generally no fever. Two affected members of the family were studied in detail in hospital, and six were interviewed in their homes; information about the rest was obtained by questionnaire.

The disorder was strikingly uniform in character in the affected members of this family. It began in most cases in infancy or childhood and appeared to persist throughout life (in one case for 80 years); it tended to become less severe and less frequent as age advanced.

The familial distribution is typical of a simple dominant (heterozygous) Mendelian character. Harry Harris.


An investigation has been made into the incidence of rheumatic complaints in miners by means of a field survey arranged to include control groups of non-mining males and of females from mining and non-mining families. The gross incidence of rheumatic complaints was not found to be appreciably different in miners and non-miners, but there was evidence of an earlier onset in miners, as shown by a higher incidence in the fourth decade. The miners' statements indicated that they lost more working time from rheumatic complaints than non-miners. Rheumatic pain in miners was chiefly in the lumbar and sciatic distribution, and pain in these sites was largely accounted for by the increased incidence of rheumatic complaints in the fourth decade and for the increased loss of working time in miners. Miners also showed an increased incidence of knee pain. Tentative diagnoses made in the field indicated that the lumbar sciatic pain may frequently result from disorders of the intervertebral discs. There was also evidence of an increased incidence of osteo-arthritis in the miners. A study of invaliding records made under the Essential Works Order showed that invaliding from the mines was due most commonly to chest conditions, rheumatism coming second in importance. Those invalided for rheumatism complained chiefly of low-back sciatic pain. The incidence of rheumatic complaints in members of the miners' families was lower than in the general populations and considerably lower in miners.—[Authors' summary.]


The author reviews 135 cases of "brachial neuritis", which he classifies into three groups:

1. 120 cases with symptoms due to a lesion of a cervical intervertebral disk;
2. 14 cases of costo-brachial compression;
3. 4 cases of "brachial neuritis" presenting signs similar to those caused by a disk prolapse, but which were shown to be due to a neoplasm.

The cases in Group 1, the only ones to be discussed, are divided into two categories: (a) 86 cases in which a root lesion was present as a result of disk prolapse; (b) 34 cases in which the disk lesion was part of a cervical degenerative spondylitis. The former occurred mainly in the 35-50 age group and only 12 per cent. of patients gave a history of antecedent trauma. Stiffness of the neck occasionally preceded other symptoms, and recurrent attacks were encountered. In general, however, three phases could be distinguished in the development of the syndrome:

1. An irritative phase, in which subjective sensory changes are marked;
2. A phase of compression, with more accurately localized pain, objective sensory loss, and alterations in the segmental deep reflexes;
3. A paralytic phase (rarely reached), with diminution of pain and paraesthesiae, and obvious (though not extreme) muscle wasting. The lower three cervical disks are most frequently affected, the 6th, 7th, and 8th cervical nerves being involved: other root affections are rare. A central prolapse of a cervical disc produces symptoms by indentation of the spinal cord rather than by complete bilateral compression: pain in the neck or upper limbs is rare, spasticity of both lower limbs is a characteristic finding, and signs of a lower motor neurone lesion may or may not be present in the arms.

In cases of disk degeneration neck and occipital pain, rarely radiating beyond the shoulders, is the invariable complaint. Neurological examination is usually negative, and radiographs do not enable differentiation to be made from disk herniation, the value of radiography in these cases being limited to the exclusion of other causes of root compression, such as diseases of the vertebrae.

Conservative treatment will give relief in the majority of cases of disk prolapse, and surgical intervention is required only very rarely, being absolutely indicated only in the presence of cord compression. Spontaneous resolution, due to the shrinking and fibrosis of the herniation, usually occurs. When a prolapse is actually present, manipulation is contraindicated for fear of cord damage. The author's cases were treated by immobilization in a padded cardboard collar, worn for at least 4 weeks after relief of symptoms, the average period being 8 to 10 weeks. In eighteen cases where this failed, treatment by bed rest and head traction was then adopted, traction being continued for 7 days after relief of
symptoms and a Minerva plaster then applied for 6 weeks. Surgical intervention was necessary only in four cases.

The report includes a review of the anatomy, physiology, and pathology of cervical intervertebral disks and numerous illustrative case histories. J. V. Crawford.


A radiological survey, at the University of Michigan, of 43 cases of well-defined tuberose sclerosis revealed certain typical skeletal changes. In seventeen of the cases radiographs of the skull showed scattered sclerotic plaques in the vault and twenty of the thirty patients whose hands and feet were examined radiographically had localized cyst-like areas of bone destruction in the phalanges or wavy periosteal new bone formation along the shafts of the metatarsals and metacarpals, or both kinds of changes together.

These highly selective osseous lesions, for which there is no explanation, are so typical, and were so strikingly similar in the cases examined, that they may be considered as valuable aids in the diagnosis of tuberose sclerosis. A. Orley.

**Studies of Paget’s Disease (Osteitis Deformans).** Lake, M. (1951). *J. Bone Jt Surg.*, 33-B, 323. 9 figs, 38 refs.

The author discusses two of the complications of Paget’s disease of bone—sarcoma and fracture. The incidence of sarcoma as estimated by various authorities ranges between 2 per cent. and 15 per cent., but it is probable that the true figure, allowing for the many cases of Paget’s disease which escape diagnosis, is less than 2 per cent. In an analysis of 95 cases reported in the literature, to which the author adds seven further cases, it is noted that the age incidence of Paget’s disease in cases complicated by sarcoma follows closely that in uncomplicated cases, and that the tumour is much commoner in males than females. The commonest site for development of sarcoma, which bears no definite relationship to the site of maximal incidence of Paget’s disease, is the femur. Chemical investigations show that the serum alkaline phosphatase level in Paget’s disease often rises when sarcoma supervenes and falls on amputation. Prognosis is very poor, survival for more than 2 years being rare and 5 years being the longest recorded period of survival.

Fracture, probably the commonest complication of Paget’s disease, most often occurs in the femur, the tibia and pelvis also being common sites. Bones are most easily broken in the vascular stage of the disease, and at this stage there is no disturbance in the rate of union of the fracture. Decalcification due to immobilization is increased in Paget’s disease, particularly if renal failure is also present. Open reduction and skeletal fixation may be performed, but the bone is extremely vascular and the marrow cavity may be absent. In the sclerotic stage, union is delayed. Peter Ring.


Osteitis pubis, also called periostitis or osteochondritis pubis, is a self-limiting osteonecrosis of the non-suppurative type, which begins at the symphysis and can extend back to the ischial tuberosities. It occurs chiefly as a post-operative complication in urologic surgery. Differential diagnosis is important, and lies between a true osteomyelitis and metastatic malignant disease. Diagnosis is important because of the excellent response to roentgen therapy. From 1924 to June, 1950, 116 cases were recorded in the literature, 83 of these being since 1947. The outstanding symptom is excruciating pain. This pain occurs with abrupt suddenness 3 to 8 weeks after an otherwise successful urological operation, and spreads from the pubis to the thighs; any movement of the trunk produces violent spasms of the muscles, due to the pull of muscles attached to the diseased bone, the disability lasting many months. Slight swelling and tenderness are the main physical signs.

Radiological appearances are negative in the prodromal stage. In the destructive stage changes can be seen on the medial aspects of the body of the pubis, extending medially and laterally. This is followed by decalcification; sequestrum formation does not occur. After 2 to 8 months calcification sets in and is complete in 6 to 12 months.

The two main criteria of diagnosis from a frank osteomyelitis are the absence of fever, and of sequestrum formation; these never occur in osteitis pubis. The prognosis is excellent, but full disability may last 3 to 6 months, some incapacity lasting for 12 months. The two main theories of its origin are that it is due to:

1. Infection in a traumatized pubic bone;
2. Aseptic necrosis of the bone.

Treatment aims at alleviating the pain and shortening the course of the disease; x-ray therapy in conjunction with other measures achieves both of these. A dose of 75 to 100r, with 200 kV, 1 mm. Cu, three times a week, is recommended until the acute symptoms subside, and then at gradually spaced intervals thereafter until satisfactory alleviation is achieved. I. G. Williams.


A review of previous reports on the Speranskii spinal pumping treatment of arthritis is given and the results in a new series of cases treated in the Madison General Hospital, Wisconsin, are described. The technique used was slowly to withdraw and reinject 10 ml. of cerebrospinal fluid twenty times, each phase taking at least 45 seconds. Finally, 10 ml. was withdrawn.

Only six of 26 cases of rheumatoid arthritis and one of five cases of ankylosing spondylitis showed major improvement. The results in osteo-arthritis were better, marked improvement occurring in seven out of eleven cases. Erythrocyte sedimentation rate was unaffected. There were no protracted ill effects from the treatment, though nausea and headache lasting up to 10 days occurred in eighteen cases. Improvement could not be correlated with such reactions. Details of four cases in which dramatic improvement occurred are given.

The authors are [rightly, the abstracter considers]
cautious of their conclusions, but feel that the treatment warrants further trial. In a final note a death from cerebellar pressure cone following Speranskii pumping is recorded. A malformation is presumed, but not proved.

H. F. Turney.


The authors from the Mayo Clinic, review the literature on the effects of various physical agents on intra-articular temperatures. Because of the existence of contradictory reports they decided to study in the trained dog the effects of certain physical agents on the temperatures in the treated and contralateral knee-joints, and compare the simultaneous effects on subcutaneous and intramuscular temperatures in the treated area.

The physical agents used were: hot packs, short-wave diathermy, microwave diathermy, ice-packs, and percutaneous electric stimulation. In order to determine the influence of vasoconstrictors and vasodilators, adrenaline, vasopressin, nitroglycerin, histamine, and pyrogens were also given singly intravenously.

The authors found that hot packs, short-wave diathermy, and microwave diathermy raised the intra-articular temperature as well as the temperature of the adjacent muscles and subcutaneous tissues. No reflex increase in the temperature of the contralateral knee-joint was noted. Ice-packs had the same effect, but in the opposite direction, and also had no cooling effect on the contralateral joint. Repeated electrical stimulation produced no change in the temperature of the knee-joint, but a slight rise in the subcutaneous and intramuscular temperatures respectively. Intravenous injections of vasoconstrictor and vasodilator drugs produced no significant change in the temperature of the joint and adjacent tissues. Vasopressin, however, produced a gradual but definite reduction in the intra-articular temperature as well as in the intramuscular and subcutaneous temperatures. M. H. L. Desmarais.


Sciatica

Imbibition of Fluid as a Cause of Herniation of the Nucleus Pulposus. CHARNLEY, J. (1952). Lancet, 1, 124. 6 figs, 1 ref.

The author does not consider that protrusion of the intervertebral disk is satisfactorily explained as due to external mechanical factors acting on a "degenerating" disk, and he adduces evidence which suggests that intrinsic causes in the disk may be more important than external factors. Acute lumbago usually starts without recognizable injury, often following exposure to cold after a latent period, while the pain is unlike that usually associated with an injury; this is maximal almost at once and is relieved by complete rest, whereas in acute lumbago the patient is often relieved somewhat if he is able to move a little. The acute stage lasts between 2 and 3 weeks, quite unlike an injury, and is often preceded by a prodromal phase lasting some 24 hours.

In experiments on the cadaver the author found that when a fresh specimen of lumbar spine was frozen and sawn in half longitudinally, one half being immersed in normal saline for 24 hours and the other merely allowed to thaw out, the central portions of the nuclei pulposi in the former half projected far more than those in the latter. Moreover, whereas the protrusions disappeared in the control specimen on exerting longitudinal traction, those in the specimen which had been immersed did not, showing that an increase in volume had taken place.

By some further experiments [the description of which is a little difficult to follow] he was able to prove that internal tension of some degree is generated in the nucleus pulposus when immersed in saline. He therefore advances the hypothesis that under certain conditions the intervertebral disk may acquire an abnormal amount of fluid and that the consequent increase in internal pressure constitutes the acute attack of lumbago. A spontaneous protrusion may then occur or a slight injury complete the bursting of the annulus fibrosus, with conversion of the clinical picture of lumbago into that of sciatica. He concludes that "if this hypothesis should prove correct it opens up the future possibility of prophylactic treatment of lumbago by medical means". Ronald Furlong.


The upper surface of an adult cervical vertebra is concave transversely with an upward projecting lip on either side. This lip was called by Trolard the processus uncinatus; by Luschka, the eminentia costaria; and by Giraud, the processus lunatus. The present author prefers to use the term "uncinate process". On the bodies of C5 and C6 the uncinate processes are placed laterally; on C7 they are dorso-lateral. The neurocentral joints of English anatomists lie between the uncinate process and a corresponding facet on the vertebra above. Luschka called this joint hemarthrosis intervertebralis lateralis, and Trolard called it the unco-vertebral articulation. These joints have, however, been regarded as artefacts by other anatomists. The present author believes that these so-called joints are part of the annulus fibrosis of the intervertebral disk, and regards the function of the uncinate process to be to restrict excessive lateral movement in the cervical spine. The so-called neurocentral or unco-vertebral joint he prefers to regard as the uncinate part of the intervertebral disk. He divides disk lesions into nuclear herniations and annular protrusions. Nuclear material may extrude
centrally, laterally, or within the foramen, when the uncinate part of the disk is fissured. These latter extrusions may conceivably involve the issuing nerve and produce root pain. Annular protrusions are the result of disk degeneration, when the disk bulges in all directions. When osteophytes are present these may take the form either of ventral spurs or of marginal lipping; the former may not be, but the latter are invariably associated with disk degeneration.

This is an important anatomical study of the cervical spine, and particularly of the so-called neurocentral articulations, and casts some light on knowledge of osteoarthritis of the spine. Lambert Rogers.


Intervertebral-disk lesions are the commonest causes of low backache and sciatic pain. A considerable proportion of patients recover spontaneously, even though myelography shows that the prolapse remains unchanged. Operative treatment relieves nearly all patients of sciatic pain, but a considerable proportion still experience low backache. The causes of failure in such cases include wrong diagnosis, delay in treatment, and poor selection. Patients with widespread disk disease, and those with disk lesions associated with other conditions such as spondylolisthesis, do not react well to excision of the prolapse alone. Damage during the operation, particularly if the laminectomy is extensive, increases the risk of spinal weakness, and traction of nerve roots may give rise to foot-drop.

A comparison carried out at the Massachusetts General Hospital of the results in fifty patients with disk lesions who were subject to simple excision of the disk with those in 150 subjected to excision with spinal fusion showed that with excision alone the mortality was lower and convalescence shorter, but that post-operative back symptoms were commoner than in the other group. Of all patients undergoing disk operations, 97 per cent. reported satisfactory relief of sciatic pain. Peter Ring.

Technique and Results of Diagnostic Disk Puncture and Injection (Discography) in the Lumbar Region. [In English.] Lindblom, K. (1951). Acta orthopaed. scand., 20, 315. 15 figs, 4 refs.

Disk puncture and injection (discography) has been carried out on 150 patients with ruptured intervertebral disk. The technique is as follows: On a lateral film the distance from skin to disk centre is measured, and with the patient lying prone with pads to straighten the lumbar lordosis a double needle of corresponding length is inserted. The outer needle enters the spinal canal and the inner needle the centre of the disk. A mixture of 35 per cent. dione and 5 per cent. procaine is injected; the normal disk is completely filled by 0.5 ml., but a ruptured disk may take considerably more. Distension of a normal disk produces a low backache, but distension of a pathological disk reproduces the symptoms originally complained of by the patient. Normally the lower two or three lumbar disks are punctured.

The discogram in the ordinary subject shows two dye-filled spaces along the upper and lower vertebral margins joined by an irregular streak of dye through the centre of the disk. In the early stages of degeneration there is projection of dye into or through the annulus. It may outline the disk prolapse or spread along the nerve roots. As degeneration proceeds the two layers of dye spread along the entire vertebral surface of the disk, often outlining marginal osteophytes. Puncture with a fine needle does not appear to injure the normal disk and is considered to be of greater diagnostic value than myelography. Peter Ring.


This paper is based upon a series of 117 patients who have undergone operation for displaced intervertebral disk and been followed up for 1 to 5 years. In 99 of these cases a disk protrusion was found at operation; in eleven of the remainder no abnormality was discovered at the time of exploration, and some other lesion was found in seven. The protrusion was lumbo-sacral in 73 cases, at the interval between L4 and 5 in 28, and at that between L3 and 4 in two; in four cases a double protrusion was revealed. The author considers that trauma is not an important factor in the aetiology of lumbar disk protrusion, and the radiological examination has little value in diagnosis except in excluding other forms of spinal disease.

At follow-up it was found that backache was absent in 47 and present but slight in 45, and there was disability in 24 cases. Sciatic pain was absent in 67, slight and occasional in 22, and persistent in eleven cases. The results were less satisfactory in the group in which there was a negative finding on exploration than in patients from whom a disk protrusion had been removed.

J. E. A. O'Connell.


The elastic properties of the human intervertebral disk, with particular reference to its contribution to the function of the spine, have been studied by the author at the University of Liverpool. Several (up to five disks) were obtained from each of 51 cadavers and compressed in an Olsen compression-testing machine by successive increments of 50 lb. (22.6 kg.) up to 500 lb. and their load then reduced again to zero, the machine indicating the changes in thickness of the disk. After two such tests had been made, an incision was made into the centre of the disks through the postero-lateral part of the annulus fibrosis and the test repeated. Similar tests were carried out on sections of the spine containing four vertebral bodies and three disks, and the effects of compression by a load of 50 lb. for periods up to 48 hours were also studied.

From the findings in these tests it is concluded that the disk is an organic elastic structure capable of maintaining great loads without disintegration, but that its elasticity is interfered with at certain ages and when there
are general or local pathological conditions, such as wasting diseases or avascular lesions of the vertebrae.

St. J. D. Buxton.


In carrying out experiments at the University of St. Andrews on the rabbit's intervertebral disk, the authors accepted at the outset that any conclusions that might be reached could not be held to be directly applicable to man, but they hoped that useful data for further research would be provided.

In each of seventy rabbits damage was done to a lumbar disk by a transverse incision in the ventral part of the annulus fibrosus, allowing escape of the nuclear pulposus, and the condition of the disk studied in animals killed immediately after operation and at frequent intervals subsequently, so that it was possible to study the healing of the annulus, the changes in the deep fibres, and those in the nuclear tissue. The normal structure of the disk in rabbits and the effects of trauma are described, and microphotographs are reproduced to amplify the text.

The authors' findings, after 2 years' work, are that in the rabbit a superficial wound in the annulus heals rapidly, but subsequently the disk undergoes cartilaginous and bony change so that disk and vertebra become ankylosed and the normal joint mechanism is no longer possible. The site of the nucleus pulposus is eventually occupied by a dense pad of fibrocartilage.

The authors consider that the investigation of the relative importance of degenerative changes in the annulus fibrosus and of trauma to the disk appears to be of primary importance in the elucidation of the aetiology of prolapse of the nucleus pulposus.

[This paper and that by W. J. Virgin (above) constitute an important addition to knowledge of this problem and should be read in full. The illustrations are of high quality, and the references cover all the important British, American, French, German, Italian, and Scandinavian contributions to the literature.]

St. J. D. Buxton.

Non-Articular Rheumatism


The author continues his anatomical observations on the human cervical spine (see Acta chir. scand., 1951, 101, 345 and 457) with a description of some of the soft tissues surrounding the nervous structures. The fascia of the posterior longitudinal ligament is prolonged laterally and is continued through the intervertebral foramina to take part in the periradicular structures. This fascia affords some protection to the spinal cord in cases of multiple dorsal disk protrusion, and it also counteracts the outward displacement of the radicular nerves. The epineural sheaths are held firmly in position, and those of the upper plexus trunks are further reinforced by ligaments attached to the transverse processes above.

This arrangement gives protection to the nerve when traction is applied to the plexus. The presence of the operculle fibreux of Forestier at the external orifices of the intervertebral foramina could not be confirmed. The tresseaux fibreux of Soulé consist chiefly of epidural vessels. The article is effectively illustrated. L. Crome.


The author briefly reviews the evidence, built up over the last 10 years, in favour of the efficacy of a-tocopherol in the cure or improvement of Dupuytren's contracture, and expounds a hypothesis for its mode of action. He then describes the effect of this substance on 22 cases of Dupuytren's contracture treated in the Rochester General Hospital, New York, and claims nine cases cured, six improved, and seven failures. In the cases cured and in most of the improved the disability had been of short duration—under 5 years—and there was minimal deformity.

The author has also applied the method to cases of frozen shoulder: six patients were treated successfully, but a further twelve derived no benefit. Dennis Walker.


The author claims that the local intramuscular injection of benzyl salicylate (Scott, Brit. med. J., 1943, 2, 510) is an advance upon existing methods for the treatment of fibrositis. He also expresses the view that the essential cause of fibrositis [which he does not clearly define as a clinical entity] may lie within the bone marrow, and not within the muscle or other soft tissues as is normally assumed. He suggests that the signs and symptoms of this disease may be "indications of some derangement of a normal physiological function or interplay between bone-marrow and muscle".

[Further pathological work on these lines should clearly be undertaken.]

W. S. C. Copeman.


This interesting paper deals with simple or traumatic tenosynovitis as distinct from pyogenic or granulomatous affections of the tendon sheath. The latter may occur in other parts of the body, while simple tenosynovitis is most commonly confined to the dorsum of the forearm proximal to the wrist joint. As in the majority of cases the responsible lesion is above the upper limit of the tendon sheaths and crepitus or creaking is an important sign, it is suggested that a better name would be peritendinitis crepitanus.

A series of 544 cases is reviewed; of these 419 were classed as peritendinitis crepitanus, and 125 as simple tenosynovitis. The annual incidence in a motor-car factory employing 12,000 workers was about forty cases.
The main aetiological factors in order of frequency were: unaccustomed work, return to work after absence, local "strain", simple trauma, and repetitive effort associated with speed. In some cases more than one of these factors were present.

Five cases of peritendinitis crepitans were explored and the tendon sheath found to be normal. Biopsy showed that the deep fascia and tissues around the muscles were oedematous and bulging; the muscle bellies were dark and swollen. Microscopically all the tissues showed increased cellularity from proliferating fibroblasts. These biopsy reports are important as they show definitely that the lesion is not in the tendon sheath but at a higher level.

The authors maintain that in treatment the best results, with the smallest recurrence rate, were achieved by partial immobilization in "perspex" splinting; 116 cases were so treated, with a recovery period of 12 days and a relapse rate of only 6 per cent. In the 125 cases of simple tenosynovitis, 66 occurred in the extensor of the hand and the remainder in the extensor and peroneal tendons of the leg. Only two cases developed De Quervain's disease. Direct local trauma was the commonest cause. Here again the authors found that incomplete fixation in a perspex splint produced better results than complete immobilization in plaster.  

E. C. B. Butler.

2 figs, 6 refs.

The author points out that more attention should be paid by rheumatologists to the various syndromes which come under the heading of non-articular rheumatism in view of the fact that such patients constitute the majority of those attending rheumatism clinics. She describes the clinical syndrome of panniculitis, which is one such condition, and quotes illustrative case-records. She then describes the results of her important investigations into the pathology of the condition by means of deep skin biopsies in a small series of cases. Her own discussion of these findings may be quoted:

"In panniculitis the character of the pain, and the pins and needles and numbness, suggest that the small nerve-endings in the dermis are involved. In the areas which are usually affected, with the possible exception of the pectoral region, the skin is usually held down closely to the underlying tissues. Any increase in density of the dermis, together with a rapid increase in subcutaneous fat and possibly sodium with water retention, could cause pressure on small nerve-endings. The aggravation of symptoms by warmth might be due to dilatation of the small blood vessels in the dermis, adding to the tension in the affected tissues.

"Day (J. Physiol., 1949, 190, 380) has shown that with changes in pH or electrolyte balance, collagen fibres do not participate in connective-tissue swelling, but that the hydration of the interfibillary tissue is very greatly increased; and Bartter and others (J. clin. Invest., 1950, 29, 950) have demonstrated that ACTH causes retention of sodium and chloride in extracellular fluid. It seems possible that in panniculitis there may be abnormal water retention; clinically, Copeman [personal communication to the author] finds that giving cortisone to patients with panniculitis increases the severity of the symptoms, and that temporary but very real relief results from dehydration. My own experience, although small, confirms that a strict low-sodium diet (1 g. sodium daily) will give temporary relief from symptoms.

"There would appear to be substantial evidence to support Copeman's theory that panniculitis results from endocrine dysfunction; it seems possible, however, that the important change may be in the collagen layer of the dermis rather than in the fatty tissues, though this can be proved only by larger series of skin biopsies."

The author concludes that "it is evident that this syndrome should be renamed, for the term panniculitis is incorrect and misleading."  W. S. C. Copeman.

General Pathology


Electrophoretic analysis by the conventional Tiselius method was carried out on three subjects with rheumatoid arthritis on seven, seven, and eight occasions respectively, before a course of cortisone in two of the subjects, and at intervals afterwards in all three. Total protein estimation was not done, and the amounts of the individual constituents are expressed as a percentage of the total protein. Cortisone was given for 27 to 30 days with a total dose of between 2-1 and 1-7 g. for each subject. The analyses were not continued beyond the period of cortisone administration. No consistent changes were noted and the authors conclude that the fluctuations observed were random in nature.

[There are marked discrepancies between the data given in the table and those on the graph which make interpretation difficult.]

E. G. L. Bywaters.


The authors examined histologically the hearts of 63 tuberculous patients and found granulomatous lesions in the myocardium in thirteen. They consider seven of these lesions identical with the so-called Aschoff's bodies; and draw the conclusion, not now greatly disputed, that these bodies are non-specific and may occur in a variety of infective diseases.

J. W. McNee.


In three cases of scleroderma in which death was due to renal failure, two distinctive lesions were found in the vessels of the kidney. The first of these consisted in a concentric, mucoid, intimal thickening of the proximal parts of the intralobular arteries, while the second was characterized by fibrinoid necrosis in the terminal parts of these arteries and in the afferent arterioles. The consequent ischaemic changes in the cortex were presumably responsible for the renal insufficiency.

R. Hepinstall.
ANNALS OF THE RHUMATIC DISEASES


The purpose of this investigation, carried out at the Canadian Red Cross Memorial Hospital, Taplow, Berkshire, was:

(a) to investigate the speed of reconstruction of skin hyaluronic acid after its breakdown by injected hyaluronidase in normal subjects and in cases of acute rheumatic fever and rheumatoid arthritis;

(b) to observe the effects of ACTH and cortisone on such reconstitution.

An intradermal injection of 0·2 ml. of standardized hyaluronidase solution was made into four sites on the inner aspect of each forearm and in control areas being measured after 1 hour and the spreading ratio calculated. The process was repeated at 2-hourly intervals until the spreading ratio was less than 1·24, which was calculated to be the minimum figure indicating a significant difference. When the spread in the enzyme-treated area failed significantly to exceed the spread in the control area it could be concluded that the barrier to spread in both areas was the same as that of the skin hyaluronidase acid had been fully reconstituted. A second method consisted in injecting hyaluronidase solution into sites on each forearm at 12-hourly intervals, all the sites on the right arm being tested with haemoglobin solution 48 hours after the first enzyme injection, and all sites on the left arm 6 hours later, giving a range of observations from 12 to 54 hours at 6-hourly intervals. Confirmation of the measurement of spread and that the injection was into the enzyme-treated area was obtained by infra-red photography.

The normal reconstitution time (estimated from observations on 27 normal adults and children) varies with age and lies between 24 and 42 hours. Reconstitution was prolonged in rheumatoid arthritis (55 cases) and in acute rheumatic fever (109 cases), but returned to normal levels in the latter during treatment with salicylate, ACTH, or cortisone, and during convalescence. In nineteen patients with active tuberculosis and a raised erythrocyte sedimentation rate and in two other non-rheumatic subjects normal readings were obtained. It is concluded that in both rheumatoid arthritis and rheumatic fever an alteration in hyaluronic acid metabolism is likely.

René Mendez


The authors draw attention to the role of the scalenus minimus muscles in the production of the "scalene syndrome". They describe in detail the signs and symptoms which occurred in a housewife aged 35 who had suffered from unilateral brachialgia with circulatory changes for 6 years. Pain and paraesthesia were more prominent on the medial side of the hand and forearm, and there was subjective weakness without wasting. The positive findings included intense tenderness over the root of the neck, associated with exacerbation of the pain by traction on the limb, which also obliterated the pulse. Cyanosis occurred when the arm was dependent. The sensory loss was extensive; the deep reflexes were normal and the pain was not relieved by head traction.

At operation the scalenus minimus did not seem to be causing mischief. After division of the scalenus minimus the 8th cervical and 1st thoracic nerves showed signs of having been compressed by the muscle as they crossed the first rib. The post-operative course was satisfactory. The anatomy and relations of the muscle are described in detail, and brief mention is made of a similar case cured by operation.

L. W. Plewes

The Coexistence of Rheumatic and Arteriosclerotic Heart Disease in Patients over the Age of 40 Years. CHASNOFF, J., and SILVER, A. (1951). Amer. Heart J., 42, 809. 6 refs.

The authors studied the clinical and necropsy records of 66 patients above the age of 40 years in whom unequivocal evidence of rheumatic heart disease was discovered post mortem, in order to ascertain to what extent arteriosclerotic heart disease coexisted. Of 27 patients (40·9 per cent. of the series) in whom atherosclerosis was found, fourteen had significant narrowing of the coronary arteries, and seven of these had definite occlusions with myocardial infarction.

A clinical diagnosis of coronary artery disease had been made in eighteen cases, but in seven of the eighteen this was not confirmed at necropsy. In thirteen of these eighteen cases the diagnosis of concomitant rheumatic heart disease was not even suspected clinically. In five cases in which the diagnosis of combined rheumatic and arteriosclerotic heart disease was made ante mortem, none showed post-mortal evidence of coronary disease. Since 69·5 per cent. of the whole group of patients were women, the reported frequency of coexistence of the two diseases is even more significant.

The authors conclude that there is little justification for the apparent reluctance of clinicians to make the dual diagnosis in patients with rheumatic heart disease in the arteriosclerotic age group. They also review the literature pointing to the coexistence of these diseases in patients over 40 years of age, and consider that the difficulty in diagnosing rheumatic heart disease in older subjects is partly due to the fact that clinicians are insufficiently aware of its frequency in this age group.

K. G. Lowe


ACTH, Cortisone, and Other Steroids


The production of acute arthritis in unilaterally nephrectomized rats by means of repeated injections of deoxycorticosterone acetate (DCA) was first demonstrated by Selye in 1944, and has ever since remained a controversial subject in view of the wide discrepancies in results obtained by different investigators. The present author, who in 1946 was unable to confirm Selye's results, returns to the problem and concentrates on the technique of nephrectomy as the most likely cause of the discrepancies.

The experiment described was based on an anatomical finding—namely, the existence in immature rats, such as those used by Selye, of one or two accessory adrenal arteries arising from the left renal artery, in addition to those arising from the aorta seen in the adult animal. These accessory adrenal arteries may be inadvertently interrupted during the operation of nephrectomy. The author has shown (J. Anat., Lond., 1951, 85, 12) that interruption of an adrenal artery in the rat or rabbit results in an area of necrosis in the zona fasciculata of the adrenal cortex.

A series of thirty Wistar albino rats, weighing from 30 to 55 g. were divided into three groups of ten, three or six rats from each litter being divided equally among the three groups. In Group I the left kidney of all rats was removed after placing a ligature around the pedicle close to the hilum, carefully avoiding any branches arising from the renal artery. In rats of Groups II and III the pedicle of the kidney was seized with fine curved artery forceps so as to include the inferior adrenal arteries, and the kidney then removed. Throughout the experiment all rats were given 1 per cent. saline to drink instead of tap-water and were fed on a diet similar in composition to 'purina fox chow'. From the fifth day after the operation 2 mg. of a fine DCA suspension in 0-1 ml. of a 0-1 per cent. aqueous solution of cetrimide was injected twice daily into animals of Groups I and II. Animals of Group III were receiving injections of equal volumes of a control solution containing no DCA.

Arthritis developed in three rats of Group II, and in a milder form in two rats of Group I. The left adrenal gland of all five arthritic rats showed an area of necrosis in the cortex restricted to the zona fasciculata. A similar lesion, but involving the outer part of the zone only, was found in the left adrenal of both arthritic rats of Group I, in which at necropsy constrictions by fibrous tissue of the accessory adrenal arteries were demonstrated. All the non-arthritic rats of Group II and three others from Group I showed areas of focal necrosis in the left adrenal cortex, but these either involved the whole width of the cortex or at least the full width of two zones—the zona fasciculata and zona glomerulosa. The remaining rats of Group I showed no focal necrosis of the adrenal cortex. The differences in extent and character of the lesions in arthritic and non-arthritic rats appeared to be conditioned by the degree of ischaemia, which in its turn depended upon the number and size of the inferior adrenal arteries. Histochemically, the adrenal cortices of the arthritic rats differed from those of normal rats and also from those of their non-arthritic litter-mates.

Since in the rat the zones of the adrenal cortex are relatively independent, the zona glomerulosa being concerned with the formation of the salt-regulating fraction of the adrenocortical secretion and the zona fasciculata with the carbohydrate-regulating fraction, necrosis of the zona fasciculata alone may be expected to lead to a diminished production of the latter. The resulting imbalance between the two fractions of the adrenocortical secretion is further enhanced by the administration of DCA.

Thus it appears that unilateral nephrectomy sensitizes to the action of DCA, not by virtue of the removal of a kidney, but by an inadvertent interruption of the accessory adrenal arteries, or by their involvement in fibrous tissue resulting from the operation.

[This is a very important paper which not only provides an adequate explanation for numerous failures to repeat Selye's experiment, but may influence our attitude to the conception of the "diseases of adaptation."] A. Swan.


The authors describe the effect of intra-articular injections of cortisone and of hydrocortisone in cases of rheumatoid arthritis and also in a variety of other arthritic and peri-arthritic conditions. In rheumatoid arthritis one knee was usually the joint injected, the other knee being used as a control. Cortisone acetate (25 mg.) had no consistent beneficial local effect in seventeen injections, but hydrocortisone acetate (25 mg. or 37-5 mg.) was immediately efficacious in reducing joint temperature, swelling, and pain in all of the 178 injections made. The duration of this effect varied from 2 days to 10 weeks, but in most cases was from 6 to 8 days.

The authors then used intra-articular hydrocortisone in the treatment of cases of osteo-arthritis (mainly of knees, but also in some other joints), acute traumatic arthritis, acute gouty arthritis, and various inflammatory conditions of bursae (including the subdeltoid bursa). They found that the injections caused dramatic relief of pain and recovery of mobility, more marked and often more permanent in the more acute conditions.

It is suggested that the reason for the difference in effect of cortisone and hydrocortisone may be found in their relative solubility. Whereas cortisone is slightly less soluble in water than hydrocortisone, it is about seven times as soluble in plasma and therefore, presumably, in synovial fluid. The relative insolubility of hydrocortisone may enhance its local effect by ensuring slower dispersion from the joint. B. E. W. Mace.


The hormone treatment of arthritis by intramuscular
injection of testosterone propionate is a form of "steroid therapy". The favourable results obtained in ten out of twenty patients suffering from rheumatoid arthritis are reported. Optimum dosage and the relevant literature are discussed. In the author's opinion, the preliminary results of his investigation justify further research in this direction. [Author's summary.]


The author has previously reported the results of prolonged uninterrupted cortisone therapy in a series of patients with rheumatoid arthritis (Brit. med. J., 1951, 2, 19). By using initial suppressive dosage and then gradually reducing the amounts in step-like fashion it proved possible to retain satisfactory, although incomplete, control of the disease in approximately two-thirds of the patients with a small maintenance dose. In those cases, however, in which the disease was severe the high dosage required for its control often could not be tolerated owing to unwanted side-effects of various types. Therapeutic limitations of this nature have led investigators to search for steroidal substitutes which might possess similar anti-rheumatic properties. Most of these have proved therapeutically inert, the only exception being Kendall's Compound F, which is now called "hydrocortisone" (17-hydroxy-corticosterone).

In this paper the author reports the results of comparative tests of the anti-rheumatic effects of hydrocortisone (free alcohol), hydrocortisone acetate, cortisone (free alcohol), and cortisone acetate given orally for short periods to small groups of patients with rheumatoid arthritis. Their relative potencies were assessed by comparing the clinical response to initial suppressive doses (150 to 200 mg. daily for 2 days followed by 100 mg. daily) of each drug in the same patient, and by determining the maintenance dose of each required to uphold a similar degree of clinical improvement. Hydrocortisone (free alcohol) was found to possess the greatest anti-rheumatic activity when given by mouth, and its action appeared to be more rapid than that normally expected with cortisone acetate. The relative incidence of endocrine side-effects from the various preparations could not be estimated in these short-term studies with any accuracy.

W. S. C. Copeman


The authors report the results of a clinical trial carried out at Bellevue Hospital, New York, of 3-hydroxy-2-phenylcinnchoninic acid (HPC) in the treatment of ten cases of rheumatoid arthritis and six of rheumatic fever, confirming the findings of Blaushard and others (Bull. Johns Hopk. Hosp., 1950, 87, 50), and in addition record the treatment of five cases of gouty arthritis with this drug. HPC was given in a daily dosage of 20 to 40 mg./kg. body weight divided into three doses preferably given after meals. The total dose ranged from 5.4 g. to 81.4 g.

The results of treatment in gout were very satisfactory, and the drug is considered useful in this condition, especially where there is intolerance of, or resistance to, colchicine. Results in rheumatic fever and rheumatoid arthritis were comparable to those achieved with adequate salicylate therapy. One or more toxic reactions occurred in sixteen out of the 21 cases, and four cases relapsed on discontinuing treatment. Toxic manifestations included frequency of micturition, dysuria, nocturia, impairment of renal function, nausea, vomiting, diarrhoea, erythema, vesication, pruritus, menstrual delay, paraesthesiae, and Bradycardia. Harry Coke.


Treatment with ACTH or cortisone was given in seventy cases, including 24 cases of chronic polyarthritis, five of infective polyarthritis, twelve of rheumatic fever, six of ankylosing spondylitis, three of gout, five of ocular disorders, two of myocardial infarction, and single cases of various vascular disorders. Cortisone was administered for 13 to 64 days in a total dosage of 1,275 to 4,850 mg.; the dosage of ACTH varied according to the preparation used. No case was observed for more than 3 months after the cessation of treatment. The complications of this form of therapy are discussed.

It was found that in the cases of polyarthritis improvement was marked in those of more recent onset, but that administration of gold salts in conjunction with cortisone probably gave more favourable results. As has also been reported by others, cases of rheumatic fever responded well, and in three cases of ankylosing spondylitis marked improvement was obtained. ACTH in association with colchicine was considered beneficial in acute attacks of gout. Benefit was also obtained in cases of myocardial infarction, periarteritis nodosa, and Buerger's disease. Kathleen M. Lawther.


It has been stated that corticotrophin and cortisone inhibit synovial permeability, and that their beneficial action in the rheumatic affections is due to this action. The authors, working at Iowa University, attempted to confirm this in animal and human experiments.

Phenolsulphonphthalein (PSP) was injected into the ankle joint of rabbits and constant hydration maintained; bladder contents were withdrawn at 15-minute intervals for 2 hours. Urinary dye content was measured by spectrophotometric methods. Treated animals received corticotrophin and cortisone in varying doses, either for some days before, or on the day of, experiment; some
animals were given intra-articular cortisone. Renal function as assessed by intravenous injection and subsequent urinary assay of the dye was unaltered by hormone therapy.

In the human study PSP was injected into the knee joint of patients with rheumatoid arthritis. Both corticotrophin and cortisone were given in therapeutic doses, and the experimental technique as for animals was used. Urinary excretion of the dye was estimated before and during parenteral and intra-articular injection of the anti-inflammatory agents. The effect of intra-articular hyaluronidase on synovial permeability was also observed.

The time for maximum or total excretion of PSP was not significantly influenced by parenteral corticotrophin or cortisone in man or animals. Intra-articular cortisone caused marked retardation of dye excretion, but particulate blocking effect cannot be excluded. Hyaluronidase alone, or with parenteral hormonal therapy, did not alter dye excretion. Maximal clinical response to these drugs in rheumatoid arthritis was not accompanied by changes in joint permeability to PSP.

The authors, though not denying that the drugs under study alter synovial permeability, suggest that the PSP test is inadequate.

J. N. Harris-Jones.


The authors reviewed the literature on the effects of hormones on dermal spread, with particular reference to their inhibitory action on hyaluronidase. His own investigations were carried out on thirty white rabbits, half of which were given 15 i.u. ACTH subcutaneously in two doses daily for 5 days, and the remainder 50 mg. cortisone subcutaneously in two doses daily, also for 5 days. The spreading experiments were performed before the hormones were given, and also 2 hours after the ninth injection, 0.1 ml. normal saline being injected into the left flank and an equal volume containing a standardized solution of hyaluronidase into the right flank. After the first hour an equal volume of Evans blue or Indian ink was injected into both sides; 24 hours later the areas were traced and measured with a planimeter.

The results are tabulated and show that the hyaluronidase spread was reduced in the animals receiving ACTH and cortisone, while in the controls the spread was increased in all by cortisone, and in most of them by ACTH. Earlier work had shown that ACTH and cortisone reduce the dermal hyaluronic acid content, so that the hyaluronidase would have less substrate on which to act, with a resultant decrease in spread. In the absence of hyaluronidase, the hormones having increased dermal permeability by their action on hyaluronic acid, there would be an increase in spread. The lack of consistency of ACTH in this respect is to be studied further. It was concluded that there was no direct inhibition by the hormones of the enzyme hyaluronidase, a fact which has been confirmed in vitro.

R. Sf. J. Buxton.


The weight, cholesterol content, morphology, and zonal thickness of the adrenal glands were determined in 126 patients examined post mortem, including otherwise healthy children and adults who died suddenly as the result of trauma (fifteen cases), patients with pituitary disease (three cases), those given corticotrophin or cortisone (33 cases), and 65 others with various diseases.

The mean weight range of the adrenal glands of adults with endocrine disease was higher than that of the healthy subjects (6.3 to 18.4 g., with a mean of 11 g., compared with 6.1 to 13.5 g. and a mean of 9.3 g.); a linear correlation was found between adrenal weight and mean cortical thickness (obtained from forty thickness measurements in each case, made on tracings of a magnified projection).

Cholesterol content ranged between 4.7 and 14.9 g. per 100 g. wet weight (mean 9.6 g. per 100 g.) in healthy adults as compared with a somewhat decreased amount in diseased patients (0.5 to 11.3 g. per 100 g.; mean 5 g. per 100 g.).

In three cases with pituitary tumour the cortex was thinner and the gland smaller, and the cholesterol content was low. Increase in thickness was due to widening of the zona fasciculata, but there was little specific difference between diseases, nor were glands from cases of disseminated lupus erythematosus, rheumatic fever, and rheumatoid arthritis different from those in cases of other diseases, whether the patient had or had not been given hormone therapy. The adrenals of two patients who died while on massive corticotrophin therapy (over 2 g.) showed a great increase in weight (to 28 g.), with hyperplasia and hypertrophy affecting all zones. In patients who died 9 days or more after the discontinuance of corticotrophin therapy the glands appeared no different from those of patients who had not been given such therapy, nor were specific changes seen in patients who had received less than 2 g. of either hormone. The adrenals of some of the patients who had received large amounts of cortisone showed atrophy, but there was no atrophy in a patient receiving 5-2 g. in 18 days. Patients who died 19 days or more after cessation of a long and intensive course of cortisone therapy showed no atrophy or morphological change.

E. G. L. Bywaters.


During a period of 16 months a total of about 18,000 tablets of 3-hydroxy-2-phenylcinchoninic acid (HPC) were used in clinical trials (mostly on patients suffering from so-called collagen diseases) at the University of Utah College of Medicine. In the 21 cases of rheumatoid arthritis treated, the daily dosage varied from 15 to 50 mg./kg. body weight for periods up to 16 months, whereas three patients with rheumatic fever received between 22 and 36 mg./kg. for 10 to 42 days. Two patients with scleroderma, four with disseminated lupus
erythematous, one with gouty arthritis, and two with osteo-arthritis were also treated.

The author was able to confirm the finding of other workers that HPC is a useful agent in the treatment of rheumatoid arthritis, but he doubts whether it is superior to sodium salicylate, in the treatment of rheumatic fever; nor was he impressed with its efficacy in disseminated lupus erythematosus and scleroderma. Side-effects were mainly confined to toxic skin reactions and diarrhoea, and it is suggested that the high incidence of the former could be accounted for by exposure to sunlight (all patients were ambulant). Experiments in vitro showed that the protein-binding ability of HPC was greater for serum albumin than for serum globulin or mucoprotein.

D. Preiskel.


Ungar, in work published in 1945 and subsequently, claims to have demonstrated in splenic extracts two pharmacologically opposed substances which he named "splenin A" and "splenin B". The former is probably a derivative of ascorbic acid and the latter an ester of fatty acids with a complex alcohol. He later succeeded in demonstrating splenin B in human serum in various pathological conditions, including rheumatoid arthritis. Greene also found splenin B in the serum of patients with rheumatoid arthritis, but never in healthy persons, whose serum contained only splenin A. After successful treatment with ACTH, serum from rheumatic patients contained splenin A but no splenin B. Ungar believes that both substances are produced in the spleen, and that their production forms part of the general adaptation syndrome.

In the present work, the authors set out to investigate the effects of sera from normal subjects and from patients with rheumatoid arthritis on the bleeding-time of guinea-pigs. Pooled, freeze-dried sera were used from which chloroform-soluble and acetone-soluble extracts were made. The former is said to contain splenin A and the latter splenin B. In a series of carefully controlled experiments, it was shown that the chloroform extract from normal serum decreases the bleeding time, and acetone extract from rheumatoid serum increases it. The results are statistically valid, and are shown in detail in tables. The authors conclude that a factor or factors present in the splenin A extract of normal serum reduces bleeding time, but is absent from similar serum extracts in rheumatoid arthritis. A factor or factors is present in the splenin B extract in rheumatoid arthritis that increases bleeding time, but is absent from normal serum. They add that their experiments give no indication of the manner or place of production of these substances.

Ellis Dresner.


The authors, in experiments carried out at the National Heart Institute, Baltimore, Maryland, studied the differences in the eosinophil content of blood from the splenic vein and femoral artery of the intact dog following the administration of ACTH (corticotrophin) or adrenaline in an attempt to determine the relationship of splenic function to the eosinophil count in the circulating blood. In no case was there a significant net increase in the eosinophil content of the spleen, but in three out of seven experiments with adrenaline and in one with ACTH there was a significant splenic output of eosinophils. There were no significant differences in the haematocrit determinations, and arterio-venous differences in neutrophil count observed were quite independent of those in the eosinophil count simultaneously determined.

The authors conclude that the spleen does not significantly retain or destroy eosinophils during the development of eosinopenia on stimulation of the adrenal cortex. On the other hand, as under certain conditions eosinophils were expelled into the general circulation when other factors were causing eosinopenia, it appears possible that the spleen may be capable of storing cells of one type and releasing others into the circulation.

John F. Wilkinson.


This paper reports the results of treatment of various diseases with cortisone and ACTH. The pathological process was significantly altered and there was clinical improvement in certain cases of acute leukaemia, disseminated lupus erythematosus, rheumatoid arthritis, and idiopathic thrombocytopenic purpura.

Among the patients with acute leukaemia, the only ones with remission were those in whom definite manifestations of adrenocortical stimulation were observed. It is suggested that the dose should be great enough, and treatment sufficiently prolonged, to produce either clinical remissions or proof of adrenocortical stimulation.

Observations on the effect of treatment on the levels of the eosinophils revealed that in ten of the 46 courses of treatment given, the level before treatment was so low that further significant reduction could not be expected. In the remaining 36, definite eosinopenia developed in eleven, while in 25 the eosinopenia was present but less marked. Only one patient with definite eosinopenia failed to show other evidence of cortical stimulation; urinary 17-ketosteroids were not measured in this case.

Three patients without eosinopenia showed definite signs of increased cortical function, one showed facial changes, and two a marked rise in urinary 17-ketosteroids.

A. Brown.


Experimental evidence indicates the presence of ACTH in varying fractions of placental tissue and shows that it is produced in large quantities by this organ. The Lyons' procedure for extraction of ACTH from pituitary
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tissue is not applicable to the extraction of ACTH from placental tissue and blood.

Administration of various fractions of crude placental extracts to normal or hypophysectomized mice produces a marked inhibition of hyaluronidase-enhanced spreading with essentially complete inhibition of exogenously added enzyme. These fractions are completely without effect in adrenalectomized mice and are without effect when injected intradermally at the site of the hyaluronidase injection. The inhibitory effect of placental extracts is not due to the presence in them of measurable quantities of steroids of the adrenal cortical type (cortisone or Compound F).

There is a similarity between the inhibitory effects produced by the placental fractions and the results following administration of pituitary ACTH, chorionic gonadotrophins, and heat-inactivated chorionic gonadotrophins. The presence of ACTH activity in placental extracts is also shown by the depletion of adrenal ascorbic acid and a fall in circulating eosinophils that occurs after their injection into hypophysectomized rats and mice.—[Authors' summary.]

Acquired Hemolytic Anemia treated with Corticotropin. 
The authors give an account of two cases of acquired haemolytic anaemia (in a girl of 19 and a boy of 17 months) treated with ACTH. Clinical and haematological remissions were obtained in both instances within 5 to 10 days. The Coombs test was markedly positive in both patients and became negative after treatment in the female. It is thought that antibiotics also played a part in the production of this remission. In the second patient a relapse occurred after one month, but further remissions were obtained with two subsequent courses of ACTH. The patient, however, died of pneumonitis.
The authors believe that ACTH is useful in the treatment of acquired haemolytic anaemia as it appears to diminish the fragility of globulin-coated erythrocytes.
R. Winston Evans.

Employing the MEFI strain of poliomyelitis virus, injected intracerebrally into mice in doses of 100 LD50, the authors found that cortisone or ACTH increased the number of deaths and shortened the period of survival very considerably, the effect being most marked with cortisone. Other experiments suggested that the virus in cortisone-treated mice was present in much higher concentrations in the spinal cord 24 and 48 hours after the injection than it was in controls.
The Lansing strain of poliomyelitis virus is generally unable to produce symptoms or kill golden hamsters, but when it was injected into five animals receiving cortisone (5 mg. cortisone acetate at the time of injection and another dose 3 hours later) four of them became paralysed, on the 3rd, 8th, 11th, and 28th day, respectively. In other experiments it was found that cortisol-treated mice died much more rapidly from a viscerotropic strain of Rift Valley fever virus than did controls; and further that the Coxsackie virus multiplies more rapidly, and that the Columbia SK strain of encephalomyocarditis virus produces lesions earlier in cortisone-treated animals.
[These experiments increase the already impressive volume of evidence that cortisone and ACTH have profound effects in increasing the susceptibility of animals to many forms of bacterial and virus infection.] R. Hare.

Intravenous ACTH therapy was given in the Boston City Hospital to ten patients with bronchial asthma, 10 mg. being added to each litre of a 5 per cent. solution of glucose. Of this preparation, 3 litres, containing 30 mg. ACTH, was infused in the first 24 hours. As improvement occurred the dose was reduced to 10 or 15 mg. ACTH daily. The total administered ranged from 10 to 210 mg. in periods up to 9 days. Relapse followed within a short period in two of the seven patients whose symptoms disappeared, and in the other three there was a certain degree of improvement. No patients failed to obtain some relief, although the follow-up period was short (from 1 to 8 weeks only).
The authors claim that, as compared with intramuscular injection, intravenous therapy is cheaper; it is also more effective, since in at least one case relief was obtained, with fall in eosinophil count, after intramuscular treatment had failed. No allergic reactions were noted. It is pointed out that when treatment is terminated fever and bronchitis may follow, and for this reason concomitant antibiotic therapy is recommended. K. Gurling.

The author describes the case of a boy of 3 years of age who was severely burnt in a petrol explosion. The boy was admitted to hospital in June, 1950, not severely ill but with considerable skin loss over the trunk and extremities. He was given blood transfusions and a satisfactory urine output was obtained on the 4th day. Dressings were applied locally, and the superficial burns healed; the deep sloughs separated, and considerable discharge continued. In spite of penicillin, and for a time aureomycin, he remained febrile. In the 5th week skin grafting was begun, and while some autografts took, the homografts from his mother sloughed. After 11 weeks further homografts were performed, and soon separated. At 15 weeks, pinch grafts were done and most of these were washed away in the discharge. By the 24th week there were no signs of healing; the boy had received more than 4 l. blood, but had a progressive anaemia, and his loss of appetite was resulting in an inadequate protein intake. ACTH was started after the 28th week, 3.8 to 15 mg. being the daily dose, and
more than 800 mg. were given over 16 weeks. Auto-
grafting after 5 days resulted in 100 per cent. take, and the
graft was seen to spread afterwards. He was less
irritable, took his food, and put on weight, at the same
time starting to crawl about and stand up. At the end
of the course of ACTH the laboratory tests were normal,
but some hyperostosis of the frontal bone was visible
radiologically. He was discharged in June, 1951, and
when seen 2 months later was well; there was complete
healing without contractures and only some stiffness
on walking remained.  
R. St. J. Buxton.

Treatment of Radiation Sickness with ACTH.  
Taber,  
Radiology, 57, 702.  24 refs.

The theory that the adrenal cortex is in some way
associated with the constitutional effects of radiation
(Selye) and reports that exogenous adrenocortical
hormones have proved effective in some hands in the
 treatment of radiation sickness have provided the author
with a rationale for the clinical trial of small doses of
ACTH.

Among patients receiving x-ray therapy for malignant
lesions, fourteen were treated by intramuscular injection
of 10 mg. ACTH, repeated daily or thrice weekly as
necessary. Prompt relief of symptoms is claimed after a
few injections in twelve of the patients, prolonged treat-
ment being necessary in one, and results were inconclusive
in another, who died of his primary disease during
treatment. A composite table gives such
details as dosage and symptoms [but not over-all treatment times].
The total volume doses in this series ranged from 0·26 to
3·65 M.g.r. [all remarkably low]. The author states
that the doses of ACTH given were so small that “no
appreciable changes were found in the excretion studies”.
To prove that the dosage employed was nevertheless
pharmacologically active, groups of white mice were
exposed to total body radiation of 300, 600, 900, and
1,200r. The protective effect of “comparable” doses
of ACTH was thereafter assessed in terms of survival.
[No quantitative explanation of “comparable doses” is
offered. The treatment of alternate patients would have
provided a much simpler and certainly more valid
method of assessment.]  
E. C. Easson.

Studies of the Effects of Cortisone and Pituitary Adreno-
corticotropic Hormone (ACTH) in the Sprue Syndrome.
Adlersberg, D., Colcher, H., and Drachman, S. R.
(1951).  
Gastro-enterology, 19, 674.  6 figs, 16 refs.

The effect of corticophelin and, subsequently, corti-
sone on five cases of idiopathic steatorrhoea was studied.
After 1 to 3 days of therapy there was, in general, a
marked improvement in the clinical condition. There
was an increased sense of well-being and increased
appetite. Diarrhoea disappeared and the stools became
formed, but steatorrhoea remained present, though
usually diminished. The absorption of vitamin A in
some cases was improved, and in others cortisone brought
about a considerable gain in weight.

[From the results presented it seems likely that ACTH
and cortisone had a beneficial effect on these patients,
though with a condition such as sprue, in which there are
notoriously marked remissions and relapses, a much more
carefully controlled investigation would be necessary
before one could be certain that the effects were all due
to ACTH or cortisone.]  
G. A. Smart.

Cortisone in Idiopathic Steatorrhoea.  
Badenoch, J.  
(1952).  

At the Radcliffe Infirmary, Oxford, two untreated cases
of idiopathic steatorrhoea and two partially treated cases
were given cortisone in doses of 100 mg. intra-
muscularly daily for 4 weeks. Slight decreases in fat
excretion were observed in all patients, but the decreases
were not statistically significant. Subjective improve-
ment occurred in three of the four cases. The effect on
the excretion of nitrogen was variable and showed no
appreciable benefit.

C. L. Cope.

Effect of Adrenocorticotropic Hormone on the Diuretic
Response to Water in Panhypopituitarism.  
Chalmers, T. M., and Lewis, A. A. G.  
(1951).  
Lancet, 2, 1158.  4 figs, 15 refs.

In healthy persons a diuresis occurs between 30 and
90 minutes after taking about a litre of water; such a
diuresis does not occur in panhypopituitarism or in
Addison’s disease under similar circumstances. The
authors, noting that ACTH restored the diuretic response
in cases of panhypopituitarism, investigated the cause of
the phenomenon. They observed six patients with
panhypopituitarism and one with Addison’s
disease.

In the patients with panhypopituitarism it was found
that a normal diuretic response after the ingestion of
water occurred up to about 30 hours after the end of a
course of ACTH, whereas before the ACTH had been
given there was no such diuretic response. The
glomerular filtration rate was estimated, and, although a
slight rise occurred during ACTH therapy, the increase
was not very marked and was insufficient to account for
the diuresis. Lack of absorption of water from the
alimentary tract was not a cause of failure of diuresis,
since normal haemodilution occurred after the ingestion
of water.

The action on a patient with Addison’s disease of
vasopressin injected intravenously before and after cortisone
therapy was investigated, and no essential difference was
found in the results. The authors concluded from this
that the hormone was not inactivated more rapidly after
the cortisone had been given than before. In one patient
whose plasma was found to contain anti-diuretic sub-
stances there was nevertheless a normal diuresis. On the
other hand, in another case no diuresis was obtained,
thought the plasma contained no anti-diuretic substance.

The authors conclude that the failure of the diuretic
response in panhypopituitarism and in adrenal deficiency
is due to failure of the tubular reabsorption of water to
decrease in response to the ingestion of water. Whether
the cause of this failure to respond lies in defective renal
tubules or in defective osmoreceptors, or in both, the
authors were unable to determine, but the essential point
is that cortisone repairs it and so enables a normal diuretic response to occur.  

G. A. Smart.

Effect of Intravenous Testosterone on Nitrogen and Electrolyte Metabolism.  


4 figs, 9 refs.

Testosterone was dissolved in a 25 per cent. aqueous solution of human serum albumin and doses of 162 and 195 mg. respectively were given intravenously to two normal men. Urine was collected every 24 hours. For 7 to 10 days after the injection there was a positive nitrogen and phosphorus balance, and for 5 days there was water retention and disappearance of creatine from the urine. The testosterone concentration in the blood fell within 90 minutes to undetectable levels (less than 20 μg. per 100 ml.) though α,β-unsaturated ketosteroids equivalent to only 2 mg. of testosterone were excreted in the urine during the first hour and none thereafter. There was a raised excretion of 17-ketosteroids during the first 2 hours after the injection, accounting for 70 to 80 per cent. of the injected testosterone. There was also a temporary rise in phosphorus excretion before there was any alteration in nitrogen excretion. Two other normal men given lower doses of testosterone intravenously (25 and 101 mg. respectively) showed little or no alteration in nitrogen balance.

The results suggest that a small part of the injected testosterone is absorbed into the tissues and continues to be active for several days, but that the bulk of material is metabolized and excreted within 24 hours. A slight rise in urinary 17-ketosteroids coinciding with the end of nitrogen retention may represent the ultimate metabolites of this retained testosterone.  

Peter C. Williams.

Metabolic Effects of Compound S (11-Desoxy-17-hydroxycorticosterone) in Man.  


In this study of the metabolic activity of 11-desoxy-17-hydroxycorticosterone (Reichstein's Compound S) two healthy young men were given constant diets and the effects on their metabolic balance of Compound S acetate in doses of 200 to 400 mg. per day, both orally and intramuscularly, were investigated. The following determinations were made: daily fasting values for blood sugar, haematocrit, blood reduced glutathione, and total circulating eosinophil cells. Total lipid and free and total cholesterol levels were determined at 2- to 4-day intervals, and glucose tolerance and serum sodium, potassium, and chloride concentrations at the conclusion of each metabolic period. Daily urinary total nitrogen, uric acid, glucose, creatinine, sodium, potassium chloride, 17-ketosteroids, and formaldehydegenic steroids were also estimated. In addition, in one subject, the ketogenic fraction of the urinary 17-ketosteroids was determined.

Compound S was not found to effect any of the above determinations except for the 17-ketosteroids; these were found to be significantly increased when Compound S was taken by mouth, but not when it was given intramuscularly. The increase appeared to be in the ketogenic fraction. One patient with Addison's disease was also given Compound S by mouth and in this patient, too, there was an increase in the urinary 17-ketosteroids.

The authors conclude that the liver was responsible for
the degradation of Compound S to 17-ketosteroids, and in a footnote they state that after the completion of the paper they investigated the effect of 400 mg. of Compound S on a patient with atrophic cirrhosis of the liver. Only a small increase in the urinary 17-ketosteroids was observed, much less than that obtained in the control patients and in the patient with Addison's disease.

G. A. Smart.

Slow-release Medium for Adrenocorticotrophic Hormone.

The authors used a test based on decrease in weight of the thymus in rats to study the effectiveness of a slow-release preparation of ACTH. The hormone was incorporated in 5 per cent. beeswax in arachis oil in a concentration of 10 mg. per ml. Three daily doses of 1 mg. led to a maximal decrease in thymic weight and body growth of nesting rats aged 4 to 10 days, comparable with that resulting from administration of 0.2 mg. cortisone daily. A total dose of 3 mg. was almost as effective in one injection as in three, and the maximal effect did not appear for some days. Similar results were obtained in adult rats, in which a single injection of 8 mg. ACTH in wax-oil was almost as effective as four daily injections of 2 mg. Reducing the beeswax content from 5 per cent. to 2 per cent. led to a marked loss of effect. ACTH in saline or arachis oil alone had no certain effect on thymic weight, nor did administration of the wax-oil medium without ACTH. The use of this slow-release medium was thought to increase the effectiveness of ACTH at least ten-fold.

Robert de Mowbray.


ACTH was given by continuous intravenous infusion to eleven patients with chronic polyarthritis (including two cases of psoriatic arthritis) and to four patients with severe asthma. The technique of choice was to introduce a polythene catheter into one of the saphenous veins; with the use of heparin, infusion could be continued for periods up to 20 or 30 days. The usual dose of ACTH was 5 mg. daily, given in 1 l. isotonic glucose solution (saline being contraindicated by the risk of oedema), but signs of overdose in some cases demanded a reduction to 3 mg. daily.

A striking diminution in pain and increase in mobility were observed in all the patients with arthritis, usually by the first day and invariably by the second, even in cases in which treatment with ACTH intramuscularly had had little effect or in which doses of 75 mg. or more daily, given intramuscularly, were necessary to produce even partial remission. The patients with asthma were almost completely relieved after 2 days' treatment. Depression of the eosinophil count and lowering of the erythrocyte sedimentation rate were achieved more constantly than with intramuscular ACTH, but the incidence of induced hormone resistance and of relapse following cessation of treatment appeared undiminished. Complications were essentially those typical of ACTH therapy and of intravenous infusion.

H. McG. Giles.


In this paper is described the "enormous oak which has grown from the acorn that Addison unobtrusively planted in Guy's Hospital in 1855"—Addison's monograph On the Constitutional and Local Effects of Disease of the Supra-renal Capsules is discussed, and it is noted that of the eleven cases described by him only four can be confidently accepted as being true cases of his disease. When Addison wrote, the nervous system was normally thought to be the sole co-ordinating mechanism of the body. Hormones were far in the future. Yet Addison seems to have had the germ of an idea that non-nervous co-ordinating mechanisms might exist as indeed had Richard Lower 200 years earlier. The views of de Bordeu, George Gulliver, A. A. Berthold, and Claude Bernard are also noted, and special attention is given to Pavy's criticisms of Bernard's work.

From this point the development of endocrinology is reviewed through the work of Brown-Séquard, Hilton Fagge, Ord, Oliver and Schäfer, and many others until the outstanding contribution to adrenal research of Swingle and Pfiffner is reached. The physiology and biochemistry of steroids in general, and cortisone in particular, are then discussed in some detail, and stress is laid on the theory that cortisone does not act directly on a toxin or noxious stimulus, but is effective in conferring on a cell the ability "to withstand abnormality in the internal environment".

Calvin P. B. Wells.


Abstracts

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