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; Pararheumatic (Collagen) Diseases; 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 research into the scope and modus operandi of steroid therapy.

Acute Rheumatism


During the past 3 years sixty patients suffering from cardiac rheumatism have been treated with ACTH (corticoteraphin) at the Institute of Therapeutics (Academy of Medical Sciences), Moscow. In twenty cases there was no established cardiac lesion, the majority of these patients undergoing their first attack of rheumatism. The other forty patients had an established valvular lesion, which in some cases was causing circulatory disturbances. All had a recurrence of the rheumatism. In addition to routine investigations the blood histamine and hyaluronidase levels, the serum protein pattern, and the blood and urinary levels of steroid hormones were estimated before, during, and after treatment. ACTH was given on the second or third day after admission for a period of 4 to 6 weeks in an initial dose of 60 mg. per 24 hrs, which was gradually decreased to 10 mg. per 24 hrs. The total dose ranged from 700 to 1,000 mg.

Patients in their first attack of rheumatic fever responded to the treatment rapidly and satisfactorily, and no toxic effects were seen. During the period of follow-up (1 to 3 years) only one patient developed a permanent cardiac lesion (mitral incompetence), while the rheumatism recurred in two cases. Patients with established rheumatic lesions did considerably less well, however, a satisfactory result being obtained in only 22, no improvement being noted in eighteen. Toxic reactions, particularly oedema, were frequent, and there was recurrence of the rheumatism in eight cases during the period of observation. The hyaluronidase and histamine content of the blood was raised in the majority of patients in the acute stage, but tended to return to normal levels as the result of ACTH administration, especially in patients who improved clinically. ACTH therapy also caused a fall in the serum γ- and α-globulin levels when these were originally raised. In all the patients investigated the administration of ACTH caused an increase in the blood and urinary levels of adrenocortical steroids.

In comparing the results of ACTH therapy with those of the usual antirheumatic substances the author considers that ACTH is more rapid in action and more complete in effect, resulting in fewer recurrences, but it would appear to the author to be unsuitable for the treatment of patients with established rheumatic cardiac lesions.

Marcel Malden.


An analysis is presented of the diagnoses reached in 65,044 examinations of children at the New York City Department of Health Cardiac Consultation Service Clinics during the period 1943 to 1953 inclusive, the object being to determine whether there had been a change in the relative incidence of organic heart disease following rheumatic fever. Some 80 per cent. were first examinations, but the percentage of re-examinations rose from an average of 14 during the first half of the period of 26 during the second. The cases seen in the clinics each year were divided into three broad diagnostic groups—non-cardiac, possible heart disease, and organic or potential heart disease. There was a sharp rise in the percentage of non-cardiac cases from 1951 onwards, which is considered to be due partly to the increase in the number of re-examinations and partly to a change in the type of case referred.

Patients with "organic or potential heart disease" were again divided into four sub-groups as follows:

(1) Rheumatic heart disease—history of rheumatic fever with positive heart signs;
(2) Potential heart disease—history of rheumatic fever but no signs of heart disease;
(3) Unknown heart disease—organic heart disease of rheumatic type without a history of rheumatic fever;
(4) Congenital heart disease.

In 1943 60 per cent. of the children with a history of rheumatic fever had detectable heart disease when
examined. This percentage steadily fell to about 30 in 1948, and has remained at the lower level ever since. The authors point out that this decrease in rheumatic heart disease is in keeping with the findings of other investigators. They also note that 86 per cent. of the patients with a history of rheumatic fever were referred to the clinics after the first attack. The incidence of organic heart disease was about 35 per cent. higher in those with a history of more than one attack of rheumatic fever than in those who had had only one known attack.

E. H. Johnson.


The authors have studied the reproducibility of the erythrocyte sedimentation rate (E.S.R.) in sixty patients with rheumatic fever, the E.S.R. being determined by two methods simultaneously, each in duplicate—that of Westergren and a similar method in which heparinized blood was used instead of citrated blood. Blood for all tests was collected at one venepuncture, and the tubes were set up within an hour under identical conditions. The E.S.R. was read at the end of an hour. The packed cell volume and the plasma fibrinogen level were determined on the heparinized blood samples.

No abnormality of the sedimentation process itself was noted. Discrepancies between a pair of tubes were common with both methods, especially at the initial blood examination—that is, before treatment—in cases of acute rheumatic fever. The average arithmetical difference between the readings of duplicate tubes containing heparinized blood was 7·8 mm. and of tubes containing citrated blood 1·3 mm. With clinical improvement and a fall in the plasma fibrinogen level discrepancies became smaller and less numerous. Discrepancies of more than 20 mm. were noted in thirteen instances with heparinized blood and in one instance with citrated blood. The authors conclude that in following the course of rheumatic fever the E.S.R. with heparinized blood may be seriously misleading. David Friedberg.


Previous investigations have shown that in the U.S.A. the incidence of rheumatic heart disease in children is directly correlated with latitude, ranging from three cases per 1,000 children at 25 degrees N. (Florida) to 45 per 1,000 at 45 degrees N. (Wyoming). At the National Children’s Cardiac Hospital (University of Miami School of Medicine), Florida, the authors have investigated the characteristics of beta-haemolytic (Group A) streptococcal infections in the school children of Miami in an attempt to explain the low incidence of rheumatic fever in the South. A total of 6,400 cultures were prepared from throat swabs monthly for 2½ years from 740 children aged 6 to 9, and cultures for Group-A streptococci from single swabs from another 1,200 children.

The over-all monthly incidence of positive cultures was 11·2 per cent., and 25 to 40 per cent. of the children harboured Group-A streptococci at least once during any one school year (8 months). The distribution of streptococcal types was similar to that in other reported studies. Antistreptolysin O (A.S.O.) titres were determined on 1,400 blood samples from the children. Higher titres were found in children whose throats had yielded Group-A streptococci than in those with negative results. In serial A.S.O. titre determinations a significant rise (two or more tubes) was found in 50·7 per cent. of those with positive cultures. Only 8·6 per cent. of bacteriologically negative children showed a significant rise in A.S.O. titre.

From these results it is concluded that about 40 per cent. of children in this age group in Miami harbour Group-A streptococci in the throat at some time during each school year, and that half of these, that is, those showing a rise in A.S.O. titre, must be regarded as cases of true streptococcal infection of the upper respiratory tract. On the basis of the postulate commonly accepted in the U.S.A. that 3 per cent. of untreated Group-A infections proceed to rheumatic fever, the administrative area in Florida studied should have yielded 212 cases of rheumatic fever among the 35,350 school children at risk in the relevant period. In fact no cases occurred in this area and only 73 in the whole State. The authors discuss the definition of streptococcal infection, and deduce the importance of climatic and environmental factors in the aetiology of rheumatic fever. E. J. Holborow.


The results are reported of an investigation carried out at the University of Colorado, Denver, into the changes in body weight and exchangeable potassium ion content in thirteen children aged 5 to 15 years with acute rheumatic fever who were receiving large doses of cortisone or corticotrophin (ACTH) (5·5 to 9·4 mg. per kg. body weight daily). The duration of treatment ranged from 57 to 124 days. All the patients were having a regular hospital diet with supplementary food on demand, and received in addition 2 to 3 g. potassium chloride or citrate daily. In eight of the patients clinical signs of hyperadrenalism developed. There was an increase in body weight of at least 10 per cent. in twelve patients, the gain being more than 20 per cent. of seven of them. In spite of some variability, the general tendency was for the gain in weight to be progressive. After intravenous injection of a solution containing 1·5 μc. radioactive potassium (42K) per kg. body weight the 42K content of all specimens of urine voided during the following 20 hours was measured. The data thus obtained were used to calculate the exchangeable potassium ion content per kg. body weight. This value fell consistently in all cases, with signs of hyperadrenalism of at least 5 mEq. per kg. body weight. There was, however, no consistent pattern in the value for total body potassium, although the serum potassium concentration was within normal limits in all cases and the serum sodium level in all except two.
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From these results the author suggests that the increase in body weight cannot be accounted for by sodium and water retention or by increase in muscle content, and that it may be due in part to a rise in the total fat content of the body. 

H. F. Reichenfeld.


A study is reported of the immunological response to subcutaneous injection of Brucella antigen in fifty healthy children and 42 who were convalescent from, or had healed, rheumatic fever, the average age of the children in both groups being 10 years. The methods were similar to those used in a previous investigation in adolescents (Wagner and Rejholec, Ann. rheum. Dis., 1955, 14, 243). Specimens of serum from both groups were studied at 7 and 14 days for the titre of Brucella agglutinin and incomplete antibody. In the rheumatic group there was a significantly greater response in incomplete antibody titre by the seventh day and in agglutinin by the fourteenth day than in the controls. Within the rheumatic group there did not appear to be any correlation between the immunological response and the severity of the cardiac lesions. The authors consider that the higher anti-streptococcal antibody level normally seen in rheumatic patients need “not necessarily be explained as a consequence of multiple exposure to the infectious agent”. They refer to the finding of Kuhns and McCarty (J. clin. Invest., 1943, 33, 759) that there was no difference between rheumatic patients and healthy subjects in the response to diphtheria toxin, but they note that their own tests were performed after primary inoculation of the antigen.

E. G. L. Bywaters.


The incidence of recurrences of acute rheumatism and streptococcal infections in fifty rheumatic children receiving 200,000 units benzathine benzylpenicillin daily by mouth was compared with that in 56 similar children receiving 1,200,000 units benzathine benzylpenicillin every 4 weeks by intramuscular injection. There were no recurrences in the latter group, but three children in the former group who did not take the tablets regularly experienced a recurrence of rheumatic fever. There was no difference between the two groups in the incidence of streptococcal infections as shown by a rise in the anti-streptolysin-O titre. An allergic reaction to penicillin was observed in only one of the patients receiving the antibiotic by mouth in contrast to four in the group given intramuscular injections; in addition, in twelve other patients in the latter group the injections had to be discontinued because of pain or emotional disturbances.

Winston Turner.


**Chronic Articular Rheumatism**

(Rheumatoid Arthritis)


Unusually chronic ulceration of the leg associated with rheumatoid arthritis was seen in six patients (three males and three females) at the Middlesex Hospital, London, the duration of the rheumatoid arthritis varying from 6 to 20 years. All the patients had had at least one course of gold injections and some had received phenylbutazone as well. There was a history of dermatitis following gold therapy in four cases. Subcutaneous nodules were noted at some stage of the disease in all cases. The ulcers were single or multiple, indolent, always on the lower limbs, and frequently about the ankle-joints. There was a history of painful induration which in the course of a week or two broke down to give a punched-out ulcer. There was no evidence of venous stasis in the affected legs. Histologically, the margin of the ulcer was formed by vascular granulation tissue, and there were necrotic bands of tissue in the base; occasionally giant cells were seen. The ulcers were very slow to heal even with rest in bed. Skin grafting was tried and failed in three cases, while in three recovery followed steroid therapy. L.E. cells were present in the peripheral blood in four cases.

Discussing the significance of these findings the authors express the view that the ulcers are manifestations of disseminated lupus erythematosus, which is closely related to rheumatoid arthritis. *William Hughes.*


The introduction of a new steroid in the treatment of a collagen disease calls for investigation of its metabolic effects as well as its anti-inflammatory action. This report on the metabolic effects of prednisone ("meti-corten"—Schering) in rheumatoid arthritis is from the University Hospital of Copenhagen. Three female patients with chronic rheumatoid arthritis were studied in the metabolic ward of the hospital over periods of 48, 72, and 64 days respectively.

In all three patients a reduction in the urinary excretion of 17-ketosteroids followed administration of prednisone, indicating that, like cortisone, prednisone represses adrenal cortical function.

In all three patients nitrogen balance became negative. If the diet is kept constant, nitrogen balance is restored after loss of a certain fraction of tissue proteins. If an ad lib. diet is allowed, negative nitrogen balance is less pronounced, and increased protein intake soon results in retention of tissue proteins. The transitory negative nitrogen balance sets no limitation to the clinical use of prednisone, if renal function is unimpaired.

Administration of prednisone was found to be associated with excretion of sodium and retention of potassium, without any alteration in the concentration of the two ions in the serum. Most other reports conclude that prednisone has no effect on sodium and potassium metabolism. The degree of sodium excretion in the authors' experiments suggests a primary effect of prednisone on sodium metabolism, and not merely a result of regression of intra- and peri-articular oedema.

Electrophoretic analyses and estimations of serum proteins were made at regular intervals. Before treatment, total serum protein was normal, but showed alteration in the albumin/globulin ratio due to excess of \( \alpha \) and \( \gamma \) globulins. During administration of prednisone \( \alpha \) and \( \gamma \) globulins were reduced, and albumin concentrations rose towards normal limits. These changes were associated with a fall in the erythrocyte sedimentation rate.

*Kenneth Stone.*


The authors, working at the Medical Clinic of the University of Turku, Finland, have tried to determine the prevalence of the "thyrohypophyseal" syndrome in rheumatoid arthritis; and to see if administration of either somatotropin, or the thyrotropic hormone, has any effect on rheumatoid arthritic symptoms.

Somatotropin is the growth hormone secreted by the eosinophil cells of the anterior pituitary. It has been found that in rats after thyroidectomy it can produce peri-artitis nodosa and arthritis; and in intact guinea pigs degenerative cartilage changes.

The thyrotropic hormone is secreted, with ACTH and gonadotropin, by the basophil cells of the anterior pituitary. In the absence of thyroid hormone it causes a characteristic accumulation of an acid mucopolysaccharide in connective tissue.

The "thyrohypophyseal syndrome" names a syndrome caused by over-production of thyrotropic hormone: oedema of the lids, puffiness round the eyes, obliteration of the upper fronto-palpebral sulcus, malignant exophthalmos, facial and temporal oedema, localized myxoedema.

This syndrome has been found in 44 per cent. of 148 patients suffering from rheumatoid arthritis. Similar signs were found in 10 per cent. of a control series of one hundred patients.

Neither somatotropin nor thyrotropin was found to have any effect on the symptoms of rheumatoid arthritis.

*Kenneth Stone.*

These studies from Boston, Mass, U.S.A., are designed to see if hormone-induced changes in mineral and nitrogen metabolism in a patient with rheumatoid arthritis can be correlated with exacerbations or remissions of rheumatoid activity. Balance studies were performed on one male patient with typical rheumatoid arthritis during administration of cortisone, desoxycorticosterone, testosterone and corticotropin, singly and in various combinations. The results are shown graphically for nitrogen, phosphorus, calcium, sodium, chloride, and potassium.

The main conclusions are:
1. Rheumatoid activity could not be correlated with alterations in electrolyte, calcium, phosphorus, or nitrogen balance.
2. Corticoid-induced remissions and the ensuing exacerbations were not related to gains and losses of intracellular or extracellular fluid as estimated from external balance data.
3. Initial losses of potassium appeared in all but one experiment (testosterone + cortisone) when treatment was associated with improvement. Similar losses, however, were nored during treatment periods not associated with improvement.
4. The observations by Selve of the antagonistic effects of desoxycorticosterone and cortisone in relation to inflammatory processes could not be confirmed. Neither desoxycorticosterone nor testosterone had any effect on rheumatoid activity. The constant antiinflammatory effects of cortisone were not modified by desoxy-corticosterone or testosterone. Kenneth Stone.


Prolonged Treatment of Rheumatoid Arthritis with Prednisone. Comparison with Cortisone Therapy and Clinical Considerations. (Il trattamento prolungato con prednisona della artrite reumatoide confronto con la terapia cortisonica e considerazioni cliniche.) BONOMO, L. (1957). Reumatismo, 9, 47. 4 figs, 16 refs.


Treatment of Rheumatoid Arthritis with Prednisolone. (Tratamiento de la arthritis reumatoide con prednisolona.) LÓSADA, M., and FRANCE, O. (1956). Rev. med. Chile, 84, 611. 2 figs, 18 refs.


(Osteo-Arthritis)


At the University of Pittsburgh the authors have studied a “stratified random sample” of the population in an attempt to determine the relation between the presence of x-ray evidence of osteo-arthritis and the occurrence of pain and other symptoms and signs of the disease. Of the 478 persons examined (constituting only 60 per cent. of the original sample), there was radiological evidence of osteo-arthritis of the hands and wrists in 115, and of the knees in 65. In all cases information was recorded regarding:

1. History of pain in the joint concerned;
2. Observed motion on movement;
3. Observed tenderness;
4. History of swelling;
5. Observed swelling;
6. Morning stiffness (which is regarded as a generalized phenomenon even though the patient may point out an area where it is worst).

Analysis of these data from several points of view gave results consistent with the hypothesis that morning stiffness and x-ray signs of degenerative joint changes are quite independent. Proceeding from this assumption the authors found that morning stiffness was more frequently associated with pain than were x-ray changes at both sites, although the difference was less marked with the knees than with the hands. When those subjects with definite radiological evidence of degenerative joint disease were considered separately it was found that as the incidence of pain increased, so did that of morning stiffness both in the hands and in the knees. In the hands joint swelling did not occur in the absence of morning stiffness, whereas this was not entirely true for the knees, in which a few cases swelling was reported with no history of morning stiffness. When those persons who reported morning stiffness were studied in more detail they appeared to have an earlier onset of arthritic symptoms than those without morning stiffness, with involvement of a greater number of miscellaneous peripheral joints, more joint swelling, and attacks of pain of longer duration. Classification of this group according to the American Rheumatism Association’s criteria for the diagnosis of rheumatoid arthritis showed that 26 per cent. met the criteria for probable rheumatoid arthritis and 41 per cent. for possible rheumatoid arthritis. The authors therefore consider that most of these patients with morning stiffness were suffering from rheumatoid arthritis, and that the degenerative joint changes seen in the radiograph were purely incidental.

In summary, the survey demonstrated that 70 per cent. of the subjects in whom osteo-arthritis changes were revealed by x rays were asymptomatic, while the remainder could be divided into three groups:

1. Those who had obvious rheumatoid arthritis and incidental degenerative joint changes.
2. Those with no morning stiffness, a late onset of symptoms, and mild pain usually without swelling.
3. An intermediate group in whom morning stiffness was the predominant feature and in whom the possibility is that the symptoms were due at least in part to a rheumatoid component. B. M. Ansell.


The object of this study from the Washington University School of Medicine, St. Louis, was to investigate the role of age in the susceptibility of the articular cartilage to osteo-arthritis in mice fed on a high fat diet.

The stock diet of Purina Laboratory Show of 146 male mice strain C.57 B.L. was enriched with 25 per cent. lard for a 5-month period, 49 receiving this from 1-5 months of age, 51 from 6-11 months, and 46 from 12-17 months, and the animals were then killed at approximately 18 or 24 months. The knee joints were removed whole, fixed, and decalcified, and then examined histologically. The findings were compared with those obtained previously on stock-fed animals and animals fed the same high fat diet commencing at 1, 6 or 12 months and continuing to death.

The over-all effect was a temporary weight increase, particularly in the younger mice, and no interference
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with normal life-span. In comparison with the stock-fed mice, there was a marked increase in rate of appearance and incidence of osteo-arthritis change in the animals receiving a high fat diet from 1-5 months, while in the other two groups there was a very slight increase in total incidence. When compared with those animals who were maintained on a high fat diet throughout life, the over-all incidence and severity, together with rate of progression, was considered greater in those receiving the continuous diet than in those who had it only for a short period. It was concluded that limited feeding of a high fat diet had a less injurious effect, particularly in older animals, and it was suggested that the decreased susceptibility in the older joints might be related to a decreased susceptibility to growth-promoting stimuli.

B. H. Ansell.


This paper from the Rheumatological Institute of the University of Rome describes the use of the electron microscope in the study of collagen from articular cartilages in osteo-arthritis. Isolated collagen fibres were prepared by the technique of Monteleoni and Boni (no details given). Preparations from three examples of osteo-arthritic cartilage were compared with non-arthritic specimens from old individuals. No abnormalities were found, either in the general appearance of the collagen fibres or the periodicity of their cross-striation.

N. A. Nixon.


(Spondylitis)


The results of the treatment of ankylosing spondylitis by x rays are discussed and the published results are reviewed. The objective findings after treatment are compared with the improvement in symptoms reported by the patients. A follow-up report is given on 122 patients treated more than 3 years previously. In 25 per cent. of the patients, the disease had progressed since treatment, the advanced disease showing a greater tendency to progress than the early disease. At the time of the follow-up examination, active disease was present in 25 per cent. of patients. Eighty-one per cent. of the patients were at work and 72 per cent. were able to continue with their normal work. The correlation between activity of the disease as assessed clinically and the erythrocyte sedimentation rate was poor.

The complications and sequelae of x-ray treatment are discussed. The possibility of an increased risk of leukaemia is mentioned and its significance discussed in relation to the management of patients in the future.

[Author's summary.]


The authors are convinced that rheumatoid arthritis and ankylosing spondylitis are, fundamentally, variants of one and the same disease. After surveying the literature in search of support for their thesis they report three cases in which rheumatoid changes in peripheral joints—and in one case psoriasis—were present in addition to typical ankylosing spondylitis. Photographs and radiographs of the spine and various joints in each case are reproduced.

L. Michaelis.


Radiotherapy and Ankylosing Spondylitis. (Radiothérapie et spondylite ankylosante.) Audet, L. (1956). Laval méd., 21, 1215.


(Miscellaneous)


In a study carried out at Sampierdarena Municipal Hospital, Genoa, the authors have compared the ther-
peutic value of a combination of 325 mg. acetyl-salicylic acid, 0.5 mg. prednisolone, and 50 mg. ascorbic acid given in tablet form with that of cortisone and acetyl-salicylic acid given separately in the treatment of rheumatic disorders.

In one case of recent acute rheumatic fever and four cases of active rheumatic fever of long standing or in relapse which were treated with six to twelve tablets daily, there was relief of the clinical condition within 3 weeks and no side-effects were seen. The combination was then tried as the sole medicament on five patients with moderate rheumatoid arthritis; all five improved when given six tablets daily for 3 months, although therapy had to be interrupted for a week in one case because of gastric upset.

In ten further patients with rheumatoid arthritis treated with three to six tablets daily according to their clinical requirements for 2 to 3 months in addition to gold therapy [dosage not stated], the results during a 6-month period of observation have been good. In two cases expected exacerbations following gold injections were apparently suppressed by the tablets. Of the last five rheumatoid arthritis patients, who were being treated with cortisone, three improved after receiving six of the tablets daily for one month instead of the cortisone; the other two patients relapsed.

In the treatment of other conditions ten patients with acute osteo-arthritis of the knees with effusion improved on taking six tablets daily for 10 to 20 days; three patients with lumbar osteo-arthritis were relieved after taking six tablets daily for 6 days, and one patient with sciatica was relieved after 10 days of the same dosage, but another was not improved. Lastly, twenty patients with fibrositis responded to six tablets daily given for 4 to 6 days.

It is considered that the side-effects of prednisolone and acetylsalicylic acid are minimized when they are given in combination, and there even appeared to be a synergism between these two components of the tablets.

G. H. Blair.


Radiological examination of the bone of 35 patients with struma lymphomatosa (Hashimoto’s disease) revealed that seven had Paget’s disease. The diagnosis of Hashimoto’s disease was confirmed in all cases on histological examination of thyroid tissue obtained at biopsy and the diagnosis of Paget’s disease in two cases on bone biopsy. Brief reports of the seven cases are given. The incidence of Paget’s disease in the general population has been estimated radiologically at 2·4 per cent., and from necropsy findings at about 3 per cent. On the basis of these figures the incidence of Paget’s disease in patients with struma lymphomatosa is considered to be highly significant. Paget’s disease preceded the thyroid disease in three patients and followed it in four. The author does not advance any reasons for the association of these two diseases, or any views on a common aetiology.

J. N. Harris-Jones.


Although intermittent hydralroth is not rare, fewer than 180 cases have been reported. An analysis of 101 of these shows that the sex incidence is about equal (52 males and 49 females) and that age at onset is usually 20 to 50 years. The author describes three additional cases, all in females. In the first case intermittent swelling of the right knee started at the age of 41 years and recurred at intervals of 9 to 13 days, the attacks bearing no relation to menstruation. The results of laboratory investigations were normal. A course of gold injections was followed by a remission which has lasted 5 years. In the second case symptoms were first noted at the age of 27 years, there being painless swelling of the right knee. Thereafter the patient experienced pain and swelling of both knees at intervals of 2 to 4 weeks for some years, apart from short remissions following illnesses. Again the results of laboratory tests were normal, and the joint fluid was sterile. Rest in bed and corticotrophin injections did not affect the periodicity of the effusions. A remission which followed radiotherapy has now lasted for 4 years. The patient in the third case had had prolonged rest in bed at the age of 19 years and again at the age of 27 years for acute “rheumatism” in the legs. When she was 45 intermittent hydralroth developed, recurring in both knees every 8 days and accompanied by fever. The erythrocyte sedimentation rate was increased and radiographs of the knees showed some osteoporosis. Rest in bed and antihistamine drugs appeared to give temporary relief. The effusions suddenly ceased when the patient was 48, but intermittent swelling of the eyelids was noted for some months after this. The remission has now lasted for 5 years.

The cases described in the literature fall into two groups—one in which the periodic effusions were not accompanied by any evidence of joint damage and those in which a rheumatic disorder was already present. In his discussion the author shows that none of the many causes postulated for this condition, or the many treatments advocated, has any very firm basis. Spontaneous remissions and relapses are common. He considers that gold therapy is worth further trial, and that radiotherapy and synovectomy may also produce remissions.

B. E. W. Mace.


The relationship between arthritis and psoriasis was investigated by analysing three groups of patients at Stoke Mandeville Hospital: (1) 42 with psoriasis and arthritis, of whom 34 had “erosive arthritis” (a term which the author uses in preference to “rheumatoid arthritis” in order not to prejudice the issue), six with degenerative joint disease, one with rheumatic fever, and one with gout.
Ocular Complications

Lesion blennorrhagica.

Keratodermia

Uveitis with psoriasis and “erosive arthritis”, 94 per cent. gave a negative D.A.T. response, and this suggests that the joint condition in these cases forms an entity distinct from rheumatoid arthritis. A less likely explanation is that the psoriasis modifies the arthritis. Clinical differences from the classic picture of rheumatoid arthritis in Group 1 included a high incidence of distal interphalangeal joint involvement (58 per cent.), a combination of ankylosing spondylitis and peripheral arthritis in three cases, and a generally milder course than in Group 2. Nail changes characteristic of psoriasis were seen in 87 per cent. of Group 1 as against 18 per cent. of Group 3. The psoriasis seen in Group 1 differed in some respects from that in similar cases reported in the literature, in that it was not extensive, never pustular, not unduly resistant to treatment, and did not usually affect the palms and soles.

[This is a notable contribution to a controversial subject.] G. W. Csonka.

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Disk Syndrome


Gout


Pararheumatic (Collagen) Diseases


Klemperer has estimated that the kidneys are involved in 60 per cent. of all cases of disseminated lupus erythematosus, while other authorities accept a figure of 90 to 100 per cent. The kidney may be affected in a variety of ways, the disease taking the form of focal nephritis,
diffuse glomerulo-nephritis, or the nephrotic syndrome, and there is no characteristic clinical picture. A study of the pathological anatomy, however, suggests that the typical findings are a combination of the so-called "wire-loop lesions", the appearance of haematoxyphil bodies, and fibrinoid swelling of the glomeruli resulting in partial (focal) or total necrosis. Somewhat similar changes are seen in scleroderma. In long-standing cases the above picture tends to be blurred by the usual appearances of chronic glomerulonephritis. With the onset of renal symptoms there develop certain immunological reactions. The factor responsible, which is associated with the gamma-globulin fraction of the serum proteins, seems to be suppressed by prolonged cortisone therapy, but can be made to reappear under suitable provocation. It can also be absorbed by extracts from healthy kidneys and may be regarded as having the properties of an auto-antibody. Experimentally, it has been shown that the auto-antigenic reaction arises from changes in the vascular endothelium of the glomeruli. Antibodies against the cellular constituents of the blood have also been demonstrated. These factors do not represent the primary cause of the disease, but a secondary product of the disease process; nevertheless, they vitally affect the course of the illness.

Cortisone (or prednisone) and corticotrophin (ACTH) give the best results in therapy. They suppress inflammatory changes in the tissues and the development of primary or secondary pathogenic antibodies, though the antigen-antibody reaction as such remains unaffected. Kurnick has suggested an attack on the causal factor by repeated intramuscular injections of fresh blood or leucocytes; the authors discuss the theoretical basis of this suggestion and offer criticisms of their own. [The original paper should be consulted for details.] 

D. Freiskel.


A retrospective study has been made of 111 proven cases of polyarteritis nodosa which had been under care in nine teaching hospitals during the period 1946 to mid-1953. In seven patients the appearances were atypical; these were not considered further. The study provided new information particularly with regard to classification, aetiology, and blood-pressure changes. It seemed that the most useful classification was one based on the presence or absence of lung involvement. Cases with lung involvement tended also to show a number of other features which were not seen, or were only rarely seen, in the other group. The chief of these were a respiratory illness initiating and generally dominating the disease, blood and tissue eosinophilia, granulomatous polyarteritis, and necrotizing lesions not demonstrably related to arteries. These features are described, and are contrasted with the findings in cases without lung involvement. The possible relation of the syndrome to other diseases is discussed, and some previous reports are reviewed.

The aetiology of the disease remains uncertain, but there is evidence of an association with preceding respiratory infections (especially those due to streptococci) and with rheumatic fever. Further investigation is needed to determine the relative importance of the infection and its treatment; at present the infection itself is chiefly suspect. In a few cases the disease appears to have been due to sensitivity to drugs of the thiouracil group; the evidence by which other drugs have been incriminated is weak.

An attempt was made to correlate blood-pressure changes with the urinary and necropsy findings in the 86 cases in which blood-pressure records were adequate.

(1) Among the 48 patients whose blood-pressure remained normal, recent renal polyarteritis and glomerulitis were common, but healed lesions were rare.

(2) Of the seventeen patients who were observed to develop hypertension during the course of the disease, all but three showed healed renal polyarteritis or glomerulitis at necropsy, and urinary abnormalities had preceded the first rise in pressure in all patients of whom data were adequate.

(3) In 21 patients the blood-pressure was high when first measured, but in all but two the first record was made months or years after the onset of the disease; the necropsy findings were the same as in Group 2.

It is concluded that the development of hypertension in polyarteritis nodosa is associated with the healing stages of renal polyarteritis or glomerulitis.—[Authors' summary.]

Treatment of Polyarteritis Nodosa with Cortisone: Results after One Year. REPORT TO THE MEDICAL RESEARCH COUNCIL BY THE COLLAGEN DISEASES AND HYPERSENSITIVITY PANEL (1957). Brit. med. J., 1, 608. 4 refs.

An attempt was made by the Collagen Diseases and Hypersensitivity Panel of the Medical Research Council to assess the value of cortisone in the treatment of polyarteritis nodosa, and the results after one year are presented in this paper. It is pointed out that random allocation of patients to an untreated group was not possible because of the known poor prognosis if patients are untreated and the rarity of cases of this disease. Patients were admitted to the trial only after the diagnosis had been confirmed histologically by a panel of pathologists. With a few exceptions the initial dosage of cortisone was 200 mg. daily; if the response was poor the daily dose was raised by 100 mg. each week until signs and symptoms were suppressed or intolerable side-effects occurred; if symptoms were suppressed with 200 mg. daily, an attempt was made to reduce the daily dosage by about 50 mg. each week, the course finishing in the sixth week.

Of 25 patients originally selected for this trial, seventeen were finally accepted; there was also a control series of nineteen histologically proved cases with onset of the disease before the introduction of cortisone. Unfortunately the groups differed in many respects, particularly in the incidence of hypertension, which was present in eight of the controls but in only one of the treated group.

For comparison of results, therefore, the groups were further subdivided into those with and those without hypertension. At the end of one year's observation it was found that only seven of the nineteen controls were still
alive, compared with fourteen out of the seventeen patients in the treated group. Excluding the patients with hypertension, however, the figures were seven out of eleven and thirteen out of sixteen respectively.

The authors conclude the discussion as follows: "To maintain suppression of symptoms may require doses of cortisone which provoke troublesome and occasionally dangerous side-effects. Whether the treatment is better or worse than the disease is a matter on which we have no unequivocal evidence to present."

J. N. Harris-Jones.


The authors have reviewed the records of 270 patients with classic dermatomyositis seen at the Mayo Clinic between 1916 and 1954. Of these patients 179 were female and 91 male, a ratio of very nearly 2 : 1. There was a family history of the disease in only one case. Some type of malignant disease accompanied the dermatomyositis in eighteen cases (6·7 per cent.). Although it has been claimed that the incidence of malignant disease is unduly high in patients with dermatomyositis, the authors were satisfied that in their cases the malignancy was incidental, the age range of the eighteen patients being 40 to 72 (mean 55) years.

Cushing's syndrome was observed in two young female patients, and it appeared to have an ameliorating effect on the dermatomyositis. The clot test for lupus erythematosus gave a positive result in two cases, and in a further two patients the skin eruption had the characteristics of pityriasis rubra pilaris. Dysphagia of some degree occurred in 60 per cent. of the patients and an [unstated] number of cases of abdominal pain, gastrointestinal bleeding, and perforation of multiple gastric ulcers also occurred. Osteoporosis was recorded in thirty patients and calcinosis in 28, but there did not appear to be an obvious correlation between these two complications; calcinosis was most frequent in patients under 16 years of age, of whom 29·1 per cent. were affected.

In recent years 62 of the patients have been treated with cortisone, of whom 28 improved, nine obtaining a permanent remission. In fifteen cases the disease appeared to have been un influenced by treatment, and eleven patients died despite the treatment. Complications of cortisone therapy included hypertension, diabetes mellitus, and osteoporosis. In view of the short periods of treatment with cortisone the authors are unwilling to draw hasty conclusions, but they consider that cortisone treatment was of definite value, and in some of their cases was life-saving. J. N. Harris-Jones.


In this report from the Mayo Clinic are reviewed the case records of 235 patients with localized scleroderma seen at the Clinic during the period 1923-54. They were divided into two groups:

1. Those with linear lesions and plaques of morphea (191 cases).

2. Those with generalized bilateral, symmetrical morphea (44 cases).

Of the 191 patients in Group 1, 146 were female, a ratio of females to males of 3 : 1. The histories showed that the onset of the illness was frequently associated with trauma, infection, surgical operation, pregnancy, the menarche, or the menopause. A table showing the location and distribution of the lesions is given. Arthralgia, commonly limited to the side of the skin lesion, occurred in 44 per cent. of this group. Raynaud's phenomenon, usually involving the ipsilateral limb, was recorded in eight cases, migraine in 31, and epilepsy in six. A large range of skeletal abnormalities, mostly involving the vertebral column, were observed and are tabulated. Residual pigmentation was noted in 82 patients, and facial hemiatrophy in 38.

Individual histories (with photographs) from both groups of cases are given. J. N. Harris-Jones.


Cogan's syndrome consists in ciliary injection with granular infiltration of the cornea but no changes in the iris or fundus, together with tinnitus, severe vertigo and nystagmus, and rapid progressive deafness. There are no signs of systemic disease except eosinophilia and elevation of the erythrocyte sedimentation rate. Young males are most often affected. Cases of Cogan's syndrome associated with periarteritis nodosa have been reported by Oliner et al. (New Engl. J. Med. (1953), 248, 1001), and by McNeil et al. (Ann. int. Med. (1952), 37, 1253).

The present author has seen four cases in which the two conditions were associated in the past 3 years, and here reports two of them. The first patient, a man of 28, developed fever, diarrhoea, and cough, with deafness, vertigo and tinnitus, and interstitial keratitis. All pathological tests gave negative results (except for positive reactions to Salmonella paratyphi B and ragweed) and all antibiotics tried proved useless. Cortisone applied locally cured the eye condition. There was severe residual deafness and loss of cold caloric responses. In the other case there was total loss of caloric responses, severe deafness, and recurring diarrhoea with fever. There was a family history of asthma, but no personal sensitivity was found. Except for the ear symptoms, improvement was obtained with cortisone and blood transfusions. In both cases at some time during the course there was lymphadenopathy and enlargement of the liver and spleen. F. W. Watkyn-Thomas.


The author, from the Royal Victoria Infirmary, Newcastle upon Tyne, reports three cases in which careful
study of serial sections post mortem suggested a common vascular aetiology, the clinical and gross pathological findings being respectively of systemic lupus erythematosus, scleroderma, and dermatomyositis. Small arteries and arterioles of skin and of internal organs showed hyaline or granular material partly or totally occluding the lumen. It was adherent to endothelium, contained round cells and polymorphonuclear leucocytes, and appeared later to be covered by endothelium so as to lie deep to the intima. Further study suggested conversion of this material into fibrous thickening. The author considers, in view of these findings, that there is much to be gained by adopting the term "viscero-cutaneous collagenosis" to include a wide range of clinical entities "provided we could be sure what the term 'collagenosis' implies". John T. Ingram.


Controversy is still rife concerning the nature and origin of the fibrinoid material which is found in the lesions of the collagen diseases and of a great variety of inflammatory conditions. The authors have developed a technique using fluorescein-labelled rabbit antiserum against human fibrin which, they claim, is more sensitive than the conventional staining methods for the detection of fibrin. Such antiserum has been shown to be specific for fibrin and fibrinogen. Working at Harvard Medical School and the Children's Hospital, Boston, they have been able to demonstrate the presence of a specific reaction in a variety of lesions containing fibrinoid from cases of disseminated lupus erythematosus, rheumatoid arthritis, dermatomyositis, rheumatic fever, subacute and chronic glomerulonephritis, and periarteritis nodosa.

It is pointed out that the finding of fibrin (or some other, hypothetically, insoluble derivative of fibrinogen) in the fibrinoid lesion does not rule out the presence of other substances in fibrinoid material, but merely indicates that there has been a local conversion of fibrinogen to fibrin. This might be brought about by tissue breakdown products acting upon an excess of plasma proteins (of which fibrinogen is one) in the tissue, and the authors' findings give no indication as to the nature of the aetiological agents causing such tissue breakdown in the collagen diseases.

The article is well illustrated and the full details of the techniques employed are recorded. R. E. Tunbridge.


General Pathology


It has been claimed by Steffen (Schweiz. Z. allg. Path. Bakt. (1955), 18, 287; Abstracts of World Medicine (1956), 19, 138) that an organ-specific antibody exists in the blood in rheumatic diseases which is demonstrable in vitro by its reaction with lyophilized human tissue cells in the presence of a known amount of an anti-human-globulin serum (Coombs serum). The extent of the reaction can be determined by titrating the residue of Coombs serum against a mixture of human Rh-positive erythrocytes and incomplete Rh antibody.

The present authors, working at the University of Vienna, have repeated this work, keeping closely to Steffen's method and using skeletal muscle, heart muscle, or a mixture of skeletal muscle, heart muscle, and joint capsule as the source of the lyophilized cell substrate. A total of 163 tests were performed on one hundred patients (48 with rheumatoid arthritis, fifteen with acute rheumatic fever and carditis, two with subacute bacterial endocarditis, two with chronic rheumatic heart disease, and 33 without rheumatic disease. Duplicate tests on the same specimen of blood in a number of cases showed poor reproducibility despite strict precautions to standardize the reagents. The results are reported in terms of the highest and the lowest titres obtained, together with an extensive statistical analysis. Although there was a significant trend towards a higher consumption...
of Coombs serum in the test when performed with blood from rheumatic subjects, the authors found that the test failed to distinguish correctly between rheumatic and non-rheumatic subjects in from 30 per cent. to 38 per cent. of cases, depending on the definition adopted for a positive result. [The authors do not distinguish between the various rheumatic diseases studied.]

Allan St. J. Dixon.


At the University of Oklahoma School of Medicine an attempt was made to correlate changes in the serum protein and glycoprotein levels with the severity of the inflammatory activity in rheumatoid arthritis. The method employed was paper strip electrophoresis, the protein being stained with bromphenol-blue-zinc-sulphate and the glycoprotein with the periodic-acid-Schiff reaction. The various fractions in the developed strips were measured with a recording photometer, the total serum protein content being determined by the biuret reaction and the total serum glycoprotein content by the tryptophan method. The seromucoid content was also determined. The clinical activity of the rheumatoid process in the 33 patients studied was assessed in four grades, from “none” to “severe”. A control group of thirteen healthy subjects was also studied.

As the severity of the rheumatoid activity increased there was a rise in serum globulin levels, particularly those of the $\alpha_1$ and $\alpha_2$ fractions, and a corresponding decrease in the albumin level. There was a marked increase in serum levels of those glycoproteins associated with the $\alpha_1$- and $\alpha_2$-globulin fractions, this increase being in excess of the protein increase.

Clinical activity was closely correlated with the glycoprotein level considered in relation to the serum protein with which it is bound—the polysaccharide: protein ratio—the $\alpha_1$- and $\alpha_2$-glycoprotein levels, the seromucoid level, and the $\alpha_2$-globulin level. The authors point out, however, that this elevation of the $\alpha_2$-globulin level has been noted in many other inflammatory conditions and also that the apparent elevation of the glycoprotein level in excess of those of $\alpha_1$ and $\alpha_2$ globulin may in part be due to an increase in the level of the seromucoids, which have similar electrophoretic mobilities. Using the technique described, the amount of carbohydrate bound to albumin was found to be low compared with data previously obtained by salt fractionation. It is suggested that this may be due to appreciable amounts of carbohydrate-rich globulin being obtained with the albumin sample in the latter process.

It was concluded that of the various indices studied, the total serum glycoprotein level showed the highest correlation with the clinical activity of the rheumatoid process.

B. M. Ansell.


This paper consists essentially of a record of the results of the routine performance of the C-reactive protein test on 1,262 occasions on 729 patients admitted to the U.S. Public Health Service Hospital, San Francisco, with 123 different clinical diagnoses. In tabulating the results the authors group their cases in seven diagnostic categories.

Positive results were found during the acute phase in nearly all infectious bacterial diseases, with less frequent positive results in viral diseases and the more chronic infections. A positive reaction tended to be present in infections associated with gastro-intestinal disease and diabetes, severe congestive heart failure usually with mild pulmonary infection, acute coronary insufficiency, pulmonary infarction, acute rheumatic fever, rheumatoid arthritis, penicillin-sensitivity reactions, and malignant conditions with metastases, and during the first 24 to 48 hours after a major surgical procedure. A negative result is particularly noted as usual in acute infective hepatitis, cerebral thrombosis, and destructive lesions of the central nervous system. The authors consider that the test is more “sensitive” than the erythrocyte sedimentation rate in the presence of inflammatory or necrotic processes.

[It is difficult to deduce any “evaluation” of this test from this report, which is fundamentally a record of experience on a wide and general basis.]

Harry Coke.


Studies on the Mucoproteins of the Serum and Mesenchymal Tissues in Rheumatic Diseases. (Studio sulle mucoproteine del siero e sui mucopolisaccaridi di tessuti mesenchimali nella malattia reumatica.) RADINO, G. (1957). Reumatismo, 9, 121. 7 figs, 19 refs.

ACTH, Cortisone, and Other Steroids


In this communication from the Peter Bent Brigham Hospital, Boston, the authors posit the hypothesis that the delayed diuresis which occurs after a water load in patients with Addison’s disease is due to abnormal distribution of the ingested water in the body rather than to faulty renal response. To test this hypothesis they investigated the changes in the water content of plasma and erythrocytes, calculated from changes in the haemoglobin concentration and in the haematocrit, after a conventional Robinson-Power-Kepler water-excretion test in normal subjects and treated and untreated patients with adrenocortical deficiency.

The test showed that in thirteen healthy subjects there was a hypotonic expansion of the plasma volume with a transient increase in erythrocyte hydration until diuresis occurred during the second hour after the ingestion of the water load. The erythrocyte volume then rapidly returned to normal, although the increase in plasma volume persisted until after the fourth hour. In ten patients (five men and five women) with untreated Addison’s disease there was a significantly greater and more persistent increase in erythrocyte water content than in the normal subjects, but plasma hydration did not differ significantly either in degree or duration from normal. The delay in water diuresis thus parallels the erythrocyte water content rather than the degree of plasma dilution.

It seems reasonable to assume that excessive hydration may also occur in other cells of the body, and the authors suggest that this abnormality in fluid distribution is the cause rather than the consequence of the delayed water diuresis in Addison’s disease. The abnormality can be completely corrected by the administration of 100 to 200 mg. cortisone, as was shown in a further group of six patients, and was then accompanied by a normal diuretic response to the water load. However, the erythrocytes of patients with Addison’s disease exhibit no abnormal permeability to water when exposed to increasing haemodilution in vitrō, nor does hydrocortisone have any effect on their permeability. The authors therefore suggest that the abnormal changes found in vitrō may be related to the persisting excretion of antidiuretic hormone, and that cortisone can correct the abnormality by inhibiting the secretion of this hormone.

Robert Mahler


An attempt was made at Sheffield Royal Infirmary to investigate the role of the adrenal glands in the metabolic response to operation by studying water, electrolyte, and nitrogen balance, as well as urinary excretion of 17-keto-steroids and 17-ketogenic steroids, in patients undergoing bilateral adrenalectomy and oophorectomy for mammary carcinoma. The eight subjects were between the ages of 30 and 58 years and had widespread soft-tissue and often bony metastases following a previous radical mastectomy for mammary carcinoma. A full study was made of seven patients, two of whom underwent a one-stage bilateral adrenalectomy and oophorectomy, while five were studied during removal of the second adrenal gland some 10 to 14 days after removal of the ovaries and one gland. All these patients received cortisone throughout the study, the five undergoing the second adrenalectomy in doses of 200 mg. daily and the other two doses of 150 and 100 mg. daily respectively, starting 3 to 12 days before the operation. (Investigations in the eighth case were limited to the blood electrolyte and eosinophil changes.

A slight fall in serum sodium and chloride levels was noted, which was of a similar order to that seen in “normal” patients undergoing surgery. The balance data were compared with those obtained in similar studies on patients undergoing partial gastrectomy and showed the same tendency to retention of sodium and chloride and loss of potassium. Although the retention of sodium and chloride was less and the loss of potassium greater in the authors’ subjects, the differences were not significant. The range of values in the nitrogen-balance studies was wide and the average loss less than has been reported in patients undergoing gastrectomy. The authors suggest that this difference may be attributed to the debilitated state of their patients and to the fact that in five cases there had been a previous recent operation, the negative nitrogen balance in the other two cases being greater than the average despite a lower dosage of cortisone. All remained in positive fluid balance.
Although the excretion of ketogenic steroids before operation varied with the amount of cortisone administered, there was a wide variation, from 29 to 53.4 mg., in the mean daily post-operative output of the five patients who were all receiving the same dosage of cortisone and had been subjected to the same operative procedure. This variation could not be related to the patients' weight, daily urinary volume, or general condition, and it was therefore thought to be due either to individual differences of metabolic pattern or to varying ability to mobilize intramuscular cortisone. In two cases the eosinophil count showed no rise following a pre-operative suppression by cortisone, while in the remainder it remained high before operation and was depressed for only a few days immediately after operation, after which it returned to or exceeded the pre-operative level.

It was concluded that the pattern of metabolic response to trauma in these patients fell within the accepted "normal" range and therefore that variations in adrenocortical steroid levels are not essential either for the initiation or maintenance of metabolic changes after surgical operation. B. M. Ansell.


The author reports his experience at Westminster Hospital, London, in the treatment of 150 patients rendered deficient in adrenocortical hormone by adrenalectomy, performed in five cases for malignant hypertension, in two for Cushing's syndrome, and in 143 for metastatic malignant disease. Of the last-mentioned group of patients 65 survived more than 6 months, the two patients with Cushing's syndrome remain alive and well, but only one of the five patients with malignant hypertension survived more than 2 years, the others dying at 10, 12, 12, and 19 months, respectively, after operation.

The greatest therapeutic problems arise in maintaining the patients subjected to adrenalectomy because of metastatic malignant disease, the chief variables to be studied in these cases being the salt and water balance, the cortisone requirements, and the activity of the underlying malignant disease process. The author emphasizes the difficulty in differentiating between the symptoms and signs of water and sodium imbalance and of cortisone deficiency. Thus, apathy, anorexia, nausea, and vomiting may be due to water intoxication, sodium loss, or cortisone deficiency; the last may be absolute, as occurs in omission of the usual dosage, or relative, when due to intercurrent infection or extension of the malignant disease. Of the salt-retaining agents at present available, cortisone and hydrocortisone may provide adequate substitution in many cases. Aldosterone is the most potent sodium-retaining, potassium-eliminating hormone yet isolated from cortical extract, but it has been shown that in adrenalectomized man aldosterone given alone does not prevent signs of adrenal deficiency (Maclean et al., *J. clin. Invest.* (1955), 34, 951).

Recently 9α-fluorohydrocortisone has been found to be a more potent salt-retaining agent than hydrocortisone itself, but used alone it is too potent for practical use. However, in combination with cortisone acetate, doses of 0.125 mg. 9α-fluorohydrocortisone may be of great value, especially in patients who are themselves able to detect early symptoms and signs of mild salt deficiency; in cases of severe salt deficiency a larger dose (1 mg.) of 9α-fluorohydrocortisone may be required. Until this preparation became available, deoxycortone acetate was a useful supplement to cortisone therapy, and liquorice root and its extracts also exert a mild deoxycortone-like action; when administered to adrenalectomized subjects in conjunction with cortisone, glycyrrhetinic acid causes some retention of sodium and chloride, but has a stronger water-retaining effect.

In the author's series of adrenalectomized patients the hypertensive group remained well on a daily dose of 50 mg. cortisone acetate with no additional salt-retaining agent, and similarly no problem regarding salt and water balance arose in the cases of Cushing's syndrome. In the group with metastatic malignant disease, however, control was more difficult. Initially they were mostly controlled on cortisone alone in a daily dose of 50 mg., but in many cases salt deficiency developed later and additional therapy with deoxycortone acetate or 9α-fluorohydrocortisone was required. The author stresses the importance of maintaining adrenalectomized subjects on full substitution therapy and has found that the required daily dose of cortisone ranges from 37.5 mg. to 50 mg. In an adrenal crisis, intravenous hydrocortisone, 100 to 300 mg. in a saline infusion given over 6 to 24 hours, has proved the best treatment; for the crisis in patients with severe salt loss 9α-fluorohydrocortisone may be infused intravenously in one-twentieth of the dose of cortisone.

John Lister.


At the Ospedale Maggiore, Turin, the authors have treated 38 patients (47 joints) suffering from various rheumatic diseases with prednisolone tertiary butylacetate given by intra- or peri-articular injection, the dose employed varying from 20 to 60 mg. In six cases an injection of hydrocortisone acetate was later given into the same joint after a suitable interval and the effects of the two substances compared.

In seventeen cases of rheumatoid arthritis of varying severity and duration, 28 injections produced complete or nearly complete local improvement on fifteen occasions, fair improvement on seven, slight on two, and had no effect on four; the effects were temporary and lasted longest in those cases which had improved the most. There was no apparent correlation between the size of dose and the result. In fourteen cases of degenerative joint disease, 24 injections were given (nineteen into the knee and five in the hip). In the knee-joint these produced great improvement in nine instances, moderate in five, slight in one, and none in four. Of the cases of
hip-joint disease, none was greatly improved, one being moderately and two slightly improved, and two unchanged. Again, no correlation with dose level was found.

Hydrocortisone was given to three patients with rheumatoid arthritis and three with osteo-arthritis. Comparison was difficult, but the authors formed the impression that if the two drugs are given in equal doses a greater response is to be expected from prednisolone. This drug was also tried in one case of gout, three of de Quervain's tendon-vaginitis, and three of peri-artthritis of the shoulder, with moderate benefit in a few cases. David Friedberg.


In this paper attention is drawn to the observation that steroid therapy, in doses which control symptoms, begins to lose its beneficial effect within a few months and that serious side-effects may develop. It is argued, therefore, that rheumatoid arthritis should, in the first instance, be treated with the more traditional remedies in the hope of inducing a remission; such remissions are known to last from a few months to many years. If no success is achieved in 12 to 18 months, then steroid therapy should be considered. In general, maintenance doses tend to be too high; for example, the administration of 15 to 20 mg. prednisone daily, if continued for a long period of time, will usually lead to trouble. According to Hench, a patient may suffer at one and the same time from endogenous hypocorticoidism and exogenous hyper-corticoidism. Hence even a slight reduction in dosage is likely to aggravate symptoms considerably.

Physiologists have calculated that the human body produces daily 25 mg. corticoids, expressed as hydrocortisone, daily, which corresponds to 5 mg. prednisone. On the basis of these observations the authors recommend that the steroid should be given at 6-hrly intervals, and that after giving 15 to 20 mg. daily for an initial period of 5 to 10 days, the dose should be reduced to the minimum necessary for maintenance. For this purpose 1 mg. tablets of prednisone are required so that a reduction of 1 mg. every 3 days can be effected until the required maintenance dose is reached. This varies with the individual, but is usually found to lie between 5 and 10 mg.

(In the discussion that followed the presentation of this paper, Weill-Hallé referred to an injury he himself had sustained a year previously to two cervical vertebrae; the resulting brachial neuralgia had been intractable, but had yielded finally to prednisolone, of which 6 to 7 mg. was still required daily, any attempt to reduce this dosage to 3 or 4 mg. being followed after a few days by recurrence of symptoms. This maintenance dose had not caused any of the usual side-effects which, as suggested, might depend on pre-existing, if unsuspected, organic defects. In his reply the author agreed as to the spectacular effects of prednisolone in relieving pain due to trauma, but pointed out that this case stressed the possibility of a state of dependence developing even in non-rheumatoid conditions.) D. Preiskel.


At the Rheumatic Centre of the Ospedale Maggiore, Turin, the authors have studied the effect of treatment with prednisone on the glucose tolerance curve and the insulin sensitivity curve in two groups of patients suffering from rheumatoid arthritis. The first group (seventeen cases) had been receiving the drug for some time and were on maintenance doses; the second group (six cases) had received 40 mg. prednisone daily for 8 days. Glucose was given at the level of 1 g. per kg. body weight and insulin in doses of 0.15 unit per kg. body weight. [For the detailed results for each case, which are given in tables, the original paper should be consulted.]

Despite the long-continued administration of prednisone in Group 1, the fasting blood sugar level was normal, the highest figure recorded being 119 mg. per 100 ml. In about half the cases in this group and occasionally also in the second group a "lag curve" of glucose tolerance was found, without a succeeding hypoglycaemia. A similar proportion of cases in each group showed slightly increased sensitivity to insulin. The authors point out that the degree of departure from normal was variable, but in no case marked. They conclude that prednisone does not interfere with glucose metabolism as seriously or as frequently as cortisone and hydrocortisone.

David Friedberg.


At the Clinic of Infectious and Tropical Diseases of the University of Naples the author carried out four groups of investigations on the influence of prednisone and prednisolone on immunity. Two groups of experiments were carried out on human subjects.

(1) The effect was studied of the prolonged administration of prednisone in high doses (40 to 60 mg. daily according to body weight for 14 days) on the development of active immunity in ten patients in the later stage of convalescence from typhoid fever who received high doses of typhoid vaccine intravenously during the same period; a control group of ten patients also received the vaccine, but without any prednisone.

(2) The effect of prednisone in similar doses was studied on the development of active natural immunity in patients suffering from typhoid fever, one group of twelve...
patients receiving the steroid from the seventh to the eleventh day of the disease, and another group of twelve receiving it from the fifteenth to the twentieth day. (The second group received 1·5 g. chloramphenicol daily for the first 10 days, and 1 g. for the following 18 days.) It was shown that in the early stages of the disease there was a diminution of active natural immunity when either prednisone or chloramphenicol was given. After the eleventh day of the illness, neither prednisone nor chloramphenicol had any influence. In convalescents hyperimmunized with large doses of typhoid vaccine, prednisone reduced the rate of formation of antityphoid agglutinins only slightly and in an inconstant manner.

In experiments on rabbits it was shown that the injection of prednisolone at a rate of 5 mg. per kg. body weight daily prevented the formation of antibodies in animals given three intravenous injections of antityphoid vaccine in 3 days. On the other hand prednisolone did not affect antibodies already formed or injected in large doses (10 ml. serum with a titre of 1 : 40,000) for passive immunization. In the prevention of formation of antibodies in the rabbit, prednisolone appeared to be twice as effective as the equivalent dose of cortisone.

V. C. Medvei.

Some New Negative Results observed in Experiments with Cortisone and Hydrocortisone. (Croton Oil Dermatitis, Schick-Test, Ultraviolet Radiation Dermatitis, Herpes Simplex and Vaccinia of the Cornea, Mitotic Effect of Cetylic Ointment.) (Quelques nouveaux résultats négatifs observés au cours d'expériences avec la cortisone et l'hycrocortisone. (Dermitis au huile de croton Schick-test, dermite aux rayons ultraviolets, herpes simplex et vaccine de la cornée pousée mitotique par unguentum cetylicum.) Musso, E. (1956). Acta endocr. (Kbh.), 21, 77. 2 tables, 13 refs.

The dermatitis in the guinea-pig produced by croton oil was not influenced by cortisone injections. The reaction of guinea-pigs after intra- and subdermal injections of diphtheria toxin was not affected by cortisone injections.

The erythema produced by ultraviolet radiation in man was not influenced by cortisone injections nor by treatment with 2·5 per cent. hydrocortisone ointment. Both the corneae of rabbits were inoculated with herpes simplex or vaccine Lancy. One eye was treated with drops of 2·5 per cent. hydrocortisone acetate every second hour for 10 days. No difference in the evolution of the infections was seen in the two eyes. G. von Bahr.


Clinical and Biological Findings and Practical Considerations concerning the Unfavourable Side-Effects of Prednisone Therapy in Rheumatic Diseases. (Rilievi clinico-biologici e considerazioni pratiche sugli effetti collaterali sfavorevoli della terapia prednisonica delle malattie reumatiche.) Daneo, V. (1957). Minerva med. (Torino), 48, 87. 40 refs.


Abstracts

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