ABSTRACTS

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

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

The section “ACTH, Cortisone, and other Steroids” includes abstracts and titles of articles dealing with research into the scope and modus operandi of steroid therapy.

Acute Rheumatism


Investigations were carried out at the Rheumatic Fever Research Institute, Chicago, into the significance of the colour development in the deproteinized “serum blank” on heating with the sulphuric-acetic acid mixture used in the well-known diphenylamine reaction of Dische for the estimation of sialic acid in glycoprotein complexes. This colour is also probably due to sialic acid, and estimation after heating with the sulphuric-acetic acid mixture alone, although less sensitive than the diphenylamine method, is simpler and obviates the “allergic reactions” in many technicians. Indoles, pyroles, and tryptophan produce colour with this reagent, but are considered to be removed by protein precipitation with hot 5 per cent. trichloracetic acid. The reagent which the authors recommend is one of 5 per cent. sulphuric acid and 95 per cent. glacial acetic acid heated in a boiling water-bath for 30 minutes. The colour is determined spectrophotometrically at 530 mp.

The supernatant solution remaining after precipitation of the serum protein with hot 5 per cent. trichloracetic acid was dialysed, frozen, and lyophilized, and contained 17 per cent. hexoses, 3-5 per cent. hexosamine, 13 per cent. sialic acid, and 5-8 per cent. nitrogen. The colour absorption curves obtained after treatment of this material with the sulphuric-acetic acid and diphenylamine reagents were practically identical with those obtained with pure sialic acid. Serum from healthy subjects gave an optical density of 0-265±0-019 units. Higher levels were found during the “acute phase” of acute rheumatic fever, tuberculosis, and cancer. Serial determinations were made in comparison with the erythrocyte sedimentation rate (Wintrobe) as an expression of rheumatic activity. The raised sialic acid levels were usually 2 weeks later in returning to normal than the erythrocyte sedimentation rate, and also persisted after the C-reactive protein reaction became negative.

Harry Coke.


In a previous paper (Ann. Eugen. (Camb.), 1953, 17, 177; Abstracts of World Medicine, 1953, 14, 342), the authors estimated the familial incidence of rheumatic fever in 462 Belfast families ascertained through an affected child and first visited in 1950-51. They now present further information obtained on revisiting the same families in 1955. Of the original 462 families, nineteen were not traced. In the remainder, 28 sibs of the original families who previously unaffected have now developed rheumatic fever. The revised figures for the percentage of sibs affected are now: with neither parent affected 6·4 (±0·7), with father affected 14·3 (±3·4), with mother affected 9·9 (±2·4). The corresponding figures for the risk to sibs, calculated by Haldane’s q method, are 11·2 per cent. (±1·1), 22·1 per cent. (±4·9), and 16·6 per cent. (±3·6) respectively. In 51 families ascertained through an affected mother, one of the original 156 children has since had a first attack of rheumatic fever, making ten in all.

The authors note that any attempt to estimate proportions of sibs affected in sibships whose members have not reached early adult life is bound to result in an underestimate of the true familial incidence of the disease.

C. O. Carter.


To obtain information concerning the anatomy of the rheumatic tricuspid valve for use before subjecting a patient to tricuspid valvotomy, the author, at University College Hospital, studied 21 specimens from cases of rheumatic tricuspid valve disease. Reviewing the literature he points out that the tricuspid valve is anatomically much weaker than the mitral valve as regards the prevention of incompetence, a point which was emphasized in his findings in the diseased valves. The mitral valve was found to be affected in all the cases (the aortic valve in fourteen), and this diseased mitral valve...
valve tended, in contrast to the tricuspid valve, to be further protected from incompetence by its large anterior cusp. Of the five valves showing well-marked stenosis, four were considered to be incompetent also, while in eight of the sixteen showing slight or no stenosis there was probably considerable incompetence. The author found it difficult to see the fused commissures from the atrial aspect, so that presumably they would also have been difficult to palpate at valvotomy during life.

J. B. Wilson.


In investigations carried out at the Hôpital de Versailles the concentrations of total cholesterol, cholesterol esters, and free cholesterol in the blood were measured frequently during the course of the illness in ten patients with acute rheumatism and in two patients with mitral stenosis and manifestations suggesting active rheumatic carditis. It was found that during the active phase of the disease the total cholesterol and cholesterol ester levels in the blood were low, and that these rose during convalescence. In fact the blood cholesterol level varied inversely with the erythrocyte sedimentation rate. The total cholesterol content of the blood in early convalescence was about 100 per cent. above that in the acute phase. It subsequently fell, but not to the original value. The significance of this change in the level of blood cholesterol is obscure, but it is suggested that the determination of the blood cholesterol content may be of help in assessing the progress of the disease.

[It should be noted that all the patients studied were receiving treatment with "deltacortisone".]

C. Bruce Perry.


An attempt was made at Sheffield Children’s Hospital to elucidate the mechanism of the "rebound" phenomenon, or transient relapse, sometimes seen following the cessation of treatment in patients with acute rheumatism. In all, 110 patients were studied and according to their treatment fell into five main groups:

1. Seventeen were treated with low doses of salicylates only, and again only one exhibited a rebound.

In twenty of the 34 cases in which a rebound occurred this consisted in elevation of the erythrocyte sedimentation rate only, but in fourteen there were other clinical features. It is noted that rebounds were no more frequent after treatment with hormones than with salicylates in large doses, but were far fewer when small doses of salicylates were employed. A rebound was frequently associated with septic lesions (particularly in hormone-treated cases), the presence of beta-haemolytic streptococci in the throat, and a long illness before treatment was instituted. The incidence of the rebound was also high in adolescent girls.

C. Bruce Perry.


This paper reports studies carried out at the Canadian Red Cross Memorial Hospital, Taplow, the Postgraduate Medical School of London, and the Royal Berkshire Hospital, Reading, on 52 patients (28 at Taplow and 24 at Reading) with Schönlein–Henoch purpura. The maximum incidence was between the ages of 10 and 12 years, only seven of the 52 being over 12, and the sexes were equally affected. The onset in the majority of cases occurred between October and February. Four of the 52 patients had a second attack within one year of the first, and one had three attacks. In all, 56 attacks were witnessed.

The characteristic rash, which starts as a pink maculopapule and within a few hours flattens and becomes dull red and later purple, finally fading after 3 or 4 days, was observed in all but one attack. Joint pain and swelling occurred in 38 attacks, abdominal manifestations (colicky pain) in 33, and melaena in ten, while one patient on two occasions developed an intussusception. Haematuria occurred in 23 attacks and localized patches of oedema were seen in 23 patients. Treatment seemed to have little effect and there was rapid and complete recovery except in about 10 per cent. of cases, in which proteinuria and haematuria persisted.

Although there was a history of a preceding infection of the upper respiratory tract in 41 attacks, in only seven out of thirty cases were Group-A β-haemolytic streptococci isolated from the nasopharynx within a week of admission to hospital, and raised antistreptolysin-O titres were found in only seven out of nineteen cases. This is in marked contrast to a series of 107 cases of rheumatic fever examined during the same period, in which the incidence of a raised antistreptolysin-O titre was 76 per cent. Thus despite the close clinical and pathological similarity between Schönlein–Henoch purpura, rheumatic fever, and acute nephritis, there is no clear evidence that the former invariably follows infection with Group-A β-haemolytic streptococci.

C. Bruce Perry.

Certain aspects of the physical environment, the financial status of the family and the emotional climate of the home life of 120 children suffering from rheumatic fever were investigated. Similar inquiries were attempted for one hundred children not suffering from rheumatic fever who were in the same group and also came from the same socio-economic group; these children constituted the control group. A number of factors occurred more frequently in the families with children with rheumatic fever, and for some of these the differences were statistically significant compared with the control group. The number of families involved were, for some of these conditions, too few to justify their being considered as directly associated with the aetiology of rheumatic fever.

Overcrowding occurred in 31 per cent. of families with children with rheumatic fever, compared with 19 per cent. of controls. Of children with rheumatic fever 26 per cent. were living in damp houses, compared with 13 per cent. of controls. In 56 per cent. of the families with children with rheumatic fever, income was judged to be marginal or inadequate, compared with 34 per cent. of the controls; in addition, 42 per cent. of the mothers of the former group compared with 13 per cent. of the controls were rated poor managers. Of mothers of children with rheumatic fever, 21 per cent. were judged to have a low maternal efficiency, compared with 5 per cent. of mothers of the control group. Once again it is considered that the total number of families involved is too small to justify a claim that low maternal efficiency is of itself a factor in the aetiology of rheumatic fever. Of families with children with rheumatic fever 66 per cent. and 57 per cent. of families in the control group, were considered neither to initiate nor to avoid social activities outside the family. Of families in the control group 47 per cent. went out together regularly, compared with 29 per cent. of families with children with rheumatic fever. Of mothers with children with rheumatic fever, 61.5 per cent. were judged to be inadequate in their relationship with their child who had rheumatic fever; this figure contrasted with 28 per cent. of the controls. More than 50 per cent. of children in both groups came from the outer residential suburbs.

The observations in six areas—namely, housing, crowding, dampness, income, maternal efficiency, and mother-child relationship—were compounded for both groups. This analysis showed a high incidence of families with children with rheumatic fever to be inadequate in four, five and six areas compared with the controls, the three most commonly recurring factors being income, maternal efficiency and mother-child relationship. Other areas investigated were the parents' health, the routine of the household, undue desire for social advancement, separations from the mother, conjugal relationships, the attitude of fathers, the influence of grandparents, and the child in school. In the main the effects of these influences upon the children of both groups were similar, being in the direction of assisting the child's growth and development. In none of the areas investigated was the difference between the families with children with rheumatic fever and the control group sufficiently pronounced to justify a cause and effect relationship in the aetiology of rheumatic fever. However, the study did reveal the poor quality of family life in a significant number of families with children with rheumatic fever. —[Author's summary.]


The authors have determined the plasma fibrinogen concentration, as a possible measure of rheumatic activity, in 33 patients between the ages of 10 and 46 with febrile migratory polyarthritis diagnosed as rheumatic fever who were treated with aspirin at the Clinical Chemotherapeutic Research Unit of the Medical Research Council, Western Infirmary, Glasgow. The blood salicylate levels were maintained between 30 and 45 mg. per 100 ml., as determined by Trinder's method. The concentration of fibrinogen in the plasma was estimated gravimetrically at 0, 4, 7, 14, and 21 days, and on discharge. It fell regularly and consistently, in contrast to Ernstene's findings (Amer. J. med. Sci., 1930, 180, 12). The authors attribute this fall to the effect of the salicylate [although no control series was studied]. When aspirin was temporarily discontinued the plasma fibrinogen level rose in six of the patients, only to fall again when a second course was given. [There is no mention of the erythrocyte sedimentation rate.]

The authors conclude that the results provide definite evidence that salicylate does more than relieve symptoms. E. G. L. Bywaters.


As continuous chemoprophylaxis with oral sulphonamides or penicillin has been found to be very effective against recurrences of rheumatic fever the authors consider that one of these drugs should be given as a routine to all patients convalescent from this disease. At the Canadian Red Cross Memorial Hospital, Taplow, Bucks, such routine prophylaxis has been in use since 1951, and all patients are given a supply of one of these drugs on discharge. The aim is to continue with this prophylaxis regularly until the patient reaches 20 years of age. Nevertheless, after the patient returns home this measure is frequently abandoned either because of parental apathy or because of the opposition of the general practitioner on medical or financial grounds or through ignorance. An examination of the reasons for medical opposition shows that most of them have some degree of validity, but it is suggested that the advantages of routine prophylaxis far outweigh its occasional possible disadvantages, which are avoidable. It is considered a matter for regret that relatively few hospitals in Great Britain practise such routine prophylaxis.

John Lorber.

Of 252 young patients admitted to the Royal Alexandra Hospital for Children, Sydney, in the period 1951-56 with a diagnosis of rheumatic fever or chorea, 86 were given penicillin orally as a prophylactic, the remaining 166 children serving as controls, of whom 71 received a course of sulphadiazine (0.5 g. twice daily for varying periods). For purposes of comparison the whole series of patients was divided into four groups according to the number of attacks they had undergone; attacks occurring within 3 months of the previous one were considered as relapses and not as recurrences. Penicillin was administered as soon as the diagnosis was definite, being given intramuscularly initially and then orally in the form of tablets containing 100,000 units benzylpenicillin three times a day half an hour before meals. Administration was continued for 3 to 52 months (average 22 months) and the children in both groups were periodically reviewed.

There were six deaths in the series, all from rheumatic carditis and all in the control group (one after the first attack, four after the second, and one after the third). In the penicillin-treated groups there were three recurrences whereas ten recurrences developed in the patients given sulphadiazine, and seventy in those receiving no form of drug prophylaxis (61 representing a second attack and nine a third). Of four children in the treated group who subsequently stopped taking penicillin, two later suffered a recurrence, while of four children receiving penicillin who were found at some stage to have Lancefield Group A β-haemolytic streptococci in their throat, none developed a recurrence. It is suggested that these cases may indicate that a higher dose of penicillin is required for prophylaxis. The recurrence rate after the first attack in children given no prophylaxis conformed to the natural history of the disease, a second attack occurring in nearly 70% of cases within 5 years, with a peak incidence in the second year.

In view of the significant reduction in recurrences in patients receiving penicillin it is suggested that this treatment should be given prophylactically throughout childhood and adolescence, and probably even longer, to all children developing an attack of rheumatic fever or solitary chorea.

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ABSTRACTS


Chronic Articular Rheumatism
(Rheumatoid Arthritis)


At the Institute of Microbiology, Pilsen, Czechoslovakia, the antistreptolyhaluronidase and the sheep-erythroocyte agglutination tests (Heller's modification) were performed on the sera of 145 patients with rheumatoid arthritis and thirty patients with ankylosing spondylitis. The majority of the patients were actively ill. In the rheumatoid arthritis group, the antistreptolyhaluronidase level was raised in 15 per cent. of patients, did not approach the levels customarily found in rheumatic fever. The sheep-cell agglutination reaction was positive in 81 per cent. Statistically there was no positive correlation between the two tests. In practice the results of these two tests were found to be useful in differentiating atypical rheumatic fever from early rheumatoid arthritis.

Of the patients with ankylosing spondylitis negative results in both tests were obtained in two-thirds, while in the remaining one-third the reaction was positive in one or both tests. In these patients the antistreptolyhaluronidase titre was only slightly raised in those giving a positive reaction, a finding similar to that in the rheumatoid arthritis group and unlike the findings in patients with rheumatic fever. G. W. Csonka.

Quantitation of the Activity of Rheumatoid Arthritis.

This is the sixth in a series of articles from Temple University School of Medicine, Philadelphia, in which the senior author has endeavoured to establish an acceptable clinical index of activity in rheumatoid arthritis. In two previous papers (Amer. J. med. Sci., 1956, 232, 150 and 300) he described what he terms the "articular index" and the "systemic index". In the present paper is recorded a correlation between these two which is considered to support the previous claim that the systemic index measures the activity of the disease with reasonable accuracy. This index is based on such general manifestations as can be objectively measured—stiffness, fatigue, strength of grip, erythrocyte sedimentation rate, and aspirin requirements. The claim for its reliability has hitherto rested, however, upon indirect evidence and "clinical impression".

It is now reported that simultaneous paired determinations of the systemic and articular indices in eighty unselected cases of active rheumatoid arthritis showed a striking correlation between the two. As the articular index is based upon the simplest and most reliable type of clinical observation of the degree of joint function it is considered that this correlation indicates a high degree of reliability. The authors recommend use of their articular and systemic indices as rapid and reasonably accurate methods for recording the activity of, and summarizing the joint findings in, rheumatoid arthritis.

W. S. C. Copeman.


The authors describe the earliest changes observed in rheumatoid arthritis of the carpal bones and illustrate them in a series of radiographs. These changes may occur before involvement of the articular surfaces and sometimes even before the onset of any clinical symptoms. They consist in cystic areas within the bones, sometimes with opaque areas, and in other cases a diffuse osteosclerosis is seen. The carpus may show a gradual slipping towards the ulnar margin, while eventually the semilunar may be almost in contact with the styloid process of the ulna. The appearance of the carpal bones in a young adult may come to resemble that of an old man. In one of the authors' cases these early changes were present for 5 years before the onset of symptoms, but when symptoms eventually appeared there was a rapid progression of the disease, with advanced radiological changes.

John H. L. Conway-Hughes.


The authors have studied 22 cases in which aortitis
and aortic endocarditis were associated with rheumatoid spondylitis or rheumatoid arthritis observed over a period of 20 years at the Massachusetts General Hospital, Boston. The patients had signs of aortic regurgitation without evidence of mitral stenosis; those suspected of having had syphilis or preceding attacks of rheumatic fever were not included in the study.

Serological tests for syphilis gave negative results. Three of the patients developed pericarditis, eight anagina pectoris, and ten congestive cardiac failure. All but six of the 22 patients died, a cardiac lesion being the cause of death in thirteen cases. Post-mortem examination was carried out on nine patients. Secondary amyloidosis was present in three cases. The aortic valve rings were found to be dilated. The valve cusps showed varying degrees of fibrosis, with thickening and retraction; the cusps were usually separated rather than adherent, though a few adhesions were seen. The aortitis was characterized grossly by discrete intimal plaques extending from the valve for about 2.5 cm. distally into the ascending aorta, the coronary ostia being distorted by these lesions in two cases. Microscopically, the intimal thickening was the result of subendothelial connective-tissue proliferation and increase in mucinous ground substance. Irregular focal destruction of the media associated with ingrowth of vascular granulation tissue was noted. There was also fibromuscular thickening of the vasa vasonum, with obliteration of the lumen in some instances.

C. E. Quin.


Agammaglobulinemia is a rare condition characterized clinically by repeated attacks of bacterial infection, resulting from a gross immunological defect. From the 58 cases so far reported there appear to be two forms—congenital, occurring in children, and acquired, in which the lack of response to infection appears in later life. In several of these reported cases "rheumatic" symptoms were noted—for example, joint pain and tenosynovitis—and in eight there appeared to be rheumatoid arthritis. The authors describe three cases—two in which the condition was apparently acquired in adult life, and one, in a child, of congenital agammaglobulinemia. The association of agammaglobulinemia with other "collagen" diseases—scleroderma, dermatomyositis, and (probably) disseminated lupus erythematosus—is discussed.

The authors point out that the pathogenesis of rheumatoid arthritis has been much related, in theory, to some form of hypersensitivity, to antibody formation or to disturbance of gamma-globulin metabolism. The fact that rheumatoid arthritis can co-exist with agammaglobulinemia makes theories involving anaphylactic or immunological mechanisms less attractive, if not untenable. In patients with agammaglobulinemia, however, bacterial allergy does develop in spite of the defect, and it is therefore still possible that rheumatoid arthritis may have an allergic basis.

B. E. W. Mace.


An inquiry into the nature of the anaemia associated with rheumatoid arthritis was carried out at the Royal Bath and White Hart Hospital, Harrogate, in which fifteen in-patients with active rheumatoid arthritis were studied. The erythrocyte life-span was measured by Dacie and Mallison's modification of Ashby's technique, cells from 800 to 1,200 ml. blood being transfused and the normal life-span of the erythrocyte being taken as 100 to 120 days. In ten of the cases studied the rate of erythrocyte destruction was increased, the life-span varying from 30 to 90 days. The serum bilirubin level and the reticulocyte count were within normal limits with a single exception. The faecal urobilinogen content and the osmotic fragility of the erythrocytes were determined in six cases and were normal in all. In five of seven cases storable iron was demonstrated in the sternal bone marrow and there was no response to intravenous iron therapy, the increase in haemoglobin level being less than 2 g. per 100 ml. blood.

It is concluded that "latent haemolysis, demonstrated by abnormally short survival-time of normal red cells, is a factor in the production of anaemia in certain cases of active arthritis". In addition, the bone-marrow response to haemolysis in these cases was less than would be expected if marrow function was normal, and erythrocytes were produced that were deficient in haemoglobin. This deficiency not being apparently due to a lack of iron: there is an extensive discussion of the literature of these and related phenomena.

Harry Coke.


Rose's test and the L-agglutination test are known to be of value in the diagnosis of rheumatoid arthritis of long standing. The authors now describe in detail a method by which it is possible to support the early diagnosis of rheumatoid arthritis. By extraction of beta-streptococci Type 3 (Lancefield Group A) with acetamide, an extract was obtained which gave positive haemagglutination in 21 (71-8 per cent.) of 32 samples of serum from patients with Stage-I rheumatoid arthritis. Rose's test was positive at this stage in only 5:1 per cent. As control sera, donor's blood from the transfusion service was used and 20 per cent. of ninety such sera gave a positive streptohaemagglutination reaction.

In the late stages of rheumatoid arthritis the proportion of positive reactions with this method was approximately the same as in the early stages, while the percentage of positive results in the Rose and L-agglutination test increased. Both complete and incomplete antibodies were demonstrated, and a complement-fixation test using the streptopcoccal extract gave a positive result in some patients though it seemed to be less sensitive than the
streptohaemagglutination reaction. The authors state that the streptococcal extract is not group-specific, since it reacts to sera of Groups A, C, and D. It is thermo-
labile and in this, as in some other characteristics, it is similar to the so-called L-antigen.  G. W. Csonka.

Long-Term Results in Early Cases of Rheumatoid Arthritis treated with either Cortisone or Aspirin. MEDICAL RESEARCH COUNCIL/NUFFIELD FOUNDATION JOINT COMMITTEE ON CORTISONE, ACTH, AND OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES (1957). Brit. med. J., 1, 847. 6 refs.

This is the third report of a comparative study of the use of cortisone and aspirin in the management of 61 cases of rheumatoid arthritis. When the investigation started in 1951 a criterion for treatment was a history of rheumatoid arthritis of only 3 to 9 months' duration. The patients were aged 17 to 59 years, and in each case four joints or more were affected, with bilateral disease of the hands, wrists, ankles, or feet. In the majority of cases the sheep-cell agglutination test yielded a positive result at least once. [For previous reports see Brit. med. J., 1954, 1, 1223, and 1955, 2, 695; Abstracts of World Medicine, 1954, 16, 405, and 1956, 19, 229.]

The therapeutic trial in its original form was discontinued after the second year, and the present report reviews the condition of the 53 patients remaining under observation 3 to 4 years later. At that stage the mean daily dosages of cortisone and aspirin in those still taking these drugs were 66 mg. and 3.5 g. respectively. Cortisone therapy had been discontinued in four cases owing to the advent of side-effects such as dizziness, hypertension, dyspepsia, and moon-face. The results of treatment were evaluated by assessment of the general functional capacity, the number of remissions, and the average haemoglobin level and erythrocyte sedimentation rate. Changes in porosis and erosion were estimated by studying the radiological appearances of the hands and feet. With regard to the outcome of treatment, there appeared to be no significant advantage in employing cortisone therapy; in fact, some patients preferred aspirin. Administration of these drugs brought about remission in 25 per cent. of cases, but the disease remained very active in a similar proportion.  A. Garland.


The differential sheep-cell agglutination test of Rose and Waaler is now well known as an aid to the diagnosis of rheumatoid arthritis; an important part of this test appears to be the reaction between the gamma globulin coating the sheep erythrocytes and a factor (the R factor) in the serum of the rheumatoid patient. Recently, however, Singer and Plotz (Amer. J. Med., 1956, 21, 888; Abstracts of World Medicine, 1957, 22, 50), described a modification of this test, in which, instead of sheep cells, polystyrene latex particles of uniform size (0.8140 μ) are used.

The present authors, at the British Columbia Medical Research Institute, Vancouver, have subjected the sera of 105 patients with rheumatoid arthritis to this modified test and to the standard Rose-Waaler test. The latex test gave a positive result in 76 cases, and the Rose-Waaler test in 38. In a further 81 cases of other rheumatic or collagen diseases, no positive results were obtained with the standard test, but in one case of osteoarthritis the latex test gave a positive reaction. The authors consider that the latex fixation test shows a degree of specificity comparable with the best of the various modifications of the sheep-cell test, and moreover, the materials required can be more easily obtained and stored.  B. E. W. Mace.

Clinical and Radiological Studies of the Diencephalo-
hypophyseal Region in Rheumatoid Arthritis. (Rilievi clinico-radiologici della regione diencefalooipofisaria nell'artrite reumatoide.) RIZZI, D., and CAVALLO, A. (1957). Reumatismo, 9, 114. 5 figs, 20 refs.

The authors, working at the University of Bari, have estimated the area of the sella turcica in 31 patients (thirteen males and eighteen females) suffering from rheumatoid arthritis, the area being determined from a study of lateral radiographs. The normal area was taken to be 95 sq. mm. in the male and 90 sq. mm. in the female. In 24 cases (about 70 per cent.) the area was reduced. The smallest area recorded was 33 sq. mm. in a 50-year-old woman. Abnormalities in the clinoid processes were noted in ten of the patients. The detailed results are tabulated.

The authors consider that the clinical features suggest a dysfunction of the "diencephalon-hypophyseal system", and point out that in four cases there was hyperthyroidism, in two signs of forme fruste hypoadrenalism, and one patient had acromegaly. The various theories of the aetiology and pathogenesis of rheumatoid arthritis are discussed, the role of the pituitary gland being emphasized. The authors claim that there is a frequent association between reduction of the area of the sella turcica and unbalanced pituitary function in rheumatoid arthritis.  David Friedberg.


The great pharmacological potency of the steroid hormones has been abundantly demonstrated since their introduction in 1949 for the treatment of rheumatoid arthritis and other disorders. The problems associated with their employment to the best advantage and greatest safety have not yet, however, been completely solved, more especially when they are used for long-term treatment, as is the rational tendency of their modern use.

The authors discuss in this paper what they refer to as "the calculated acceptable risk" of "hypercorti-
sonism" embodied the decision to embark upon the long-term treatment of patients with any of these hormones. They discuss the clinical signs and symptoms of this condition and the need for slow and gradual reduction in the dosage of exogenous hormones. They stress the difficulties associated with this procedure, and outline the technique they have adopted. They emphasize the difference between the therapeutic effect achieved by optimally tolerated doses of cortisone and other steroid hormones, note the effects of chronic mild hormonal overdosage in patients with rheumatoid arthritis, and comment on certain special dangers associated with the latter. W. S. C. Copeman.


This paper summarizes the results of a number of urinary steroid studies carried out during 1954-55-56 at the King Gustaf V Research Institute, Stockholm. Insufficient detail is given to allow a critical assessment of the findings.

(1) The total 17-ketosteroid (17-K.S.) excretion per 24 hrs of one hundred typical patients with rheumatoid arthritis fell within the lower limits of normal.

(2) The main ketosteroids found on chromatographic separation both before and after the administration of ACTH or cortisone showed the same pattern in rheumatoid arthritis as in normal subjects.

(3) The blood content of "free hydrocortisone-like" steroids of ten patients were within the limits found for normals both before and after ACTH. [The authors comment that the method used, that of Nelson and Samuels, is still open to criticism.]

(4) Using the 17-ketogenic steroid (17-K.G.S.) assay for urinary corticosteroids, the authors found the mean excretion of twenty rheumatoid arthritis to be 50 per cent. below those of healthy persons.

(5) A study of the adrenal response to an intravenous infusion of ACTH, measured as urinary 17 K.S. and total 17-hydroxy corticosteroids (17(OH)CS), showed a lower response in patients (fifteen) than in healthy persons (25).

(6) Using the method of Appleby and Norymberski for the assay of urinary steroids with a 17-ketol side chain and subsequently isolating the 17-ketosteroids formed, they confirmed the presence of 17-α-hydroxy pregnanolone in both rheumatoid and normal urine.

(7) They estimated the percentage of ketonic and non-ketonic, 11-oxo and 11-desoxy steroids derived from urine after hydrolysis with β-glucuronidase, oxidation with sodium bismuthate, reduction with potassium borohydride, and Girard separation. The pattern in the four rheumatoid patients differed from that in two normal subjects.

(8) They measured the urinary output of 17 K.G.S. and 17(OH)CS from eight normal subjects and seven rheumatoid arthritis before and after the administration of ACTH. They found an abnormal relative increase in the 17(OH)CS output in the patients which disappeared after ACTH administration. [The 17(OH)CS assay measures the same corticosteroid metabolites as the 17 K.G.S. assay and 17-20 ketols as well, but the difference between the assay results cannot be taken as a measure of the excretion of 17-20 ketols.] The above findings "mostly strongly suggest" to the authors a disturbed steroid metabolism in rheumatoid arthritis and do not definitely exclude "primarily altered adrenal cortical function".

(9) In collaboration with Genzel and Robbe, they studied certain aspects of steroid metabolism in seventeen healthy women during and after pregnancy. They found high blood levels of hydrocortisone-like steroids, and in the urine an increased breakdown of hydrocortisone to 17 K.S., a great increase in progesterone metabolites, and a reduction of dehydroepiandrosterone, androsterone and etiocholanolone [the latter suggesting reduced rather than an increased corticosteroid production]. "These findings indicate that the favourable effect of pregnancy on rheumatoid arthritis is not produced by steroids from the adrenals but probably by placental steroids."

(10) They found that nine patients with acute hepatitis had pathologically low amounts of 17 K.G.S. in their urine. This suggested that the effect of hepatitis on rheumatoid arthritis might be due to altered steroid metabolism rather than to increased steroid production. H. F. West.


This report extends earlier observations of the authors on intermediary carbohydrate metabolism in rheumatoid arthritis. These observations included the demonstration of a hitherto unknown phosphorylation process and also of an organic phosphorus fraction soluble in trichloroacetic acid. This fraction was absent, or nearly so, in normal individuals. The authors have now undertaken measurements of the quantitative difference between the total phosphate and orthophosphate in the soluble fraction obtained after precipitation of synovial fluid with 5 per cent. trichloroacetic acid. The "difference phosphorus" value was found to be significantly greater in rheumatoid arthritis than in other types of joint disease, and a similar increase occurred also in serum. Preliminary investigations suggested a relation between "difference phosphorus" and serum iron; during clinical improvement the former declined in concentration as the latter rose. Although the "difference phosphorus" was also abnormally high in ankylosing spondylitis and in cancer, the phosphorus-containing fraction in rheumatoid arthritis could be distinguished by its more complete hydrolysis after treatment with hot hydrochloric acid. In normal individuals the "difference phosphorus" fraction contains adenosine triphosphate, creatine phosphate and nucleotides; the nature of the substances responsible for the pathological values in rheumatoid arthritis and cancer is now being investigated. Alan G. S. Hill.

Impressed by the high incidence of arthropathy, often indistinguishable from that of rheumatoid arthritis, in cases of systemic lupus erythematosus, the author has tested serum from a number of patients with rheumatic disorders for the L.E. phenomenon. The method adopted was that of Snapper and Nathan (Blood, 1955, 10, 718). The clinical material comprised two hundred cases of rheumatoid arthritis [calculated from the number and percentage of positive results, the actual total having been omitted], one case of systemic lupus erythematosus, and 106 cases of ankylosing spondylitis, degenerative joint disease, etc.

The L.E. phenomenon was demonstrated in the case of systemic lupus erythematosus, and in four (2 per cent.) of the patients with rheumatoid arthritis—with doubtful results in three further cases. None of the control group had a positive test. Surveying the clinical features of the cases of rheumatoid arthritis with a positive reaction, the author finds grounds for believing that in three instances the patient may in fact have had subacute lupus erythematosus. Among the special manifestations in this group were episceritis, erythema multiforme, pleural thickening, "atypical" pulmonary infiltration, asthma, very rapid erythrocyte sedimentation rate, and hyperglobulinaemia.

All three patients were being treated with steroids when the L.E. phenomenon was demonstrated, but none showed signs of hypercortisonism. The cases of rheumatoid arthritis with "doubtful" results presented no special features. Positive preparations were incidentally observed to exhibit more rapid lysis of cells than negative preparations.

[Cases of rheumatoid arthritis with a positive L.E. cell test have been reported by other authors. Careful follow-up and histological investigations, when feasible, should reveal whether these are true examples of systemic lupus erythematosus.]

Alan G. S. Hill.


In an investigation of serological reactions in rheumatoid arthritis, the author has studied the agglutination of living and autoclaved streptococci (dependent respectively on the "L" and "O" antigens) and of sensitized sheep erythrocytes. He has used the inter-relationships of these reactions, and the ability of certain tissue polysaccharides to inhibit them, as the basis for a tentative explanation of the pathogenesis of rheumatoid arthritis.

Specimens of serum from ninety cases of rheumatoid arthritis were examined; streptococcal "L" agglutinins were present in 55-6 per cent., "O" agglutinins in 56-7 per cent., and agglutinins for sensitized sheep cells in 81-1 per cent. The corresponding figures in controls were 0-7 per cent., 1-5 per cent., and 3-3 per cent. Absorption experiments showed that the haemagglutinating factor was not identical with the streptococcal agglutinins, and after electrophoresis of serum on filter paper the former was found in the fast moving γ globulin band, and among the β globulins, while the latter migrated with the slow moving γ fraction. The haem-agglutinating factor was able to activate "L" but not "O" agglutination. Among the serum proteins only γ globulin (Cohn Fraction II), could inhibit haemagglutination when added to the rheumatoid serum-sensitized sheep cell system. On the other hand, only Fractions I and, to a lesser extent, IV-4 inhibited streptococcal agglutination. The reactivity of a rabbit streptococcal "O" immune agglutinin was inhibited only by Fraction I. Streptococcal agglutination could also be inhibited by hyaluronic acid, sodium hyaluronate, and a substance obtained by autoclaving human synovial tissue. Haem-agglutination was unaffected by these substances.

The author believes that these inhibition experiments imply that antibodies against mesenchymal tissue are formed in patients with rheumatoid arthritis. He points out that the "O" antigen of human pathogenic Group A streptococci contain N-acetylglucosamine, which is also yielded by the depolymerization of hyaluronic acid, such as occurs in rheumatoid arthritis. He suggests that rheumatoid arthritis is initiated by an increase in the activity of specific enzymes which are concerned in the formation and degradation of mesenchyme. This increased activity gives rise to connective tissue degradation products "foreign" to the body. These substances stimulate the formation of antibodies directed against mesenchymal tissues and initiate a chain reaction of further mesenchymal degradation and antibody formation.

[The experimental observations are interesting and possibly important, but a wide gap remains to be bridged before they can firmly support the author's theory about pathogenesis.]

Alan G. S. Hill.


From the Anti-Rheumatism Centre of the Faculty of Medical Science, Buenos Aires, the author describes small cystic swellings occurring adjacent to Heberden's nodes in six patients with osteo-arthritis. One of these cysts was removed, and on histological examination showed replacement of collagen, reticulin, and elastic fibres by clear mucoid. The mucoid could be broken down by hyaluronidase. The skin over the cysts was atrophic and had lost the normal papillae, while the base- ment membrane was discontinuous. A fibroblastic and cellular proliferation encapsulated the cyst. He briefly reviews the literature, notes that the cysts do not communicate with the terminal interphalangeal joint, and concludes that they represent a reaction of the skin to the pressure on the corium of the underlying bony prominence. — Allan St. J. Dixon.


(Spondylitis)


Because of certain dangers in the deep x-ray treatment of ankylosing spondylitis it is important to establish the diagnosis of this disorder beyond doubt so as to avoid exposing any patient to risk unnecessarily. Among a series of 530 patients attending a special spondylitis clinic at Manchester Royal Infirmary the author has found that about one in five is not a genuine case of spondylitis ankylopoietica. These atypical cases all showed involvement of the sacro-iliac joints, but they also presented unusual clinical or radiological features suggestive of other diseases, such as rheumatoid arthritis, Reiter's disease, acute rheumatism, or psoriatic arthritis.

He has therefore studied the occurrence of spondylitis in the above conditions to see how far it was possible to establish an exact diagnosis.

(1) In rheumatoid arthritis clinical involvement of the spine is uncommon and although some radiological evidence of disease can be demonstrated in about 50 per cent. of these cases, the radiological changes differ in many respects from those of ankylosing spondylitis. Involvement of the cervical spine is more common; here the joint spaces are narrowed but there is absence of the characteristic “bambooning” of the spine seen in ankylosing spondylitis.

(2) In rheumatic fever spinal lesions are rare, but nineteen cases of such lesions were identified among 2,000 patients with acute rheumatism; all nineteen patients had suffered repeated attacks of rheumatic fever and all had valvular lesions of the heart. The differential sheep-cell agglutination test was negative in all of the sixteen cases tested. The sacro-iliac joints were involved in half these patients and the radiological appearances in many cases were indistinguishable from those in ankylosing spondylitis. However, the history of the disease, the ligamentous laxity, and the effusion into the peripheral joints all helped to clarify the diagnosis in difficult cases.

(3) Of the twenty patients with Reiter's disease four had developed severe restriction of spinal movements and some showed radiological involvement of the sacro-iliac joints. However, a history of dysentery or urethritis together with the occasional incidence of keratodermia or iritis were pointers to the correct diagnosis.

(4) There was some spinal involvement in eleven out of 68 cases of rheumatoid arthritis complicated by psoriasis. But whereas extensive involvement of the peripheral joints was found in these cases, radiological involvement of the sacro-iliac joint was not a notable feature.

There were also changes in other areas in the spine, but these were more suggestive of rheumatoid arthritis than of ankylosing spondylitis.
The author concludes by stressing that exact diagnosis is of great importance in these cases, since treatment by deep x-ray therapy may be of real benefit in cases of true ankylosing spondylitis but is useless in the other conditions.

William Hughes.

**Structural Disorders and Destructive Lesions of Bone in Ankylosing Spondylitis.** (Troubles de la structure osseuse et lésions destructives au cours de la spondylarthrite ankylosante.) JACQUELINE, F. (1956). J. Radiol. Electr., 37, 887. 5 figs, 18 refs.

The author describes how destructive lesions in the spine of patients with ankylosing spondylitis may present different appearances, depending on whether the lesion is very active or stabilized. Two types of ankylosing spondylitis have to be distinguished. In the first there is a slow progress over many years; in this type osteoporosis is rare but there is marked bridging of the vertebrae. In the second type the progress is much more rapid and bridging of the vertebrae appears much more slowly, but there is marked generalized osteoporosis and ankylosis of the intervertebral articulations. The two types may occur in the same patient at different times.

Destructive lesions in the second, active, type are confined to the angles of the anterior vertebral margins. Destruction in the vertebral bodies may also sometimes be seen in stabilized cases following trauma, but in such cases is usually confined to areas where there is marked bridging of the vertebrae, whereas in the active type it may be diffuse. Three cases of ankylosis of the hip-joint with marked destructive changes in the femoral head are described. The term “destruction” in relation to ankylosing spondylitis is really a radiological one, the so-called destruction being produced by intense osteoporosis and condensation. These appearances later disappear, to be replaced by bony ankylosis. In a few rare cases true anatomical destruction of the spine occurs, when it is similar to that found in the hip-joints.

John H. L. Conway-Hughes.

**Ankylosing Spondylitis and Radiotherapy.** (Spondylarthrose rhizomelique et radiotherapie.) CÔTÉ, P. (1957). Laval méd., 22, 447. 5 refs.

(Miscellaneous)


Arthritis has long been recognized as a complication of psoriasis, and since this latter condition is not infrequently associated with rheumatoid arthritis the question has arisen whether the joint changes are entirely due to the associated condition or whether psoriatic arthritis is itself a disease entity. The authors of this paper from the Cleveland Clinic, Ohio, review the literature, and on the basis of the radiological findings in the hands of fifteen patients with psoriasis and arthritis suggest that such patients may be divided into two groups. [Unfortunately, no reference is made to the incidence of skeletal involvement when all cases of skin affection are included.]

In the larger group (eleven cases) the usual radiological manifestations of rheumatoid arthritis were clearly present—generalized demineralization of bone, narrowing of the joint spaces, erosion of articular surfaces, and soft-tissue swelling around the affected joints. [One illustration also shows early ulnar deviation of the fingers.]

The significant features in these cases were the generalized nature of the bone changes and particular involvement of the proximal interphalangeal joints. Parallelism between the psoriasis and the arthritis, or the simultaneous waxing and waning of symptoms of both conditions, led the authors to conclude that psoriasis acts as a non-specific stimulus for the exacerbation of an existing arthritis, particularly arthritis of the rheumatoid type. The remaining four cases were true cases of psoriatic arthritis with different radiological features. No generalized demineralization of bone was seen, and destruction was noted in one or more distal interphalangeal joints, with little or no change in the proximal joints. This destruction was articular in type, leading later to fibrous or bony ankylosis, but some hypertrophic change was also seen around the margins of the affected joints. There was a tendency to psoriatic involvement of the finger nails in those digits where underlying arthritic changes of this type were present. R. O. Murray.


At the Goldwater Memorial Hospital and New York University—Bellevue Medical Center, New York, the uptake by the thyroid of radioactive iodine (131I) was estimated in thirteen euthyroid subjects before and after the administration of 800 mg. phenylbutazone daily for 4 days. A consistent and marked reduction in 131I uptake was observed in all cases, the fall being to levels ranging from 10 to 37 per cent. of the control level. The concentration of the drug in the blood was estimated in eight cases and was found to be within the limits observed during its therapeutic use in rheumatic conditions. After discontinuation of the drug for 7 days the 131I uptake had risen again to the control level in two out of three cases reinvestigated, and to 80 per cent. of that level (from 14 per cent.) in the third case.

The authors note that in spite of this demonstrable suppression of thyroid activity phenylbutazone does not produce hypothyroidism or goitre when given for long periods. They therefore reinvestigated 131I uptake in four patients who had been given phenylbutazone continuously for periods ranging from 16 to 97 days. From these studies it appears that the thyroid-inhibiting effect of the drug begins to wear off after 4 days, although there may be some residual effect even after 97 days. To determine the mode of action of phenylbutazone it was administered together with pituitary thyroid-stimulating hormone (T.S.H.) in three of the cases previously investigated. It was found that the inhibiting action of the drug was abolished by the subcutaneous injection of 10 units T.S.H. for 4 days. It is suggested that the drug probably acts by suppressing pituitary function.

An analogue of phenylbutazone, 4-(phenylthioethyl)azo-1:2-diphenyl-3:5-pyrazolidinedione was also investigated. In this a phenyl-thio-ethyl side-chain has been substituted for a butyl group. This drug was shown to...
have no thyroid-depressing effect, although it has some anti-inflammatory action and is said to be a powerful uricosuric agent.

T. D. Kellock.


At Stanford University School of Medicine, San Francisco, the effects of prolonged administration of phenylbutazone were studied in one hundred patients—sixty with rheumatoid arthritis, twenty-three with ankylosing spondylitis, four with arthritis and psoriasis, and thirteen with mixed arthritis. The daily dose of the drug ranged from 100 to 600 mg., but most patients received 300 to 400 mg. daily, and the duration of the treatment varied from 12 months to 4½ years.

Initially there was a Grade-I response (complete remission) or a Grade-II response (major improvement) in 91 patients; the initial response in the remaining nine was Grade III (minor improvement). The original favourable response was maintained throughout the period of treatment in ninety patients. Toxic effects included rash (three cases), stomatitis (five), dyspepsia (fifteen), vertigo (two), transitory visual blurring (two), purpura (two), and agranulocytosis (two). Administration of the drug was successfully resumed later in all these patients. One patient died from haemorrhage from a duodenal ulcer.

Laboratory examination at the end of the period of study did not reveal any abnormality of the blood cells or any evidence of hepatic damage.

C. E. Quin.


The pancreatic enzyme trypsin is said to have an anti-inflammatory action. From the University of Barcelona the results are reported of the treatment of scapulo-humeral periartthritis by periarticular injections of a similar proteolytic ferment, \( \alpha \)-chymotrypsin, which has the advantage that it can be used in aqueous solution and causes far less local pain than an oily suspension of trypsin. In the fourteen patients treated, ten with acute or subacute and four with a chronic condition, the periarticular tissues were infiltrated with 5 mg. \( \alpha \)-chymotrypsin dissolved in 10 ml. sterile normal saline, treatment being given on alternate days for 2 weeks, and then less frequently according to the degree of improvement.

The results are considered to be superior to those of any other treatment in current use. The first injection brought prompt relief of pain in most of the acute cases, and the range of movement at the shoulder quickly increased. Almost complete cure, with only a slight painless limitation of rotation remaining, was achieved with from eleven to nineteen injections. Remedial exercises were also employed.

Kenneth Stone.

CORRIGENDA

Volume 16, p. 318

RELATION OF HIGH MOLECULAR WEIGHT PROTEINS TO THE SEROLOGICAL REACTIONS IN RHEUMATOID ARTHRITIS


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It is regretted that the two parts of Fig. 3, page 318, column 2, were accidentally transposed. The Figure should appear as follows:

Fig. 3.—Ultracentrifugal patterns of the euglobulin fractions prepared from the serum of a patient with rheumatoid arthritis dissolved in 5 per cent. saline, acid pH 3, urea, and mercapto-ethanol. The dissociation of the 22S peak in acid and urea is accompanied by an increase in the amount of 7S and 19S material. The mercapto-ethanol caused a loss of both 19S and 22S material.