ABSTRACTS

This section of the ANNALES 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


In an investigation at the New York Hospital—Cornell Medical Centre—of the effect of hormone therapy on the course of rheumatic carditis, the history of one hundred patients treated without hormones was compared with that of 55 receiving hormone therapy. The hundred control patients experienced 165 attacks of active carditis between 1930 and 1955. Their ages varied from 3 to 18 years; 72 of the attacks were initial and 93 recurrent. Careful study of the cases occurring in the two 10-year periods 1935-45 and 1945-55 showed that there had been no significant difference in the type and severity of the disease. In one-fourth of the patients, chorea, and in one-half polyarthritis, accompanied the carditis, and in about 12 per cent. of the attacks subcutaneous nodules were observed. The duration of active carditis was less than 2 months in 20 per cent. of the attacks, 2 to 4 months in 30 per cent., and from 4 months to over a year in 50 per cent. The follow-up period varied from 3 months to 21 years and averaged 9 years. During this time, increase in cardiac physical signs rarely occurred without an obvious attack of carditis, and murmurs regressed in one-third of the patients.

The 55 patients (aged 4 to 19 years) receiving hormones were observed during 1949-55, and in all cases treatment was instituted within 3 to 21 days of onset. The attacks in 25 cases were initial and in thirty cases recurrent. The carditis in the hormone-treated group appeared to be slightly more severe than in the controls. The hormones used—corticoterphin, 25 units intramuscularly every 6 hours for 4 days, and then 20 units 6-hrly for 3 days; cortisone, 100 mg. orally 6-hrly for 4 days and then 80 mg. 6-hrly for 3 days; and hydrocortisone, 80 mg. 6-hrly for 4 days and then 60 mg. 6-hrly for 3 days—were equally effective. In the majority of cases, bradycardia developed on the second day; transient hypertension was occasionally noted towards the end of treatment. In most cases, heart size decreased and new murmurs regressed by the third to seventh day. After therapy, most cases in which treatment was started in the third week developed transient fever and joint pains on the fourth to seventh day, and in three cases evidence of carditis was observed, but this regressed spontaneously. The duration of active carditis was less than 2 months in all cases, in two-thirds of them being less than one month. It was found that the earlier therapy was started, the shorter was the duration of the carditis. While all the control patients had evidence of residual cardiac damage at the end of the attack, 84 per cent. of the hormone-treated group had no evidence of residual damage, or, in the case of recurrent attacks, of an increase in residual cardiac damage. During the follow-up period of 6 months to 5 years, murmurs regressed in two-thirds of the total group (as compared with one-third of the control patients).

In eight additional cases receiving 7 days' hormone therapy one to 4 months after the onset of carditis there was no apparent effect on the disease. It is urged that it is essential that hormone therapy should be started as early in the course of the attack as is possible while the lesions are still reversible.

C. Bruce Perry


In this paper from the Bogomoletz Medical Institute, Kiev, the author describes his experience in the treatment of 28 cases of rheumatic chorea with a regimen of complete rest and prolonged sleep. The children were nursed in wards of two or three beds only, with shaded lights, and isolated from noise but well-ventilated, in which the daily routine was strictly observed, the time allowed for talking, playing, and reading being very limited. Once daily a teacher read or told the patients a story which was specially selected as being not likely to arouse any emotional tensions.

Drug therapy consisted of phenobarbitone, 0.02 to 0.05 g. twice a day, with bromides and "pyramidon" (amidopyrine), 0.25 to 0.3 g. four times a day. The dose of phenobarbitone was usually decreased after the first 2 weeks, and in the majority of cases could be omitted after the third week as the rhythm of spontaneous sleep developed. With these measures periods of prolonged
sleep were easily achieved. Early in the investigation it was realized that 16 to 18 hours of sleep per day was too much, and thereafter the aim was 13 or 14 hours of sleep out of the 24, divided into 11 or 12 hours during the night and 2 or 3 during the day.

The results in the 28 children, who were suffering from chorea of all degrees of severity, treated by this method during 1951-2 were contrasted with those in a comparable group of thirty children treated in 1950 with the same drugs but without this regimen of prolonged sleep. The comparison showed that the addition of prolonged sleep shortened the duration of the illness and had a beneficial effect not only on the neurological and psychological manifestations of the illness, but also on the course of the cardiac complications. Marcel Malden.


It has been established that most patients with acute rheumatic fever show evidence of recent infection with β-haemolytic streptococci of Lancefield's Group A, and that such patients have a significantly greater antibody response than those with uninfected infections. It has further been shown that in infants and young children antibody response increases with age, and it has been suggested that this may be due to conditioning of the antibody-forming organs by repeated exposure to streptococcal antigens. This observation, together with the rarity of rheumatic fever in very young children, has been held to support the concept that sensitization to streptococci or their products is closely related to the pathogenesis of rheumatic fever. In an attempt to elucidate this problem the authors have estimated the antistreptolysin-O titre in 107 rheumatic children at the Canadian Red Cross Memorial Hospital, Taplow, Bucks. Only those children were chosen who were seen in their first attack of acute rheumatic fever within 4 weeks of the onset of symptoms and were under 12 years of age. The highest titre found within 4 weeks of admission was recorded for this survey. Simultaneous throat and nose swabs were examined for Group-A β-haemolytic streptococci and previous upper respiratory-tract infections noted. No age difference in the frequency of positive swabs or preceding upper respiratory-tract infections was found. The twenty children who were under the age of 6 years showed a significantly lower frequency of raised antistreptolysin titres and a significantly lower mean titre than those over that age; this is regarded as indicating that the pathogenesis of rheumatic fever is not primarily related to the sensitization to streptococci or their products. G. W. Csonka.


The syndrome which occurs after cardiomyotomy in patients with rheumatic heart disease is discussed in this paper from Maimonides Hospital of Brooklyn and the State University of New York. It is characterized by fever and pleuropericardial chest pain, congestive heart failure, pleural effusion, polyarthritis, arhythmia, abdominal pain, subcutaneous nodules, haemoptysis, and psychosis; there is laboratory evidence of a non-specific inflammatory process. In the majority of cases the initial episode is observed within one month of operation, and there are recurrences up to 28 months afterwards.

A series of 84 patients (26 men) with mitral-valve disease who were subjected to cardiomyotomy were observed; 58 had pure mitral stenosis, and in 48 rheumatism was considered to be completely inactive. Of the 84 patients, 58 were given cortisone prophylactically in a dosage of 75 to 300 mg. daily for 3 to 6 weeks after operation, while 26 served as controls. The syndrome occurred in eight of the controls; in the cortisone-treated group it occurred while the drug was being taken in four and after the drug was withdrawn in seventeen. Although the syndrome developed in two patients in whom there was clinical evidence of active rheumatism before operation, there was no clear correlation between the incidence of the syndrome and the pre-operative evidence of possible rheumatic activity or the presence at operation of Aschoff bodies in the auricular appendages.

Once established, the course of the syndrome was unaffected by antibiotic therapy and was not definitely influenced by salicylates or amidopyrine (“Pyramidon”), although these produced gradual and partial reduction in temperature. Cortisone (50 to 300 mg. daily) was given as a therapeutic measure to 21 patients during 65 attacks of the syndrome; in 62 of these attacks fever subsided in 24 to 36 hours. Adequate doses of the hormone brought about dramatic relief of pain in the chest and joints, but it did not affect pleural or pericardial effusions or the chest pain and fever ordinarily associated with thoracotomy. Occasionally the addition of cortisone to a treatment regimen appeared to abolish arrhythmia or to lessen the degree of heart failure. Although three patients needed cortisone almost continuously for 5 to 12 months, no undesirable side-effects were noted. There were two deaths in the control group, while in the treated group there was one death from pulmonary oedema 16 days after operation; in this last case florid rheumatic endocarditis and myocarditis were found post mortem, and the authors consider that the dosage of cortisone given was too low.

It is suggested that the syndrome results from trauma to a heart already affected by rheumatism, although, as the authors point out, it differs from rheumatic fever in several important respects. D. Emile-Smith.


The authors describe a study of 31 female and two male patients with functional stenosis of the tricuspid valve of rheumatic origin who were treated at the Hôpital Lariboisiere, Paris. In fifteen cases the diagnosis was
confirmed at operation or post-mortem examination, but anatomical confirmation of the lesion was not possible in the remaining eighteen. Operation to relieve the stenosis was performed in four cases, in all of which mitral stenosis was also present and was dealt with at the same time. Haemodynamic studies suggested the presence of tricuspid stenosis in the others.

Tricuspid stenosis may be diagnosed by cardiac catheterization before the classic signs of the condition appear. The coexistence of tricuspid stenosis in a patient with mitral stenosis may be suspected if the second pulmonary sound is not increased and if there are signs in the aortic area. In addition, radiography may show marked enlargement of the heart to the right and an absence of pulmonary congestion. Minimal right axis deviation may be found in the electrocardiogram, occasionally accompanied by right bundle-branch block, but no evidence of right ventricular hypertrophy. At cardiac catheterization tricuspid stenosis is diagnosed by an increase in the right atrial diastolic pressure and a pressure gradient across the tricuspid valve; in some cases exercise may be required to demonstrate this change. The pulmonary vascular pressures are usually lower than would be expected from the degree of mitral stenosis, unless the tricuspid valve is incompetent as well as stenosed. The cardiac output is reduced.

In three of the present cases a successful tricuspid valvotomy was performed and seven other cases have been reported in the literature; the operation appears to be a useful one.

H. E. Holling.


In this paper is reported part of a follow-up study, initiated in 1949, of children who had been treated for rheumatic fever at Herrick House, Bartlett, Illinois. On reviewing the follow-up records of one hundred children examined in 1955 it was found that:

(1) Almost one-third were no longer under medical supervision;
(2) Two-thirds were not receiving any prophylactic treatment;
(3) Many children failed to adjust satisfactorily at school and at home on discharge from hospital.

An attempt was made to find the cause for this unsatisfactory state of affairs, but the reasons varied from case to case. It is emphasized, therefore, that all efforts to prevent relapses in rheumatic fever will be unsuccessful if reliance is placed solely on the co-operation of the patient and his parents. An educational programme is necessary so that:

(1) Physicians, nurses, school-teachers, and others who come into contact with these patients may be fully informed of advances in the study of the disease;
(2) The best care can be given to convalescents;
(3) Full use can be made of prophylactic measures.

Further, there is need for social services ensuring adequate rehabilitation of the rheumatic patient on return to his own environment. The authors conclude that all this necessitates a carefully-planned community programme.

C. Bruce Perry.


A comparative study of the skin sensitivity to serum in 34 children with rheumatic fever, chorea, or inactive rheumatic heart disease and 166 children with other ailments, mostly non-infectious and unrelated to rheumatic fever, is reported from the University of Helsinki. A drop of serum obtained by centrifuging blood withdrawn within the hour was placed on the skin and a scratch made through it, taking care to avoid drawing blood. A control scratch was made through a drop of saline. A cutaneous reaction—namely, a weal surrounded by erythema which appeared within 10 min. and faded in 30 min.—was seen in a number of cases, the result of the test being interpreted as positive when the serum gave rise to this skin reaction and control saline did not. About 10 per cent of the control children gave a positive reaction to sera obtained from controls and from children with rheumatic fever. A similar proportion of children with rheumatic fever gave a positive response to control sera, but the proportion giving a positive response to sera from rheumatic children was much higher, a skin reaction being observed in sixty out of 73 tests. There was no correlation between the result of the test and the treatment given, but the strongest reaction occurred when the test was carried out in children in the acute stage of rheumatic fever with sera from patients in the same stage of the disease.

E. G. L. Bywaters.


During 1946 to 1949 inclusive, at the Children's Medical Clinic, Lyons, 88 children suffering from rheumatic fever were treated with salicylates in doses of 5 to 12 g. by mouth daily for 3 to 6 months. In the following 4 years either corticotrophin (ACTH) or cortisone was used in treating 90 similar children. The dose of ACTH varied between 50 and 200 mg. (2 units) daily, that of cortisone from 100 to 200 mg. daily, and the duration of treatment from 11 to 150 days, with an average of 30 days; at the end of this course of hormone therapy salicylates were given for another month or two.

In a retrospective review of the results it was considered that the two groups were comparable as regards age and sex incidence, the condition of the heart on admission, the duration of the symptoms before treatment began (18 and 20 days respectively), and the proportion of patients who had had previous attacks. Those treated with hormones have naturally been observed for much shorter periods, but the minimum period of follow-up was fixed at 6 months after the onset of the disease. The authors conclude that the use of hormones represents a great advance in the treatment of rheumatic fever. The
clinical progress was more rapid in all respects and toxic phenomena were far less frequent than with salicylates. There were seven deaths among those treated with salicylates as compared with only two in the hormone group, although the latter included seventeen cases of severe pancarditis as compared with only eleven such cases in the salicylate group. There was no difference in the incidence of valvular damage among the survivors in the two groups.

[The conclusions drawn from this study must be accepted with reserve because there was no definite prearranged plan of treatment in either group and the two groups were not treated concurrently.] John Lorber.


From the Paediatric Institute (Academy of Medical Sciences), Moscow, the results are reported of the histological examination of necropsy material from 22 children who died of rheumatic fever. The patients’ ages ranged from 7 to 15 years, and the duration of the disease from 20 days to 8 years. The material was subdivided into three groups:

1) The first group consisted of eleven cases described as “dyscirculatory encephalopathy” which showed the following histological changes in the brain: congestion, perivascular lacunae and focal perivascular haemorrhages, degenerative changes in the vascular walls to the point of fibrinoid necrosis, degenerative changes and necrosis of the cortical nerve cells, and glial proliferation as well as marked proliferative changes in the ependyma.

2) “Exudative meningo-encephalitis”, six cases. Here, as well as the changes observed in the first group, there was focal infiltration with polymorphonuclear leucocytes, lymphocytes, plasma cells, and histiocytes which was mainly perivascular, both in the meninges and in the substance of the brain. Glial proliferation was very marked.

3) There were five cases of “proliferative encephalitis”, in two of which the disease started as chorea. The characteristic lesions were “gliogranulomata”, which are described as distinct from Ashoff nodes and consisted of lymphoid, histiocytic, and microglial cells.

A. Swan.


In this study of hereditary factors in acute rheumatism, the index cases were 287 patients (137 male and 150 female) from a total of 368 with rheumatic fever who (when children) had attended the Institute of Pathological Medicine, Florence, between 1940 and 1955. The parents and sibs of these patients were visited and examined for signs of rheumatic fever, the criteria for this being long-lasting fever with diffuse arthritis, or chorea even without any joint involvement, or valvular heart disease of rheumatic type. The parents and sibs of three hundred children attending the clinic for other illnesses were visited and examined in the same way and served as a control group.

The rates of incidence in the two groups were as follows (those for the rheumatic families being given first): fathers 15·6 per cent and 2·6 per cent; mothers 21·9 per cent and 3·0 per cent; brothers 11·4 per cent and 1·6 per cent; sisters 14·7 per cent and 2·1 per cent; sons 8·1 per cent and 1·6 per cent; and daughters 11·3 per cent and 2·4 per cent.

In four instances both parents of an index patient had rheumatic fever, and in these families five out of eight children, that is, one in four of the sibs of the index cases, were affected.

The authors note that no single genetic hypothesis would fit their findings; their preference is for a dominant gene with reduced penetrance. None of the following disorders showed an increased incidence among the relatives of the rheumatic index cases: asthma, urticaria, vasomotor rhinitis, Quincke’s oedema, and degenerative connective tissue disorders.

C. O. Carter.


In many diseases the efficacy of treatment can be measured in terms of duration of symptoms, and with this in mind the authors, at the Canadian Red Cross Memorial Hospital, Taplow, have analysed the duration of 206 attacks occurring in 170 consecutive patients suffering from chorea. Five patients who died between one and 15 weeks from the onset were excluded from the analysis.

The mean duration of the attacks was 19 weeks and the range between one and 117 weeks. The authors consider that these and other modes of expressing duration are unsatisfactory in a mixed group of patients who are admitted to hospital at varying intervals after the onset of their illness, and they prefer to use the life-table technique, relating the recovery rate at any stage of the disease to the patients under observation at that particular time. Charts are provided to show the differences resulting from such an interpretation. It was found that from the moment the diagnosis of chorea was proven the recovery rate was generally rapid in those patients who were observed to develop chorea while in hospital. It is suggested that abortive attacks may be quite common and may remain unrecognized, and that these may be partly responsible for the large number of cases of mitral stenosis in adult life in which no history of previous rheumatic fever or chorea is elicited. John Lorber.


As rheumatic fever “seems less severe and occurs less frequently in Miami than reported elsewhere” [in the U.S.A.], a detailed study of the prevalence of Group-A
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β-haemolytic streptococci in the throats of Miami school-children and of the immunological response of the host was undertaken to see whether bacterial factors alone could explain the difference. During the 8 months from October, 1953, to May, 1954, paired throat swabs were examined monthly and the serum antistreptolysin-O (ASO) titre determined bimonthly in 417 representative school-children from Grades I and II. For technical reasons it is probable that streptococci were recovered from less than 100 per cent of those children who harboured them, and that the figures obtained certainly do not overestimate the true prevalence of streptococcal infection. Yet altogether 126 (35.9 per cent) of the children gave at least one positive swab, and nine types of Group-A β-haemolytic streptococci were isolated, the types in order of frequency being 12, 1, 4, 3, 28, 31, 33, 23, and 44. The average ASO titre was higher and individual values were more frequently elevated in carriers than in those giving negative swabs. None of the carriers developed clinical rheumatic fever or scarlet fever, nor were the “nephritogenic” Types 12 and 4 associated with clinical nephritis. Thus the relatively low incidence of rheumatic fever and other serious streptococcal disease in this area cannot be attributed to rarity of pathogenic streptococci, and some other reason must be sought.

[The results of this careful and detailed study are set out in a manner which allows comparison with findings in other areas.]

*Allan StJ. Dixon.*


**Clinical Study of Rheumatic Heart Disease.** BANERJEE, J. C. (1956). *Indian Heart J.,* 8, 39. 11 refs.

**Critical Evaluation of the Present Concepts of the Aetiology and Epidemiology of Rheumatic Fever and Rheumatic Heart Disease.** CHAND, D. (1956). *Indian Heart J.,* 8, 27. 3 figs. bibl.


**Interpretation of Laboratory Tests in Rheumatic Fever (Interpretation des épreuves de laboratoire dans la maladie de Bouillaud).** MAURICE, P. (1956). *Brux.-ménd.,* 36, 1847. 7 refs.


Chronic Articular Rheumatism
(Rheumatoid Arthritis)

Course of Rheumatoid Arthritis during Four Years of Induced Hyperadrenalism (IHA). 

The authors, working at the Presbyterian Hospital (Columbia University), New York, have studied the effects of prolonged hormone therapy ("induced hyperadrenalism") in 68 cases of rheumatoid arthritis (four initially juvenile) and seven of ankylosing spondylitis. Most of the cases of rheumatoid arthritis were chronic and had ceased to respond adequately to "conservative" treatment (rest, aspirin, and gold therapy). The disease had been present for over 3 years in 90 per cent of cases; 75 per cent of the patients were female; 66 per cent were between 40 and 60 years of age. Progress was estimated:

(1) Subjectively, by ascertaining the degree of joint pain, stiffness, tenderness, and functional capacity;

(2) Objectively, by noting the amount of joint swelling and effusion, deformity, nodules, synovial pouches, and tenosynovitis;

(3) Clinically, by measuring the erythrocyte sedimentation rate (E.S.R.), pyrexia, haemoglobin value, body weight, differential sheep cell agglutination titres, and the results of streptococcal agglutination tests;

(4) By observing the radiological changes in the joints.

The adrenocortical hormones were given for periods ranging from 6 months to 3½ years, 63 of the patients receiving cortisone only, four ACTH (corticotrophin) only—seven received both hormones on separate occasions—and one hydrocortisone. The dosage was "as commonly employed elsewhere"; only one patient was given 100 mg. cortisone daily after the first 2 years, the dosage being smaller in the remainder. In addition, all the patients were given aspirin, 36 to 72 grains (2·4 to 4·8 g.) daily; in twelve cases phenylbutazone for 1 to 8 months, and in five gold therapy for 9 to 18 months, were given in an attempt to reduce the required daily dose of hormone.

The treatment had no apparent effect on the progression of bone and joint damage and of deformity. Disease activity, as estimated by elevation of the E.S.R., persistence of mild anaemia, and positivity of the differential sheep cell and streptococcal-agglutination reactions, was similarly unaffected. New nodules appeared in 28 patients. Subjectively, moderate to marked relief of joint symptoms was described by the majority of patients and persisted to the same degree throughout treatment. The dosage of the hormones was regulated to give sub-optimal relief of symptoms, in order to eliminate untoward reactions which tended to occur with the higher doses. Functional capacity was correspondingly increased with the relief of symptoms. Phenylbutazone and gold therapy had no appreciable effect in reducing the hormone dosage required. Remissions occurred in five cases after 10 to 25 months' treatment, but three of these patients relapsed.

The usual side-effects associated with such hormone therapy were observed, that is, psychiatric phenomena, cardiovascular and electrolyte disturbances, peptic ulceration, infections, metabolic and endocrine disorders, and skin and superficial tissue changes. These events tended to occur most frequently in patients with associated disease and debility, and necessitated hormone withdrawal in 37 cases, in ten temporarily and in 27 permanently.

The authors conclude that there is a place for prolonged hormone therapy in a limited, selected, group of patients with severe rheumatoid arthritis of long duration which has not responded to rest, aspirin, and gold therapy, provided that these patients are free of any major contraindication to hormone therapy, and do not require doses of cortisone exceeding 100 mg. per day. They suggest that borderline cases should receive a preliminary trial course of hormone therapy for 4 or 5 weeks, but that a return to simpler treatment should be made as soon as the patient's condition allows it.

[The simultaneous administration of aspirin, although stated to have little effect, tends to limit the value of these results, which the authors attribute solely to the hormone therapy.]

M. Kendall.


From the Canadian Red Cross Memorial Hospital, Taplow, Bucks, comes this report of a comparative therapeutic trial of cortisone and aspirin in the treatment of juvenile rheumatoid arthritis (Still's disease), which for this purpose was defined as starting before the age of 16. Of the 25 children in the trial, thirteen were treated with cortisone and twelve with aspirin, the selection being random and the two groups being almost identical at the beginning of treatment.

The standard dosage of cortisone for the first week was 300 mg. on the first day, 200 mg. on the second, and then 100 mg. per day for 5 days, after which the maintenance dose was determined. At the end of one year the dose of cortisone was between 50 and 100 mg. per day in six patients; of the remaining seven, one had been changed to aspirin, having derived no benefit from cortisone, one had been excluded from the trial because of dislocation of the hip after 6 months, and the remaining five did not need medication. The dosage of aspirin for older children was 6 g. a day for the first week, 2 g. a day for the second week, and then between 3 and 6 g. a day. At the end of one year regular aspirin treatment was maintained in only six of the original twelve patients, in a dosage of 1·3 to 4 g. a day, the other six needing no regular medication. X-ray films were taken of the affected joints in all cases before treatment and at the end of one year.

Assessment of the results showed that these were comparable to those in the similar trials in adult patients carried out under the auspices of the Medical Research Council, except that in the present trial a higher proportion of patients improved than was the case with the adults. In both treatment groups the children improved clinically and functionally to a similar extent. Radiography showed that there was an increase in the number...
of patients with erosions, this number rising from three before treatment to six at the end of one year in the cortisone group, and from two to five in the aspirin group. Side-effects attributable to the drugs were few and not serious.  

Kenneth Stone.


The authors, in this paper from the Veterans Administration Hospital, Bronx, New York, report experience of two serological tests for rheumatoid arthritis which were carried out in 1,576 patients. The sheep erythrocyte agglutination (S.E.A.) test was performed with selected sheep erythrocytes sensitized with a 1-in-20,000 dilution of antiserum (one-tenth of the basic agglutination titre) in 2 per cent sheep serum (complement inactivated). Naturally occurring agglutinins were first absorbed from the test serum. The titration was carried out in saline and in dilutions of sheep serum, the result of the test being considered positive if the titre in sheep serum diluent was fourfold or greater than that in the saline diluent. In the gamma-globulin or Fraction-II (FII) test a suspension of tannic-acid-treated sheep erythrocytes in buffered saline sensitized with pooled human gamma globulin was added to the test serum in saline dilutions. A positive reaction was one in which maximal agglutination was observed at a dilution of 1 in 28 or more.

The results of the first test performed in each patient, which are tabulated, were as follows. In peripheral rheumatoid arthritis 62 per cent of 331 patients gave a positive reaction to the S.E.A. test whereas 69 per cent of 180 gave a positive reaction to the FII test. When the two tests were carried out simultaneously on serum from 46 patients correlation was good in 39 instances and poor in seven. Of patients suffering from rheumatoid arthritis with spondylitis 26 per cent gave a positive reaction to the S.E.A. test and 33 per cent to the FII test. A much smaller percentage of patients with rheumatoid spondylitis alone gave positive reactions (2·1 and 3·6 per cent respectively). In patients with psoriasis and arthritis the percentage of positive reactions was 22 to the S.E.A. test and 29 to the FII test. Among patients with other arthritic conditions no group showed any significant incidence of positive results higher than 10 per cent, although some positive results were obtained in all, particularly in lupus erythematosus [for results in other\ types of connective tissue disease the table must be consulted]. Of 560 patients without any arthritic condition only three gave a positive reaction to the S.E.A. test and only two to the FII test.

The percentage of initial positive reactions in rheumatoid arthritis increased with the severity of the disease and the degree of incapacity, although two patients gave a positive reaction simultaneously with the onset of clinical symptoms. Of patients with nodules 95 per cent gave positive reactions to the S.E.A. test.

In most instances the results obtained with joint fluid were similar to those obtained with serum. [This paper will repay detailed study.]

L. E. Glynn.


The introduction of the Waaler-Rose test marked a great advance in the serological diagnosis of rheumatoid arthritis. The original test, in which whole serum was used, was relatively insensitive, detecting only between 40 and 60 per cent of cases. In this paper from the New York University College of Medicine, an investigation is reported which appears to carry this advance much further. The agglutinating factor in rheumatoid arthritis serum was concentrated in the euglobulin fraction by dialysis against M/150 citrate-phosphate buffer at pH 5·8 for 2 days. The euglobulin dissolved in isotonic saline buffered at pH 7·0 was then used in place of the whole serum in the Waaler-Rose test. With this reagent the results were positive in 76 out of 83 cases compared with 62 (out of 83) when the whole serum from the same patients was used.

Many of the false negative results obtained with whole serum are apparently due to the presence of an inhibitor substance that remains in the supernatant fluid when the euglobulin is precipitated. In non-rheumatoid subjects, however, a considerable proportion of this inhibitor substance is precipitated with the euglobulin. This difference of precipitability in rheumatoid and non-rheumatoid subjects has been developed into a highly selective test for rheumatoid arthritis. Whereas the inhibitor substance was absent from the euglobulin fraction of all the 83 patients with rheumatoid arthritis, it was present in 96 per cent of controls. In a second series of 46 patients and 38 controls, the test gave the correct result in every instance.

The results of these tests in patients with Still's disease, spondylitis, and psoriatic arthritis lent support to the view that of these three conditions only Still's disease is to be identified with rheumatoid arthritis. L. E. Glynn.


At the University of Oklahoma School of Medicine, Oklahoma City, the authors have attempted to correlate the results of various laboratory procedures with the clinical activity of rheumatic disease (excluding osteoarthritis, non-articular rheumatism, and gout). "Clinical activity" was determined by the assessment of the degree of morning stiffness, the sleep pattern, the presence of malaise, fatigability and weakness, acute joint manifestations, fever, appetite, and physical performance, and compared with the results of the estimation of serum glycoprotein (non-glucosamine) content, the C-reactive
protein test, the Ziff euglobulin modification of the haemagglutination test, and determination of the anti-streptolysin-O titre, the Wintrobe erythrocyte sedimentation rate, and serum γ-globulin level.

The closest correlation was obtained with the serum glycoprotein and the C-reactive protein determinations, while that with the erythrocyte sedimentation rate was barely significant. In patients with rheumatoid arthritis or "rheumatoid spondylitis" the haemagglutination test showed no correlation with clinical activity, although it showed a raised titre in 63 out of 66 cases of rheumatoid arthritis. The serum γ-globulin value was similarly generally raised in rheumatoid arthritis, but also showed no correlation with activity of the disease. Determination of the statistical correlation among the various tests showed a high correlation only between the serum glycoprotein level and the C-reactive protein test results.

[The whole of the authors' deductions depend essentially upon the method of assaying "clinical activity", which is not as yet on a generally agreed basis.]

Harry Coke.


The L.E.-cell test was carried out at the University of Arkansas School of Medicine, Little Rock, Arkansas, on the blood of 79 patients with rheumatoid or a rheumatoid-like arthritis, and on twelve patients who were known to have systemic lupus erythematosus. In eighteen cases a positive L.E. test result was obtained. Comparison with the clinical and physical findings revealed that in all of the eighteen patients showing an L.E. positive reaction more body systems (pulmonary, gastro-intestinal, renal, or cardiovascular) were involved than in those giving a negative L.E. reaction.

Although reluctant to affirm that a positive L.E. test result is pathognomonic of systemic lupus erythematosus the authors recommend that in every patient presenting with rheumatoid arthritis the L.E. test should be performed, as a positive test may give warning of multi-systemic disease. They add that the present results offer no clarification of the relationship between systemic lupus erythematosus and rheumatoid arthritis. E. G. Rees.


At the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases 25 patients with "disabling progressive rheumatoid arthritis" varying in duration from 3 to 28 years were allocated at random for treatment with either hydrocortisone or prednisolone. The average quantities given daily were approximately 50 mg. and 15 mg. respectively in divided doses [presumably by mouth]. [No mention is made of any other therapy employed concurrently.] Assessment was made in each case before starting treatment and again after 12 and 24 weeks—the functional status (graded according to a defined scale), the number of joints actively affected, hand grip (measured with a rolled-up sphygmo-}

manometer cuff inflated to 15 mm. Hg), haemoglobin level, and erythrocyte sedimentation rate being determined, and radiographs taken of the hands and feet.

No statistically significant difference in the results of treatment was found between the two groups, although those obtained with prednisolone were slightly the more favourable. Moderate degrees of dyspepsia occurred in more than half of each group, with one severe case in the group given prednisolone, and moon-face occurred in nine cases in each group; hypertension developed during treatment with prednisolone in one case, and pitting oedema in three cases, two being in the prednisolone group. [No mention is made of electrolyte studies during the trial, and it would appear that the patients were given a normal diet.]

The author concludes from her results that prolonged prednisolone therapy is not justified in this type of case.

J. Warwick Buckler.


Investigations were carried out at Karolinska Sjukhuset, Stockholm, into the nature of the factor present in the blood and joint fluid in rheumatoid arthritis which is responsible for the agglutination of sensitized sheep's erythrocytes in the Waaler-Rose test. Sera which gave a positive haemagglutination reaction were subjected to electrophoresis and the different fractions tested separately. As expected, the factor causing the reaction was found with the gamma-globulin fraction but did not correspond with any of those normally found in health. Experimental findings suggested that it is a protein body which is probably bound to another radical. Haemoglobin is not involved in the reaction, since it is the stroma of the erythrocytes which becomes "sensitized".

It was found that a haemagglutinating factor could be produced experimentally in rabbits by injecting serum or synovial fluid from appropriate patients. However, the factor thus produced had only a low haemagglutinating titre and its demonstration was made difficult by the development in the animal of an anti-factor. A haemagglutinating substance was also produced by culturing certain unclassified cocci isolated from the pharynx on connective tissue (joint capsule or tendon), the bacteria-free filtrate having properties similar to those of the human factor, though it was not possible to prove complete identity. This haemagglutinating factor is probably produced by the enzymic action of the bacteria on the connective tissue, and it is suggested that the factor present in human blood in rheumatoid arthritis is also the product of an abnormal enzymic process involving the connective tissue.

G. W. Csonka.


In many cases of Still's disease and rheumatoid arthritis there is a characteristic rash, and the present


ABSTRACTS


The nature and significance of extra-articular lesions in rheumatoid arthritis are discussed in this paper from the University and the Northern General Hospital, Edinburgh. Of ninety cases of rheumatoid arthritis seen at necropsy, sixteen showed extensive visceral involvement. Lesions were found in the endocardium in seven cases and in the myocardium in five; active pericarditis was noted in one case, healed pericarditis in three cases, and pericardial fibrosis with obliteration of the space in a further three. Arteritis was recorded in nine cases, lymphadenopathy in four, and amyloidosis in four. Clinically, the outstanding feature was the terminal emaciation, which was observed in all except one of the patients. Evidence of pleurisy was found in twelve cases, and in seven of these no aetiological factor other than rheumatoid arthritis was noted. In all four cases in which amyloidosis was found at necropsy there was diarrhoea associated with intermittent pyrexia during life.

Histologically, the extra-articular lesions were of three kinds—granulomata, non-specific inflammatory lesions, and amyloid deposits; more than one of these might be found in any individual case. In eight cases the extra-articular disease was considered to be the cause of death, while in seven others it was a contributory factor.

The literature on visceral extension of disease in rheumatoid arthritis is reviewed. In the authors' view the arthritis is non-specific and part of a more widespread "rheumatoid disease". They do not consider that the available evidence justifies the inclusion of rheumatoid arthritis among the so-called "collagen diseases".

William Hughes.


This paper from Temple University School of Medicine, Philadelphia, reports an inquiry into the measurement of the duration of morning stiffness as a reliable sign of activity of the disease process in rheumatoid arthritis. Morning stiffness has long been recognized as an early and almost universal feature of this disease process, and the author here presents data collected over a period of 10 years in one hundred consecutive cases. It is shown that the duration of severe stiffness is correlated roughly with the erythrocyte sedimentation rate as measured by Cutler's technique (maximum 5-min. fall). On the other hand it appears to be related to such features as age, sex, duration of the disease, and haemoglobin level. The author considers, therefore, that since most patients can note accurately the duration of morning stiffness, this should be recorded as a routine and will serve as an index of progress or the reverse.

W. S. C. Copeman.


For many years the erythrocyte sedimentation rate (E.S.R.) has been accepted as a rough guide to the degree of activity of the systemic disease in cases of rheumatoid arthritis. Unfortunately its estimation may be carried out in a number of different ways, the results of which are not comparable with each other. The present author advocates Cutler's method, which differs from the others in common use in that a wide-bore tube is used and that the fall of the erythrocytes is measured not only at the end of an hour, but also at 5-min. intervals during that hour. The shape of the curve constructed from these readings being considered to provide additional information regarding the degree of activity present. As a measure of the slope of the curve, the maximum fall in any 5-min. period (the 5-min. E.S.R.) is recorded.

It is considered that the results of a statistical analysis of the findings in ten cases of rheumatoid arthritis going into remission "indicates a trend toward normal, both for individuals and for the group, which is sufficiently regular to validate the Cutler 5-min. E.S.R. as a quantitative index of systemic rheumatoid activity". The author suggests other methods, such as Westergren's, that should be evaluated in a similar manner.

W. S. C. Copeman.


(Osteo-Arthritis)


At the Cook County and Presbyterian Hospitals, Chicago, of 182 patients with chronic (and in most cases stationary) degenerative arthritis who received placebo tablets containing 0.3 g. lactose for periods ranging from 4 weeks to 26 months, 105 (59 per cent) were improved for one month or more. About one-half of the patients initially relieved by the placebo later complained that the tablets did not help them. The 77 patients who reported no improvement with the tablets from the start were given saline injections and 44 (57 per cent) appeared to benefit from these. As expected, the placebo was of most effect in patients with the milder degrees of arthritis.

In the improved cases there was rapid decrease of pain, increased mobility, and later decrease in the swelling of 37 of these patients benefited continuously for 6 months or more. The group of patients who derived no benefit included some who had not responded to any form of medication, including drugs known to be pharmacologically effective in arthritis, such as salicylates and phenylbutazone. The authors point out that it is important to realize that there is a “placebo effect” in all types of treatment of a conscious patient and that this accounts for the great number of different substances offered for the management of arthritis.

G. W. Csonka.


In this paper from the Institute of Rheumatology of the University of Rome, the authors discuss the hypothesis that there exists a systemic osteo-artritic syndrome that is distinct from osteo-arthritis secondary to trauma or synovial inflammation and also distinct from that due to ageing of the joint tissues. As a contribution towards the elucidation of this question they have sought evidence of a generalized disturbance of capillary permeability in cases of osteo-arthritis by means of a modification of Landis’s test. They cite evidence in the literature in support of their contention that vascular factors play an important part in osteo-arthritis, and draw attention to an association with hypertension in their own and other cases.

G. W. Csonka.
Ocular Ochronosis with Alkaptonuria and Osteo-Arthritis.


(Spondylitis)

Patients with ankylosing spondylitis are said to be unusually susceptible to leukaemia. Since the literature does not contain a description of the bone-marrow findings before and after radiotherapy the present authors, in this paper from the University of Cambridge, report the results of bone-marrow examination in 28 patients with ankylosing spondylitis. Marrow hypercellularity was found in five of the ten patients who had received one or more courses of irradiation of the spine and in six out of eighteen patients who had had no irradiation previously; thus, it is not related to previous radiotherapy. The myeloid-erythroid ratio was normal in both groups; there was, therefore, no evidence of stimulation of the bone marrow by the dosages of radiation given to the spine.

The increase in cellularity affected all the formed elements of the bone marrow, the myeloid and erythroid cells both showing normal maturation. The only abnormalities detected were an increase in the number of plasma cells in ten patients and an increase in the eosinophil count in four. This is explained on the basis of a body reaction to foreign protein, associated with an increase in the plasma globulin fraction; the plasma protein values were not studied, however, in the present investigation.

G. H. Blair.


Rheumatoid spondylitis was discovered in five out of one hundred cases of aortic insufficiency which were seen at Georgetown University School of Medicine, Washington, D.C., for surgical correction of the valve lesion. There was thus some selection of cases, both as regards the severity and the type of valve lesion, although the authors state that in several hundred cases of mitral stenosis they have not observed one in which there was associated rheumatoid spondylitis.

The findings in these five cases were remarkably similar. All the patients were males (sixty of the original hundred were males) and all showed possible disease activity, as evidenced by a raised erythrocyte sedimentation rate and anaemia. The spondylitis was severe, having lasted for an average of 23 years. None of the patients gave a history of syphilis; only one had had rheumatic fever and one peripheral rheumatoid arthritis (no residual manifestations). The known average duration of heart disease was 10 years; in the authors' view the clinical signs were those of gross aortic incompetence, although mitral diastolic murmurs were heard. Of the five patients three died suddenly. At necropsy on two of these the mitral valves were normal and no Aschoff bodies were found; the aortic valves were thickened, shortened, and incompetent, but had no commissural irregularity or obliteration. In one case all layers of the aortic root were involved.

The authors state that a direct relationship must exist between rheumatoid spondylitis and heart disease, particularly that affecting the aortic valve.

J. Warwick Buckler.


At the laboratories of the Faculty of Medicine, Nancy, tests of respiratory function were carried out on 61 patients with ankylosing spondylitis, of whom 44 were free from respiratory affections but nevertheless showed diminished function. The mean value for total vital capacity in the patients was 3,120 ml., as against 4,463 ml. in 363 control subjects. The maximum volume of air expired during the first second after a forced inspiration was also diminished as compared with controls. The authors state that these changes are due to strictly mechanical factors consequent to costo-vertebral ankylosis which combine to limit the functional respiratory
potential under effort. The anatomical changes and their effect on respiration are irreversible and persist after the disease has ceased to be active. G. W. Csonka.


In an investigation of nearly one hundred patients [actual number not stated] with ankylosing spondylitis for changes in the skin it was found that 65 per cent showed varying degrees of scleroderma-like abnormalities, especially in the lumbar area. Histological examination was carried out on biopsy specimens in 28 cases of these, the skin was found to be normal in four, but the others gave a positive MacManus reaction and showed deficient elastic fibres in the skin sections. In the more severe cases the abnormalities extended to the anterior aspect of the trunk. The high incidence of these skin changes suggests that in ankylosing spondylitis the connective tissue is profoundly affected. [No clinical details of the patients nor of the type of preceding treatment are given.] G. W. Csonka.


Spondylitis ankylopoietica is commonly thought to be a disease beginning at puberty or during adolescence. The authors present four cases occurring in children, two of which were typical cases involving the whole spine in children aged 11 and 12 years, respectively; with a history of stiffness and pain for several years; the third was an early case in a child aged 11. The fourth case, however, occurred in a child aged only 34 months, and was manifested by rigidity and calcification in the cervical spine, associated with generalized Still's disease of 2 months' duration.

The authors consider that rheumatoid arthritis and ankylosing spondylitis are two quite distinct diseases. They suggest that an infantile form of spondylitis ankylopoietica occurs more frequently than is thought, but is usually confused with rheumatic fever, the spinal changes becoming apparent only during adolescence. The differential diagnosis is discussed. David Friedberg.


The term ankylosing sacro-iliitis is used by the authors to describe a syndrome which they discuss and differentiate from other types of sacro-iliitis and from spondylitis ankylopoietica. Essentially there is an ankylosing process involving the sacro-iliac joints and no other. Clinically the condition is characterized by lumbosacral or sacro-iliac pain on one or both sides, sometimes radiating to the coccyx but without signs or symptoms suggesting involvement of the rest of the spinal column or of rheumatoid arthritis. The radiographic changes in the sacro-iliac joints are those of spondylitis ankylopoietica; the rest of the vertebrae are normal. The natural history of the syndrome is extremely diverse, rendering prognosis difficult. In this paper from the Ospedale Maggiore, Turin, two cases are described clinically; in both, signs localized to the sacro-iliac joints had been present for over 15 years.

[The only laboratory investigation mentioned is that one patient had an erythrocyte sedimentation rate (Westergren) of 20 mm. in the first hour; treatment is not discussed.]

There is a detailed discussion, with many references to the literature, of the differentiation from the other rare conditions affecting the sacro-iliac joints, including sacro-iliac arthrosis, epiphysitis, osteo-chondritis, sacroliliitis of infective, rheumatoid, tuberculous, and senile degenerative origin, and sacro-iliitis condensans. The authors admit that ankylosing sacro-iliitis may be a precursor or a forme fruste of spondylitis ankylopoietica and suggest that the diagnosis be kept provisional, bearing in mind the possibility of spread to other spinal segments. David Friedberg.


(Miscellaneous)


"Butadion" is a newly synthesized compound related to phenylbutazone, being the sodium salt of 1:2-diphenol-4-N-butyl-3:5-dioxypyrazolidin. It is a white crystalline powder which, in contrast to phenylbutazone, is readily soluble in water. At the Second Moscow Medical Institute the author has observed the effect of this preparation on 43 patients with rheumatic fever and 17 with rheumatoid and other forms of non-specific polyarthritis.
The cases of rheumatic fever fell into three groups:

(1) In twenty cases there was polyarthritis without pronounced cardiac involvement. These patients received 0·6 g. butadion daily in divided doses at first, the dosage being reduced to 0·45 g. and then 0·3 g. daily with clinical improvement. The response was very rapid, joint pains disappearing on the first or second day of treatment, the leucocyte count becoming normal within 18 days, and the erythrocyte sedimentation rate (E.S.R.) falling to 20 mm. in one hour within 21 days on the average. The mean total dose of butadion was 18·3 g.

(2) In fifteen cases there was a recurrence of rheumatic fever in a patient with evidence of previous rheumatic carditis. The initial dose of butadion in this group was 0·6 to 0·8 g. daily and the total dose averaged 20 g. Clinical improvement was just as rapid as in the first group and the leucocyte count fell to normal even sooner, though reduction of the E.S.R. was delayed.

(3) Eight patients without joint manifestations, but with cardiac involvement, most of them having a subfebrile temperature and mild leucocytosis, received an unspecified dosage of butadion, which again brought about rapid clinical improvement, with a fall of the E.S.R. and leucocyte count to normal values within 16 days.

There was pronounced improvement in the cardiac symptoms and signs in the 43 patients in the series who had evidence of carditis. A careful watch was kept on the leucocyte count during treatment, but only in seven out of the sixty cases did the level fall below 5,000 per c.mm., the lowest value recorded being 3,800 per c.mm. On the other hand in five patients with relative leucopenia before treatment (4,200 to 5,000 per c.mm.) the figures increased to between 6,000 and 8,000 per c.mm. with treatment. The author is therefore cautiously optimistic about the possible danger of agranulocytosis due to treatment with butadion.

In the seventeen cases of non-specific polyarthritis treated with butadion other methods of treatment had been unsuccessful. This heterogeneous group consisted of cases of exudative, proliferative, and other forms of acute joint disease, ten of the patients being gravely ill. With a daily dose of 0·6 g. butadion the general condition improved just as rapidly as in the cases of acute rheumatic fever, but the local lesions were slow in clearing up.

A. Koby.

These tablets were employed "as a therapeutic adjuvant" in the treatment of 42 patients with active rheumatoid arthritis who showed evidence of increased capillary fragility in the form of petechiae appearing spontaneously or on the application of a pressure-cuff to the arm. It was not stated what other forms of treatment were given. They received initial doses of 400 to 1,000 mg. daily hesperidin-ascorbic-acid [presumably 200 to 500 mg. of each] according to the severity of their arthritis. This was later reduced to a maintenance dose of 300 mg. daily. Capillary resistance became normal within 2 months in 35 cases, which are reported to have shown a greater improvement than the remainder in respect of weight gain, reduction in erythrocyte sedimentation rate, reduction in joint swelling, and (possibly) increased resistance to upper respiratory tract infection during an observation period of 7 years; two patients in the latter group died of unrelated causes during that time. Similar benefits are claimed to have resulted from the administration of 300 mg. hesperidin-ascorbic-acid daily to seventeen patients with various manifestations of osteo-arthritis. Improvement in general health and reduction in joint pain were observed.

[The authors' claims are based on clinical impressions only, without controls, and no clear evidence that this treatment has a direct effect on the joint lesions is presented.]

G. H. Blair.

Erythema Nodosum as a Manifestation of Sarcoidosis.


The relationship between erythema nodosum and sarcoidosis was studied at the Middlesex Hospital, London, in a group of patients (seven men and twenty women, mostly young adults) suffering from the former condition. The Kveim test revealed the characteristic nodule of sarcoidosis in nineteen cases, and sarcoid tissue was found on biopsy examination of erythematous lesions (two cases), lymph nodes (four cases), skin (five), and liver (four). In 24 of the 27 cases chest radiographs showed enlargement of the hilar lymph nodes; the lymphadenopathy was bilaterally symmetrical and the enlargement persisted for an average of 6 months. In a few cases transient parenchymal mottling developed after the swelling of the nodes had subsided. No abnormality was found in the erythrocyte or leucocyte count, but there was a marked increase in the erythrocyte sedimentation rate.

Polyarthritis with pyrexia and sweating developed in seventeen patients either before or during the attack of erythema. Acute rheumatism was diagnosed in four cases, but there was no evidence of cardiac damage or of abnormal antistreptolysin titres; furthermore, the response to salicylate therapy was poor. The results of the Mantoux test were of little assistance in determining the aetiology of the condition—since the test was not carried out before the illness it was impossible to decide whether conversion was of recent origin.

The authors emphasize the importance of histological examination in the differentiation of the sarcoidosis

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syndrome from erythema nodosum due to other causes; the prognosis is favourable in erythema nodosum associated with sarcoidosis. A. Garland.


The authors fully review the literature concerning the use of ACTH and cortisone in Reiter's syndrome, and point out the difference of opinion which exists as to the effectiveness of these methods of treatment. They report in detail the clinical findings and the result of hormone treatment in ten patients under hospital care for Reiter's syndrome. Their experience is that ACTH and cortisone when given in adequate doses for a long enough period of time are effective in suppressing the symptoms, but that the course of the disease is not shortened by the treatment. It is considered that while ACTH and cortisone are not curative agents they are valuable in the treatment of Reiter's syndrome in order to keep the symptoms under control. J. R. Hudson.


The author examined 31 male patients with urethritis who, after periods ranging from 2 days to 2 weeks, presented polyarthritis with passing attacks of conjunctivitis. 21 cases had had more than one attack and eight more than three. X-ray examination of the sacroiliac joints showed slight sclerosing of one joint in thirteen of the cases with two or three attacks, and distinct changes of the joints in five of the cases with more than three relapses. Adequate treatment seems to be afforded by a suitable antibiotic with butazolidin. G. von Bahr.


This paper, based on a study of 237 cases of uveitis, demonstrated no association either between osteoarthritis and uveitis or between classical rheumatoid arthritis and uveitis. A marked association was seen between uveitis and spinal arthritis, and between uveitis and Reiter's disease. It is suggested that non-granulomatous uveitis may be divided into two groups: the first associated with spondylitis and occurring in males, and the second having no rheumatic association and occurring equally in men and women. A. G. Cross.


Treatment of Rheumatic Conditions with Local Hydrocortisone. Two Years' Experience. (Tratamiento de algunos procesos reumáticos con hidrocortisona local. Dos años de experiencia.) Sans Solà, L., and Barceló, P. (1956). Rev. esp. Reum., 6, 480. 15 refs.


Immediate and Late Results of Minute Doses of Adrenaline given Intravenously in Rheumatism. (Les effets immédiats et éloignés de l'adrénaline intra-veineuse en microdoses en rhumatologie.) Arsov, D. (1956). Rhumatologie, 3, 117. 1 fig.


Minor Trauma and Rheumatism. (Traumatismes benins et rhumatismes.) JOORS, M. (1956). *Scalpel (Brux.),* 109, 1053.


Sialography in Chronic Rheumatism. (La scialografía del reumatismo crónico.) LUCHERINI, T., CERVIN, C., and FIUMICELLI, A. (1956). *Policlinico, sez. prat.,* 63, 1081. 9 figs.

Disk Syndrome


In the opinion of the authors, myelography is still a very useful procedure in the diagnosis of lesions of the intervertebral disks if carefully performed, but it is emphasized that errors in interpretation will continue to occur if an inadequate amount of contrast medium is used, an insufficient number of films taken, and exploration of the vertebral canal is incomplete. The average amount of contrast medium needed is 6 ml., but the authors state that as much as 24 ml. may be used. [This seems to be an excessive amount, unless adequate removal can be ensured.] The advantages of myelography are that it allows the entire spinal canal to be visualized, that it is of value in differentiating tumours from disk protrusion, and that it indicates the presence of multiple lesions. “Pantopaque” is less irritating than “lipoiodol” and is more easily removed, but its absorption rate is very slow (1 ml. per annum) if it is not removed.

Diskography is of additional value when a bulging annulus is observed, and is useful in demonstrating the amount of disk degeneration present. It is also of value when myelography is negative and in the diagnosis of atypical back pain and sciatic syndromes. It should not be performed when rupture of the disk has occurred, as there is then a greater risk of local nerve-root injury due to distortion of the cauda equina, while severe local symptoms may result from the extradural extravasation of the contrast medium used (iodine) if there is an opening through the annulus fibrosus. The authors do, however, recommend diskography in cases of long-standing low back pain as a means of demonstrating possible underlying degenerative disk disease with or without mild protrusion not visible in the myelogram. They advise initial investigation by myelography, which, they say, will give positive findings in over 90 per cent of cases with a typical clinical history and objective neurological signs. In cases in which the myelographic findings are equivocal or negative, a history atypical, the physical and neurological signs negative or minimal, and the response to treatment unsatisfactory, diskography is recommended.

*J. MacD. Holmes.*


Three cases are reported in which, in association with cervical spondylopathy, there was an ocular syndrome characterized by a diminution of the visual acuity and...
alterations of the fundus and visual field. The ocular symptomatology responded favourably to treatment of the vertebral affection. M. Marin-Aguirregomozcorta.


Gout


Pararheumatic (Collagen) Diseases


After a short review of the literature on the treatment of lupus erythematosus with the anti-malarial drug "resochin" the authors describe the results obtained with this drug in the treatment of ten cases of lupus erythematosus discoides, four of chronic lupus erythematosus disseminatus, and one of lupus erythematosus acutus occurring in patients aged between 16 and 51 in whom the disease had been present for periods ranging from 6 months to 21 years. In five cases the patients were given a course of 1 to 4 tablets (each 0.25 g.) daily by mouth for 3 weeks to a total of 50 tablets (12-50 g.) while the remaining ten received 1 or 2 tablets daily to a total dose of 20 g.

After the first course three patients were clinically cured, nine greatly improved, two slightly improved, and in the acute case a remission of 73 days was obtained. The improvement was maintained for 2 or 3 weeks after cessation of treatment, but in a number of cases in which a mild relapse occurred a second course of treatment was given, but only one patient required a third course. At the end of one year from the beginning of treatment five of the fifteen patients were clinically cured, seven greatly improved, and two slightly improved; the patient with acute lupus erythematosus has had two remissions so far and still remains under observation. Among the side-effects attributed to the drug were slight loss in weight, general weakness, headache and giddiness, anorexia, and in a few cases pruritus in the affected skin areas. No change in liver function or in the blood picture was observed. Investigation of the photosensitivity of the skin before and after treatment showed that two patients had lowered sensitivity, one increased sensitivity, but the rest were unaffected. H. Makowska.

Clinical Significance of the L.E. Clot Test. Brustning, L. A., Stickney, J. M., Pease, G. L., and Reed, W. B. (1956). A.M.A. Arch. Derm., 73, 307. 5 figs, 9 refs. The records of 112 patients whose blood, when tested at the Mayo Clinic in 1951 and 1952, gave a positive reaction to the L.E.-cell test, have been reviewed with the object of assessing the value of the test more fully. The patients were divided into three groups, according to the clinical picture:

1. Typical (42 per cent);
2. Partly typical (35 per cent);
3. Frankly atypical (23 per cent).

In the last group weakly-positive responses to the L.E. test were the rule, and not infrequently only one such response was obtained on repeated testing. The average age of the patients in this group was 45 years (compared) with 35 years for those in whom the clinical picture was typical and rheumatoid arthritis was the chief complaint. Of the 25 patients in this group, seven had died, but in none of these was there any evidence of systemic lupus erythematosus at necropsy. The authors conclude that when the result of the test is weakly-positive its significance is uncertain. The test is a great aid in the diagnosis of systemic lupus erythematosus, but the results will "not serve for prognostic purposes".

E. G. Rees.

Comparison of Chloroquine and Gold in the Treatment of Lupus Erythematosus. Crissey, J. T., and Murray, P. F. (1956). A.M.A. Arch. Derm., 74, 69. 3 figs, 6 refs. Results in the treatment with chloroquine of 24 cases of chronic discoid lupus erythematosus were compared to a standard derived from treatment of 66 cases with gold sodium thiosulfate. There was no significant difference in the proportion of cases that responded to these drugs. Cases treated with chloroquine responded more rapidly than those treated with gold. There was a significantly greater number of recurrences within a year after chloroquine treatment than after gold. No detectable correlation was observed between the duration of the disease before and the duration after treatment with either gold or chloroquine, or, in chloroquine-treated cases, between the age of the patient and the duration of the disease. There was a small amount of negative correlation between the patients' ages and the duration after treatment in cases treated with gold.

Serious side-effects following chloroquine therapy were not seen. Visual disturbances and incubus were observed. Chloroquine is superior to gold aesthetically and in ease of administration. [Authors' Summary.]

Treatment of Chronic Lupus Erythematosus with Resochin. (Beitrag zur Resochinbehandlung des chronischen Lupus erythematodes.) Thiel, E. (1956). Derm. Wschr., 133, 660. 12 figs, 9 refs. The author, at the Charité Hospital, Berlin, has treated 101 patients with chronic lupus erythematosus with...
“resochin”, an acridine derivative. Compared with “atebrin” (mepacrine) resochin does not produce any skin discoloration and acts more quickly, but relapse after discontinuation of treatment occurs with both drugs.

The dosage of resochin was 375 to 500 mg. daily by mouth for 7 to 10 days, later reduced to 250 mg. daily, and finally to 125 mg. and maintained at that level until improvement or a total of 20 g. had been given. In case of relapse a second course proved effective. Local treatment was also given in addition (or alone in some cases) and consisted in the injection of up to 2 ml. 10 per cent resochin with 2 per cent “jenacain-adrenaline” in the proportion of 2 to 1 into each lesion to a total of 5 ml. per patient, this being repeated at 8-day intervals. The injection produces a violent burning sensation.

Of the 85 female and fifteen male patients, 79 were asymptomatic at the end of treatment and seven did not respond at all. Some of the cured cases had previously failed to respond to atebrin. The side-effects due to resochin, which were fewer and less severe than those of atebrin, included headache, vertigo, mild gastro-intestinal upsets, and loss of weight in some cases. In ten cases intolerance of atebrin resochin produced no side-effects.

F. Hillman.

Discoid Lupus Erythematosus treated with Plaquenil.


“Plaquenil” (7-chloro-4-[4-(N-ethyl-N-β-hydroxy-ethyl amino)-1-methylbutylamino]quinoline), a quinacrine type of drug, was given to seven patients suffering from chronic lupus erythematosus who had responded only partially to other forms of treatment, and in this paper from the University of Illinois College of Medicine and Cook County Hospital, Chicago, the results are described. Each patient received an initial dosage of three 200-mg. tablets daily. Only one patient experienced any side-effect—namely, an attack of vomiting—and treatment was resumed satisfactorily on a smaller dosage after a fortnight’s rest. Some involution of the lesions was observed in all cases, and the dosage was reduced to two tablets daily at 2 to 3 weeks. In two cases there was complete involution and in the remainder at least 40 per cent involution. No changes were observed in the blood or urine as a result of this treatment. There was no skin staining. Preliminary experience suggests that plaquenil is less toxic than other anti-malarial drugs of this type.

E. H. Johnson.


A clinical study is reported of the effect of “plaqueunil” [see above] in the treatment of 22 patients with discoid lupus erythematosus, six of whom had not been treated before, eleven had not responded satisfactorily to previous treatment, and five had been unable to tolerate other medication because of severe side-effects. The dosage initially was two 200-mg. tablets four times a day. If this dose was well tolerated and there were signs of improvement the dosage was reduced slowly, usually by 200 mg. every few days. Over a trial period of 4 months seventeen patients showed more than 50 per cent improvement while nine became free from all signs of disease activity. Side-effects—notably diarrhoea, intestinal cramps, nausea and dizziness—necessary cessation of treatment in fifteen cases; after a rest period treatment was resumed with a smaller dosage, which was usually tolerated.

The authors conclude that plaquenil offers considerable promise in the treatment of discoid lupus erythematosus, but that further study, particularly of the effective dosage, is required.

E. H. Johnson.


The results obtained with cortisone and corticotrophin in the treatment of diffuse scleroderma have been generally regarded as disappointing. In this paper from the National Institutes of Health, Bethesda, Maryland, a trial of prednisone in six patients (four females and two males) suffering from progressive symmetrical scleroderma is reported, the dosage of the drug being 20 to 30 mg. a day for uninterrupted periods of 6 weeks to 41 months. In all the cases there was improvement in the skin, with lessening of pigmentation, swelling, and tightness, and peripheral vasomotor changes were less marked. The most favourable response was obtained in patients with polyarthritis. One patient with pulmonary involvement experienced relief of exertional dyspnoea. Gastro-intestinal symptoms were not influenced. Facial rounding was noted in four patients, in two of whom acne developed. In the four females there was an increased growth of hair on the face and limbs.

E. W. Prosser Thomas.


In an attempt to elucidate the nature and pathogenesis of the collagen diseases, experiments were carried out at the Pasteur Institute, Paris, in which an acid solution of collagen (“collagen A” of Nageotte) was treated with solutions of various mucopolysaccharides normally present in mammalian connective tissues, such as chondroitin sulphuric acid and heparin, and of various inorganic salts and bacterial extracts. Chondroitin sulphuric acid and heparin, within certain limits of concentration and pH, each combined with collagen to form a fibrillar precipitate which disappeared on adding calcium chloride. Of the eleven inorganic salts tested, calcium chloride was found to be incapable of precipitating collagen in any concentration, and ammonium sulphate had a weak precipitating action in high concentrations only, whereas sodium chloride, bromide, iodide, and sulphate, strontium chloride, bromide, and
iodide, sodium salicylate, and acid sodium tartrate all precipitated collagen when added in moderate concentrations, some being also active in low, and others in high concentrations. Bacterial endotoxins and their cleavage products varied in their precipitating activity and in the stability to heat and resistance to calcium chloride of the precipitates obtained. Thus the endotoxins of Salmonella typhosa, S. enteritidis, and Eschericia coli produced poorly-formed, microfibrillary precipitates, whereas the products of Staph. aureus gave rise to long fibres.

The effect of various combinations of these substances was also studied. The addition of mixtures of heparin and sodium chloride and of chondroitin sulphuric acid and staphylococcal endotoxin caused no precipitation, whereas a mixture of heparin and S. typhosa endotoxin added to the collagen solution resulted in the formation of a microfibrillar precipitate resembling that produced by the endotoxin alone, but with different physical properties.

In the light of these observations it is suggested that the abnormality present in connective tissue in the collagen diseases is a derangement of the collagen mucopentasaccharide bond brought about by the presence of certain electrolytes in non-physiological concentration or of organic substances, especially of bacterial origin, not normally present.


The author [who is a recognized authority on systemic lupus erythematosus and its treatment] reports from the University of Southern California, Los Angeles, his experience with the new steroids prednisone and prednisolone in the treatment of 31 patients (of whom 26 were female) with this disease; the diagnosis was confirmed by the L.E.-cell test in 25 cases. Steroid therapy had already been established in 21 cases with cortisone or hydrocortisone, the remaining patients being either untreated or receiving antimalarial drugs. Prednisone was given in thirteen cases for periods up to 58 months and prednisolone in nine cases up to 30 months; in the remaining nine cases both drugs were given in successive courses. The dosage of prednisone ranged from 10 to 120 mg. per day and of prednisolone from 10 to 160 mg. per day.

As judged by the clinical response, haemoglobin level, and suppression of the L.E.-cell phenomenon, prednisone was found to have up to ten times the potency of cortisone, the average therapeutic ratio being 5 to 1, while it was about four times as active as hydrocortisone. Prednisolone was on the average five times as active as cortisone. The average maintenance dose of prednisone was 22 mg. per day. The author advises dietary restrictions and the administration of antacids and anti-cholinergic drugs for all patients receiving large doses of prednisone in order to prevent the high incidence of peptic ulceration previously noted following the use of this steroid. Sodium retention, though less than with cortisone, has also occurred after large doses of prednisone and low-salt diets were therefore found necessary. One patient in the series developed a duodenal ulcer while undergoing treatment, and a "Cushingoid appearance" was noted in thirteen cases and acme in five. The most serious side-effect of the steroids, however, was the development of severe diabetes mellitus in two patients (one of whom had a family history of the disorder), necessitating withdrawal of the steroid or the institution of Insulin therapy.

Patients receiving anti-malarial drugs before treatment with prednisone continued with this therapy in conjunction with the steroid therapy. Reviewing this series the author suggests that steroid therapy should be reserved for the more severe cases, since salicylates and anti-malarial drugs have proved an adequate form of treatment for earlier and milder cases.

J. N. Harris-Jones.

Studies on Periarteritis Nodosa, with Special Reference to Cardiac and Renal Involvement and Possible Aetiological Factors. [In English.] Bäckman, H. (1956). Acta med. scand., 154, 441. 6 figs, bibl.

The author reports his observations on fourteen cases of periarteritis nodosa studied at Turku University, Finland. The diagnosis was confirmed by biopsy in two cases and at necropsy in the remainder. The study was mainly directed to the cardiac and renal changes in the disease, and an attempt is made to correlate these with the clinical findings. Before the cases are described, many of them in detail, the historical and aetiological aspects of the disease are discussed.

The cardiac lesions were found predominantly in the myocardium and pericardium, and in the latter site were associated with retrosternal pain and pericardial friction rubs. Angina was not common. Congestive heart failure was the cause of death in most of the fatal cases. Renal lesions were both more frequent and more severe than those found in the heart. Typically, arterial obliteration was seen with accompanying areas of infarction, but aneurysms were occasionally present. Urinary abnormalities were found in eleven instances, and in six cases there were renal infaracts. Hypertension was observed in eight of the patients known to have renal lesions, and was generally associated with long-standing renal changes. The erythrocyte sedimentation rate was usually raised, and eosinophilia was found in four patients. Involvement of the liver was also present in three cases.

J. N. Harris-Jones.


Six cases of kerato-conjunctivitis sicca associated with rheumatoid arthritis, polyarthritis nodosa, lupus erythematosus, and Boeck's sarcoidosis are briefly described.

The cases provide further evidence that keratoconjunctivitis sicca occurs in association with a variety of conditions of probably interrelated aetiology and pathology, and that Sjögren's syndrome is but one of such associations.

C. A. G. Cook.
ABSTRACTS


Case report of an aboriginal bush worker aged 22 who suffered from pulmonary tuberculosis, circumscribed scleroderma of the left portal region, and keratitis in the left eye. The corneal lesion consisted of a group of small, white, circular, of and cornea. There was very little infiltration of the ulcerated area. As this process proceeded, fresh nodules appeared, so that the whole of the cornea was affected. The lesion remained localized to the cornea. After about 4 months, the condition improved concurrently with improvement of the scleroderma of the portal region, 2 months later the last ulcer had healed, and the eye had good vision, with a few residual opacities in the substantia propria. Treatment consisted of atropine, aureomycin and, when the ulcers had healed, cortisone.

A. G. Leigh.


A young man presented at the clinic with slight swelling of the lower lids, giving the clinical picture of blepharitis. The red, swollen appearance of the lesion and the depressions left by digital pressure led to a diagnosis of lupus erythematosus, which was confirmed by histopathological examination. All other parts of the body were normal. A short course of treatment with Resochin and bismuth resulted in a cure.

[Authors’ Summary.]


A middle-aged woman developed bilateral central retinal arterial occlusion during the course of periarthritis nodosa. The author believes that the occlusion was due to local involvement of the vessel wall at the level of the lamina cribrosa.

S. M. Drance.


Non-Articular Rheumatism


General Pathology


The author has determined the plasma protein pattern and the erythrocyte sedimentation rate (E.S.R.) in one hundred children aged 4 to 13 years who were under copyright.
treatment for acute rheumatism during the period 1951-4. For observation purposes the patients were divided into three groups as follows:

(1) 24 patients with endocarditis and five without;
(2) Nine with endocarditis and 27 with endo- or myocarditis;
(3) Twenty with diffuse myocarditis and five with pericarditis. All patients in this group had cardiac enlargement, tachycardia, and dyspnoea, and some also had rheumatic nodules, annular rashes, and polycythaemia.

The remaining ten children were suffering from chorea without cardiac involvement.

The results showed that in all three main groups the total plasma protein content was within the normal range, although in Group 3 it varied at the lower limit. In all groups the plasma globulin level was raised by 55 to 60 per cent, particularly in Group 3, in which the rise persisted longer. In Groups 1 and 2 the plasma gammaglobulin level was raised by 20 to 25 per cent and in Group 3 by 25 to 30 per cent. The E.S.R. in all groups was raised to 50 to 60 mm. per hour, the maximum sedimentation occurring in the first 15 to 30 min. The E.S.R., however, was not found to have any prognostic significance.

In the ten children with chorea rheumatica but without cardiac involvement it was found that the changes occurring in the plasma proteins were insignificant.

Edward D. Fox.


As a contribution to the solution of the problem of early diagnosis of rheumatic carditis, the authors describe an immunological test, based on the experimental work of Cavelti (Schweiz. med. Wschr., 1948, 78, 83: Abstracts of World Medicine, 1948, 4, 223). The latter showed that the intraperitoneal injection of killed streptococci and an emulsion of cardiac tissue in the rat and rabbit produced antibodies to heart tissue and also inflammatory changes such as myocarditis and endocarditis. Further, the sera of patients with polyarthritis and various "collagen" diseases have been shown to contain antibodies to a mixture of heart, muscle, and joint tissues, demonstrable by the indirect Coombs test.

In the present study, carried out at Hanusch Hospital, Vienna, the authors therefore tested the sera of 52 patients for auto-antibodies to a preparation of heart tissue, using the Coombs test. Nearly all of 25 cases of clinically active rheumatic carditis gave a positive test result, but of four cases of bacterial endocarditis, only one showed a doubtful positive reaction. Out of nine cases of old rheumatic carditis three showed a positive test result, whereas among five patients with various nonrheumatic ailments, in only one, a case of nephro lithiasis, was the reaction positive. The authors present a [somewhat elaborate] theory of the causation of rheumatic carditis, involving the formation of auto-antibodies.

G. Loewi.


The serum transaminase (glutamic oxalacetic aminopherase) level was estimated in patients with various diseases at the Veterans Administration Hospital (Vanderbilt University School of Medicine), Nashville, Tennessee. The serum level of the enzyme in healthy control subjects [number unstated] ranged from 10 to 45 units per ml. serum.

In all cases of acute myocardial infarction the level was increased to three to twelve times the normal, falling to normal values in 2 to 4 days. In one patient with acute rheumatic pericarditis, however, there was only a slight temporary elevation, the level falling to normal after administration of cortisone, and normal values were invariably found in other types of heart disease, including angina of effort, calcific aortic stenosis, chronic rheumatic valvulitis, acute pulmonary oedema with hypertensive cardiovascular disease, auricular flutter of 48 hours' duration, left bundle-branch block, old healed cardiac infarction, arteriosclerotic heart disease, and idiopathic benign pericarditis.

Raised serum enzyme levels were found in two patients with muscle necrosis resulting from ischaemia due to arterial disease. The level was also found to be increased during exploratory thoracotomy [in an unstated number of patients] and remained so for periods of 2 days to 2 weeks afterwards; this again may have been owing to muscle injury. High serum levels (56 to 1,900 units per ml.) were found in twenty patients with jaundice due to cirrhosis, carcinoma of the pancreas, acute and chronic hepatitis, and infarction of the liver or other abdominal viscera. The serum enzyme levels in liver disease could be correlated with the serum protein levels, the amount of cephalin flocculation and thymol turbidity, the prothrombin time, the serum cholesterol, alkaline-phosphatase, and bilirubin levels, and with the degree of cellular necrosis demonstrated by liver biopsy. Transaminase was found in the bile in concentrations of 25 to 60 units per ml., and the serum levels remained fairly constant in cases of extrahepatic obstruction with a progressive rise in the serum bilirubin level, suggesting that regurgitation of bile was not a major source of the high serum enzyme levels found in liver disease.

Robert de Mowbray.
protein level being carried out. The present authors have simplified the technique and now measure only the erythrocyte sedimentation rate (E.S.R.) and plasma protein level. At the Institute of Rheumatology, University of Rome, they have employed this modified test in eight cases of chronic inactive rheumatoid arthritis, twenty of active rheumatoid arthritis, eight of ankylosing spondylitis, and in ten healthy control subjects.

The E.S.R. was raised and the plasma protein level lowered in all the cases of active rheumatoid arthritis and in seven of the eight cases of ankylosing spondylitis, while only one of these values changed in the eighth case of ankylosing spondylitis and in two of the eight cases of inactive rheumatoid arthritis; in the other arthritic patients the alteration in the values was not "notable". [The results in the controls are not stated, and it is regrettable that in the case of the patients no actual figures are given.] From this study the authors conclude that such a test is of diagnostic value in the rheumatic disorders and is a pointer to the role of capillary permeability in the pathogenesis of these diseases. David Friedberg.


The sequence of changes occurring in the nucleus during formation of the L.E. cell were observed in smears of the buffy coat of defibrinated blood of patients with systemic lupus erythematosus, the smears being taken at 15-min. intervals after collection. Many variations in the pattern were noted, and when the nuclear alteration was focal, not generalized, the resulting inclusion body tended to be lumpy or flaky. The authors state that L.E.-like cells differ from typical L.E. cells in that the inclusion bodies are unevenly stained and have residual chromatin structures; they often have prominent and dark margins.

In thirteen patients with systemic lupus erythematosus and eight controls the numbers of L.E. cells, L.E.-like cells, and rosettes per 1,000 neutrophils in preparations from bone marrow or peripheral blood were recorded. As regards the controls, the number of L.E.-like cells varied, rosettes were present in half of them, and in one patient suffering from rheumatoid arthritis L.E. cells were found. In the authors' view the L.E. cell is not specific for systemic lupus erythematosus, but "the reliability of the diagnosis is increased in proportion to the number of typical L.E. cells seen". They suggest that a quantitative report on the results should be given whenever the L.E. test is performed. E. G. Rees.


From the Central Lenin Institute of Haematology and Blood Transfusion, Moscow, eleven cases of osteomyelopoeitic dysplasia are described and four of them discussed in detail. Of these four the condition was chronic in three with marked splenomegaly, and in the fourth was subacute, the spleen being barely palpable. Photomicrographs of bone marrow smears, radiographs of bones, and two electrophoretic curves of the serum proteins are reproduced [the marrow smears rather unsatisfactorily]. In two cases there was hyperglobulinaemia and an abnormal serum protein electrophoretic pattern. All four cases had one unusual feature in common, namely, a predominance of periosteal sclerosis over endosteal sclerosis. The pathogenesis of the condition is discussed [and the authors' views are well expressed in their choice of the title of the paper. Apparently no histological sections of bone marrow were made and no trephine biopsies attempted]. A. Swan.


The amino-acid hydroxyproline constitutes 13 per cent of collagen and 1 to 2 per cent of elastin and is present in no other protein of the body. At New York University College of Medicine the daily urinary excretion of this amino-acid was studied in 64 patients, 48 adults and sixteen children. Of the adults, sixteen had rheumatoid arthritis, eight had one of the other collagen diseases, eight were normal, and the remaining sixteen suffered from a variety of non-rheumatic disorders. The colorimetric method of Wiss was employed and was shown to agree well with other methods, including the reliable isotopic derivative technique. Only the total hydroxyproline excretion was determined, since the average free hydroxyproline in urine did not exceed 3 per cent of the total either in the normal subjects or in the patients. The daily urinary excretion of hydroxyproline in normal adult individuals averaged 21.8 mg. (range 15 to 33 mg.). The amino-acid was present almost entirely in the bound form, which is relatively stable in acid solution, and for the most part was freely dialyzable, suggesting that it is a peptide of low molecular weight. The excretion of total hydroxyproline was not influenced by the oral ingestion of up to 4 g. 1-hydroxyproline or 1-proline, but was markedly increased (up to 5-fold) by the ingestion of these amino-acids in the form of 28 g. gelatin. These results suggest that free hydroxyproline is not synthesized into collagen directly, but that proline is first converted into a peptide, is subsequently oxidized to hydroxyproline, and later incorporated into collagen. No apparent difference was observed in the urinary excretion levels of total hydroxyproline between healthy adults and the patients with the non-rheumatic diseases; the patients with rheumatoid arthritis and other collagen diseases showed values which were somewhat higher than in the normal subjects, but these were not considered significant on account of the wide degree of scatter of the results. In the children, who were aged 5 to 14 years, the excretion of total hydroxyproline was two to three times that in adults, averaging 64 mg. daily (range 38 to 126 mg.), and was associated with a rise in the percentage of this amino-acid of the total amino-acid..
excretion. This finding is discussed, but is considered to be unrelated to the activity of any particular disease process.

Harry Coke.


The present communication, one of a series of reports on a study of the histochemistry, electron microscopy, and diffraction radiography of collagen, describes the histochemical properties of the residue after the extraction of carbohydrates from collagen with a 0·1 M solution of disodium phosphate at pH 9, followed by the removal of globular protein with 5 per cent sodium chloride solution and of procollagen with a citrate buffer at pH 4. This residue, which has been given the name of "collastromin" by the author, contains sulphated mucopolysaccharides which are rendered more demonstrable histochemically by the removal of the procollagen. It was also noted that argyrophil fibres became visible in the material.

The author discusses the application of these findings to certain problems in pathology, for example, those of fibrinoid degeneration. The argyrophil fibres visible in fibrinoid tissue are considered to represent a protein of collastromin rendered visible by the replacement and removal of procollagen.

L. Crone.


At the Sloan-Kettering Institute and the Memorial Centre for Cancer and Allied Diseases, New York, the authors have applied the methods described in detail in earlier papers (Lab. Invest., 1955, 4, 69; Amer. J. Path., 1955, 31, 687; Abstracts of World Medicine, 1955, 18, 346, and 1956, 19, 90) to the investigation of certain renal diseases. The serum globulin of rabbits immunized against human globulin was coupled with fluorescein, and sections of normal and diseased kidneys obtained from human subjects at necropsy treated with the fluorescein–globulin conjugate. It was shown by specific absorption and blocking tests that any fluorescence resulting in the sections was due to the presence of human γ globulin.

The ratio of glomerular to tubular fluorescence, measured photometrically, averaged 1·2 in sixteen control subjects. (Only three of these kidneys were histologically normal, the others showing nephrosclerosis, pyelonephritis, or other lesions.) Increased fluorescence of the glomerular capillary walls increased the ratio to between 1·9 and 2·8 in cases of lipid nephrosis (one), combined acute and subacute glomerulonephritis (two), acute glomerulonephritis (four), and renal amyloidosis (one), while in a case of periarteritis nodosa with acute nephritis the ratio was raised both in the glomeruli and in the vicinity of necrotic arteries.

It is concluded that in the diseases investigated γ globulins are deposited in the glomeruli, and the theory is advanced that these are, at least in part, antibodies against antigens which have become fixed there, the pathogenesis of these conditions being of an "immunoallergic" nature.

[Although their findings are suggestive, the authors have in fact done no more than to demonstrate the deposition of γ globulin in the glomeruli in certain diseases. It has yet to be shown that this is due to the presence of antibodies against particular antigens and not to local, non-immunological changes favouring non-specific accumulation of γ globulin.] M. C. Berenbaum.


ACTH, Cortisone, and Other Steroids


There is a good deal of clinical evidence that cortisone in very large doses depresses the bodily defences against infection. In an investigation carried out at King's College, University of London, into the mechanism of this depression guinea-pigs were injected intramuscularly with 5, 10, or 25 mg. cortisone acetate daily for 1, 2, 3, or 4 weeks. These doses were calculated to be, weight for weight, much higher than those given clinically. [However, the authors did not take into account the unusual size and activity of the guinea-pig's adrenal cortex—an adrenalectomized guinea-pig may need as much as 12-5 mg. cortisone acetate a day by mouth to keep it alive. Since the authors give their injections intramuscularly it is probable that their animals were overdosed, though not to the extent that they assume.]

The effects of this treatment on phagocytic activity in the reticulo-endothelial system on the total and differential leucocyte counts, and on the gamma-globulin level in the serum were studied, and the findings are summarized [with very few exact data]. To determine the first of these effects trypan blue was injected daily for 6 days before the animals were killed and the intensity of vital staining judged from the number of dye granules seen within the cells of spleen, liver, and lymph nodes. During the first 2 weeks of treatment phagocytic activity was depressed, many of the animals died, and the lymph nodes and spleen were reduced in size. Phagocytic activity recovered during the third and fourth weeks of treatment, mortality was low, and the lymph nodes showed signs of hypertrophy. Similarly during the first 2 weeks of treatment the total leucocyte count was halved owing to a reduction in number of both lymphocytes and granulocytes, and the serum gamma-globulin concentration was reduced to about one-half the normal value. During the second 2 weeks the total leucocyte count returned to normal, though the lymphocyte count was still about one-quarter of the normal and the serum gamma-globulin concentration remained depressed.

It is suggested that the dangers of intercurrent infection are likely to be greatest during the early stages of clinical treatment with cortisone in large doses, and antibiotics should perhaps be given as well during this time. It is also suggested that cortisone should be given locally rather than systemically.

Peter C. Williams.


It has been shown that secretion of pepsin and gastric acid is increased when there is hyperactivity of the adrenal cortex and reduced in Addison's disease. In studies of the influence of adrenal activity on the stomach carried out at the Peter Bent Brigham Hospital and Harvard Medical School, Boston, the daily 24-hour excretion of uropepsin was used as a quantitative index of gastric secretory function. A unit of uropepsin activity was arbitrarily defined as the amount which, during 30 min. of incubation at 37°C in the standard assay, released 0·04 mg. tyrosine-like substances. The mean 24-hr. uropepsin excretion in 265 healthy subjects was 3,670 units, in 205 patients with active duodenal ulcer, 8,470 units, and in ninety patients with gastric ulcer, 5,670 units.

However, in twelve patients with Addison's disease given deoxy corton acetate alone the mean 24-hr output of uropepsin was 540 units; this represented an 85 per cent reduction from the normal mean excretion and was paralleled by a 75 per cent reduction in 17-ketosteroid excretion.

In eleven patients with Addison's disease receiving 12·5 to 50 mg. cortisone daily the uropepsin excretion was normal.

Similar doses of glucocorticoid in the healthy individual produced a much smaller increase in the excretion of uropepsin; to obtain a similar increase in excretion in healthy individuals, daily doses of the order of 200 to 300 mg. glucocorticoid were necessary.

The uropepsin excretion of patients with Cushing's disease was 100 per cent above the normal, while in patients subjected to bilateral adrenalectomy it fell immediately after the operation, rose to about 8,000 units during administration of high doses of cortisone, and subsequently fell to and remained within normal limits when a basic maintenance dose of cortisone had been established.

Peptic ulcer developed or there was symptomatic exacerbation of a previously existing ulcer in seven patients with Addison's disease who were receiving maintenance doses of cortisone. The authors suggest that antacid therapy may be indicated for patients with Addison's disease maintained on long-term glucocorticoid therapy.

P. A. Nasmyth.


During a period of one year 25 patients, or approximately one in every three hundred, subjected to operation
at the Memorial Center for Cancer (Cornell University), New York, showed signs of adrenal cortical insufficiency such as hypotension persisting despite transfusion and the administration of vasopressor drugs, depressed respiration, or delayed emergence from anaesthesia. These signs were found most frequently in the elderly, the chronically debilitated, the morbidly nervous, and the patients with disease or absence of the adrenal glands. The treatment recommended is the intravenous infusion of 100 mg. hydrocortisone dissolved in 500 ml. saline or 5 per cent dextrose solution. The histories are appended of seven cases in which acute adrenal insufficiency supervened during or after anaesthesia and was successfully treated in this way.

The mechanism of action of hydrocortisone is uncertain. However, adrenal cortical hormones are known to be necessary for the maintenance of peripheral vascular tone, and any hypotension which occurs as a result of shock will diminish cortical activity by reducing the blood flow to the adrenal glands, causing acute cortical deficiency.

Mark Swerdlov.

Trial of Cortisone and ACTH in Infective (Non-Specific) Polyarthritis of Children. (Опыт применения кортизона и адrenaокортикотропного гормона у детей с инфекционным (неспецифическим) полиартритом).


The author reports the results of the treatment with cortisone or ACTH (corticotrophin) of thirteen children all of whom were suffering from infective, non-specific polyarthritis, which in two cases had been present for at least 18 months. Previous treatment with prolonged courses of salicylates, antibiotics, and amidopyrine in conjunction with physiotherapy and orthopaedic measures had had little effect. Cortisone was given in doses of 100 mg. daily (in a few cases 150 to 200 mg.), this dose being lowered to 25 to 50 mg. if oedema or a rise in blood pressure developed. The dose of ACTH was 30 to 40 units daily, gradually decreasing to 7 units daily. Usually only one course of treatment lasting 14 to 38 days was given. A detailed description of five out of the thirteen cases is presented to illustrate the effect of the hormones.

The author’s conclusions from this trial of ACTH and cortisone is that all the children showed a quick and sometimes striking response in their general state, the temperature falling quickly to normal, with disappearance of pain and joint swellings and lessening of contractures. The increased erythrocyte sedimentation rate returned to normal in nearly all the cases observed. Edward D. Fox.


Relevant knowledge of compounds secreted by the adrenal cortex and their metabolism is reviewed. Experiments are discussed which give information about the action of corticotrophin in man. Difficulties in evaluating the response due to variations in the activity of different batches of corticotrophin are stressed. After making due allowance for these difficulties, it is possible to define a “spectrum” of response in individuals with various pathological entities. Particular attention is drawn to the response of patients with idiopathic hirsutism, and the effects are contrasted with those in hypopituitarism and normal childhood on the one hand, and in adrenal cortical virilism on the other. Comparisons are made between the effect of exogenous corticotrophin and the endogenous stimuli produced by surgical trauma.

A condition of “basal hypo-adrenal corticalism” is defined and its significance discussed. The possibility of synergic action between corticotrophin and a factor associated with growth hormone, gonadotrophins, and thyroid hormones is considered. There seems little doubt that thyroid hormones are of great importance in the responsiveness of the adrenals. Evidence concerning the existence of a potentiating factor to corticotrophin for the stimulation of adrenal androgens is shown to be worthy of consideration. A similarity in the behaviour of certain adult male obese subjects to that of hirsute women is noted and contrasted with others bearing a superficial resemblance to patients with Cushing’s syndrome.

Attention is drawn to clinical problems in relation to alterations of cerebral activity in patients with Addison’s disease and hypopituitarism and to difficulties which arise when space-occupying intracerebral lesions may be present. A patient with long-standing encephalitis has been studied, with particular reference to the secondary endocrinological phenomena which ensued, and the significance of these is discussed. Recent advances and ideas in relation to the diagnostic problems in Cushing’s syndrome and in patients with adrenal cortical tumours, particularly when hypocalcaemia and renal symptoms are present, are considered and supplemented with additional observations.—[Author’s Summary.]