ABSTRACTS

Acute Rheumatism


A study of the effect of oral penicillin in preventing recurrences of rheumatic fever was carried out on 126 children in a special school in Chicago for cases of rheumatic heart disease. The subjects were divided into two groups, comparable as to sex, race, age, and economic level, one being used as a control. A further control group of eighty children at another similar school were selected in the same manner but were not in contact with those undergoing prophylactic treatment.

Penicillin was given in the hope that it might be possible to eliminate haemolytic streptococci and so to prevent or lower the incidence of rheumatic fever. For the former purpose, throat swabs from all the groups of children were examined at intervals during the course of treatment. At the end of 4 months' treatment with 50,000 units of penicillin twice daily, throat swabs showed no improvement in the treated group.

As it was thought that this dosage might be causing penicillin-resistance in the organisms the dosage of penicillin was changed to 1 mega unit daily for 5 days, repeated five times in the school year. This was found to cause a maximum reduction in streptococci in throat swabs from the treated children lasting for at least 3 weeks after the short course.

As a result, in the third year of the experiment, treatment was given in the first week of each calendar month throughout the school year and consisted of 200,000 units four times, or 250,000 units thrice daily for 7 days. With this dosage the penicillin-treated group showed a consistently lower infection rate than the control group from the same school. Owing probably to the lessened cross-infection risk, the latter group showed a markedly lower infection rate than did the group from the second school, in which the rate was similar, on the one occasion of comparison, to the rate among children in an ordinary school.

The recurrence rate of rheumatic fever in each of the 3 years remained steady at about 20 per cent. in the school where there was no prophylaxis. In the school with prophylaxis the rate among those given penicillin was consistently less than in the control group, though of smaller proportionality than in the first and second years. In the third year, however, there were no recurrences among the treated children, as compared with 11 per cent. among the untreated. This is regarded as a highly promising result.

During the second and third years, while penicillin was being given in larger doses for short periods, there was no evidence of the development of penicillin resistance among haemolytic streptococci of groups A, B, or C, in a total of 274 strains examined.

Reginald St. A. Heathcote.


An analysis was made of 400 cases of rheumatic fever during convalescence, the patients being men between the ages of 18 and 25 at an American Naval Hospital. Full clinical reports in a standard form were rendered weekly by the ward medical officer, an attempt being made so far as possible to exclude bias from the previous week's laboratory findings. A series of estimations of the Weltmann reaction (coagulation of the patient's serum when incubated with differing concentrations of calcium chloride solution) and the Cutler erythrocyte sedimentation rate (E.S.R.) were made in each case; only those cases with more than four estimations of both were included in this series. A total of 2,552 estimations of each test were performed.

Of the 400 cases fifty showed clinical activity of the rheumatic process during the initial period of convalescence. The results of the Weltmann test showed agreement with the clinical opinion in 60 per cent. of the estimations performed, and the E.S.R. agreed with the clinical findings in 70 per cent. Many of the discrepancies observed were confined to the results of tests on only four patients; when these were allowed for the correlations became 93 per cent. and 90 per cent. respectively.

When the disease became clinically inactive in these 46 patients, there was correlation with the Weltmann reaction in 99 per cent. of estimations and the E.S.R. in 93 per cent. Of the 350 cases without clinical activity there was correlation in 98·1 per cent. of Weltmann reactions and in 85·9 per cent. of E.S.R. estimations.

Statistical analysis of these figures proved that a disproportionately large number of those estimations of the E.S.R. showing a discrepancy were confined to a few patients. When 22 patients with four or more abnormal readings of the E.S.R. were excluded, the correlation became 92·2 per cent. No persistent discrepancies with the Weltmann reaction were noted.

The authors conclude that the Weltmann reaction is of great value in the assessment of activity of the rheumatic process, especially when there is no correlation between the E.S.R. and the clinical opinion.

[It is perhaps unfortunate that the authors have used as one of their yardsticks their own modification of the Cutler technique, the test they describe being almost entirely}

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Westergren reaction performed in a Cutler tube. Workers using the Wintrobe technique have found a much higher correlation between the clinical activity and the erythrocyte sedimentation rate.

A. Michael Davies.


This paper describes biochemical investigations carried out by the authors on seven adults with rheumatic fever under treatment with salicylate. As a result of these tests they conclude that, although the primary mode of action of salicylate remains uncertain, the principal pharmacological actions of the drug are: (1) induction of respiratory alkalosis, and (2) stimulation of protein catabolism. The details of these actions are as follows:

(1) It is shown by the authors that as the plasma salicylate level rises, the plasma carbon-dioxide content falls and the plasma pH rises. This correlation shows that carbon dioxide is removed from the plasma by the lungs (probably by the stimulating action of the drug on the vagal nerve-endings causing hyperpnea) much more rapidly than the fixed base is excreted by the kidneys. Hence the H2CO3 : NaHCO3 ratio diminishes and the plasma pH therefore rises. In other words, salicylate appears to induce respiratory alkalosis, clinically manifested by deep breathing.

(2) Protein catabolism profoundly alters the water balance of the body. At first, reduction in intracellular (protoplasmic) water content occurs followed by diminution in extracellular (tissue and plasma) water content, indicated by a fall in plasma volume and the development of a diuresis. It is shown that the former is associated with relief of joint pain and swelling, and the latter with a fall in erythrocyte sedimentation rate.

The authors also observed that salicylate, besides promptly relieving acute manifestations of rheumatic fever, produces a "special salicylate syndrome" with hyperpnea, sinus bradycardia, peripheral vasodilatation, nausea, vomiting, tinnitus, deafness, and drowsiness leading to mental confusion and coma. This syndrome appears when acute manifestations of rheumatic fever are eased and the authors found that the promptness of relief of rheumatic symptoms and the severity of the special salicylate syndrome are both directly related to plasma salicylate level; the higher this level the quicker the disappearance of fever, tachycardia, and joint pain and swelling, and the more intense the symptoms of the added salicylate syndrome.

S. Karani.


Stirile horse serum was injected into 24 young rabbits on the 1st and 20th days, each animal receiving 10 ml. per kg. intravenously on each occasion. Twelve rabbits were given sodium salicylate from the day of the first serum injection. Two daily doses were given orally at 10 a.m. and 4 p.m. and a larger dose was injected subcutaneously at 10 p.m. The final dosage used was 150 mg. per kg. orally and 200 mg. per kg. subcutaneously, a total of 500 mg. per kg. Treatment was continued up to the 26th day, when the surviving animals were killed and their hearts removed for section. In assessing the severity of the lesions produced in each animal (corresponding to those seen in the experimental production of rheumatic fever), marks were awarded for the presence of intermuscular and perivascular infiltration, Aschoff-like bodies, valvular lesions, and muscle and collagen degeneration. The incidence of vascular and valvular lesions was considerably reduced by the treatment with sodium salicylate. The mechanism by which this inhibition is produced is still uncertain.

It may be that the in vitro activity of salicylates in inhibiting the activity of hyaluronidase is involved. This enzyme is said to play a part in the breakdown of interfibrillar cement in rheumatic fever.

G. B. West.


A Clinical and Statistical Study of the Course and Prognosis of Rheumatic Heart Disease. III. Rheumatic Valvular Defects in Persons Over 45. (Studio clinico-statistico sulla evoluzione e prognosi della cardiopatia reumatica. III-1 vizi cardiaci di origine reumatica nei soggetti di età superiore a 45 anni.) MASINI, V. (1949). Cuore e Circol., 33, 76.


**ABSTRACTS**

**Cardiac Changes in Rheumatic Arthritis.**


**Rheumatic Fever with Nodules in a Child of 7 months.**


**Chronic Articular Rheumatism (Rheumatoid Arthritis)**


The Plummer-Vinson syndrome, usually seen in middle-aged women, is characterized by hypochromic anaemia and dysphagia; occasionally, the changes in the oral epithelium suggest a deficiency of the vitamin-B complex, though administration of the latter alone does not cure the condition. The relation between it and Sjögren's disease (dacryo-sialo-adenopathia atrophicans) has been discussed by Godtfredsen, who observed 23 cases of the disease and found that in thirteen there was dysphagia and in three the complete Plummer-Vinson syndrome; most of his patients had a chronic progressive polyarthritis. Felty's syndrome is characterized by rheumatoid arthritis, splenomegaly, and leucopenia, and may be associated with a pronounced dysphagia. Anaemia is a common factor in all three conditions.

The author describes Felty's syndrome in one male and one female patient; both had severe dysphagia and the woman had advanced cancer of the uterine cervix. He discusses the advisability of splenectomy and quotes the conflicting views of various authorities. He hints that patients with Felty's syndrome do not form a homogeneous group and suggests that the presence of cancer in the second case described was not coincidental. In support of this view he mentions a paper by Ayre (Amer. J. Obstet. Gynec., 1947, 54, 363) who sought to establish a connexion between cervical cancer and nutritional deficiency.

D. PREISKEL.

**Copper Morrhuate in Treatment of Rheumatoid Arthritis.**


The authors describe preliminary results with copper morrhuate in the treatment of rheumatoid arthritis. Their studies started in 1943 when they gave intravenous injections of cod-liver oil to seven patients. In two of these patients a striking therapeutic result was obtained, bedridden patients being able to resume full activity after six injections. Reactions were, however, so severe in two cases that the method was abandoned.

The next stage was the employment of ethyl morrhuate in a series of cases by intramuscular injection. In four cases out of seven pain was relieved, physical signs diminished, the patient gained weight, and the erythrocyte sedimentation rate fell after a course of twenty injections of 50 mg. every other day. Tolerance was perfect.

The authors have now prepared a colloidal solution of copper morrhuate which remains stable indefinitely. Each ampoule contains 50 mg. morrhuate and either 2 or 10 mg. copper. The preparation may be given intravenously, in which case injection should be very slow, or intramuscularly, in which case procaine must be added. A course consists of 24 to 32 injections, at first of 2 mg. copper, then of 10 mg. two or three times a week. The effect of this preparation is greater than that of ethyl morrhuate. No serious reaction has been observed. In a series of 117 cases improvement has been obtained in about 30 to 35 per cent. This low figure is attributable to the fact that cases have not been selected.

S. S. B. GILDER.

**Effects of Delta 5 Pregnenolone in Rheumatoid Arthritis.**


The authors claim, in this further paper on the relation of steroid metabolism to rheumatoid arthritis, that the synthetic steroid Δ5-pregnenolone, when administered in adequate dosage by intramuscular injection, will cause a remission in the course of rheumatoid arthritis, and that this remission can be maintained by means of a suitable scale of dosage. When the injections are stopped the activity of the disease will return within a few days. No toxic effects of any sort have been observed in patients given daily injections for periods up to 4 months.

It is claimed that although pregnenolone takes much longer to become effective than do cortisone or pituitary adrenocorticotrophic hormone, its lack of toxicity and low cost of manufacture are determining factors in favour of its use. High dosage is essential, the average effective daily dose being in the neighbourhood of 200 mg. Once symptomatic improvement has become manifest, 100 mg. daily will generally prove sufficient to maintain it. It is stated that a new substance which permits the employment of still larger dosage without toxicity symptoms is at present under test. Full reports on thirteen cases are appended.

[W. S. C. COPEMAN]

**Diagnostic Value of Histologic Lesions of Striated Muscle in Rheumatoid Arthritis.**


Biopsy or necropsy specimens of muscle from the deltoid and gastrocnemius were examined by serial section in 57 cases of rheumatoid arthritis, ten of ankylosing spondylitis, 21 of acute rheumatism, 101 of various other conditions, some involving the joints, and in thirteen healthy volunteers. Focal cellular lesions similar to those described by other workers were found in 56 per cent. of the cases of rheumatoid arthritis, but also in three of the normal controls and in 25 per cent. of the non-rheumatoid group as a whole. Various other laboratory investigations were performed, such as determination of the erythrocyte sedimentation rate and estimation of the serum content of streptococcal.
agglutinins and agglutinin of sensitized sheep erythrocytes. None of these threw any light on the mechanism of production of the histological lesions, and the authors conclude that muscle biopsy is of little value as a diagnostic procedure in rheumatoid arthritis.

G. J. Cunningham.


(Osteo-Arthritis)


The author suggested in 1940 that the condition causing "cracking" of the jaw should be called "temporomandibular arthrosis" as he considers that it is a degenerative, non-infective disease of the joint and that the characteristic snapping "is merely one of several symptoms in the more serious cases." He has studied 138 examples in the last 9 years and finds it commonest between 20 and 30 years old (though the total age distribution is wide), the sex-ratio being 44 female cases to one male case. He considers that there are many pre-disposing causes, but emphasizes the importance of dental irregularities with resulting repeated trauma from an abnormal bite. This produces pain and stiffness which is later followed by restrictive movement of the joint, which may even interfere with nutrition. Deviation of the chin to the affected side on opening the mouth was a conspicuous sign in over one-half of the unilateral examples. X-ray examination, with or without arthrography, often showed changes in the joint, but the eurythreotic sedimentation rate was normal and other pathological tests gave negative results.

Emphasis is laid on the need for an expert dental opinion in deciding the cause and suggesting conservative methods of treatment, which are often successful, but are protracted and expensive in Denmark. The indications for operation, which was carried out in about 1 in 4 of the author's cases, are listed, the most important being progressive limitation of movement and frequent locking. Some form of local analgesia is preferred by the author who uses the posterior approach (Bockenheimer-Axhausen) to divide adhesions and usually to excise the meniscus, with occasional removal of the condyle. Good results were obtained in 32 of 34 cases (33 patients) after a follow-up of 6 months to 8 years, and there were no complications, apart from partial and transient facial paralysis, in ten cases. Eric I. Lloyd.


The author suggests that muscular insufficiency is an important factor in the development of osteo-arthritis of the hip, and that the deformities in the femoral head and acetabulum are the result of misdirection of the physical strain. He presents his impressions (rather than a statistical analysis) of the results in 111 cases treated by vitallium-mould arthroplasty. The best results were obtained in osteoarthritis (89 cases). In atrophic arthritis nine cases) and Marie-Strümpell disease (three) the operation proved disappointing, whereas no success was achieved in tuberculous arthritis (two). In cases of an un-united fracture of the neck of the femur (three), old slipped upper femoral epiphysis (two), and septic arthritis (two) unsatisfactory results were obtained, whereas a good result was obtained in one case of fracture dislocation.

The posterior (Kocher) approach to the hip joint was used in every case, and on no occasion was a blood transfusion necessary. The femoral head alone was remoulded, only loose pieces of bone or redundant synovial membrane being removed from the acetabulum. Post-operative treatment consists of 4 weeks in bed, during which time assisted, active, and resisted hip exercises are carried out in all directions, together with exercises for the lumbar spine. Complications in the author's series included infection (one), dislocation (three), transient foot-drop (one), and spur formation on the femoral neck (one). Bone absorption in the acetabulum is noted frequently, and on account of this the author does not advise burring out the cavity of the acetabulum. There were no operative deaths.

Good results, with freedom from pain and adequate function as regards return to work and activity, were obtained in 65 out of 111 cases. A satisfactory result, with the emphasis on alleviation of pain, was obtained in a further sixteen cases, and doubtful or poor results were obtained in thirty cases, which included all the cases of tuberculous, atrophic, and Marie-Strümpell arthritis.
[In the discussion following the presentation of this paper, Smith-Petersen pointed out that this method differs from his own, in which the necessity of the accurate re-shaping of both sides of the joint is stressed, together with the freedom of movement of the vitallium mould in the acetabulum and on the femoral head. He also pointed out that the posterior approach would be less satisfactory in cases of osteo-arthritis when the anterior acetabular bone is hypertrophied, which is frequently the case.]

This paper would be of much more value if based on a scientific study of results, though the practical difficulties of carrying this out in the area of Winnipeg, Manitoba, where the author works must be fully realized.

W. A. Law.


A technique is described for the relief of pain from chronic arthritis of the hip, in which procaine is injected into the obturator nerve from in front as it leaves the obturator foramen, and into the nerve to the quadratus from behind where it lies on the posterior surface of the ischium. Nineteen patients out of 23 treated by this method had immediate and complete relief of pain, and eighteen had increased movement. The relief of pain lasted for periods ranging from 36 hours to 3 months.

[The authors' conclusion that, in addition to being a useful means of treatment for coxalgia, this method should be used as a therapeutic test before surgical denervation of the hip, deserves careful consideration by orthopaedic surgeons.]

L. W. Plewes.


In this paper the technique and results of operations for partial denervation of the hip joint for the relief of pain in cases of chronic arthritis are discussed. The authors describe four definite patterns of pain arising from disease of the hip joint: (1) Obturator (medial aspect of thigh); (2) Posterior (buttock); (3) Femoral (anterior thigh); (4) Lateral (lateral aspect of thigh). Only patients with the obturator and posterior patterns of pain are considered suitable for operation. Obturator neurectomy may be performed by intrapelvic or extrapelvic approach, but in the authors' experience the latter approach gives much less satisfactory results. Both operations are illustrated and described in detail. Posterior denervation may be performed at the same operation.

Partial denervation was performed in 48 cases where conservative therapy had failed and major operative procedures were contraindicated. During an observation period after operation ranging from 3 to 20 months, 66 per cent. of the patients were appreciably relieved of pain. Most of the failures occurred in those cases where the extrapelvic approach was used for obturator neurectomy. Electromyographic tracings are reproduced showing the marked effect of intrapelvic section of one obturator nerve on adductor spasm in a case of bilateral osteo-arthritis of the hip, the tracing from the untreated side remaining as a control.

L. W. Plewes.


The best position for obtaining a radiographic view of the metacarlo-carpal joint of the thumb is described in detail, the importance of placing the hand in full pronation being stressed. Several illustrations of the results of this technique are given. A light plastic splint is recommended for immobilization of the joint when the latter is the site of osteo-arthritis.

John Charney.


Excision of the trapezium is recommended for osteo-arthritis of the carpo-metacarpal joint of the thumb. The operation has been performed eighteen times, and indifferent results were encountered in only two cases. Both the poor results were in cases with general arthritic changes. The results in the remaining sixteen cases were uniformly encouraging. Details of the technique are described.

John Charney.


Rhizotomy was performed in 44 cases of painful conditions of the hip-joint during 1943-46. A follow-up questionary after 2 to 5 years gave the following results: of 22 males, nine had satisfactory improvement, four had some improvement, and nine had none; of 22 females, four had satisfactory improvement, five had some improvement, and thirteen had none. Different roots were cut for the relief of pain. The author sees no reason for section of more than the sensory root of L 4, but he suggests that excision of the posterior root ganglione might give better results.

J. Agerholm-Christensen.


(Spondylitis)


Basing their treatment on the work of Oppen­grad, the authors performed parathyroidectomy in four out of five cases of ankylosing spondylarthrosis, and thyroidectomy with ligation and resection of the thyroid artery in the other case (in this case the parathyroids could not be located). In four cases the calcium level in blood was normal, and in one case there was hypercalcaemia (17.5 mg. per 100 ml.); this case was the only one in which an adenoma of the parathyroid was found and in which there was a post-operative fall in the blood calcium level greater than the usual 1 to 3 mg. per 100 ml. In all cases there was a remarkable improvement in subjective symptoms immediately after operation, but except in one case this improvement was temporary and lasted only for a few months or years. The rationale of this procedure is not clear, and the


(Miscellaneous)


Bone involvement by hydatid disease occurs in 2-1 per cent. of all cases. The bones affected are the vertebrae, pelvis, femur, and humerus. The vertebrae are affected in 33 per cent. of cases of bony involvement. Infection occurs in childhood, but hydatid growth is so slow that symptoms do not appear before adult life. The onset is usually shown by either dislocation or collapse of a vertebra or by signs of pressure on the cord. Five cases are reported, in four of which there were signs of cord pressure. Growth is slow at first, but becomes rapid once the hydatids have escaped from the bone. The cysts in bone are as a rule small, but one case in which there was a large cyst is reported. They may begin anywhere in the cancellous tissue of the vertebral body, pedicles, or laminae. Extra-osseous lesions are prone to degenerative change.

The diagnosis is difficult. Radiological signs, though not conclusive, are as a rule more advanced than the duration of symptoms would suggest. The trabecular pattern is destroyed, but the “bunch of grapes” appearance found typically in the ilium is not seen. The intervertebral disc is not involved. There is no periosteal reaction except when secondary infection has occurred. Massive sequestration is rare, but small sequestrae may be present.

In differential diagnosis the following conditions must be considered. (1) Pyogenic osteomyelitis. In both diseases involvement of adjacent vertebrae is common, but in osteomyelitis there is fever, loss of the intervertebral disk, and marked periosteal reaction. (2) Tuberculous spondylitis. The cold abscess may resemble the extra-osseous extension of hydatid disease, but the site of infection, the rarefaction, and loss of the disk spaces are distinctive. (3) Secondary carcinoma. Periosteal reaction is absent, but complete destruction of a single vertebra is the rule. (4) Haemangioma produces a honeycomb rarefaction, without periosteal reaction, confined to one body. (5) Bone sarcoma occurs in the young, though the extra-osseous extensions may suggest those of hydatid disease. Secondary elsewhere make the diagnosis clear. (6) Syphilitic spondylitis affects chiefly the cervical spine; there is a combination of bone destruction and new bone formation, with the development of spurs. Similar changes are seen in Charcot’s disease of the spine. The “bunch of grapes” appearance, if present, may simulate fibrocystic disease or multiple myeloma. Large cysts must be differentiated from simple bone cysts, chondroma, and osteoclastoma.

The disease is very chronic. The time of survival of the four patients who died was 5, 19, 7, and 12 years. Two of the only surviving patient is paraplegic but has lived for nine years. Most patients had undergone numerous laminectomies, with very variable results owing to the inevitable recurrence of pressure on the cord even if this could be temporarily relieved.

J. G. Bonnin.


An anthropological survey of Miao peasants living in Shih Men K’an in Kweichow Province of Southwest China revealed a very high incidence of “arthritis” and joint ankylosis amongst the adult population of neighboring villages. These changes proved typical of fluorosis and analysis of the water supplies showed concentrations of fluorine up to 6-28 parts per million. The villagers stated that the disease started at about 10 years of age and in acute cases caused death at about 18. In chronic cases, however, the patient often lives severely crippled, to the age of 50. The skeletal changes in one patient who died of a fractured cervical spine—from a trivial fall—was observed and studied. All the bones were thickened, porous, and brittle. The intervertebral disks were ossified and the whole vertebral column was fused into one long bone. Analysis of the bones revealed a fluorine content nearly twenty times that of normal bones used as controls.

C. Bruce Perry.


Because periarteritis nodosa may affect more than one organ or system of the body, the disease gives rise to bizarre and diverse clinical manifestations. It is true that the symptomatology includes fever, asthenia, and loss of weight, but these symptoms are common to many diseases. The diagnosis of periarteritis nodosa should be considered, however, when additional symptoms are produced by vascular abnormalities. Furthermore, the diagnosis should be borne in mind in cases of subacute or chronic conditions of obscure aetiology and when patients are suffering from two apparently unrelated conditions, such as neuritis and nephritis. Biopsy examination of muscles, nodules, and abdominal organs may prove to be of the utmost value.

In a man, aged 36 years, biopsy examination of the left gastrocnemius muscle revealed the lesions of the disease. Significance was attached to the presence of fever, hypertension, haematuria, and muscle pain. Variable changes were detected in the reflexes, and subcutaneous nodules were found in the limbs.

Necropsy findings confirmed the diagnosis in three male patients whose ages ranged from 22 to 34 years. The first patient had fever, hypertension, haematuria, uraemia, and subcutaneous nodules. The heart was found to be...
enlarged, and there was evidence of pericarditis. Anaesthesia and pareses developed in the upper limbs. Haematemesis was a terminal event. Widespread lesions were observed at necropsy. Evidently the haematemesis had been due to periarteritis nodosa, for the disease had affected the arteries in a large gastric ulcer. Vascular lesions in the brachial plexus were responsible for the neurological signs. In the second patient the presence of the disease was suspected because the chief manifestations were fever and hypertension combined with changes in the renal tract and nervous system. The third patient required a laparotomy for a perforated peptic ulcer. In other respects his symptoms were somewhat similar to those experienced by the other patients, yet his medical attendants made no fewer than seventeen different diagnoses of the illness.

A. Garland.

Arthralgia and Arthritis Caused by Infectious Hepatitis.


The authors regard "arthralgia" as a lesion of a joint associated clinically with local pain, stiffness, and tenderness on pressure. On the other hand, when swelling of the joint is present, the patient is said to have an "arthritis". However, "it was often difficult for the patient to distinguish the muscle pain from the joint pain". On the basis of such a group of clinical premises an investigation was carried out on the joint manifestations of 150 patients (93 female and 57 male; 82 less and 68 more than 30 years of age) who suffered from infective hepatitis. Jaundice developed in all cases. The joint manifestations were present in the pre-icteric stage in eighteen patients, in the pre-icteric and icteric stages in nineteen, and in the icteric in nine only. Often "arthritis" or "arthralgia" was the presenting feature of the disease and it lasted for periods varying from a week to 3½ months.

The authors go so far as to suggest that the presence of "arthralgia" or "arthritis" may be of value in the differential diagnosis of jaundice. I. H. Milner.


The mucinoses are characterized by the accumulation of mucin in the cutis. They may be classified in two main groups: the myxoe demas or metabolic mucinoses, and the secondary or catabolic mucinoses.

Of the metabolic mucinoses the most common is generalized myxoe dema associated with hypothyroidism. The localized myxoe demas may be papular, lichenoid, or nodular, occurring on any part of the body and associated with hypothyroidism. They may occur with past or present thyrotoxicosis as bilateral, irregular, firm plaques, often, but not necessarily, on the pre-tibial area (myxoe dema circumscriptum thyrotoxicum), or they may rarely be present as widespread papules with no signs of thyroid dysfunction. Localized myxoe demas with hypothyroidism responds to thyroid medication. The pre-tibial type is related to pituitary hormone activity.

Secondary or catabolic mucinoses are a group in which excess mucin is probably formed as a degeneration product of connective tissue. They are found in sarcomata, fibromata, and lipomata.

It is possible that a considerable part of the mucin in myxoe dema circumscriptum thyrotoxicum is the mucopoly saccharide hyaluronic acid. In two patients with this condition hyaluronidase (150 turbidity reducing units per ml.) was injected into the pre-tibial lesions daily for 10 days. The lesions became softer and flatter and several months later areas of soft normal skin were found within the area of injection.

S. T. Annin.


An investigation was carried out to determine the importance of changes in the cholinesterase and histamine content of the blood in allergic states. The cholinesterase activity of cells and serum was estimated by the methods of Alles and Hawes in the blood of a series of allergic subjects. The values were found to fall mainly within normal limits and there was no relation between variations in the level of cholinesterase activity and in those of other constituents of the blood, including serum protein, serum chloride, erythrocytes, or haemoglobin. These results confirm those of other workers.

The blood content of histamine in allergic subjects was estimated by means of dialysis through viscos tubing and by the Code method. The addition of histidine to fresh whole blood, with and without incubation for 15 minutes at 37° C., led to no increase in histamine content. Blood histamine values were found to be consistently lower during the summer months. The incubation of blood with the allergen to which the patient was sensitive led to no significant increase in histamine content. These findings are at variance with those of Katz and Cohen (J. Amer. med. Ass., 1941, 117, 1782). The authors consider that the finding of normal cholinesterase activity in the blood does not affect the possible significance of the cholinergic nervous system in allergic states, in which there may be hypersensitivity to acetylcholine. They suggest that further work is needed to determine whether histamine is elaborated in the blood of allergic individuals.

R. S. Bruce Pearson.


Sodium salicylate in blood concentrations of the order of 50 mg. per 100 ml. confers no appreciable protection against acute anaphylactic shock in guinea-pigs. With the same technique of shock production the anti-histamine drug, "antisin", was found to protect completely against the immediate fatal effects. In passive Arthus reactions in both guinea-pigs and rabbits, sodium salicylate exerts a protective action whilst the anti-histamine drugs are relatively impotent. The same is true to an even greater extent in the case of the Shwartzman phenomenon. This protective effect of sodium salicylate is not a direct anti-histamine effect but appears to be due to some action on the local blood capillaries. The increased capillary permeability which normally occurs in such hypersensitivity reactions is thus prevented. The implications of these results in respect of rheumatic fever are briefly discussed.—[Authors' summary.]

The effect of the Duran-Reynals spreading factor or hyaluronidase on healthy human skin was investigated. Extract of bovine testes (2.5 turbidity reducing units per ml. of physiological saline) was used, 0.1 ml. being injected intra-cutaneously. The spreading effect was estimated from the profile of the wheal produced, by the use of dyes and by means of radioactive substances. The effect of hyaluronidase used in this manner was noted on allergic subjects with allergens injected intra-cutaneously or applied to a scratch at the site of previous hyaluronidase injection. The wheal resulting from injection of an allergen at such a site disappeared more rapidly than the control wheal: no wheal resulted in such a scratch test though present in the control scratch. With positive patch tests there was no spread of the eczematous reaction in skin treated with hyaluronidase.

Mantoux and trichophyton reactions in skin similarly treated showed less intense inflammation and considerable spreading.

The viscosity of the ground substance of the skin (hyaluronic acid), which is reduced by hyaluronidase, is said to be restored after 48 hours. S. T. Amin.


In describing seven cases of fibrous dysplasia of bone, the authors point out that this condition may easily be confused with single or multiple cysts of bone, with the result that three of their seven patients had been subjected to exploration of the neck for parathyroid tumour, and one of these had died. Fibrous dysplasia is a disease of many synonyms. The condition often begins in childhood with pain or spontaneous fracture. Precocious puberty may occur in females. Irregular areas of rarefaction are seen in radiographs of the bones affected—usually long bones or flat bones. Trabeculation of these areas is common. The histology of the affected bone is characterized by the presence of fibrous tissue and osteoid tissue (young bone as yet uncalcified): vacuolated giant cells with two to ten nuclei were seen in one case. The finding of a normal calcium and phosphorus level in the serum, and of solid tissue on exploration of the bone, are sufficient to exclude hyperparathyroidism, and to spare the patient an unnecessary and possibly dangerous neck exploration. N. L. Eckhoff.


A carefully controlled attempt to confirm earlier reports of the beneficial effect in the treatment of rheumatoid arthritis of the intravenous administration of amidopyrine was carried out on 62 cases of acute and chronic forms of the disease, with an equal number of control cases. With either a 10 per cent. or 23.1 per cent. solution, it was found possible to give between 0.5 and 2 g. amidopyrine daily, but only with great care under good clinical conditions. Vomiting, vertigo, and collapse (two cases) were encountered, but no granulocytopenia. There was some improvement in the arthritis as shown by diminution of pain, increased mobility of joints, and lowered erythrocyte sedimentation rate, but the results in treated cases were not significantly better than in the controls. Dushanka Wolstenholme.


The authors present two cases of haemangioma of the knee joint, a rare condition of which approximately thirty cases have been reported in the literature. Less than five of these were diagnosed correctly before arthrotomy. Articular hemangiomata are classified as (1) juxta-articular—in which, in the knee, there is a palpable tumour involving periarticular structures, particularly the quadriceps muscle: (2) intra-articular, in which the tumour replaces the synovial membrane anterior and posterior fat pad of the knee, with pressure atrophy of articular cartilage and underlying bone as possible sequelae; and (3) a combined type involving both sets of structures. The two cases described belonged to the intra-articular group, and were of a mixed histological pattern—cavernous, capillary, and telangiectatic.

Absence of thrombosis is a feature of diagnostic importance. Differential diagnosis has to be made from meniscus lesions, loose bodies, synovitis, haemorrhagic and haemorrhagic arthritis, and articular tumours. Angiography may be useful in diagnosis. The clinical features in these cases were pain after trauma (which apparently causes haemorrhage), joint effusion, and muscle atrophy. Spontaneous disappearance of a tumour may occur as a result of thrombosis, and this may be aided by x-ray therapy, but surgical excision is regarded as the treatment of choice. W. A. Law.


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The types of herniation of the intervertebral disk which have been described are the common posterior rupture causing sciatrica, a second type of herniation through the epiphysial plate resulting in Schmorl's nodes, and, more recently, anterior displacement of the nucleus pulposus, regarded by French authors as a cause of osteophyte formation on the anterior lips of the vertebral. The authors state, however, that true anterior herniation is rare because of the strength of the ligaments, and describe in this paper the condition which they find more common, in which the herniation forward takes place behind the attachment of the annulus fibrosus, the hernia burrowing obliquely into the spongy bone of the vertebral body. Coincidently this raises a lip of bone, corresponding to the epiphysial ring. The characteristic lesion is narrow in the antero-posterior direction and broad laterally. A series of tomographs illustrate this very well. Differential diagnosis from Pott's disease is most important, and depends on the facts that the hernia has more definite margins and causes slighter symptoms, while the erythrocyte sedimentation rate is not increased. Less common are confusion with persistent vertebral epiphysis and fracture of the anterior margin of the vertebrad.

Mild lumbago may be present, occasionally with some stiffness in the affected segment. There may be also a slight deformity of the vertebral column. There are frequently no clinical signs.

The pathogenesis is discussed. A series of slight injuries, especially before fusion of the epiphysis, may be causative, and non-fusion of the epiphysis is thought to play an important part. The possible relation to Scheuermann's disease is also considered.

Donald McDonald. |
| Gout |

Details of three cases of gouty arthritis treated with pituitary adrenocorticotropic hormone (ACTH) are given. The first patient was a man of 57 who had had typical recurrent attacks for 16 years. He had been treated during attacks with colchicine and a purine-free diet, and between attacks with a low-purine diet and small doses of colchicine and salicylates. Recurrences continued and became more prolonged on this regime, and the plasma uric-acid content was 5.2 to 5.9 mg. per 100 ml. during the intervals. In a subsequent severe attack the hands, wrists, elbows, shoulders, spine, and feet were all involved and the administration of colchicine, in doses increasing to the point of toxicity, with sodium salicylate and neocinopen, brought only partial relief. The uric-acid level in plasma was now 6 mg. per 100 ml. and the erythrocyte sedimentation rate 29 mm. per hour. The patient was completely disabled and unable to feed himself. A single dose of 50 mg. of ACTH was administered intramuscularly and 75 minutes later he had
practically recovered. He could now feed himself and move hands, elbows, and shoulders without discomfort. Joint tenderness disappeared and he was symptom-free for the first time in 49 days. The plasma uric-acid level was not significantly changed, but he remained free of relapse. [The period of observation since treatment with ACTH is not specified but appears to have been not less than 3 months.]

The second patient, also aged 59, had had six typical attacks in 9 years. In his latest attack symptoms progressed for a month, in spite of treatment with a low-purine diet, colchicine, and sodium salicylate. Maximal doses of colchicine brought no relief; his plasma uric acid-level was 6-5 mg. per 100 ml. and erythrocyte sedimentation rate 15 mm. per hour. He was unable to bear weight on the affected foot. One hour after a single dose of 50 mg. of ACTH he could walk and bear weight with comfort, and he has remained asymptomatic since [approximately 5 months].

The third patient, aged 41, had had recurrent gout for 11 years. An attack of 6 weeks' duration was partially relieved by injection of 50 mg. of ACTH, and a further dose of 25 mg. 6 hours later brought almost complete relief of symptoms, the duration of which could not yet be ascertained.

The authors point out that although administration of ACTH alone will bring relief in an acute attack, a rebound of gouty symptoms will usually occur afterwards. This rebound after the cessation of ACTH therapy may be prevented by giving colchicine or salicylates, or both, immediately after the ACTH.

C. L. Cope.

Non-Articular Rheumatism


The author believes that the commonest kind of headache found in eye, throat, nose, and ear practice is caused by localized tender thickenings or nodules in the posterior cervical muscles or less frequently in the temporalis, masseters, sternomastoids, or the frontal and orbicular muscles. Pain is due to sustained contraction of the muscles. According to the muscles affected the pain may be referred to the temporal or frontal regions or the orbit, less often to the ear, and very rarely to the temporal or masseter muscles, with trismus or pain in the throat on swallowing. After long-continued attacks the pain may become generalized over the whole head. Apart from sinus infections or middle-ear inflammation the condition must be differentiated from the vascular headaches—migraine or histamine headache—or Costen's syndrome.

The headache is usually non-pulsating, which helps to distinguish it from the vascular type. Often, when the pain is worst, the patient is most comfortable sitting up and supporting the head with his hands. Of all headaches [?] except those due to intracranial lesions] these are the most sustained. Usually the headache is worse in the morning and gets better during the day as the patient moves about, but if the patient's occupation demands a fixed position of the head (drivers, proof-readers) it increases during the day. As with all headaches it may be made worse by mental strain. Cold draughts are a common cause of increased pain. The majority of cases occur in early and middle adult life, but the condition is found in children, and with increasing age there may be chronic hypertrophic arthritis of the cervical spine.

Wolff and his co-workers have recorded the potentials of the head and neck muscles by electromyography while applying painful stimuli to nose and sinuses. They show that painful stimuli to anterior head structures do not cause referred pain to the back of the head, but that they do cause secondary contracture of the muscles which may persist and be a cause of pain after the stimulus has ceased. They also show that emotional tension is the commonest factor in production of sustained muscular headache. In such subjects minimal stimulation from any cranial structure can intensify already sustained muscular contracture and produce a moderately intense headache. They note too that pain from the soft tissues of the head spreads forward rather than backwards.

Vigorous action potentials can be obtained from the tender nodules but not from non-tender muscles in relaxation. Localized pain and contracture can be produced by injecting 4 to 6 per cent. saline into the neck muscles; injecting procaine hydrochloride into the painful nodules or relaxing them by heat or massage may remove the pain. Histological investigation of the nodules reveals no significant structural change. Probably they are produced by localized spasm, and the pain is due to stimulation of the afferent nerve fibres of the arterial systems of the nodule. The peculiar susceptibility of the posterior muscles may be accounted for by the fact that they are postural muscles with a special constant tonus and a lower metabolic rate than other skeletal muscles.

In two years the author saw 100 cases of headache associated with tender cervical muscles; in the same period he saw only ten cases of severe migraine and histamine headache. Of the patients 35 per cent. came for eye examinations and 65 per cent. for nose or ear examination. He emphasizes the comparative rarity of sinusitis as a cause of headache. Proetz puts the incidence at less than 5 per cent. In about 20 per cent. of cases there was a history of some previous head injury. Simons and Wolff believe that, when arachnoid haemorrhage and subdural haematoma have been ruled out, the majority of post-traumatic headaches are due to sustained contracture of the head and neck muscles.

Treatment is by physiotherapy, massage, neck-stretching, and hot and cold showers—three hours hot to half-a-minute cold—with a small nozzle spray of considerable force. “An unforeseen result of the physical therapy was the discovery of an unsuspected underlying nervous tension and anxiety in a high percentage of the patients. As the physical therapist gained the patients' confidence they gradually revealed many causes of frustration, anxiety, insecurity, or habits not conducive to relaxation and rest.”

Procaine hydrochloride was injected into the tender nodules in several cases and gave instant relief, but recurrence was usual and injections are not without danger. They should be used only for acute and early cases where prompt results are desired.

Cases of apparent indurative headache should always be fully investigated for any other condition of the head which might cause a secondary myalgia before physiotherapy is used.

In a discussion before the Chicago Laryngological and...
Otological Society (ibid., p. 294) Randolph spoke of food allergy as a cause of myalgia of the posterior cervical muscles. He found that sensations referred to the neck muscles were commonly noticed in allergic patients during the course of individual food tests for the specific diagnosis of food allergy, and that such symptoms could be experimentally produced or relieved by administration or avoidance of specific allergenic foods. A few cases were observed in which similar symptoms could be produced by house dust. His personal experience of antihistaminic drugs was disappointing but, as he remarked, as an allergist he usually saw only the patients on whom antihistamines had been tried already and had failed.

F. W. Watkyn-Thomas.


Endocrinology


Experiments are recorded to determine whether the beneficial effects of deoxycortone acetate and ascorbic acid in patients with chronic rheumatoid arthritis could be reproduced in formaldehyde-induced arthritis in rats. Three groups of rats were adrenalectomized (full details given) and 1 part in 100 of sodium chloride was added to their drinking water. After 4 days each group was injected in both hind feet with 0.1 ml. of 2 per cent. formaldehyde. The first group was then given 1 mg. deoxycortone subcutaneously daily, the second 20 mg. ascorbic acid intraperitoneally daily and the third 1 mg. of deoxycortone subcutaneously with 20 mg. ascorbic intraperitoneally daily. On the third day all the rats received a second injection of formaldehyde as before. The experiment was repeated on three further groups of normal rats and in both experiments the changes in the inflammatory process that ensued were estimated by measuring, with screw calipers, the linear cross-section at the ankle daily for 10 days. In both the adrenalectomized and normal rats the treatment given in the group receiving deoxycortone and ascorbic acid was statistically significantly greater than that afforded by either substance alone. In the adrenalectomized rats the effects in the deoxycortone group and in the ascorbic-acid group were identical, but in the normal rats the protection conferred by ascorbic acid was greater than that given by deoxycortone, which appeared to exacerbate the process. The protection given by 1 mg. deoxycortone with ascorbic acid was similar to that obtained by Selye with 5 mg. cortisone. These results appear to point to the possibility that deoxycortone and ascorbic acid are components of an essential enzyme system in relation to the anti-arthritic steroid hormone. The aggravating effects of unaltered deoxycortone may be due to the competitive substitution of this compound for the naturally-occurring hormone.

These results are thought to substantiate the reports made originally by Lewin and Wassén that simultaneous administration of deoxycortone and ascorbic acid is beneficial in chronic arthritis, and the observation of Selye that prolonged administration of deoxytocortone can induce arthritis in rats or may cause exacerbation of formalin-induced arthritis.

[It would have been of interest to know the measurements of a formalin injected lesion over 10 days without any "specific therapy". Perhaps cellulitis would be a better word than arthritis. No body weights are given, and it is not stated whether there was any general water retention in any group.]

Ellis Dresner.


Spinal osteoporosis occurring in women at the menopause is regarded as a disease entity rather than as merely one of atrophic processes that characterize advancing age. Considerable speculation exists on the aetiology of the syndrome. The author, believing that the rarefaction of bones is more likely to be due to endocrine imbalance than to dietary deficiency or achlorhydria, studied the effects of a synthetic oestrogen, dienoestrol, on calcium metabolism in women suffering from postmenopausal osteoporosis. He found that dienoestrol promotes calcium retention to its maximal only when the calcium and phosphorus intakes are both about twice the accepted optimal requirement. The suggested treatment for this syndrome, therefore, includes administration of dienoestrol (0.9 mg. daily), vitamin D (up to 10,000 units daily), and calcium glycerophosphate (30 gr. (2 g.) three times a day). Apart from these, protective orthopaedic treatment is recommended in cases with collapse of vertebral bodies.

In post-menopausal osteoporosis serum calcium, serum phosphorus, serum protein, and serum phosphatase levels are normal and the diagnosis therefore rests on the history and the exclusion of the following other conditions causing rarefaction of bones: metastases of malignant neoplasms, osteitis deformans, hyperparathyroidism, multiple myelomatosis, osteomalacia due to steatorrhea, Cushing's syndrome, and thyrotoxicosis. S. Karani.


The action of the adrenal cortex depends upon its production of three groups of hormones: (1) deoxy cortisolosterones (salt and water factor); (2) glucocorticosteroids (sugar factor); (3) 17-ketosteroids (protein factor). Various investigations were carried out to see whether in patients suffering from allergic complaints there was a relative insufficiency of the adrenal cortex. It was found that disturbances in carbohydrate metabolism were frequently, and disturbances in water and salt metabolism sometimes, present in allergic cases. No investigations were carried out on the excretion of 17-ketosteroids in such cases. The pituitary adrenocorticotropic hormone stimulates the production of adrenal cortical hormone at times of stress, and it is suggested by the authors that in allergic diseases the insufficient function of the adrenal cortex does not allow the body to acquire a power of resistance when exposed to physical or chemical stress, so that it enters into a state of exhaustion. This state is seen during the period between attacks when the patient suffers from symptoms of relative lack of cortical hormones. Thus anything that restores or increases the function of the adrenal
cortex will help the organism to overcome the state of exhaustion and prevent the onset of the next state of shock and contra-shock (Selye), which is that of the allergic attack.

A. W. Frankland.


Evidence for the antibody nature of the antihormones produced to heterologous thyrotrophic or gonadotrophic hormones includes the following: (a) complement fixation and precipitin formation as an accompaniment of antihormone action; (b) times of disappearance and union similar to those of antibody; (c) their production by reticulo-endothelial tissues; and (d) their localization in the globulin fraction of the serum proteins.

The present study deals with the development of antihormone effects to hog-pituitary adrenocorticotrophic hormone (ACTH) in 28-day Sprague-Dawley rats. Normal rats were divided into three groups. Group I (28 rats) received 1 mg. ACTH intraperitoneally 4 times weekly; Group II (24 rats) received normal saline similarly; Group III (3 rats) received 0.1 mg. ACTH 4 times weekly. Adrenal content of ascorbic acid 24 hours after the last injection was higher in Group I than in Group II at the end of one and two weeks, but fell to values equal to those in controls after 6 weeks. It was, however, not possible to ascribe this to refractoriness, since the constant weekly dose of ACTH became relatively smaller as the rats grew. The response after one hour of rats belonging to Group I to a test dose of ACTH (40 μg. per 100 g.) (assayed by the difference in ascorbic acid content of the left and right adrenal removed before and after the test injection respectively) was greatly decreased (8 to 10 per cent. compared with that in control rats given saline (27 and 25 per cent.) at both 5 and 7 weeks. There was no difference in body weight between the two groups but the adrenal weight was greatly increased in those receiving ACTH at all periods.

Serum from rats of all groups was next injected intraperitoneally into hypophysectomized rats (0.25 ml. on the first and second day and 0.5 ml. on the third day). Four to 6 hours after the last injection the injected rats were tested by receiving 60 μg. ACTH per 100 g., with assay of adrenal ascorbic acid before and after. A marked decrease in the response was noted in the rats injected with serum from Group I compared with that in those given serum from Groups II and III.

No precipitating antibodies were demonstrated in vitro when ACTH was used as antigen in concentrations between 0.003 and 0.06 mg. antigen per ml. antiserum. The author suggests that this was because rats in Group I were killed during the negative phase, which is known to follow injection and in the case of antigonadotrophin persists for about 48 hours.

The implications of this refractory state are discussed in the light of administration to man. The dosage is similar and some evidence is available that such a refractory state may develop. There is in addition a possibility that refractoriness to endogenous pituitary hormones may occur.

[For full detail of the techniques used and statistical evaluation the original should be consulted.]

E. G. L. Bywaters.


A 49-year-old man and a 59-year-old woman with rheumatoid arthritis were treated with adrenocorticotropic hormone obtained from pigs' pituitaries. Characteristic effects were noted on the erythrocyte sedimentation rate, blood picture, and 17-ketosteroid excretion. The condition in the man showed no improvement, and his associated cardiac condition deteriorated considerably (possibly on account of the retention of chloride). The condition in the woman underwent "miraculous improvement", this being associated with a fall in the eosinophil count and a fall in temperature to normal, but relapsed as soon as the treatment was discontinued.

B. Nordin.


Two cases of disseminated lupus erythematosus were treated with a Danish preparation of adrenocorticotrophin (ACTH) in doses of 10 mg. two to four times daily for 8 days. In the first case the response was dramatic. Immense subjective and objective improvement occurred within 24 hours. The erythrocyte sedimentation rate (E.S.R.) fell from 130 to 27 mm. The serum formol-gel reaction became negative; the serum globulin level fell from 4 per cent. to 2-9 per cent. The excretion of 17-ketosteroids rose by 1,000 per cent., whereas there was a distinct rise in blood pressure. Deterioration set in immediately treatment was stopped, but 3 weeks later the patient's condition was still better than it had been before ACTH treatment. In the second case clinical improvement occurred and the patient complained of considerable discomfort. There was, however, a rise in the albumin globulin ratio, and the formol-gel reaction became negative. There was temporary pyrexia after treatment. A third patient was given 4 mg. four times daily for 5 days and the condition responded well. The E.S.R. fell from 80 to 30 mm. and the serum globulin level from 3-8 to 2 per cent.

B. Nordin.


Following the introduction of adrenocorticotrophin hormone treatment for rheumatoid arthritis, the author has resumed an experiment on which he originally reported in 1942. In nine cases in which rheumatoid arthritis had been present for not more than four years, calf or human foetal pituitary was implanted in September, 1949, and six of these patients have since been discharged without subjective or objective joint symptoms, with a low erythrocyte sedimentation rate (below 5 in all but one), and in good general condition. Increased mobility and reduced oedema were observed in the joints within 24 hours of the implantation, and subsequently the weight rose and the sedimentation rate fell. There was a fall in the eosinophil count and a rise in 17-ketosteroid excretion. The results were better in patients below 40 years than in older patients.

B. Nordin.

The case is reported of a man aged 54 years with symptoms of Simmonds's disease which had progressed for 19 years. He died of cachexia and was found to have extensive fibrosis of the pituitary gland. Two years before death he fell and injured his right knee, in which arthritis and ankylosis subsequently developed. The relation of arthritis to Simmonds's disease is discussed. A. C. Crooke.


Immature mice received a daily injection of 1-25 mg. of cortisone for 6 days and mature mice were given double this dose for 9 days. All the mice lost weight and many of them died. The tretoneoprotected a fall in lymphocyte count and a corresponding increase in the polymorphonuclear leucocyte count. Pathological findings included necrotic foci in the liver, retarded development of the testes or suppression of spermatogenesis, and a failure to withstand infection (granulomatous nodules containing Corynebacterium pseudotuberculosis murium were found in the treated mice but not in control mice) or stress (leakage from a water bottle damped one of the cages and all the mice in it died within 48 hours). Weight loss was particularly great in the following tissues and organs: fat, hibernating fat, thymus, spleen, and salivary glands.

The general effects resembled the general adaptation syndrome though the adrenal cortex was atrophied. This suggests that the steroid produces the effects directly and its excess in the circulation suppresses adrenocorticotrophin secretion by the hypophysis. Peter C. Williams.


Male rats were divided into three groups. The first (10) served as normal controls, the second (6) were hypophysectomized, and the third (8) were partially hypophysectomized by removal of the rostral part of the anterior lobe and the whole of the posterior lobe. All the rats had a left adrenalectomy 48 hours after the operation and were then exposed to cold (0°C.) for one hour and killed. The ascorbic acid content of the left and right adrenal glands was compared. A great difference was observed between the content of the two glands in the control group and no difference in four rats of the hypophysectomized group, in which hypophysectomy was proved to have been complete. The third group in which the hypothalamo-hypophysial pathways were severed did not differ significantly from the control group.

In a second experiment the pituitary glands of freshly killed rats were aspirated into a needle and injected into the anterior chamber of the eye of sixteen other rats, which were hypophysectomized 24 hours later. Four weeks later left adrenalectomy was performed, the rats were exposed to cold for one hour, the right adrenals were removed, and the ascorbic acid contents of the two glands was compared. In four of the eighteen rats it was proved that transplants were viable and that hypophysectomy had been complete, and their adrenal ascorbic acid contents were compared with those of normal controls similarly exposed to cold. The reduction in ascorbic acid content of the right adrenal glands of the experimental animals did not differ significantly from that of adrenals in the controls. These experiments are regarded as evidence that the denervated pituitary gland functions and is capable of responding to acute stimulation in the absence of neurological connections. A. C. Crooke.


Male rats were hypophysectomized and their pituitary glands were collected in saline. The glands were then grafted either into their original sites in the sella turcica, or into the eye or the spleen; in thirteen of 36 rats so treated histologically viable grafts of glandular cells were subsequently found. These rats together with control groups of normal and of hypophysectomized non-grafted rats received intravenous injections of histamine (1 mg. per 100 g. body weight) after preliminary left adrenalectomy. One hour later the right adrenal was removed and the ascorbic acid content of the two adrenal glands was compared. The ascorbic acid content of the left adrenal glands of the grafted rats was intermediate between that of the normal and the hypophysectomized controls, indicating some functional activity of the graft. An hour after histamine injection the fall in ascorbic acid content, as measured by the difference between left and right adrenal gland contents, was also intermediate between those in normal and hypophysectomized controls. This showed that the grafts were able to respond to acute stimulation in the absence of a neurological or a vascular portal system as described by Harris, although they were too small to allow normal growth or prevent atrophy of the adrenal cortices. A. C. Crooke.


Further studies have been made in Stockholm on a 58-year-old patient with rheumatoid arthritis with regard to the effect of pituitary adrenocorticotropic hormone (ACTH) on the eosinophil count and on urinary excretion of adrenaline and noradrenaline. These substances were extracted and assayed by observing their effect on blood pressure in the cat, and on isolated hen's caecum. During the administration of ACTH or ACTH peptide, the number of circulating eosinophil leucocytes fell to zero; at the same time there was a decrease in the total urinary excretion of catechols, of which adrenaline rather than noradrenaline was the predominating constituent. G. S. Crockett.


The authors, working at the Serafimerlasaret, Stockholm, and the University of Upsala, describe the
Effects of the preparation of pituitary adrenocorticotrophic hormone (ACTH) and a peptic digest of ACTH protein in a case of rheumatoid arthritis in a man aged 58. The effect of the two substances was identical: there was great clinical improvement, sodium retention, increase in urinary uric acid and 17-ketosteroid output, and a decrease in the number of circulating eosinophils—all temporary effects manifested only while the preparations were being administered.

**Effects of Pituitary Adrenocorticotrophic Hormone (ACTH)**


Adrenal cortical extracts and pituitary adrenocorticotrophic hormone (ACTH) have been found to be effective in the treatment of conditions other than rheumatoid arthritis, such as rheumatic fever, lupus erythematosus, and gout. This response would seem to indicate some relationship between these various diseases (as has previously been suggested by Arnold Rich). This paper deals with the treatment with ACTH of two cases of rheumatoid arthritis, two of disseminated lupus erythematosus, one of dermatomyositis, two of rheumatic fever, and one of status asthmaticus. The purpose of the investigation was to study the clinical course, toxic complications, and the degree of stimulation and response of the suprarenal gland. These changes were assessed by means of eosinophil and total leucocyte counts and estimations of the sodium, potassium, chloride, and nitrogen balance, and the output of urinary 17-ketosteroids. Two patients, one with arthritis and one with lupus erythematosus, relapsed completely, despite prolonged treatment and increased dosage, while two others, one with lupus erythematosus and one with dermatomyositis, remained in remission. In one case of arthritis and in the case of asthma the response to the drug was dramatic. In five cases there was an eosinophilic leucopenia following treatment, and in all cases the sodium content of urine was reduced. Consistent changes in the serum sodium and chloride levels were not found. The effects on the serum potassium content and the nitrogen balance were equivocal. It would appear that administration of ACTH decreases carbohydrate tolerance, as thirteen patients developed a slight glycospuria. The excretion of 17-ketosteroids was increased in all cases. Severe potassium deficiency and also encephalopathy, either drug-induced or due to the disease, occurred in the case of acute dermatomyositis. One patient with acute rheumatoid arthritis developed signs of Cushing's syndrome after prolonged treatment: there was, however, neither hypertension nor diabetes. One case failed to respond and the patient died, the presence of antihormones being a possible explanation.

It is concluded that adrenocorticotrophic hormone obviously exerts a profound influence on collagen disease. Presumably it acts by "supporting" the adrenal, which is adversely affected in these hyperinsensitive states. The technique of repeated short courses of treatment may help to prevent toxic manifestations. The authors sound a wise warning against administration of the drug without laboratory control.


Endocrine Imbalance in Rheumatoid Arthritis and Rheuma-


**General Pathology**


Hyaluronidase was the name given by Meyer and Palmer to an enzyme found in autolysates of a type II pneumococcus which is capable of hydrolysing hyaluronic acid. The hyaluronidase activity was shown to be similar to the activity of the testicular spreading factor of Duran-Reynals, and it is now widely accepted that the two factors are identical.

In two patients with mucinous infiltrations of the skin, treated by local injections of hyaluronidase some improvement was noted. The authors make no particular claims, stating that no control injections with other materials were made and that the hyaluronidase used may have been inactivated during its preparation for injection. There is a good review of the literature.


The author reports the case of a 41-year-old woman who, for cosmetic reasons, desired treatment for a plaque of localized myxedema on each shin. These two plaques had been unaffected by thyroid extract and propylthiouracil. The left leg was treated by local injections of hyaluronidase, of which a dose of 300 turbidity-reducing units produced systemic symptoms, but smaller doses gave only local reactions. The size of
the plaque was considerably reduced by the treatment. It is suggested that this was the result of hydrolysis of the hyaluronic acid contained in the skin; but foreign-protein reaction cannot be ruled out, especially as there is some doubt about the amount of active enzyme in the preparation used. The plaque on the right leg, which was treated by incisions to allow mechanical drainage of mucin, also became much smaller. *James Marshall.*


The Significance of the Skin Reaction to Histamine in Rheumatic Subjects with Regard to Focal Toxicosis. (Die Bedeutung der Histamin-Haut-Reaktion bei Rheumatiern im Hinblick auf die Fokaltoxikose.) Müller, P. (1950). Z. Rheumaforsch., 8, 332.

Other General Articles


ABSTRACTS


