ABSTRACTS

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

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

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

Acute Rheumatism


As part of a controlled clinical trial organized by the American Heart Association, 41 patients with rheumatic fever at the Hospital for Sick Children and the General Hospital, Toronto, whose ages ranged from 4 to 41 years, were divided arbitrarily into three groups, the groups being treated with ACTH, cortisone, and aspirin respectively for 6 weeks. The results of treatment were not significantly different in the three groups. In patients receiving ACTH or cortisone the erythrocyte sedimentation rate fell more rapidly than in patients receiving aspirin, but it often rose quickly after cessation of treatment. There was no significant difference between the groups in the effect of treatment on cardiac lesions. About 75 per cent. of the hormone-treated patients had moderate or severe relapse when treatment ceased, whereas relapse was uncommon in the patients receiving aspirin.

While the authors point out that more comparative clinical trials are required, they nevertheless consider that salicylates are the most practical agents for the treatment of rheumatic fever, allowing the erythrocyte sedimentation rate to be used as a guide to progress.

Kathleen M. Lawther.


A new long-acting preparation of penicillin, N^1 : N-dibenzylethylenediamine dipenicillin-G (“bicillin”), was given to 135 children and eight adults with rheumatic fever over a 10-month period as a prophylactic against Group-A streptococcal infection. The drug was given intramuscularly in a dosage of 300,000 units once a week, or 600,000 units once every 2 weeks, or 1,200,000 units once a month, a total of 1,753 injections being given.

It was found that after injection of 300,000 units the serum concentration of penicillin was consistently low, rarely exceeding 0.2 unit per ml.; 7 days after subsequent weekly injections penicillin was detectable in the serum in a concentration of 0.02 to 0.09 unit per ml. in almost all patients. After injection of 600,000 units the drug was detectable in the serum for as long as 12 to 14 days. Ten patients received a total of 1,200,000 units in two doses, each of 600,000 units, administered simultaneously into the buttocks. Penicillin was detectable in the serum in 100 per cent. of the patients at the end of one week, in 89 per cent. at the end of 2 weeks, and in 67 per cent. at the end of 4 weeks, the concentration varying from 0.04 to 0.08 unit per ml. In another group of seventeen patients who received a single injection of 1,200,000 units, the penicillin level in the serum was assayable at the end of 3 weeks.

The authors state that in most cases a single injection of bicillin was effective in eradicating Group-A streptococci from the pharynx of carriers. In two patients urticarial reactions developed, but subsided within 72 hours. Local reactions were somewhat more severe than those observed after injection of benzyl penicillin or procaine penicillin. It is suggested that bicillin merits further trial as a long-acting prophylactic agent against rheumatic fever.

R. S. Illingworth.


The authors describe five cases seen at the Fourth Medical Clinic, Belgrade, in which subacute bacterial endocarditis was followed by a recurrence of acute rheumatic carditis, in two of the cases after a considerable interval, while in the other three the one condition passed...
imperceptibly into the other. It is this latter type of case that may prove so difficult from the point of view of treatment, for the onset of the rheumatic process, bringing with it a persistent fever and raised erythrocyte sedimentation rate, may be thought to be only a continuation of the bacterial infection. These cases the authors successfully treated with antibiotics followed by ACTH (corticotrophin) or cortisone. It is not thought that there is any fundamental difference between bacterial endocarditis in which a positive blood culture is obtained and that in which such a culture is not obtained. *G. S. Crockett.*


In this paper are reported the final results of a 5-year study of the effect of oral penicillin in preventing recurrences of rheumatic fever in Chicago school-children. [For an account of the first 3 years’ findings, see *J. Amer. med. Ass.,* 1950, 142, 20; *Abstracts of World Medicine, 1950, 7, 657.*] During the first 2 years of the study the authors found that the administration of 200,000 units of penicillin four times a day for the first week of each month from October to June caused the most satisfactory reduction in the incidence of Group-A β-haemolytic streptococci in throat swabs and in the number of recurrences of rheumatic fever of any of the schedules tried, and this was therefore adhered to for the 3rd, 4th, and 5th years. The total number of recurrences occurring during these three rheumatic-fever seasons in the treated children (totalling 133 patient-seasons) was two (1·5 per cent.), compared with 26 (16·99 per cent.) and 39 (20·21 per cent.) in two control groups (153 and 193 patient-seasons respectively). As 50 per cent. of all recurrences in Chicago occur between February and March, they suggest that in these months penicillin should be given in alternate weeks, and at other times in the year for one week each month. They do not recommend the use of lozenges, because of the development of stomatitis. They consider that prophylaxis should be continued through puberty and possibly longer. In no case was penicillin resistance found in Group-A haemolytic streptococci. Approximately 50 per cent. of the Group-A strains isolated during the 4th and 5th years could not be typed, for which no explanation is offered. *R. S. Illingworth.*


Chronic Articular Rheumatism

(Rheumatoid Arthritis)


The authors, working at the Municipal University of Amsterdam, report the results of prolonged treatment with ACTH or cortisone of eight children, aged 2½ to 15 years, who were suffering from rheumatoid arthritis. Dosage was low, namely, 1 to 3 mg. ACTH four times daily or 15 to 20 mg. cortisone twice daily.

Of the six patients observed for 3 months or more after the cessation of treatment, the results were good in four and fairly good in two. The remaining two patients were still under treatment; one was doing well on small doses of cortisone, but the other, a girl of 2½ who had had ACTH and gold salts as well as cortisone, developed nephrosis—the only poor result in the series. Although the clinical results in most of the cases were good, the final erythrocyte sedimentation rate was within normal limits in only two. Resistance to ACTH developed in two patients, but improvement was maintained with a course of gold therapy. In one case stretching of the knee at operation was only maintained with intra-articular injection of cortisone; subsequently administration of cortisone had to be stopped because of delayed healing of the wounds.

The authors conclude that children with rheumatoid arthritis can be maintained in good condition for many months on small doses of ACTH or cortisone, but that this does not render orthopaedic measures or gold therapy superfluous. *H. F. Turney.*


With the view of inhibiting the tissues’ requirements for ATP [adenosine triphosphate] chloroquine was used therapeutically in rheumatoid arthritis. Three times weekly, 0·5 g. was administered to 28 patients for 6 months without toxic effects; 21 patients improved considerably, one had complete remission, one did not improve. A view of rheumatoid therapy is offered which finds biochemical rationale for the use of chloroquine, gold, cortisone, and other anti-rheumatic agents. [Author’s summary.]
ABSTRACTS


The authors claim that the radiological changes of rheumatoid arthritis precede obvious clinical signs by months or years. It is usual to look for narrowing of joint-spaces as one of the first signs of the condition, but this, according to the authors, is a relatively late manifestation. Long before this happens there is a noticeable alteration in trabecular structure of the bones, best seen in the capitate (os magnum), together with “micro-geodic” appearances—small, clear, cyst-like areas (round or oval, encapsulated or non-encapsulated) varying in size from that of a pin’s head to that of a small pea and usually found in the carpus or at the extremities of the metacarpal and phalangeal bones. That these appearances have escaped notice for so long may be due to faulty radiographic technique and apparatus.

The trabecular changes are difficult to describe, but there is no decalcification and the bony structure tends to assume a “pumice-stone” appearance. The clear areas were found, in twenty cases out of 150, months or years before the development of the usual radiological changes in the joints. Where a portion of the circumference of such an area is missing it becomes a “marginal erosion”. The diagnosis must, of course, be made in association with the clinical picture, since similar changes have been noted, for example, in cases of herps zoster of the cervico-brachial region with trophic changes; the mechanism of production may therefore be connected in some way with the sympathetic nervous system. D. Preiskel.


ACTH (corticotrophin) and cortisone on chrysotherapy was studied in 81 cases of rheumatoid arthritis at the Rheumatological Clinic, Faculty of Medicine, Paris. The cases were divided into three groups:

1. 23 patients who developed signs of intolerance to gold.
2. Forty patients who showed no signs of intolerance; and
3. Eighteen patients who had received no previous gold treatment.

The results showed that in Group 1, sixteen patients were able to tolerate and benefit from combined hormone and gold therapy, but in most cases the effect was transient and reactions occurred after cessation of hormone therapy; in Group 2, twelve patients developed signs of intolerance to gold during or after treatment with hormones; in Group 3, five patients showed signs of intolerance during or after hormone therapy. The authors conclude that combined hormone and chrysotherapy gives reasonably good results in the treatment of rheumatoid arthritis in that remissions are induced in about 50 per cent. of cases provided that chrysotherapy is started before, or at the same time as, the hormone therapy, but that treatment with gold is useless after hormone therapy. Kathleen M. Lawther.


After a careful study of 27 cases of “chronic evolutive arthritis” in men, the authors conclude that this disease in the male differs in aetiology and course from that seen in the female. They found a history of previous gonococcal infection in seventeen of their cases.

They note that the onset, which is generally in middle life, is often monarticular and acute. These circumstances lead frequently to a preliminary diagnosis of rheumatic fever or of gout. The joints first affected tend to be those of the lower limbs, but diagnostic changes are to be looked for in radiographs of the hands and wrists. In these situations small areas of decalcification affecting the epiphyses are often present in the very early stages of the disease. These changes are accompanied by a raised erythrocyte sedimentation rate, anaemia with leucocytosis, and a positive Vernes flocculation reaction.

The origin of this syndrome is thoroughly discussed, but no single aetiology appears to satisfy all the requirements; there appeared to be some evidence that nervous, infective, allergic, and endocrine factors were concerned in most of the cases studied. W. S. C. Copeman.


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Case of Felty’s Syndrome with Abnormalities of the Blood Plasma. (Sindrome di Felty con manifestazioni emoplasmoapatiche.) MARZANI, P. C. (1953). Minerva med., Torino, 1, 861. 7 figs, bibl.


(Osteo-Arthritis)


Attention is drawn to the hitherto unsatisfactory results of the treatment of hallux valgus and hallux rigidus. The operations of hemiipheralgectomy and removal of metastarsal heads may improve the look of the foot, but in many cases they do not relieve pain and the late results are often poor. The author discusses the aetiology of hallux valgus and hallux rigidus and the various operations which have been performed in the past. He then describes the operation of arthrodesis of the great toe joint in a position of 30 degrees of extension, which he prefers to all other operations as it leads to better walking and preserves the strength and function of the great toe. A longitudinal incision is made after a tourniquet has been applied to the limb, the metatarsal and proximal phalanx is cleared, and the hard eburnated bone is removed from the lower end of the metatarsal and the proximal end of the phalanx. The two bones are then fitted together in a position of 30 degrees of dorsiflexion and 15 degrees of abduction of the toes and fixed by a metal screw extending from the lateral aspect of the metatarsal to the inner aspect of the phalanx.

Of 41 such operations for hallux valgus, 25 were satisfactory, and of seven for hallux rigidus, three were satisfactory. When allowance was made for other causes of pain in the foot or disablement a further fifteen operations were considered to be satisfactory also.

K. H. PRIDIE.


(Spondylitis)

Involvement of the Manubriosternal Joint in Ankylosing Spondylitis. (Le comportement de l’articulation manubrio-sternale dans la spondylarthrite ankylosante.) FRANÇON, F., FAIDHERBE, P., DU LAC, G., and LEBLANC, G. (1953). Presse méd., 61, 109. 5 figs, 4 refs. The authors, writing from Aix-les-Bains, point out that the manubriosternal joint is not infrequently affected in patients suffering from ankylosing spondylitis, in the same way that this disease manifests itself in the sacro-iliac and the pubic joints. This interesting lesion, although fairly common, rarely gives rise to symptoms. A number of excellent radiographs are reproduced in which lesions varying from irregularity of the joint line to complete ankylosis are demonstrable. This lesion does not generally call for special treatment, although in cases associated with pain local injections of various types may be found helpful.

W. S. C. Copeman.


(Miscellaneous)


The action of phenylbutazone ("Butazolidin") and "Butapyrin" (a mixture of phenylbutazone and amidopyrine and known also as "Irgapyrin") in 409 patients suffering from various rheumatic disorders or gout was investigated by the authors at the Stanford University School of Medicine, San Francisco. The disease conditions included, in addition to gout, rheumatoid arthritis, ankylosing spondylitis, mixed rheumatoid and osteo-arthritis, psoriasis with arthritis, and a miscellaneous group of peritendinitis of the shoulder region, osteo-arthritis, postmenopausal osteoporosis, and non-rheumatic disorders. The results in each group were assessed according to the therapeutic criteria of the American Rheumatism Association. There was no significant difference in effectiveness between irgapyrin and phenylbutazone in cases of gout, and no important difference was demonstrable in the other groups. The authors state that a "uniformly striking reduction of uric acid content in the blood [no figures given] would suggest that the action of the drugs in gout is indeed specifically concerned with the metabolism of urates". In rheumatoid arthritis the anti-rheumatic effect depended on continued administration.
ABSTRACTS


The authors report their results in a series of fifty patients with chronic arthritis treated with phenybutazone at St. Stephen's Hospital, London. Of 34 patients with rheumatoid arthritis, objective improvement was noted in twenty, no change in twelve, and two were worse; nineteen patients experienced some subjective improvement. There was no consistent change in the erythrocyte sedimentation rate. Of three patients with ankylosing spondylitis, only one was improved both objectively and subjectively, while of eleven patients suffering from osteoarthritis, seven were improved objectively, the other four remaining unchanged. Side-effects occurred in 22 patients, and varied from abscesses at the site of injection to rash. The commonest effects were gastro-intestinal symptoms and oedema, but a more serious one was massive melena, which occurred in two patients.

Discussing their findings, the authors suggest that the effect of phenybutazone is mainly analgesic and not in any way similar to that produced by ACTH. They consider that the high incidence of toxic reactions necessitates careful supervision of the patients receiving this drug, but that nevertheless phenybutazone has a place in the management of chronic joint disease.

[Unfortunately very little information about dosage is given in this paper beyond the statement that this never exceeded 1 g. per day and that the maximum total dose given was 73 g.] William Tegner.


With the object of studying the familial spread of rheumatic disease, two contrasting groups of families have been kept under observation at Yale University School of Medicine for periods of 13 to 23 years. The groups had this in common—that the contact or index member of each family had been a patient at the New Haven Hospital, Connecticut, at some time during the years 1929-39. But whereas the contact members of the larger group, numbering 122, had all suffered from rheumatic fever, the contact members of the smaller group, numbering only 35, were non-rheumatic children, and "it was not known at the time of selection that any sibling of the contact case had rheumatic fever". [Presumably this means that, so far as was known, none of the siblings had ever had rheumatic fever.]

Previous communications have been published reporting the results of this study up to 1939. The present report is concerned with the families which were still available for study in the period 1947-9, namely, forty of the original 122 rheumatic and 21 of the original 35 non-rheumatic families. [The authors seem less concerned about the loss of 68 per cent. of the rheumatic families than about the loss of 40 per cent. of the non-rheumatic families, in which group, by substitution, the numbers were increased to thirty.]

The incidence of new cases of rheumatic fever, rheumatic heart disease, or both, was found to be higher in the rheumatic families than in the controls. In most instances familial spread was according to order of birth from eldest to youngest—even though not all the members were affected—and there was a tendency for successive cases in a family to occur at progressively higher ages.

The authors found many instances in which streptococcal disease preceded the onset of rheumatic fever, and some evidence that "the occurrence of rheumatic fever in the children approximated the pattern of a single autosomal recessive gene except in the mating of two parents with the disease".

In 1930-31, when the incidence of rheumatism was at a peak, the two groups of families were comparable as regards distribution of family size and income level (the income of 90 per cent. of both groups being judged too meagre to assure adequate nutrition, clothing, and the basic essentials of family life), but poor housing and overcrowding were significantly more prevalent among the rheumatic families. This leads the authors to speculate whether the inherited factor, if it does exist, may be an altered response to repeated infection, enhanced by the presence of poor housing and overcrowding, rather than an increased susceptibility to rheumatic fever per se.

[No indication is given of the method by which the contact members of either group were originally selected. Furthermore, in the absence of evidence to the contrary, it is not unreasonable to suppose that the forty rheumatic families were the families in the original group in which most of the subsequent cases of rheumatic disease occurred and just for this reason were available for study in 1947-9. The alternative possibility that the findings are explicable in the light of the bias present in such select data cannot therefore be entirely overlooked.]

E. Lewis-Faning.


In 1944, one of the authors described the clinical and radiological forms of occipito-atloid arthritis. Many patients (30-4 per cent.) complain of orbital pain in the superior internal orbital angle, annoying sensations in the retrobulbar region, and supra-orbital pain. All
these symptoms appear or are increased with eyestrain which the authors call the "ocular mask" of this arthritis. They explain the pathogenesis of these oculor symptoms as a metameric projection of the suffering joint and muscles. Two clinical cases are presented.

(Author's summary, abridged.)


The authors report from St. Nicholas Hospital, London, two cases in which the patient was admitted with severe nasal sepsis and swelling due to a chronic ulcerating granulomatous infection and died of generalized periarteritis nodosa within 6 months. The histological appearances on biopsy of the nasal mucosa in the first case led to a diagnosis of "giant-cell granuloma of nasal sinuses" and a tentative diagnosis of periarteritis nodosa, which was later proved to be correct. In the second case sinus infection preceded by 3 months the development of a granulomatous ulcer on the septum, the macroscopical and histological appearances of which were similar to those in the first case. Death occurred later from periarteritis nodosa.

The authors review the scanty literature on this subject. Assuming that "malignant granuloma of the nose" (Woods, Brit. med. J., 1921, 2, 65) might be a variant of the syndrome, they obtained histological specimens from four cases of the latter disease, but were unable to find evidence of periarteritis. Nonetheless, in several cases of malignant granuloma of the nose reported in the literature the patient died later from periarteritis nodosa. The question whether the nasal infection is the cause of, or merely a lesion due to, periarteritis nodosa is discussed.

J. Naish.


The author here reports the use of sodium para-amino-salicylate in five selected arthritic cases: two cases of rheumatoid arthritis were given this substance orally, in a dose of 1-5 g. daily; two cases of osseous-arthritis (one of spine, one of knees) were given it orally and also parenterally into the periarticular tissues; and in one case of ankylosing spondylitis it was given in large doses by mouth and by paravertebral injection. In all these cases, the author describes dramatic improvement, which had been well maintained by smaller doses and injections for periods of 4-10 months.

[It should be noted that these cases are selected ones, and no objective criteria of progress are given: further confirmation would appear desirable.] B. E. W. Mace.


An account of the general and ocular signs—sluggish bilateral iridocyclitis, complicated cataract, and band-shaped opacity of the cornea—with description of a case. The possibility of such causes should be considered when iridocyclitis occurs in a young child.

A. A. B. Scott.


Franceschetti gives an extremely valuable survey of the ocular complications of inflammatory rheumatism and deserves special acknowledgment for his clear classification of the different forms of rheumatism.

The first group comprises the acute forms. In cases of acute articular rheumatism (maladie de Bouillaud) ocular complications do not occur, not even iritis. The author summarizes Reiter's disease and Behçet's disease under the name of rheumatoid affections.

The second group comprises the chronic forms. In adults iritis is seen especially in cases of Bechterew's disease and rheumatoid arthritis. In children there is a so-called oculo-articular syndrome characterized by signs of iritis, complicated cataract, and corneal degeneration in the form of streaks. There are two aetiological theories: rheumatoid arthritis in children, or Stull's disease. Their differentiation is not easy. Polyadenitis and splenomegaly must be regarded as indicative of Stull's disease.

Special reference is given to the affections of the sclerotic although the affections of the anterior and posterior uvea are the most frequent in rheumatism. Franceschetti mentions episcleritis, real scleritis or kerato-scleritis, and scleromalacia.

For details of the modern treatment of these affections the original paper must be consulted. The author concludes with the statement that in many cases of rheumatism the ocular alterations and complications allow a more exact and detailed diagnosis of the primary articular affection.

A. Huber.


Report of a case of a 22-year-old female with recurrent aphthous stomatitis, nodular cutaneous lesions with pain in the lower limbs, vaginal discharge, and bilateral iritis. The biopsy of a cutaneous nodule showed normal epidermis, granuloma in the derm and hypoderm, histiocytes, lymphocytes, neutrophil polynuclears, and some
eosinophils and giant cells similar to erythema exudativum multiforme. In several places there were peri-vascular nodules similar to erythema nodosum. Systemic and local cortisone considerably reduced the frequency and intensity of the muco-cutaneous attacks and cured the iritis. For 8 months the patient has continued well without any treatment. H. Moutinho.


Discussion of a personal case of the Gougerot-Sjögren syndrome with severe progressive polyarthritis and ocular lesions. Systemic injections of cortisone were effective against the arthritis but failed to improve the eye disturbances which were controlled by local instillations of cortisone. S. Vallon.


Treatment with vitamin A, thiamine, riboflavin, nicotinic acid, ascorbic acid, folic acid, Campolon, Hepar-glandol, Percorten, etc., was unsuccessful. A. Huber.


Clinical peculiarities included benign course, lack of true hypopyon, presence of fever and pain in the joints, and concomitance of acute conjunctivitis and aphthosis. The inoculation of the aqueous into chicken embryos, the haemo-agglutination test, and the complement-deviation test (antigen: allantoic membrane and amniotic liquid) gave negative results. N. Pagliarani.


A new approach to many diseases has been provided by Selye's studies of the adaptation syndrome, and those of Kendall and others on the corticotropic and adrenal hormones. A common factor, alteration of collagen, is now accepted in many dissimilar affections, such as asthma, rheumatoid arthritis, and periarteritis nodosa. Certain parts of the organism have an abundance of collagen: walls of blood vessels, synovial membranes, peritoneum and pericardium, skin, sclera, and cornea. The first alteration of collagen is a fibrinoid degeneration, followed by proliferation of fibroblasts and infiltration with leukocytes and histiocytes. More intense involvement leads to exudation of mucoid substance, alterations of tissue cells, and even to necrosis. Collagenous disease is essentially a type of hypersensitivity involving circulating antibodies and collagen which is fixed to the tissue. The relation of the adrenal gland to immune processes and the action of its hormones upon tissue of mesenchymal origin are well known. Various irritants of the anterior lobe of the pituitary stimulate the secretion of corticotropic hormones (ACTH), which in turn stimulate the adrenal gland. The final production of cortisone is the desired end-result of the reaction. In an unknown manner, this hormone alters the antigen-antibody reaction, suppressing the toxic effects of hypersensitivity and expediting the beneficial reaction of immunity. As a result resistance is increased with little alteration of collagen. Cortisone also has an inhibiting effect upon hyaluronidase. Several collagen diseases involve the eye: periarteritis nodosa, rheumatoid arthritis, scleromalacia, scleroderma, dermatomyositis, and acute disseminated lupus erythematosus.

James W. Brennan (Amer. J. Ophthal.).


Disk Syndrome


The results are reported of the treatment of 198 cases of lumbar backache and sciatica by arthrodesis according to Bosworth’s grafting technique at the Hôpital Cochin, Paris. The grafts were taken from the posterior aspect of the ilium through an extended posterior incision. The posterior incision over the iliac crest produces an area of anesthesia in the buttock and was not used unless a large graft was required. It was noted that the area from which the graft was taken remained painful for some months in many cases. Four deaths occurred. There were two cases of local scarring due to plaster pressure and one case of infection, the latter being followed by an excellent result. In twenty cases there was thrombophlebitis, one of the deaths being due to pulmonary embolism.

The functional results were excellent in 122 cases (62 per cent.) and good in 39 (19 per cent.), with failure in 33 (17 per cent.). The results were significantly less satisfactory in the 27 cases of reintervention after a previous operation for prolapsed intervertebral disk, and failures occurred in twelve (44 per cent.) of these cases. The mechanical success or failure of the graft was assessed radiologically after the fifth month. With the pelvis fixed, antero-posterior views were taken in right and left lateral rotation and then lateral views in flexion and extension of the spine. Only if no shift of the lower lumbar spine was seen was the graft regarded as successful. Immobilization was complete in 85 per cent. of cases, failure being very rare where one interspace only was grafted, but much commoner when two or three spaces had to be bridged. The site of pseudarthrosis, when it occurred, was always at the upper end of the graft, the lower part fusing well with the sacrum, probably owing to its good blood supply. Of 24 cases of pseudarthrosis, bad technique was blamed for thirteen, failure to fix the graft effectively for nine, and post-operative fails for two. The greater the number of spaces to be covered, the longer the period of immobilization necessary—for one space, one month; for two spaces, 2 months; and for three spaces, 3 months. For grafts covering a single space, rest in a flat bed only was employed, but when a larger space had to be covered, a plaster bed was used. The patient was fitted with a corset on getting up.

Failure of the graft to consolidate explained a certain number of the functional failures, but not all: of the 24 patients with pseudarthrosis, seven were comfortable. It is more interesting to study the 24 other cases where, in spite of sound fusion, pain persisted. Persistent root changes due to adhesions following long-standing sciatica were blamed in ten, lumbar osteo-arthritis in five, arthritis of the L4-5 articulation after fusion of L5-S1 in two, early immobilization and sacro-iliac arthritis in one case each, and psychological causes in three cases; no cause was found in two cases.

The results were good in 39 out of 45 cases of spinal anomalies (excluding spondylolisthesis) of the transitory type (87 per cent.), and the method is regarded as most successful for the treatment of lumbar pain, with or without sciatica, in the presence of such abnormalities. In 100 out of 147 cases of sciatica and in six out of 51 cases of uncomplicated backache a prolapsed disk was found at operation. The disk should therefore be explored before arthrodesis is undertaken. Whether arthrodesis should be carried out after the removal of a prolapsed disk is a more difficult question and the answer depends on many factors. For the patient whose work entails heavy labour, however, there is no doubt that it gives the best chance of cure and return to work.

This is an excellent summary of the fate of spinal grafts. The high percentage of success speaks well for the “H” graft with cancellous chips, a procedure which many surgeons have adopted. The notably short period of bed rest after a single-space graft is worth noting—far too much time has been spent by patients in the past in plaster beds, which should be reserved for complicated grafts involving more than a single space. The most disappointing feature of the report is the high percentage of cases of thrombophlebitis, to which the taking of the graft is probably an important contributory factor. A bone bank, if available, should reduce this complication.

J. G. Bonnin.

Full-Column Technic in Lumbar Disk Myelography.

MAINS, L., NEWMAN, C. M., and WOLF, B. S. (1953). Radiology, 60, 18. 13 figs, 8 refs.

The limitations of myelography in lumbar disk lesions, especially when small amounts of opaque medium are
used, are discussed, and a new technique, employed at Mount Sinai Hospital, New York, in which relatively large quantities of “pantopaque” are used, is described. The authors found that in 50 per cent. of cases, with the patient in the erect position, 6 ml. pantopaque reached the body of L4 and that in the remaining cases, 9 or 12 ml. was required; on a few occasions as much as 24 ml. was injected “without ill-effect”. Screen examination was reduced to a minimum, and antero-posterior, lateral, and 45-degree oblique films were taken. If no lesion was observed, then 30-degree and 60-degree oblique films, were examined before the medium was removed.

It is admitted that small defects within the subarachnoid space may be masked by the use of large amounts of medium, but on the other hand any impingement on the column of pantopaque from without, as by disk lesions, is readily seen. Radiographs taken in six cases are reproduced. Kenneth A. Rowley.


Gout


By administering glycine labelled with radioactive nitrogen (N15) and subsequently measuring the concentration of the isotope in the urinary uric acid in two normal subjects and one patient with gout, Benedict and others (Metabolism, 1952, 1, 3) showed that in gouty subjects the high blood concentration of uric acid was due to increased uric acid production. This patient was exceptional, however, in having a high urinary output of uric acid and only minor tophaceous involvement. At the Massachusetts General Hospital, the present authors, using a similar technique, have therefore studied a gouty subject with high blood uric acid content, normal renal function, and normal uric acid excretion, and a healthy control subject, both of whom were taking a low-purine diet. The cumulative excretion of N15 in urinary uric acid was similar in the two subjects, as also was its concentration in specimens taken on each of the 10 days after its administration, except for a sharp rise and fall on the 2nd and 3rd days in the case of the gouty patient. The authors therefore suggest that an increased production of uric acid does not appear to be an essential feature of gout. K. G. Lowe.


The author believes that ocular manifestations of gout are not so rare as has been supposed. He describes a number of clinical entities in which there is disease of the eye in association with gout and which respond to suitable general treatment. Iritis with a gelatinous exudate in young adults and unexplained iritis after cataract extraction in old persons should arouse suspicion. Other and better known conditions are episcleritis, tenonitis, and marginal keratitis. The author suggests that the family history may indicate the cause in young persons. A case of symmetrical conjunctival tophi is described in which crystals of uric acid were found in the blood.

P. Jameson Evans.

Non-Artricular Rheumatism


This author advocates stellate ganglion block in the treatment of bursitis and tendinitis around the shoulder girdle. The rationale of this form of treatment is that it causes great capillary vasodilatation in the area involved, resulting in absorption of the exudate. [The technique of injection of the stellate ganglion is illustrated.]

The results, which are tabulated, show that of fifty cases of acute subdeltoid bursitis, “excellent” results were obtained in 44 cases, “good” results in five, and “poor” results in one. In seventeen subacute and chronic cases the corresponding figures were twelve, three, and two. Of the total of 57 cases, thirty have been followed up for periods of 1 to 4 years, and in only two cases have there been recurrences.

Bicipital tendinitis is a difficult and often resistant condition, and in such patients as baseball pitchers [and bowlers in cricket], in whom severe forms occur which do not yield to ordinary physical therapy, the author advocates stellate ganglion block, for which he has generally employed 15 ml. of either 2 per cent. procaine or 0.15 per cent. amethocaine. The injections should be carried out with routine aseptic precautions and not lightly undertaken by untrained operators without supervision. Complications which have been reported include fatal subarachnoid injection, pneumothorax, hydrothorax, and one fatal case of an anaphylactic type of reaction (release of vagal inhibition). Only occasional vertigo from cerebral vasodilatation, or temporary paresis of the extremity due to spread of the analgesic to the brachial plexus have been observed by others.

Leon Gillis.


Writing from Duke University School of Medicine, North Carolina, the author discusses the treatment of painful shoulder, both acute and chronic, by injections into the suprascapular nerve, the aim of treatment being to eliminate pain and restore active movement.

He shows diagrammatically the variations in the distribution of the nerve supply to the shoulder joint. The rationale of the injections is that the analgesic block is said to interrupt the vicious circle of pain which is present in various shoulder conditions such as calcification about the shoulder joint, biceps tendinitis, tears of the musculo-tendinous cuff, the shoulder-hand syndrome, “frozen shoulder”, degenerative shoulder lesions, and even cervical root pain. The technique of these injections is
diagrammatically represented [and should be studied in the original]. The nerve is injected as near to the supra-
scapular notch as possible, and the angesics that have
been employed are 1 per cent. procaine and 1 or 2 per
cent. lignocaine in doses of 10 to 20 ml.

The author claims that this method of nerve block is a
very useful adjuvant in the treatment of these shoulder
conditions. He does not claim that it cures all cases,
and in some patients repeated nerve blocks may be
necessary. The procedure is simpler and has fewer
complications than stellate ganglion block, and gives
equally satisfactory results. The author believes that
sympathetic nerve block is necessary only for lesions
distal to the elbow.  

Leon Gillis.

Roentgen Therapy of Peritendinitis Calcarea of the
Shoulder. A Study of 220 Cases with Late Results.
Radiology, 59, 826. 13 refs.

The 220 cases of peritendinitis calcarea reviewed in
this paper from the Roosevelt Hospital, New York, were
divided into 107 acute cases of not more than one week’s
duration, 23 subacute cases of 1 to 4 weeks’ duration,
and ninety chronic cases of more than 4 weeks’ duration.
Follow-up was by letter and was successful in 157
cases out of 195 contacted (80.5 per cent.). The series com-
prised 119 male and 101 female patients, and the right
shoulder was involved rather more often than the left;
there were seventeen bilateral cases. The diagnosis was
confirmed by radiography of the shoulder in only 150
cases. The irradiation factors were: 200 kV, 15 mA,
0.5 mm. Cu. with 1.0 mm. aluminium filtration, and
a skin-target distance of 50 cm. The size of the field was
10 x 10 cm., and the dose was 150 r in air every other
day to a total dose of 450 to 600 r.

Of the acute cases, 91 per cent. eventually obtained
complete relief, but in only 52 per cent. was this relief
rapid. The results in the subacute and chronic cases were
less good, 69 per cent. of the former and only 52 per cent.
of the latter eventually obtaining complete relief. The authors’ conclusions are that the immediate response is
usually remarkable and most gratifying, but that complete
relief is often a gradual process. They consider that the
results are permanent.  

E. Stanley Lee.

“Dibenamine” in the Treatment of Scapulohumeral
Periarthritis. (La “Dibenamina” nel trattamento della
periartite scapulo-omerale.) MANNETTI, C., and
GALLO, G. (1953). Reumatismo, 5, 92. 17 refs.

General Pathology

A New Reaction for Rheumatic Diseases. [In English.]
31, 54. 10 refs.

In this paper from the University of Helsinki it is
described a serological test for use in the diagnosis of
rheumatic affections, slightly modified from the author’s
original technique published in 1952. The method consists
in measuring 0.25 ml. serum, drop by drop, into 2.5 ml.
94 per cent. ethanol at room temperature and refrigerating
overnight; then centrifuging at 2,500 revolutions per
minute for 5 minutes and draining. The precipitate is
covered by 1 ml. 95 per cent. sulphuric acid and examined
after 5 minutes. The reaction is regarded as positive if all
the precipitate dissolves and forms a dark brown solu-
tion; as slightly positive if there is partial dissolution with
some brown colour; and as negative if there is no dis-
solution and no colour production.

The method was used for testing four groups of sera:
(1) from 28 patients with rheumatoid arthritis;
(2) from 14 patients with rheumatic fever; and
(3) from 129 healthy blood donors.

(4) consisted of 1,263 samples of serum from the
serological laboratories originally taken for routine test-
ing from patients without rheumatic disease.

In the first three groups the sera were tested at least four
times each and an average reading taken. From the 28
cases of rheumatoid arthritis, 21 (75 per cent.) positive
results were obtained, and from the fourteen cases of
rheumatic fever nine (64 per cent.). Positive results were
associated with a high erythrocyte sedimentation rate and
a high temperature. Of the nine cases of rheumatic fever
giving a positive reaction, four out of five examined
radiologically showed joint changes caused by arthritis.
[No further details of this very unusual finding are given.]

Treatment with salicylates made no difference either
in vivo or in vitro. No positive results were obtained from
the group of healthy subjects. Sera from patients with
miscellaneous diseases were also tested, and these gave
varying proportions of positive results, the highest
percentage being obtained in liver and collagen diseases
and in some cases of carcinoma and of tuberculosis.

It is concluded that in the rheumatic diseases the result
of the test depends upon the activity or otherwise of the
process, but that the method is not specific for these
diseases.  

E. G. L. Bywaters.

“Refux” Factor in Erythrocyte Sedimentation Tests.
1 fig., 3 refs.

At the Gardner Institute of Medicine (University of
Glasgow) the methods of Westergren and of Wintrobe
for determination of the erythrocyte sedimentation rate
were compared in forty unselected patients, the Wester-
gren tube being only half filled to give a comparable
column of blood. In four cases the Wintrobe method gave
normal values, and the Westergen method raised values,
the latter results being those expected from the clinical
picture. If, however, the Wintrobe tube was filled and
the blood then withdrawn to the zero mark so that a
reflux down the sides of the tube occurred (as in the
usual method of filling a Westergen tube), a reading
comparable with that given by the Westergren method
was obtained. Similarly, a low reading could be obtained
in the Westergren tube by half-filling it with oxalated
blood and preventing a reflux. With citrated blood,
however, although the half-hour readings were sometimes
low, the prevention of reflux had no effect on the reading
at one hour.

It is tentatively suggested that the momentum gained
by the blood in flowing down the sides of the tube may
in part explain this phenomenon, but the main stress is laid on the practical importance of knowing that the phenomenon can occur and may affect the readings.

Marjorie Le Vay.


In the search for a new and useful anti-arthritic agent the effect of d-amphetamine sulfate was studied at Massachusetts College of Pharmacy, Boston, with reference to the finding that the degree of eosinopenia is a sensitive measure of adrenocortical activity. To seven selected patients two 5-mg. tablets of "dexedrine" were given thrice daily before meals, and eosinophil counts were made from finger-tip blood by Randolph's modification of Thorn's method. The counts were made at the same time on each day after 1, 5, 8, and 12 days of continuous medication.

In all cases an eosinopenia was manifested in the early stages of the experiments and was maintained for its duration, the greatest fall in the number of eosinophils occurring near the end of the test period. The average over-all drop of the eosinophil level for the whole test period was 42 per cent., the average after 12 days being 60 per cent. Three days after medication was stopped the eosinophils had returned to pre-medication levels. The degree of eosinopenia was related quantitatively to the immediate and the prolonged effect of the drug. It is suggested that all pressor amines exert a similar influence on the circulating eosinophils.

Norval Taylor.


Studies of the Agglutination of Sensitized Sheep's Erythrocytes by Human Serum from Cases of Rheumatoid Arthritis. (Untersuchungen über die Agglutination sensibilisierter Hammelerythrozyten durch menschliches Blutserum bei primär chronischer Polyarthritis.) FRANK, A., and SCHIMANSKI, J. (1953). *Z. Rheumaforsch.*, 12, 80. 8 refs.


ACTH, Cortisone, and Other Steroids


In this paper are reported two separate studies of cortisone and corticotrophin (ACTH) treatment—one in rheumatic fever, the other in juvenile rheumatoid arthritis—at the New York University College of Medicine and Bellevue Hospital, New York. It is pointed out that in rheumatic fever all the non-specific manifestations—such as fever, tachycardia, raised erythrocyte sedimentation rate, raised serum fibrinogen level, and appearance of C-reactive serum protein—return to normal with cortisone therapy. Pericarditis, with or without effusion, almost always subsides within 5 days, though this may occur spontaneously. There is evidence that cortisone has a direct, though non-specific, effect on the heart rate and thus on the myocarditis. According to the authors, it was apparent in their cases that neither cortisone (or ACTH) nor salicylates, could prevent organic heart disease or significantly shorten the duration of carditis. However, in one case, that of a child aged 2½ years, they believe that hormone therapy was a lifesaving measure. They describe the rebound phenomenon which occurs when the hormone is withdrawn in such cases; this consists in the reappearance of fever, tachycardia, or other signs of rheumatic activity, with a return of C-reactive serum protein and elevation of erythrocyte sedimentation rate. This phenomenon subsides within 20 days without the reintroduction of hormone therapy provided the natural course of the disease has ended. The authors suggest that the most suitable cases for
hormone therapy are those in which there is active, and especially severe, carditis of recent onset (less than 3 months).

In juvenile rheumatoid arthritis the administration of cortisone was followed by striking relief of articular pain and stiffness, diminution of swelling, and increase in mobility, muscular strength, and co-ordination, as well as improvement in the general condition and fall in erythrocyte sedimentation rate. Of seven patients treated, three had an acute relapse during maintenance therapy, necessitating complete rest and an increased dosage. Two cases underwent remission, and this has persisted for many months. In none of the children did any of the three more serious reactions to these drugs—psychosis, peptic ulcer, or traumatic fractures—develop. Two girls who had reached puberty menstruated normally. It is concluded that adrenal cortical hormones are of definite value in properly selected cases, but should form only a part of the regimen of treatment.

[This article contains many important observations and should be consulted in the original.]

Oswald Savage.


This paper from the Johns Hopkins University and Hospital describes the effect of ACTH (corticotrophin) and cortisone on the clinical course of sarcoidosis in fifteen cases. The age of the patients varied between 14 and 58 years.

The supply of ACTH was limited in the early part of the study, and the first three patients treated received short courses, ranging from 7 to 18 days in duration with a maximum daily dose of 100 mg., given intramuscularly, the total dose being 360 to 1,400 mg. The remaining twelve patients were given ACTH intravenously, and in three cases this was followed by the administration of "Actharin", a long-acting preparation of ACTH in gelatin. The course of intravenous ACTH extended from 12 to 42 days, the total dose being 390 to 1,650 mg., while the long-acting preparation was given for 36 to 130 days, the dose being gradually reduced from 100 to 20 mg. a day. Cortisone was given by mouth in doses of 200 mg. daily for 3 to 4 weeks, the dose being reduced towards the end of treatment. Sodium intake was restricted and a potassium supplement given.

The response to adequate treatment in all patients was dramatic, and the descriptions of individual cases leave no doubt that ACTH and cortisone suppress the activity of sarcoidosis. As might be expected, old lesions with intensive fibrosis do not respond so effectively. Uveitis was inactivated dramatically by ACTH and cortisone, and vision was improved if treatment was begun early. Relapses were common, however, and prolonged treatment was often required. Cough, sputum, and dyspnoea were all rapidly improved, and in four cases the x-ray findings after treatment were not recognizable as those of sarcoidosis. In nine out of ten patients with involvement of the skin, the lesions cleared entirely, and in four cases have not recurred. In eleven out of thirteen patients with enlarged peripheral lymph nodes complete regression occurred, and the nodes remained impalpable throughout the period of observation; in cases with enlarged mediastinal lymph nodes, however, regression was not complete and relapse occurred after treatment. Hepatic and splenic enlargement regressed completely. In four cases of the uveo-parotid type the enlarged parotid glands became normal in size during treatment, but after treatment a partial, transient recurrence took place in two of the four. Striking reductions were observed in the serum calcium level, erythrocyte sedimentation rate, serum globulin con-
centration, and cephalin-cholesterol flocculation and thymol turbidity reactions, where these had been abnormal. The development of tuberculosis, which is regarded as a possible danger, occurred in no case.

The importance of intensive initial therapy is stressed. In several cases a transient relapse, lasting 3 or 4 weeks, was observed on the cessation of treatment. Reinstitution of treatment should therefore be delayed if relapse occurs immediately after cessation of the first course.

T. M. Pollock.


There is a conflict of evidence as to the value of adrenal cortical extract (A.C.E.) in the treatment of shock, and the present investigation was undertaken at the Colorado University School of Medicine to assess its efficacy as compared with corticotrophin (ACTH) and cortisone. Albino rats were traumatized by the method of Smith and others (Amer. J. Physiol., 1951, 165, 532), and immediately afterwards received one of the following:

1. ACTH intravenously or intramuscularly in a dosage of 25 mg. per kg.;
2. cortisone orally or subcutaneously in similar dosage; or
3. A.C.E. intravenously in a dosage of 125 dog units per kg.

As judged by prolongation of mean survival time, the most effective drug was ACTH (53 per cent. and 55 per cent. prolongation), followed by cortisone (39 per cent. and 41 per cent. prolongation); A.C.E. produced a prolongation of only 18 per cent., which was not significantly different from the control figure. Circulatory improvement as judged by pulse and blood pressure was often observed after A.C.E., but not after ACTH or cortisone, whose ability to lengthen the mean survival period presumably depends on some other, non-vascular, mechanism.

H. McC. Giles.


The authors discuss the response of 45 patients with the nephrotic syndrome to 56 courses of corticotrophin (ACTH) therapy at the Children's Medical Center, Boston, Mass. The patients' ages ranged from 11½ to 21 years, and the duration of the disease from 2 weeks to 51 months. The series included patients with azotemia, haematuria, and moderately reduced renal function, but none with sustained hypertension, recent infection, uraemia, or abnormality of serum electrolyte pattern. Management included control of fluid and salt intake and routine antibiotic therapy, usually with aureomycin. ACTH dosage was 150 to 200 mg. per square metre of body surface per day for at least 8 and usually 10 days.

Diuresis occurred in 38 of the 56 courses and in 34 of the 45 patients. Of the sixteen patients in whom remission was maintained for 3 months or more, in twelve it was for more than 6 months and in six for more than 12 months. Failure of diuresis in eighteen cases is ascribed to inadequate dosage before this was determined (that is, less than 7 days) in four, and to cessation of treatment because of complications in five. In only three cases was there no apparent reason.

In addition to diuresis there was a fall of 80 to 90 per cent. in the eosinophil count and, on the average, a decrease in proteinuria. Slight azotemia tended to occur during therapy and disappear after it. Except for patients showing complications, serum electrolyte changes— an increase in sodium level, slight alkalosis, and a fall in potassium level—were consistent but slight.

Death occurred in four patients from complications of therapy— two from overwhelming Bacterium coli infections and two from hypertension; three of them had a serum sodium level well below 125 mEq per litre. Infection occurred during 6 of the 56 courses despite routine antibiotic therapy. Hypertension was common, but severe in only six of the 45 patients. Severe electrolyte disturbances—hypotonicity of extracellular fluid—was noted in 28 of the 56 courses and was corrected by the oral route.

The authors discuss the mode of action of ACTH therapy and point out that they found no way of foretelling response to treatment. The investigation was uncontrolled, but the authors do not lose sight of the natural history of the disease, and conclude that at present ACTH is the treatment of choice.

The article is very fully documented. H. Gordon.


During the treatment of lipoid nephrosis with corticotrophin (ACTH) there is not only a marked diuresis, but also a return towards normal of the values of the various routine laboratory tests. The authors, reviewing their first series of twelve children treated with ACTH at the Jewish Hospital, Brooklyn, found that recurrence of oedema was the rule. Moreover, the changes noted in the serum protein and lipid content, erythrocyte sedimentation rate, and albuminuria before diuresis started were all towards normal values; but on the return of oedema the figures reverted to their former levels.

It was decided to continue ACTH after diuresis had started and note its effect on the course of the disease, this procedure being adopted in eight cases. ACTH was given for 10 to 17 days, to promote diuresis. After a period of 1 to 2 weeks another course was given over another 10 to 17 days. The dosage was 25 mg. 6-hourly, unless a larger dose was known to be required or unless hypertension developed and the dose had to be reduced. Prophylactic antibiotics and oral potassium chloride were also given.

Clinically, all eight patients gave a similar response. After the first course there was a reduction in oedema,
and after the second a much increased appetite and good weight gain, together with the usual features of prolonged ACTH therapy. When the ACTH was discontinued the weight remained above that noted at the beginning of the second course.

In a follow-up period of 6 weeks to 8 months only one case has relapsed, after the patient had been free from oedema for 5 1/2 months. The results of laboratory investigation showed that the normal or near-normal values which were attained during treatment have been retained; and the gradual and continuous rise in serum albumin level has persisted after discontinuing administration of the drug. Complications were the same as those of single courses of ACTH therapy. Hypopotassemia was treated with generous doses of potassium chloride.

Of the whole series of twenty patients treated, three died: two during the ACTH therapy (one with persistent hypertension) and one during the administration of a long-acting preparation.

The optimum dosage is still undetermined but appears to be 150 to 200 mg. per square metre of body surface per day for about 10 days. For children under 5 this is equivalent to 3 to 4 mg. per lb. (6-6 to 8-8 mg. per kg.).

(In a note it is stated that two more children have developed oedema during the follow-up period.)

J. G. Jamieson.

Effect of Cortisone on the Clotting of Blood. Study of One Case of Haemophilic Arthritis and Four Cases of Rheumatoid Arthritis. (Efeito do Cortisone sobre a coagulação sanguínea. Observação sobre 1 caso de artítrite hemofílica e 4 de artítrite reumatóide.)


The author presents one case of haemophilic arthritis and four cases of rheumatoid arthritis treated with cortisone where variations in clotting time were observed. According to the author, there is a remarkable shortening of clotting time caused by the hormone especially in the case of haemophilic arthritis. In conclusion the author states that hypercoagulation of the blood occurs as a result of cortisone therapy, drawing attention to the possibility of accidents in its administration without a special control to prevent thrombo-embolic phenomena.

(Author's summary.)

Changes in White Blood Cell Counts after Administration of Cortisone Acetate to Healthy Ambulatory Individuals.


The effect on the leucocyte count in eight healthy medical students of administration of 50 mg. cortisone acetate by mouth and 50 mg. intramuscularly has been studied. The changes in the count following the intramuscular injection of the aqueous vehicle in which cortisone was suspended were also determined. Each of the eight subjects received the three treatments in random order, and the total leucocyte count and differential leucocyte count were estimated at intervals on each of the patients by laboratory workers who were unaware of the particular treatment given.

The authors found that 50 mg. cortisone acetate by mouth was followed during the first few hours by an increase in the neutrophil count and a decrease in the lymphocyte and eosinophil counts. By contrast, the single intramuscular injection of 50 mg. cortisone acetate was followed by a much more marked and prolonged increase in the neutrophil and total leucocyte counts, persisting for more than 14 hours, and this change seemed to be related to the discomfort at the site of injection; no changes were observed in the lymphocyte and eosinophil counts.

G. A. Smart.


The effect of cortisone on the liver function of rats given carbon tetrachloride was investigated at the University of Birmingham. Male albino rats were given 21 injections, each of 0.2 ml. carbon tetrachloride, in 75 weeks, the effect on liver function being estimated by a modified bromsulphalein retention test. Half of the animals were subsequently given cortisol intramuscularly in doses of 8-75 to 12-5 mg. to a total dose of 90 mg. in 10 days, the carbon tetrachloride being administered at the same time. A further bromsulphalein test was performed and the livers of the animals were examined microscopically.

Carbon tetrachloride caused a variable mild degree of liver damage with increased retention of bromsulphalein. Histologically there were fatty and hydropic changes in the centrolobular cells of the liver, with scanty fibrosis. When cortisone was given simultaneously, bromsulphalein excretion was markedly impaired, and histologically there was more widespread liver damage than in the animals given carbon tetrachloride only, fatty and hydropic degeneration being severe and of a general "mosaic" distribution. No such changes were observed in a small control group of normal animals which were given cortisone alone.

The damaging effect of cortisone in the presence of other liver poisons is therefore apparent. K. Gurling.


Evidence has previously been obtained by the authors that the eosinopenic activity (E.A.) of certain preparations of ACTH (corticotrophin) is not directly correlated with their activity in depleting the ascorbic acid content of the adrenal glands. They now report the results of further experiments in support of their earlier observations. The work was carried out at the University of California on normal and hypophysectomized male rats of the Long-Evans strain, 60 to 80 days old, the hypophysectomized animals being used daily for assay purposes during the first 7 post-operative days, while normal animals were used at weekly intervals. Standard methods were
used both for the eosinophil counts and for the determination of adrenal ascorbic acid-depleting activity (A.A.A.).

Analysis of the results showed there to be no correlation between the E.A. and A.A.A. of the various ACTH preparations tested, whether normal or hypophyscetomized rats were used for assay. Furthermore, treatment of the ACTH preparations with sodium hydroxide did not affect their E.A., but considerably reduced their A.A.A., whereas treatment with hydrochloric acid and heat did not affect either activity.

These observations strongly suggest that separate components of ACTH are responsible for the two types of activity. Some evidence has also been obtained which points to the presence of a third component which induces eosinophilia. Nancy Gough.

Therapeutic Test in Chronic Adrenal Insufficiency. (Le test thérapeutique dans l’insuffisance surrenale chronique.)


Writing from Nancy, the author maintains that in patients with minor degrees of adrenocortical insufficiency the diagnosis may be difficult. In such cases he gives a course of 10 mg. deoxycorticosterone acetate daily for 6 weeks. A genuine case of Addison’s disease will show clinical improvement on this regimen, whereas patients in whom there are symptoms resembling those of the disease, but due to another cause, will show signs of intolerance. A number of case histories illustrating the author’s method are given.

G. S. Crockett.

ACTH in Diagnosis of Adrenal Insufficiency (Thorn Test).


The authors discuss the various forms of Thorn test as a means of assessing adrenal cortical function and of differentiating primary adrenal failure from hypopituitarism with secondary adrenal failure. They then report their findings at Guy’s Hospital, London, in eight cases of Addison’s disease, four of Simmonds’s disease, and seven in which the diagnosis of adrenal insufficiency had been considered but not established. Three tests were performed, the four-hour test, the 48-hour intramuscular test, and the intravenous test. In the 4-hour test the patient is starved from 8 p.m. on the previous day; next morning he drinks 200 ml. water at 6 a.m., 10 a.m., and noon. At 10 a.m., 25 mg. ACTH is given intramuscularly, and at this hour and again at 2 p.m. the urinary content of uric acid and creatinine is determined and eosinophil counts made. In the 48-hour intramuscular test, urine is collected for 24 hours before and after the test, and the 17-ketosteroid content determined in both samples. On the morning of the test 25 mg. ACTH is given intramuscularly, followed by 10 mg. every 6 hours for 48 hours. Eosinophil counts are made immediately before the first injection of ACTH and 4 hours after the last injection. In the intravenous test a similar procedure is followed, except that 40 mg. LA-1-a ACTH in normal saline is given in an intravenous infusion in 18 hours, the second eosinophil count being made 2 hours later. In the last two tests the patient remains on normal diet.

The results, which are tabulated, showed that in six of the eight patients with Addison’s disease there was a fall of less than 50 per cent. in the eosinophil count, the fall in the other two, both severe cases, being 57 per cent. and 75 per cent. respectively.

In all four patients with hypopituitarism the fall in the count was less than 50 per cent.

In the group of seven doubtful cases the response was normal in four cases and subnormal in three. The ratio of urinary uric acid to creatinine in the urine bore no relation to the eosinophil count; in only two cases both of Addison’s disease, did the ratio rise to more than 50 per cent. The authors discuss in detail variations in the eosinophil count throughout the day, and note the effect of food and sleep. Errors in technique are mentioned, especially in cases in which the eosinophils are few in number, and the effect of ACTH in the presence of an eosinophilia is discussed. Variations in the urinary uric acid : creatinine ratio are discussed, and it is pointed out that the determination of this ratio has now been abandoned by Thorn and colleagues. The result of the Thorn test is not, therefore, a reliable index of adrenal cortical function, although an eosinophil response of less than 50 per cent. is strongly suggestive. The test may, however, be of some value in the investigation of a doubtful case, though in the last resort diagnosis must still be made on clinical grounds.

R. St. J. Buxton.


A case of female pseudohermaphroditism due to congenital adrenocortical hyperplasia is described.

A girl, aged 6 years 9 months, had suffered from attacks of vomiting and prostration since the age of 2. Examination revealed considerable muscular strength, axillary and pubic hair, an enlarged clitoris (known to have been enlarged since birth), and advanced bone age. The 24-hour output of 17-ketosteroids was 30 mg. There was no eosinopenic response to either adrenaline or ACTH, and no electrolyte change on administration of effective doses of the latter. Excretion of 17-ketosteroids was considerably increased by ACTH and reduced by cortisol. The effect of cortisone therapy was erratic, a fatal attack of presumed adrenocortical insufficiency occurring in the fourth week of the course (50 mg. twice weekly). Necropsy showed adrenocortical insufficiency and a normal genito-urinary tract apart from the enlarged clitoris. The axillary hair had disappeared, presumably as a result of treatment.

The authors suggest that the primary lesion was the absence of a specific enzyme system necessary for the elaboration of adrenal corticosteroids. This resulted in an excessive secretion of ACTH by the pituitary and corresponding excessive stimulation of the adrenal cortex, which could respond only by producing more androgens. It is pointed out that androgens do not, apparently, inhibit the pituitary. Prolonged cortisone
therapy has been shown by others to arrest virilization in such cases as the present one and to produce a reversion towards normal.

J. N. Harris-Jones.


The authors report in detail the clinical and post-mortem findings in four fatal cases of polyarteritis nodosa treated at the General Hospital, Birmingham. Three of the patients were treated with corticotrophin (ACTH), the total amounts given being 995 mg., 1,780 mg., and 1,690 mg. over periods of 22, 19, and 25 days respectively. The fourth patient did not receive the hormone, but underwent bilateral sympathectomy for malignant hypertension. In the first three cases more than 120 specimens of tissue from different sites were examined histologically post mortem, and showed advanced or complete healing of the affected arteries. Comparable healing of the arteries was also seen in the seventeen specimens of tissue examined microscopically in the fourth case. The authors, while recognizing the important fact that healing of the vascular lesions does not necessarily imply recovery from the effects of the disease, suggest that better therapeutic results might possibly be obtained with ACTH or with cortisone if the hormone therapy were supplemented by surgical or medical anti-hypertensive treatment.

S. Karani.


Although intra-articular injections of cortisone rarely have any therapeutic effect in chronic arthritis, the injection of hydrocortisone has been reported by a number of workers to be more successful, probably owing to its much lower solubility in synovial fluid and consequent slower diffusion; the accepted dose is 25 mg. The present authors report their results in forty cases (140 injections) treated in this manner between June and September, 1952. They comprised eleven cases of “inflammatory” arthritis (of which five were rheumatoid in type), 22 cases of osteo-arthritis, gonococcal arthritis, and post-traumatic arthritis, and seven of non-articular rheumatism.

Excellent results are claimed in rheumatoid arthritis, in which condition it is suggested that intra-articular injections are indicated:

1) in cases where the number of joints involved is small and systemic treatment can therefore be avoided;
2) where systemic cortisone is contra-indicated or where, having been tried, it has failed to influence one or two intractable joints;
3) as a preliminary to orthopaedic correction.

The results in osteo-arthritis of the hip were poor, but after an intracapsular injection, and satisfactory results were obtained in one case of Dupuytren's contracture. The authors discuss the technique of injection in rheumatic affections of the shoulder, in which encouraging, but not dramatic, results were obtained; in many cases intra-articular injection is not required and attention may have to be directed to the tendons and subacromial bursa; probably each case requires to be treated on its merits.

D. Preiskel.


The authors describe the results obtained at New York University College of Medicine with intra-articular injection of hydrocortisone (Compound F) or cortisone acetate in nine patients with rheumatoid arthritis and one with rheumatoid spondylitis. In most of the cases there were effusions and pain in the joints despite systemic treatment with cortisone. Each injection contained 25 mg. steroid in 1 ml. suspension vehicle.

Hydrocortisone was found to be more effective than cortisone, 80 per cent. of injections of the former being followed by definite objective clinical improvement and 95 per cent. by significant changes towards the normal in the properties of the synovial fluid, in comparison with 31 per cent. and 23 per cent. respectively of cortisone injections. After hydrocortisone periods of improvement lasting 27 to 90 days were observed together with a rise in the viscosity and a fall in aminotripeptidase activity of the synovial fluid. These changes were accompanied by a fall in the leucocyte count and an increase in the percentage of lymphocytes; the total protein content and the albumin: globulin ratio were unaffected.

It is suggested that the method is of some value when one or two joints remain relatively unimproved after systemic therapy, and that it permits a lower systemic maintenance dosage to be given. Hydrocortisone is considered to have a “local suppressive action on joint inflammation”. Definite conclusions concerning its value, however, must await a more prolonged trial in a larger group of patients.

Those cases in which there was bilateral effusion in the knee are described in detail.

Harry Coke.


The authors, working at University College, Dublin, have considered the possibility of an allergic element in some types of anuria, and for this reason have treated four cases of anuria with cortisone. The first patient, who was suffering from rheumatoid arthritis, was receiving cortisone when he developed pharyngitis. Administration of cortisone was stopped, and on the next day he had almost complete anuria which lasted 3 days. When the blood urea level rose to 210 mg. per 100 ml., peritoneal lavage was begun, but secretion of urine also started, the amount being 200 to 300 ml. a day. Cortisone was given, and on the next day 960 ml. urine was passed;

In a study of the effects of cortisone and ACTH on experimentally induced inflammatory reactions of the skin carried out at St. Mary's Hospital Medical School and the Statistical Research Unit of the Medical Research Council, London, thirteen subjects suffering from diseases known to respond to corticosteroids were used. The agents employed were: purified protein derivative of tuberculin (P.P.D.) and manganese butyrate by intradermal injection; histamine, morphine, pollen, and cat scurf by scratch test; and atropine by patch test. Tests were performed before, during, and at various times after treatment with ACTH and cortisone. Repeated tests were made, and results were assayed by accurate measurement of flare and induration diameter and then subjected to strict statistical analysis.

Erythema and induration response to P.P.D. was significantly reduced during hormone treatment, returning towards pre-treatment levels after cessation of therapy. Reactivity to P.P.D. was reduced between 15- and 170-fold as a result of treatment. The findings for manganese butyrate were similar but rather more variable, and reduction in reactivity was much less. Changes with histamine, morphine, pollen, and cat scurf were not considered statistically significant. Inflammatory response and itching following atropine patch-testing in sensitive subjects were abolished during cortisone treatment. The immediate or histamine reaction did not appear to be influenced by these hormones, but the more delayed type induced by P.P.D. and manganese butyrate was significantly reduced.

[These results, having been subjected to careful statistical study, appear to have established the inhibitory action of cortisone on the tuberculin response beyond reasonable doubt. The reader is referred to the original article for details of experimental technique and statistical methods.]

*J. N. Harris-Jones.*


With the object of determining the effect, if any, of administration of hormonal substances on patients suffering from alopecia areata, the authors, working at the University of Chicago, gave cortisone by mouth for 10 weeks to 22 patients with severe alopecia, mostly of the universalis and totalis types. The selection of patients, the course of the disease before treatment, the method of administration, and the therapeutic results, both clinical and histological, are described, together with some of the undesirable side-effects of the drug. There was regrowth of hair in 16 patients, in some of whom the regrowth, although not complete, was cosmetically satisfactory. In the majority of cases the regrowth was patchy. The authors do not recommend this treatment for general use.

*G. B. Mitchell-Heggs.*

ABSTRACTS

it is pointed out that injection into this joint is difficult; in the two cases (out of nine) which did well, synovial fluid was aspirated at the time of injection. A violinist with a painful Heberden's node was able to resume work thereafter 2 to 4 litres was passed daily. The patient was discharged apparently well so far as the kidneys were concerned. The second patient, who was 27 weeks pregnant, had passed very little urine for 11 days, when spontaneous delivery occurred. Cortisone administration was started on the same day. The urine volume rose, and after 26 days of cortisone therapy the patient was discharged apparently well [no renal function studies are reported]. The third patient had passed practically no urine for 5 days after a large dose of sulphamerazine. The right ureter was found to be blocked. Cortisone administration was begun, and on the next day 240 ml. urine was passed, the rate of flow rising steeply thereafter. Reduction in the dose of cortisone coincided with suppression of urine until the dose was raised again. This patient also recovered. The fourth patient passed very little urine for 7 days following prostatectomy and blood transfusion. Although he was given cortisone on the eighth day and the urine volume rose slightly, the blood urea level remained high and he died. At necropsy the kidneys were enlarged and showed old and recent lesions of glomerulonephritis, with some pus and blood in the tubules.

The authors state [rightly] that "no definite conclusions can be drawn from the three apparently successful cases, as acute anuria is prone to develop a spontaneous remission".

*G. Loewi.*


In this paper from Columbia University and the Presbyterian Hospital, New York, the authors show that cortisone markedly inhibits the synthesis of antibody protein during elicitation of a specific anamnestic or secondary immune response. In the experiments described rabbits which had been immunized to purified egg albumen 2 months previously were given a stimulating dose of antigen in the form of an intravenous injection of alum-precipitated egg albumen containing 1 mg. nitrogen. Their antibody levels were determined 12 and 6 days before the injection and on the 5th and 13th days after it. Cortisone was given intramuscularly to eight of the animals in daily doses of 25 mg., starting 4 days before the injection of antigen, and seven comparable animals not given cortisone acted as a control group.

It was found that 5 days after the antigen injection a sharp rise occurred in the antibody levels of the control animals, but those of the cortisone-treated animals remained about the same or were even slightly reduced by the 5th day. By the 13th day further increases had occurred in the control group, but there was still no change in the cortisone-treated group. Present knowledge of the effect of cortisone on antibody synthesis is briefly discussed, and it is considered that there is no reason to abandon the concept of Landsteiner that immunological reactions are chemically specific.

*C. L. Cope.*

Water and electrolyte balance before and after operation was studied at the Middlesex Hospital, London, in a group of 21 surgical patients, nineteen of them undergoing partial gastrectomy for benign peptic ulceration, one excision of the sigmoid colon for carcinoma, and one inguinal herniorrhaphy. The investigations were made for 3 to 4 days before the operation and for 1 to 8 days afterwards. An “almost constant” water and sodium intake was assured preoperatively by giving a standard mixture of “casinal” (calcium caseinate), glucose, arachis oil, and ascorbic acid in 3 l. water by slow drip down a Ryle’s tube and allowing only 1 litre of water by mouth; and post-operatively by giving intravenous fluids until the preoperative regimen could be resumed. In respect of daily electrolyte intake the patients were divided into three groups:

(1) receiving 160 to 170 mEq sodium chloride throughout;
(2) receiving no sodium from the day of the operation onwards;
(3) receiving the same amount of sodium chloride as Group 1 and also 100 mEq of potassium (except on the day of the operation, when this amount was halved).

On studying the results, three clearly separable phases were observed in the post-operative period:

(a) primary water retention, which rarely lasted more than 24 hours;
(b) early sodium retention, also in the first 24 hours;
(c) late sodium retention, starting 24 to 48 hours after operation and lasting several days.

The retention of salt and water may be continuous or interrupted, depending on the relationship of the last two. The primary water retention was found to be independent of sodium retention, and appears to result from the release of pituitary antidiuretic hormone caused by such stimuli as emotion, trauma, and drugs. Early sodium retention may be caused, at least in part, by hypotonicity of the blood resulting from water retention during the early part of the day of operation. Adrenocortical release is probably responsible for the late sodium retention and also, in part, for the early retention of this electrolyte.

A. Swan.


In this article the authors report the results of an investigation into the comparative effects of hydrocortisone (Compound F) and cortisone (Compound E).

Previous investigators have found that the former is the predominant steroid secreted by the adrenal cortex on stimulation, that it is more active in its systemic effect than cortisone, and that it is more effective in the local therapy of rheumatoid arthritis. It is also less soluble and is therefore longer acting.

In a clinical comparison of the ophthalmic use of these drugs the authors found that hydrocortisone, when given as drops or by subconjunctival injection, was superior to cortisone in eighteen out of 46 patients suffering from various diseases. The difference was most marked in four cases of vernal catarrh in which local hydrocortisone was more effective than systemic cortisone.

In an experimental comparison no significant difference was found between the two drugs in their effect on: epithelial healing; permeability of the blood aqueous barrier in the normal and inflamed eye; intra-ocular pressure changes induced by paracentesis and DFP; corneal vascularization induced by alloxan; or the healing of corneal wounds. A. Lister.


There is clinical evidence that cortisone must be used with caution in herpes simplex infections of the eye.

The authors show that in experimentally induced acute herpetic keratitis in rabbits many doses of the hormone prolong the acute phase of the pathological process, retard healing, and actually involve the risk of corneal perforation.

On the other hand, the fact that cortisone exerts an inhibitory effect upon corneal vascularization and upon the infiltrates occurring in the substantia propria may be taken advantage of, provided therapy is instituted at the appropriate stage of this disease. Official Abs. (abridged).


Twelve cases of retinitis pigmentosa were treated with ACTH parenterally with fairly good results. The authors think the favourable action of ACTH to be due to stimulation of the melanophore-hypophyseal hormone contained in this drug.

G. Cristini.


The authors sum up the conclusions of their personal clinical experience and the results of others, presenting successively: the relative value of cortisone and ACTH, the relative value of local and systemic cortisone, associated therapeutics, aetiological factors, etc. They are of the opinion that ACTH should be abandoned in ophthalmology, that almost always cortisone should be used locally, and that aetiological treatment should be continued. They mention the rare cases of drug intolerance.

H. Moutinho.


The effects, indications, and contraindications of cortisone are described. Cortisone used in a case of choroiditis did not stop relapses. M. A. H. Attiah.
Abstracts

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