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


From New York University College of Medicine comes this further report of the results in 391 children and adolescents who had had unequivocal attacks of rheumatic fever and who have been followed up in a special prophylaxis clinic, the aim being to compare the effectiveness of three prophylactic regimes. An earlier report presenting the results of the first 2 years of this study appeared in 1957 (Wood and others, New Engl. J. Med., 257, 394; Abstr. Wild Med., 1958, 23, 200). It is recalled that the three regimes were as follows:

1. 1 g. sulphasalazine daily by mouth in a single dose;
2. 200,000 units buffered potassium benzylpenicillin daily by mouth in a single dose half an hour before breakfast;
3. 1,200,000 units benzathine benzylpenicillin given by intramuscular injection every 4 weeks.

In the first 2 years of the study the attack rates for streptococcal infections per patient-year in the three groups were 24, 20, and 7 per cent. respectively, while the rates for recurrence of the rheumatic fever were 2.7 per cent., 4.8 per cent., and nil respectively.

In the present study, therefore, an attempt was made to ascertain whether the superiority of parenteral penicillin might have been due in part to the oral prophylaxis not having been faithfully carried out. Two procedures were adopted:

1. A special interview with each patient, on the basis of which prophylaxis was considered "good" if fewer than five non-consecutive daily doses had been missed during a month;
2. The patient was supplied each month with a bottle containing a known number of the pills or tablets, prophylaxis being considered "good" if the number of unused pills or tablets returned differed from the expected number by 3 to 4 for penicillin tablets, or by 3 to 9 for sulphasalazine tablets.

From the results of the interview good prophylaxis was apparently achieved by 75 per cent. of patients taking oral penicillin and by 67 per cent. of those taking sulphasalazine; by the pill count technique prophylaxis was assessed as good in 55 per cent. of patients taking oral penicillin and in 44 per cent. of those given sulphasalazine. The accumulative findings for the first 3 years of this study showed that the incidence of streptococcal infections per patient-year was now 21, 20.7, and 7.3 per cent. respectively, while the recurrence rate of rheumatic fever per patient-year was 1.9, 5, and 0.3 per cent. respectively.

The authors' main conclusions are as follows:

1. That 1,200,000 units benzathine benzylpenicillin given intramuscularly every 4 weeks is more effective in preventing both streptococcal infection and recurrence of rheumatic fever than either of the two methods of oral prophylaxis.
2. The results in the three groups showed little variation even when the oral prophylactic regimen had been faithfully followed.
3. Oral sulphasalazine is approximately equal in effect to oral penicillin in the prevention of streptococcal infections, but is superior to oral penicillin for the prevention of rheumatic fever in patients maintaining good prophylaxis.

Kenneth Stone.


At the Irvington House Prophylaxis Clinic New York University College of Medicine, 359 patients were observed in their first attack of rheumatic fever and were then followed up for 2 to 9 years (average 4.7 years).
They have been examined at monthly intervals and have received continuous antimicrobial prophylaxis.

It was found that definite evidence of cardiac enlargement, congestive heart failure, and pericardial friction rubs occurred almost exclusively in patients who had valvular involvement [this term is fully defined in the paper]. Prolongation of the P-R interval occurred with almost equal frequency in these groups—that is, those with "valvulitis", "probable valvulitis", and "no valvulitis"—but showed no correlation with the subsequent cardiac status. Thus, of those in the acute stage had valvulitis 67 per cent. (86 of 123) ended up with permanent heart disease, as compared with only 25 per cent. (13 of 52) of those with probable valvulitis and none out of the 178 who had no valvulitis. It is concluded that the auscultatory findings present during the acute attack of rheumatic fever are of primary importance in predicting the cardiac prognosis.

[The abstractor agrees with these findings and conclusion, subject to limitations of the medium-term follow-up. Later the situation may not necessarily remain the same.]

John Lorber.


The manifestations of acute rheumatic fever in the adult are described with reference to the findings in 30 patients (12 male and 18 female) aged 21 to 59 seen at Mount Sinai Hospital, New York, between 1952 and 1957. Symptoms in 28 of the thirty cases fulfilled the criteria laid down by Duckett-Jones for the diagnosis of rheumatic fever; in the remaining two cases the condition was diagnosed post mortem. Of the thirty patients, seventeen of whom were Puerto Ricans, fourteen were seen in what was thought to be the first attack, while another fourteen were known to have had rheumatic heart disease preceding the acute episode. In eighteen there was a history of an upper-respiratory infection preceding the onset of rheumatic fever, but none of these had had adequate antistreptococcal treatment. Joint involvement was the most frequent manifestation and was usually a classic migratory polyarthritis. In a series of tables the authors analyse the nature and distribution of the joint involvement and the incidence and various manifestations of carditis, the laboratory findings, and the response to treatment. Details are given of five illustrative cases. In strong contrast to the findings in juveniles, none of the adults in this series had erythema marginatum, subcutaneous nodules, or chorea. Rheumatic fever in these adults also differed from that in children in showing a higher incidence of arthritis than of carditis.

E. G. L. Bywaters.


This study of 43 patients with rheumatic fever, seen at Mount Sinai Hospital, New York City, between 1952 and 1957, was undertaken to determine the incidence, character, causation, and management of the "rebound" phenomenon, that is, the reappearance of clinical or laboratory signs of the disease after the termination of apparently successfully suppressive treatment. All 43 patients, most of whom were over 20 years of age, fulfilled the Duckett-Jones diagnostic criteria. Rebound was defined as the appearance of fever, an increased erythrocyte sedimentation rate (E.S.R.), reappearance of C-reactive protein, arthralgia, arthritis, chest pain, pericarditis, electrocardiographic abnormalities, or cardiac failure.

Of the 43 patients, 22 (51 per cent.) showed the rebound phenomenon, eight developing two "rebounds" and one four. These were most commonly manifested by fever (81 per cent.) and tachycardia (69 per cent.), and less frequently by arthralgia (56 per cent.) or arthritis (25 per cent.), while two patients developed pericarditis and five electrocardiographic abnormalities. The E.S.R. became abnormal in 97 per cent. and C-reactive protein reappeared in the serum in 92 per cent. In only two cases did the evidence of rebound depend on laboratory findings alone. In relation to drug treatment it was noted that rebound occurred in nine out of 22 patients treated only with salicylates, in seven out of twelve treated with steroids alone, and in six of nine treated by both methods. Rebound was also most frequent in those patients treated with steroids in high dosage. It did not seem to be related to duration of treatment, but only three of the patients were treated for more than 8 weeks. Abrupt or gradual cessation of therapy made little difference to the incidence, although this seemed to be lower following abrupt withdrawal of salicylates than of steroids. The rebound usually appeared on the first day after withdrawal, but in some cases was delayed until the 7th day, and lasted (in the absence of re-treatment) for periods varying between one and 29 days, the fever being short lived and abnormal laboratory findings being longer lasting. Second rebounds occurred more frequently in the steroid-treated group. The case history is presented of one patient with prolonged rheumatic fever and many rebounds who was finally discharged home taking aspirin, with a high E.S.R. and C-reactive protein in the serum after a period of 30 weeks in hospital.

The authors thus do not differentiate between relapse and rebound, believing them to be the same; nor do they consider that the phenomenon represents relative adrenocortical insufficiency (since it is seen with salicylates) nor part of a polycyclic attack. Dismissing also the theory of inadequately prolonged treatment, they incline to the view that the drugs alter the host's response to the basic pathogenic factor and conclude that the rebound phenomenon is an indication of persistent rheumatic activity necessitating re-treatment.

E. G. L. Bywaters.


In this joint study carried out at Cook County Hospital, Chicago, by members of the medical schools of
Illinois and Chicago, 385 cultures were prepared from the blood of 185 children (aged 5 to 15) suffering from treated and untreated rheumatic fever in various stages and 124 cultures from that of one hundred untreated non-rheumatic patients of similar age who served as controls.

An unusual number of positive blood cultures were found in those suffering from rheumatic fever, the organisms being short-chained, Gram-positive streptococci, often diplococcal in form; this diplococcus was found in 66 per cent. of cases which had received no treatment in the acute stage, in 22 per cent. of those in the convalescent stage, and in 10 per cent. of those in the inactive stage. It was not isolated from any of the controls, among whom the percentage of positive blood cultures (including staphylococcal contaminants) was much lower. The cultures did not show any growth of diplococcus before at least 30 days of incubation. Few of the organisms produced haemolysis in the tube test, but several showed slight β-haemolytic activity on horse-blood-agar plates; the majority of positive cultures came from cases in which less than 30 days had elapsed since the onset of rheumatic fever. It is suggested that once rheumatic fever has been initiated by β-haemolytic streptococci the disease may be continued by this additional organism described, this suggestion being based on the clinical observation that a small number of patients with chronic relapsing rheumatic fever did not show an obvious response to large intravenous doses of penicillin; there is no evidence that the streptococcus becomes resistant to the antibiotic. The literature is extensively reviewed.

[The original paper should be consulted for details of the techniques employed.]  
D. Preiskel.


At the Ospedale Maggiore, Milan, the authors have studied the clinical course and changes in various laboratory findings in two groups of patients suffering from rheumatic fever, one of which had and the other had not undergone tonsillectomy previously. They arrive at the following conclusions:

1. The macroscopic appearance of rheumatic tonsillitis, though not characteristic, is sufficiently constant in its morphological features to be recognizable.
2. The morbid histology of the tonsils as a whole indicates the existence of a hyperergic inflammatory process such as may reasonably permit the suspicion of its rheumatic nature.
3. Relapses of rheumatic fever are less frequent in patients who have undergone tonsillectomy.
4. In such patients rheumatic relapses respond more promptly to cortisone therapy and the immunological responses return more rapidly to normal.
5. In the authors' opinion tonsillectomy should be advised not only in the case of a first episode of rheumatic fever, but also in the case of relapses preceded or accompanied by tonsillitis.—[From the authors' summary.]


This paper reports the results of penicillin prophylaxis in a group of children recovered from an attack of acute rheumatism in comparison with a similar group of children receiving no prophylaxis. The children were aged 3 to 16 years and the observations were continued for periods which varied from less than a year to 5 years. Among the treated children (210 in all), who received 600,000 units of benzathine penicillin intramuscularly every 10 to 15 days for a total period of 5,120 patient-months, there were three cases of relapse of acute rheumatism—a rate of 0.06 per 100 patient-months. Among the 190 children who received no prophylactic treatment after the initial attack and were followed up for a total of 8,282 patient-months there were thirty relapses—a rate of four per 100 patient-months. A smaller group of fifty children who received no specific prophylaxis, but were given "non-specific" prophylaxis in the shape of ultraviolet light, cod-liver oil, sea baths, or dietary supplements, was studied for 1,764 patient-months, 40 relapses being observed—a rate of 2.5 per 100 patient-months. The efficiency of penicillin prophylaxis is thus clear, but the general measures were also of some value.

The length of time for which prophylaxis with penicillin should be maintained is discussed and it is shown that the majority of relapses occur within 4 years of the last attack. It is therefore suggested that prophylaxis should be maintained for a minimum of 4 years. It is further suggested that after regular prophylaxis has "ceased" prophylaxis on demand should be arranged by ensuring that when any rheumatic child develops a febrile illness a dose of penicillin adequate to eliminate haemolytic streptococci from the throat should be given without waiting to determine whether or not such organisms are present. A mixture of 600,000 units of benzathine penicillin, 300,000 units of procaine penicillin, and 300,000 of benzylpenicillin is recommended.

C. Bruce Perry.


In order to evaluate the effect of prednisone in the treatment of rheumatic fever, seventeen children with clinical evidence of active rheumatic carditis of less than one month's duration were treated at various hospitals in Baltimore with large doses of the drug. [There was no control group treated concurrently by other methods.] A prolonged course of treatment—a duration of at least 14 weeks was chosen arbitrarily—was used in the hope...

On examination of the fundus oculi in a number of cases of rheumatic fever with carditis in which visual disorders occurred the authors observed certain changes affecting the retinal blood vessels and, to a lesser degree, the optic disks. In their opinion such changes represent a local manifestation of the general effect of the rheumatic process on connective tissue and, although not specific for rheumatic fever, they can nevertheless be used in assessing the activity of the disease.

In the acute stage of a primary or recurrent attack disturbances of blood flow in the retinal arteries were noted, associated with transitory changes in the vessels such as irregularity of outline and thickening of the walls. In some cases patches of white exudate occurred which were ill defined, soft, and fluffy, and situated around the optic disk. The disk itself was sometimes congested and sometimes had the appearance characteristic of optic neuritis. In patients observed after the acute attack had subsided the blood vessels showed an early sclerosis and the areas of exudate had become smaller and better defined. The congestion and inflammatory changes affecting the optic nerve sometimes developed into atrophy of the optic disk which gave rise to serious impairment of vision. Three illustrative cases are described in detail. 

F. S. Freisinger.


In this report attention is drawn to the close relationship between acute rheumatism and thyroid dysfunction, which has been commented on by many observers, from Parry in 1872 to the present day. The results of observations on 1,600 patients have convinced the present authors that a distinct connexion exists between these two disorders. It has often been noted that rheumatism is frequently a precursor of Graves's disease, that acute thyroiditis often occurs in patients with acute rheumatism, and that during the course of Graves's disease in rheumatic subjects the onset of an acute attack of rheumatism may give rise to severe exacerbation of the thyroid symptoms. Vincent, who claimed to have found enlargement of the thyroid gland in some 67 per cent. of adult rheumatic subjects, stated as long ago as 1907 that absence of thyroid reaction in rheumatism indicated a poor prognosis. Other authors have described hypothyroidism or in some cases myxoedema as supervening on acute rheumatism.

Among the 1,600 cases of rheumatism seen by the authors at the Therapeutic Clinic, Odessa, between 1935 and 1955, symptoms of thyrotoxicosis were observed in about 10 per cent. of cases, this proportion rising in the post-war years to 16 or 17 per cent. Furthermore, of 74 patients with Graves's disease treated at this Clinic, nine gave a history of previous rheumatic polyarthritis and five had mitral valvular disease, while four more had mitral valvular disease without a history of acute polyarthritis. Increased absorption of radioactive iodine was observed in twelve out of 33 cases of rheumatism so tested; while of twenty cases of acute rheumatism in which the basal metabolic rate was determined it was raised in all, though clinical symptoms of thyrotoxicosis were found in only five. A further significant point was that in many of these cases antirheumatic treatment alone (aspirin or salicylates) banished or greatly relieved the thyrotoxic symptoms.

The incidence of myxoedema following rheumatism was much lower in this series than that of thyrotoxicosis. Two such cases are reported; in one of these patients, who had two attacks of acute rheumatic polyarthritis,
myxoedema developed during pregnancy 4 years after the second attack, while the second patient developed myxoedema 14 years after the first attack and 2 years before the second; both of these patients had also mitral involvement. While vigorous treatment of the rheumatic condition usually sufficed to allay the symptoms of thyro-toxicosis, repeated relapses of rheumatism in some cases led to the establishment of a stable toxic goitre, necessitating partial or subtotal thyroidectomy. The two patients with myxoedema required prolonged thyroid medication—in one case for 10 years. Among the hazards of uncontrolled rheumatism, therefore, must be included thyroid dysfunction, with the possibility of permanent structural and functional change in the gland, this being usually hypertrophic but occasionally atrophic in type.

L. Firman-Edwards.


From New York University College of Medicine the author reports a study of sixty children with a history of chorea who were followed up by monthly examinations for 2 to 67 months (mean 40-7 months) at the Irvington House Rheumatic Fever Prophylaxis Clinic, Irvington-on-Hudson, with the aim of elucidating the relation between streptococcal infection, rheumatic fever, and chorea. At some time during the preceding 28 months all but two of the patients had had rheumatic fever (as defined by modified Duckett-Jones criteria), and two exceptions having had only chorea. Each was given continuous prophylactic antistreptococcal treatment and at each visit a throat swab was taken, while the antistreptolysin-O and antihyaluronidase titres were determined at least every 2 months.

Of the sixty children, 41 developed no streptococcal infection during the follow-up period and there was no recurrence of chorea in these patients. The remaining nineteen patients, however, developed such infection despite the prophylactic regimen, and in three of these the chorea recurred, in one case twice. It is of interest to note that these four recurrences took place at intervals after the development of streptococcal infection (as judged by the rise in antibody titre) of approximately 5, 70, 90, and 180 days respectively, with a mean of about 87 days. These periods are contrasted with the mean interval of 10 days between the rise in antibody titre and the onset of polyarthritis or carditis in the 29 children who, despite prophylaxis, suffered a recurrence of rheumatic fever. Detailed case reports are given of the three children, in whom it was observed, the recurrence of chorea was not preceded or accompanied by clinical evidence of rheumatic fever. Only one of the four recurrences was associated with a high erythrocyte sedimentation rate and a positive result in the test for C-reactive protein in the absence of clinical signs. These findings thus provide the first reported evidence that Sydenham's chorea can follow Group-A streptococcal infection at longer intervals than, and in the absence of, polyarthritis and carditis, and indeed in the absence of any sign of "rheumatic activity". E. G. L. Bywaters.


Recent experimental findings have underlined the intimate anatomical and functional interrelationship between capillaries and connective tissue, which are of common embryological origin, and have also thrown light on the characteristic association of vascular lesions with lesions of the connective tissue in acute rheumatism and other diseases. Many authors are of the opinion that the systemic, structural, and functional damage produced in the capillaries by the rheumatic diseases is responsible in whole or in part for their pathogenesis. Cortisone, corticotrophin (ACTH), and the salicylates generally reduce capillary permeability in these diseases in parallel with their production of clinical improvement. Chlorpromazine also reduces capillary permeability, but the effect of phenylbutazone on the vessels is doubtful.

The present authors, working at the Medical Clinic of the University of Genoa and the Civil Hospital, San Remo, have studied the behaviour of capillary permeability during the treatment of cases of rheumatic fever with prednisone and dexamethasone. Clinically, dexamethasone showed a marked superiority. Among the various available methods of evaluating capillary permeability, the Landis test was preferred by the authors for its technical simplicity and dependability. This test confirmed the superiority of dexamethasone over prednisone, the latter producing no marked reduction in capillary permeability, whereas the former, in doses 6 to 8 times smaller, had a prompt and easily demonstrable effect.

This effect may, however, have been enhanced by previous treatment with prednisone. Robert E. Lister.


During the period 1938-57 about 6,000 patients with scarlet fever were admitted to the City Hospital, Cleveland, Ohio. Among these, nineteen were recorded as having concomitant arthritis or rheumatic fever (exclud- ing septic arthritis and arthritis secondary to serum sickness) during the first week of the illness, eighteen of whom were followed up to 20 years later to determine the incidence of valvular heart disease. There were twelve females and six males in the series, only three of whom had been admitted since 1946. One patient (a male aged 4 years) had died from acute rheumatic pancarditis one month after contracting scarlet fever.

Of the survivors, thirteen were examined by the authors and four by their own physician. In eight cases (44 per cent.) there were no signs of valvular heart disease and no history of acute rheumatism since the original episode. In only four patients (three females, one male) were heart murmurs of an organic character—-aortic and mitral diastolic, apical presystolic and systolic—noted at the time of follow-up. Of the remainder, however, one patient had developed signs of rheumatic pancarditis during the original illness, two had had subsequent
attacks of rheumatic fever or chorea, and in the remaining two the original arthritis had been recurrent or unduly persistent. It is therefore concluded that in ten (56 per cent.) of the eighteen cases there was evidence that the original arthritis was, or may have been, a manifestation of acute rheumatism. The authors review previous work on this complication and offer two possible explanations for the simultaneous occurrence of scarlet fever and rheumatic fever:

(1) That the patient has experienced a different streptococcal infection one to 5 weeks before that responsible for scarlet fever; or, more likely:

(2) That scarlatinal arthritis represents true rheumatic fever developing, after an unusually short latent period, as a result of infection with the scarlatinal streptococcus in persons predisposed to rheumatism.

They suggest that the present criteria for the diagnosis of rheumatic fever are too rigid, and emphasize the need for a specific diagnostic test. I. M. Librach.


The presence of the ABH and Le a blood-group substances in the saliva of healthy schoolchildren and of cases of rheumatic fever has been studied. By the ulex test 22-9 per cent. of 669 healthy schoolchildren were non-secretors, the comparable figure for 553 rheumatic fever cases was 28-9 per cent. Positive results with a precipitation test on the saliva with a rabbit anti-Le a serum were obtained in 21-2 per cent. of 1,129 healthy schoolchildren and in 27-5 per cent. of 611 cases of rheumatic fever. These two differences, significant at the 2 per cent. and 1 per cent. level respectively, would be expected if rheumatic fever could develop only in those individuals who are homozygous or heterozygous for the non-secretor gene. On the basis of this hypothesis we have shown that the incidence of rheumatic fever in the parents and sibs of patients with this disease should not, on hereditary grounds, be more than 13 and 16 per cent. greater respectively than in the general population.—[Authors' summary.]


Results of Control Examinations of Convalescents Several Years after an Acute Attack of Rheumatic Fever. (Výsledky kontrol v ústřední vojenské nemocnici v praze léčených rekonvalescentů po revmatické horečce po létě od akutní ataky.) HAUSER, J. (1959). Cas. Lék. čes., 98, 1435. 27 refs.


Chronic Articular Rheumatism (Rheumatoid Arthritis)


The author notes that German-speaking authors have made little reference to the "rheumatoid lung" syndrome, a condition first described by Ellman and Ball in 1948 (*Brit. med. J.*, 1948, 2, 816; *Abstr. Wild Med.*, 1949, 6, 101) and later more fully discussed by Ellman and Cudkowicz (*Thorax*, 1954, 9, 46; *Abstr. Wild Med.*, 1954, 16, 236) and many others. The syndrome comprises an active polyarthritis, with cough, fever, shortness of breath, and often pleocytosis. Radiologically, the lungs show net-like shadows which occasionally coalesce. Post mortem the arterioles and capillaries of the pleura and the intrapulmonary connective tissue are seen to be the primary site of attack. Other British workers, however, have reviewed a large number of cases of rheumatoid arthritis and have concluded that the pulmonary changes are not specific [for example, Aronoff and Bywaters (*Brit. med. J.*, 1955, 2, 228; *Abstr. Wild Med.*, 1956, 19, 229)].

The present author, working at the Medical Academy, Magdeburg, has reviewed 109 cases of rheumatoid arthritis. In nine of these there was no clinical evidence of any lung complications. The other hundred were examined radiologically and a number were found to be suffering from emphysema, pneumonia, or other pulmonary lesions, but there were no changes which could be attributed to "rheumatoid lung". In two of these patients who died—one of lymphatic leukaemia and the other of a septic nephritis—no significant lung changes were found at necropsy. On the basis of this study, therefore, the author also concludes that any lung changes present in patients with rheumatoid arthritis are not specific for that disease, but may be associated with any of the other collagen diseases. *D. Preiskel.*

Triamcinolone in the Treatment of Rheumatoid Arthritis.


A study of the comparative efficacy of triamcinolone and prednisolone in the treatment of fifteen patients with rheumatoid arthritis and one patient with ankylosing spondylitis is reported from the Royal Victoria Infirmary, Newcastle-upon-Tyne. All the patients received treatment with prednisolone and triamcinolone successively, the ratio of dosage being 5 : 4 by weight; the daily maintenance dosage of prednisolone ranged from 7.5 to 20 mg. The duration of treatment with triamcinolone varied from 2 to 26 weeks. Response to treatment was judged on the basis of the patient's own assessment of pain and the duration of morning stiffness as well as on the physician's assessment of functional capacity and disease activity. At regular intervals the strength of grip was measured and the erythrocyte sedimentation rate (E.S.R.) was estimated by Westergren's method.

In seven patients capillary resistance was measured by the method of Potter and Wigzell.

It was found that in respect of functional capacity, disease activity, strength of grip, and the patient's own assessment the difference between the two drugs was very small. The E.S.R., however, was lower during triamcinolone therapy in eleven cases, equal in two and lower during prednisolone therapy in three. Serial measurements of capillary resistance did not show any important difference. All except two patients lost weight while receiving triamcinolone. Diastolic blood pressure was 90 mm. Hg or more during prednisolone therapy in nine patients, and in all nine there was a fall in blood pressure during administration of triamcinolone.

Three patients who had dyspepsia while taking prednisolone experienced an increase in the severity of the symptoms when triamcinolone was given. Dyspepsia occurred for the first time in four patients during triamcinolone therapy; one of these patients had a haematemia. Lesions of subcutaneous ecchymoses developed in two cases during prednisolone administration, but regressed when triamcinolone was substituted. Two patients who were euphoric on prednisolone became calmer on triamcinolone. No change was observed in the acne, moon face, or hirsuties present in six patients when prednisolone was replaced by triamcinolone. *C. E. Quin.*


In a previous paper (*Acta med. scand.*, 1957, 157, 119; *Abstr. Wild Med.*, 1957, 22, 218) the authors reported that tanned erythrocytes coated with extracts of Group-A haemolytic streptococci were agglutinated by sera from patients with rheumatoid arthritis. In the present work, reported from St. Joseph Hospital, Heerlan, and St. Annadal Hospital, Maastricht, Netherlands, they first investigated the effect of using acetamide extracts of various other micro-organisms instead. Extracts of Gram-negative bacilli and pneumococci gave no reactions with serum from a case of rheumatoid arthritis which gave a positive result in the original test, but extracts of β-haemolytic streptococci and many staphylococcal strains gave positive reactions with this serum.

Extracts were also made from strains of α-haemolytic streptococci isolated from the throats of twenty patients with rheumatoid arthritis and of thirty normal subjects and these were used to coat tanned erythrocytes. Sera from these individuals were then tested against cells coated with extracts of autologous cocci and against cells coated with a standard Group-A streptococcal extract. Of the sera from normal subjects, none gave positive autologous reactions and four agglutinated the standard extract. Of the rheumatoid arthritis sera, three gave positive autologous reactions and eleven agglutinated the standard extract. This work, these authors claim, suggests that certain people produce antibodies against their own throat flora which play a part in the pathogenesis of rheumatoid arthritis. *E. J. Holborow.*
ABSTRACTS


In this paper from the National Institute of Hygiene and the Hôpital Cochin, Paris, the authors review in detail the results of long-term steroid therapy in one hundred patients, of whom six had ankylosing spondylitis and the remainder rheumatoid arthritis. The mean duration of treatment was 3 years, with a range of 1 to over 7 years in individual cases. All the patients are now treated with prednisone, although earlier one-third had received cortisone, hydrocortisone, or ACTH. The maintenance dose of prednisone was usually 10 mg. or even less; the authors now consider it preferable to start with a dose of this order rather than one of 15 mg. or more, and then reducing. So far as possible aspirin, phenylbutazone, and chloroquine were also given to help to limit the dose of steroid required. However, the value of aspirin in this respect was slight and the authors are “far from confirming” the conclusion reached in a British survey [no reference given] that in the long run aspirin is as valuable as, if not superior to, hormone therapy. The other drugs mentioned were often limited in use by gastric intolerance; however, when tolerance is good, chloroquine and hydroxychloroquine are valuable, and in five patients the use of these drugs ultimately enabled steroid therapy to be withdrawn. ACTH was used mainly to cover withdrawal of steroids, and the authors deprecate its use for intermittent “boosting” of the adrenal cortex.

The patients with rheumatoid arthritis were classified in four grades of severity. At the final assessment 63 per cent. showed an improvement in grade during treatment, 30 per cent. remained static, and 7 per cent. deteriorated. [There is no mention of a control group.] Before the start of steroid treatment ten of the 94 patients were classified as Grade 1 (with little restriction of physical activity); ultimately 44 could be placed in this Grade, and a further five had lost all signs of rheumatoid arthritis. Of the six patients with ankylosing spondylitis three showed improvement, mainly in peripheral joints. In regard to side-effects, gastro-intestinal symptoms were common (36 per cent., although proven ulcer occurred in only 6 per cent.): these symptoms were not related to the dosage of steroid, but their incidence was twice as high in those with a past history of dyspepsia. Osteoporosis occurred in 16 per cent., resulting in vertebral fractures in eight and fractured neck of femur in two patients. Here the danger was greatest with higher dosage (over 15 mg. daily), length of treatment, degree of immobility, and in women over 60 years of age. Of the nine deaths in the series, two were attributable to steroid therapy (gastric haemorrhage and miliary tuberculosis respectively), and three probably so (adrenal insufficiency in two cases and amyloid disease in one). The remaining four deaths were due to other causes, although possibly aggravated by sudden withdrawal of steroid therapy.

In summing up, the authors stress the need for proper precautions in order to achieve the best and very real advantages of steroid therapy. They warn particularly against the dangers of adrenal inhibition and against sudden withdrawal of steroids; they are reserved in their attitude to the new successor drugs to prednisone.

J. A. Cosh.


The authors of this paper from the University of Colorado School of Medicine, Denver, describe the clinical and necropsy findings in three patients suffering from rheumatoid arthritis in whom diffuse arteritis developed. The patients had been receiving steroid therapy for 15 months to 3 years before the onset of symptoms of arteritis and all had hypercortisonism. The first indication of the presence of arteritis was the development of symptoms and signs of polyneuritis; the patients were febrile. Gangrene of the finger tips and around the ankles developed in one patient; later, signs and symptoms appeared suggesting arterial occlusion in the heart or brain. A leucocytosis was present, the leucocyte count varying between 18,000 and 53,000 per c.mm. Microscopical examination of tissue removed at necropsy revealed polyarteritis affecting the majority of sections from the visceral and musculo-skeletal systems. The vascular lesions resembled those of polyarteritis nodosa.

Adrenocortical steroids were given in the treatment of 138 patients with rheumatoid arthritis attending the University of Colorado Medical Center in 1957. Of these, fourteen developed peripheral neuropathy—9 while receiving steroids and five over a period of 1 to 5 months after steroid therapy had been discontinued. Before the onset of peripheral neuropathy thirteen patients had received prednisone in a dosage of 10 to 20 mg. daily and one patient had received cortisone. The patients complained of pain and numbness and tingling in the hands and feet. Examination revealed sensory loss of glove and stocking type, weakness of peripheral muscles, and decreased tendon reflexes. Purpuric lesions occurred in ten of the fourteen cases. The authors consider that the peripheral neuropathy noted in these fourteen cases was due to arteritis affecting the nutrient arteries of peripheral nerves. After reviewing the literature they point out that although arteritis is known to occur in patients with rheumatoid arthritis who have never received steroids, the incidence of this complication has increased since the introduction of steroid therapy.

C. E. QUIN.


This report describes nine patients with rheumatoid arthritis who had in common severe deforming disease, subcutaneous nodules, large amounts of circulating rheumatoid factor and significant ischaemic skin changes.
and/or peripheral neuropathy. All nine had been treated with adrenocortical steroids for periods ranging from 1½ to 5 years. The incidence of subcutaneous nodules and the magnitude of the F II haemagglutination titre in these patients are significantly different from those found in a population of patients with rheumatoid arthritis. No direct correlation was found between absolute end-point titres and the clinical neurovascular complications. The association of rheumatoid arthritis of Stage III or IV, subcutaneous nodules and the presence of large amounts of rheumatoid factor in the serum may constitute a relative contraindication to the use of adrenocortical steroid therapy.—[Authors' summary.]


This article from the department of Orthopaedic Surgery of the State University of Iowa is a review of current thought upon some aspects of hand surgery in rheumatoid arthritis. In the early stages the disease may be confined to the sheaths of tendons, and complete excision of the involved sheath sometimes appears to control the progress of the disease. Tendon ruptures in rheumatoid arthritis are becoming increasingly recognized as a cause of deformity. This may be due to frictional attrition of the tendon over a rough spur of bone in the affected joint, or more commonly, to degeneration of the tendon with spontaneous rupture. This is a common cause of finger deformity, and any of the fibres of the extensor or flexor tendons may be involved. Prompt recognition of the condition, and surgical treatment by tendon transfer or grafting is imperative if function is to be retained. The deformity of the fingers is often increased by contracture of the intrinsic muscles, and may be remedied by intrinsic release, or by extensor tenodesis.

Where the joint involvement is marked, either arthrodesis of the affected joint, or occasionally arthroplasty, can achieve a considerable increase in the function of the whole hand. In the proximal interphalangeal joint, the retention of movement may be of great importance, and the author describes a prosthesis which is being developed to permit a satisfactory arthroplasty of this joint. Most surgical procedures can be carried out with safety when the disease is active, and a plea is made for the earlier consideration of surgery in these patients. Peter Ring.


In view of the rarity of neurological complications in rheumatoid arthritis the authors report two further cases seen at the Hôpital Foch, Suresnes, Paris, in which polyneuritis due to periarteritis nodosa was present as a complication of rheumatoid arthritis. Both occurred in women aged 64 in whom the rheumatoid disease had existed for 11 and 4 years respectively. Both had received courses of gold therapy in the past and more recently treatment with prednisone. Fever accompanied by generalized pain was noted in both cases. There was a leucocytosis of 15,000 per c.mm., with a preponderance of polymorphonuclear leucocytes, in one case and of 18,960 per c.mm. in the other. The neurological signs included paralysis or paresis of the extremities with absent tendon jerks, and hypoesthesia of the hands and feet; in addition there was exquisite tenderness on compressing the muscles. Muscle biopsy examination performed in both cases demonstrated periarteritis nodosa affecting the arterioles. One patient died and at necropsy widespread foci of periarteritis were found. The other recovered, but the neurological signs showed little change and gangrene developed in one toe.

The authors present an extensive review of the literature in which previous similar cases have been reported. In most the signs and symptoms were as described above, and a history of gold, copper, or steroid therapy was common, particularly the last in the more recent cases. Neurological signs, usually symmetrical, generally affect the extremities, but rarely the distribution of the cranial nerves. *Post mortem*, the arterial lesions are found to be widespread, and have been demonstrated in the heart muscle and valves, spleen, intestine, kidney, and the nutrient arteries of peripheral nerves. The treatment of such cases is extremely difficult, involving as it does the cessation of steroid therapy with the risk of serious withdrawal symptoms. These patients have often been receiving high doses of steroids and their too rapid withdrawal has been known greatly to increase the extent of the paralysis. In the authors' opinion the treatment of these neuropathies can only be prophylactic, meaning thereby that steroids should be prescribed only in exceptional cases of rheumatoid arthritis and then in low dosage. William Hughes.


For various periods during an investigation lasting 12 weeks, 24 adult patients with rheumatoid arthritis were given aspirin, a placebo, phenybutazone, and metabolite I, a derivative of phenybutazone. The last two drugs were given in doses of 800 mg. on the first day and 600 mg. on the second day; subsequently the dose was maintained at 400 mg. daily. Observations were controlled by administering the drugs in the form of a white powder in gelatin capsules of identical appearance. Throughout treatment special note was made of any changes in joint swelling, degree of tenderness, pain, morning stiffness, fatigue, speed of walking, and grip.

Apart from salt and water retention during the early phases of treatment there were no important side-effects from administration of metabolite I. The response to this drug was at least equal to the response obtained with phenybutazone. During metabolite I therapy there was highly significant improvement in grip and in the duration
of morning stiffness. On the other hand, equivocal results were obtained with completely objective measurements such as the erythrocyte sedimentation rate and joint circumference. Altogether an excellent or a good response was obtained in twelve cases.

A. Garland.


At the Arthritis Clinic of the University of Louisville 65 patients (39 female and 26 male) with rheumatoid arthritis were treated with prednisolone or prednisone, methylprednisolone, triamcinolone, or dexamethasone. Since no difference has been reported in the literature between prednisone and prednisolone, these two preparations are grouped together as "prednisteroids". The patients' ages ranged from 23 to 71 years and the average duration of the disease was 7 years. Each patient was classified in respect of severity of the disease and functional disorder according to the criteria of the American Rheumatism Association, 31 patients being in Stages 3 and 4 (moderately advanced and advanced). None of the patients had received antimalarials or gold therapy within one year of starting treatment with corticosteroids, although all had received salicylates and "basic therapy". A clinical evaluation of each patient was performed "at regular and frequent intervals". Certain laboratory studies were carried out periodically, including estimation of the haemoglobin level and haematocrit, total and differential leucocyte counts, erythrocyte sedimentation rate, total plasma protein and albumin and globulin levels, and urinary sugar and albumin content.

In 48 cases prednisteroids were given for an average period of 2 years. Methylprednisolone was given to 39 patients, of whom 32 had previously received long-term prednisteroid therapy, and 25 received triamcinolone before or after the methylprednisolone, while in seven cases methylprednisolone was the only corticosteroid given. Triamcinolone was given to 38 patients, of whom 31 had received prednisteroids and 25 were given methylprednisolone either before or after the triamcinolone, triamcinolone being the only corticosteroid given in seven cases. A firm maintenance dose of each corticosteroid was established before another was substituted. Patients served as their own controls without the administration of placebos as soon as the early part of the study was finished. This method of comparison was preferred to the double-blind method, mainly because of the dangers of interrupting corticosteroid treatment. Altogether 25 patients received prednisteroids, triamcinolone, and methylprednisolone for sufficiently long periods to allow comparative analysis of the results. The remaining forty patients did not receive all these corticosteroids and are therefore not included in the analysis. On the other hand forty patients were later given dexamethasone, enabling a preliminary comparison of the effects of this and other corticosteroids to be made.

Comparable antirheumatic effects were obtained with all compounds in the majority of cases. The average daily maintenance doses were: prednisteroids, 11-4 mg.; triamcinolone, 7-8 mg.; methylprednisolone, 8-12 mg.; and dexamethasone, 1-4 mg. The laboratory investigations revealed no consistent difference between the various corticosteroids except that glycosuria and an increase in the blood sugar level occurred more often with the prednisteroids than with the other preparations. The side-effects occurring in the 25 patients who received adequate treatment with prednisteroids, methylprednisolone, and triamcinolone are listed. The incidence of the expected manifestations of hypercortisonism and of peptic ulcer and other gastro-intestinal symptoms was similar with all compounds. Emotional disturbances, oedema, and glycosuria occurred most often with the prednisteroids and eczematous and purpuric skin manifestations with methylprednisolone. Two "new" side-effects are reported as occurring almost exclusively with triamcinolone, namely "hot flushes", erythema of the face, and increased perspiration and, more serious, muscle weakness accompanied by loss of weight, which occurred in about 24 per cent. of patients receiving this steroid. In contrast, dexamethasone had a remarkable appetite-stimulating effect and produced a striking gain of weight.

None of the steroids was outstandingly superior to the others in clinical effect and freedom from side-effects. The author concludes that methylprednisolone is probably the steroid of choice for initial treatment, but dexamethasone may prove useful for the early treatment of the underweight patient with rheumatoid arthritis.

J. Warwick Buckler.


This study of three children with Still's disease, in each of whom it took a different course, is reported from the University Paediatric Clinic, Göttingen. Although the disorder is generalized, the bones consistently tend to become demineralized and osteoporotic, and this tendency is believed to be aggravated by the modern use of ACTH (corticotrophin) and steroids, which do not necessarily arrest the disease process. The administration of vitamin D helps to counteract the tendency to demineralization, but unfortunately it also diminishes the beneficial effects of the hormones. For this reason the author suggests that the vitamin should not be given unless osteoporosis is marked; if it is given its administration should be accompanied by prompt reduction in the dosage of steroids, or they may be given intermittently, or better still completely omitted. Radiologically, in all three of the author's cases some of the changes in the bones were subsequently reversed, but it is stressed that orthopaedic measures and long-term physiotherapy form an integral and essential part of the treatment. [There is no indication of the dosage of vitamin D or the type of preparation employed.]

D. Preiskel.

Over a recent 10-year period at the Children's Hospital, Denver, Colorado, subcutaneous nodules were removed from nine children, aged 11 days to 9 years, in whom there was no evidence of rheumatic disease. The nodules were found on the limbs or on the scalp. Histological examination revealed foci of necrosis surrounded by fibroblasts and histiocytes, with scattered chronic inflammatory cells. The author concludes that the similarity of these lesions to rheumatic nodules is noteworthy.

[The photomicrographs reproduced show necrosis and a cellular “palisade”; these features are very rarely seen in rheumatoid arthritis in children (see Bywaters and others, Ann. rheum. Dis., 1958, 17, 278; Abstr. Wild Med., 1959, 25, 153) or in rheumatic fever.]

G. Loewi.


A study is reported from the University of California Medical Center, Los Angeles, of erythrocyte production and destruction and disturbances in iron metabolism (using histological, serological and radio-isotope techniques) in eighteen patients with active rheumatoid arthritis, of whom thirteen had typical rheumatoid arthritis, but five had additional complications; for instance two had “malignant” rheumatoid arthritis, two gave a positive L.E.-cell test reaction (one of these also having splenomegaly), and one had splenomegaly, leucopenia, and anaemia. The patients in the atypical group were in general more severely ill.

In nine of the thirteen patients with typical rheumatoid arthritis and in four of the atypical patients the erythrocyte volume was abnormally low. Most of these patients also had a low serum iron level, with rapid disappearance of radioactive iron (59Fe) from the plasma and an increased rate of turnover of iron. However, the utilization of 59Fe by newly-formed erythrocytes was very good in both the typical and atypical groups, only three of the thirteen patients in the typical group showing definitely abnormal utilization of 59Fe. Histological examination of the bone marrow in these patients failed to reveal any significant evidence of impaired erythropoiesis. Six of the thirteen patients in the typical group and four of the five in the atypical group showed abnormal erythrocyte survival times, but it is emphasized that this shortening of the life span cannot in itself account for the development of anaemia, since it should be compensated for by an uninhibited bone marrow. Studies of the distribution of 59Fe and radioactive chromium (81Cr) showed that in the majority of these patients this was normal. In nine of the eighteen patients the plasma volume was greater than normal, and although such an increase would not account entirely for the anaemia it would suggest that in some instances the so-called anaemia of uncomplicated rheumatoid arthritis may be due to dilution of the plasma volume. There appeared to be no relationship between the lowering of the serum iron level and the anaemia in these patients with rheumatoid arthritis. Estimation of the degree of anaemia by the haematocrit value or the actual determination of erythrocyte volume suggested that the absorption of iron in these patients was not significantly different from that in normal subjects, and it appeared that the low serum iron levels did not stimulate an increased absorption of the iron from the gastro-intestinal tract, as occurs in straightforward iron-deficiency anaemia. It has been suggested that in rheumatoid arthritis and in similar diseases there may be a defect in the mobilization of iron from the reticulo-endothelial system, but this could not be confirmed in the present study. The author concludes that severe anaemia associated with rheumatoid arthritis suggests the presence of complications such as a superimposed iron deficiency, malignant rheumatoid disease, hypersplenism, or an underlying diagnosis of disseminated lupus erythematosus.

R. F. Jennison.


Crico-arytenoid Joint. A Diarthrodial Articulation Subject to Rheumatoid Arthritic Involvement. POLISAR, I. A. (1959). Laryngoscope (St. Louis) 69, 1129. 9 figs, bibl.


Extensive haemarthrosis unrelated to severe trauma or blood dyscrasia has hitherto been considered rare. Over a recent 2-year period the author of this paper from the Institute of Orthopaedics, London, has collected details of five cases of spontaneous haemarthrosis of the knee with osteo-arthritis. In three of the cases there had been more than one episode of haemarthrosis. The onset of painful, tense swelling of the knee was very rapid, and in all cases trauma was minimal or absent. It is suggested that the haemarthrosis is due to nipping of synovial tags, perhaps in the vascular fringe round a deformed patella. Aspiration of the joint should be carried out as soon as possible, particularly if the haemarthrosis is large; disability should not then be prolonged.

J. N. Agate.


The incidence of genital infection in 82 male patients suffering from ankylosing spondylitis was investigated at the London Hospital. Previous similar studies of this subject are reviewed and the criteria for diagnosis of ankylosing spondylitis and chronic prostatitis are defined. Patients with ankylosing spondylitis as a complication of Reiter's disease and those in whom it had been recognized at the venereal disease clinic were excluded from the study.

All patients were questioned as to past genital infection, and the prostatic secretion was examined in the 72 cases in which it could be obtained; of these, sixty (84 per cent.) showed evidence of chronic prostatitis-vesiculitis. The author compares this with a maximum incidence of 25 to 30 per cent. in a control series of normal healthy males previously examined by him. Of the whole group of
patients, nine were found to have mild non-specific urethritis, while a further nine gave a history of gonorrhoea, three a history of non-specific urethritis, and eight a history of urethral infection of undetermined origin. The results of this study appear to add weight to the suggestion that there is a close link between ankylosing spondylitis and genital infection, whether gonococcal or non-gonococcal, and the author speculate on the possible prophylactic effect of the efficient treatment of genital infections.


Writing from St. Mary’s Hospital, London, the author describes the results of re-examination of 134 out of 166 patients with Reiter’s disease previously reported (Brit. med. J., 1958, 1, 1088; J. Fac. Radiol. (Lond.), 1958, 9, 44; Abstr. Wld Med., 1958, 24, 179 and 238). All were examined or re-examined radiologically for evidence of sacro-iliitis and 27 (20.1 per cent.) were found to have such evidence. The progress and clinical features in the two groups of patients, that is, those with and those without sacro-iliitis, are compared with each other and also with the course in fifty consecutive cases of classic ankylosing spondylitis seen at the hospital over the same period.

It is concluded that the development of sacro-iliitis in Reiter’s disease generally indicates that the illness was more severe from the start even though sacro-iliac joint lesions were not an important or persistent cause of symptoms. Reiter’s disease with sacro-iliitis differs significantly from ankylosing spondylitis notably in regard to age and sex incidence, type of onset, proportion of peripheral joint and spinal involvement and incidence of iritis. Conjunctivitis, keratoderma, balanitis, and plantar fasciitis, which are prominent in Reiter’s disease, do not occur in ankylosing spondylitis. The relatively high incidence of rheumatoid arthritis in the families of patients suffering from Reiter’s disease suggests that further investigation is warranted. The author concludes that, at least for the present, Reiter’s disease and ankylosing spondylitis should be regarded as separate entities.

Leslie Watt.


The results obtained with radiotherapy in 87 cases of ankylosing spondylitis seen at Charing Cross Hospital, London, are described. A single course of treatment was given, with a dosage of 600 to 300 r to the bone marrow and an integral dose of 5 to 7.5 mg./r. This was supplemented by physiotherapy and when necessary for associated depression by psychotherapy.

The cases were classified according to the severity of the disease before and the degree of remission after treatment. Of the 87 patients 75 were in remission or had made a complete recovery after 3 months’ treatment; of 74 followed up after 5 years 36 were in remission. Patients with a mild form of the disease appeared to respond more completely and more consistently to radiotherapy.

M. Wilkinson.


In this paper from St. Thomas’s Hospital, London, the author discusses the evidence for the view that pelvic infection may precipitate ankylosing spondylitis in susceptible subjects, and describes seven new cases of ulcerative colitis with sacro-iliitis or classic ankylosing spondylitis. In six of the cases in which the history was adequate the arthritis began within 3 years of the onset of colitis. He points out that a review of the literature suggests that the association of these diseases is too frequent to be due to chance. He also briefly refers to two cases of Crohn’s disease with bilateral sacro-iliitis. The progression of Reiter’s syndrome to ankylosing spondylitis is illustrated in three case histories. The sacro-iliac arthritis of Reiter’s syndrome may be more frequently unilateral but is otherwise difficult to distinguish from ankylosing spondylitis. The sacro-iliac and spinal changes in paraplegia are described and their possible relationship to chronic urinary infection is discussed.

Involvement of the sacro-iliac joints in rheumatoid arthritis is considered to be uncommon and never a dominant feature of the clinical picture.

There is evidence in the literature which suggests that prostatovesical arthritis is frequent in patients with ankylosing spondylitis, and that the thesis of pelvic infection may cause non-suppurative bone lesions is supported by the findings in two cases—one with bilateral sacro-iliac changes after a septic abortion and one with osteitis pubis and ischii following post-prostatectomy sepsis.

Discussing the vertebral venous system the author suggests that through this channel pelvic infection may cause sacro-iliac changes which in genetically predisposed patients may herald the development of classic ankylosing spondylitis. [He does not attempt to explain the occurrence of peripheral arthritis in this condition.]

M. Wilkinson.


At the State Institute of Rheumatology, Budapest, the duration of the vibration sense was investigated by means of a tuning fork in 250 patients with various rheumatic disorders. It was found that the vibration sense was prolonged to about twice the normal duration in the majority of 100 patients with ankylosing spondylitis. The reason for this finding is not known, but it is suggested that it may be due to irritation of the posterior nerve roots as a result of the narrowing of the intervertebral foramina in this disorder.

G. W. Csonka.


(Miscellaneous)


This paper from St. George's Hospital, London, represents a careful study of the results of treatment in 59 cases of periarthritis of the shoulder of a standard minimum level of severity and duration.

It has long been recognized that manipulation under anaesthesia in the acute, irritable phase generally fails to restore movement permanently and often causes an exacerbation of symptoms with a further loss of movement, whereas manipulation at a later and more quiescent phase will generally free movement without risk of recrudescence. The authors wished to discover whether, with the addition of a potent anti-inflammatory agent such as hydrocortisone injected into the joint cavity, manipulation could be carried out successfully in the acute phase and the duration of the disability shortened; nineteen cases were treated this way, 25 mg. hydrocortisone being injected at the same time as manipulation was carried out under anaesthesia and active physiotherapy given subsequently, while thirteen cases were treated with 2.5 g. cortisolone given orally over a period of one month, together with supervised active movements and palliative physiotherapy. The remaining 27 cases were treated by physical methods, sometimes followed by late manipulation under anaesthesia, but received no steroids.

The use of intra-articular cortisone combined with manipulation under anaesthesia followed by active physiotherapy was found to give considerably more satisfactory results than did the alternative methods of treatment, and the total period of disability was shortened.

W. S. C. Copeman.


At the Holy Ghost Hospital, Cambridge, Massachusetts, sixteen patients with rheumatoid arthritis and 31 with osteo-arthritis were given courses of intra-articular injection of hydrocortisone in which the interval between the injections did not exceed 2 or 3 days. The usual course consisted of three to six injections. The rheumatoid patients received a total of 116 injections in 37 courses and the osteo-arthritic patients 214 injections in 61 courses. [It should be noted that eight of the patients with rheumatoid arthritis were also receiving systemic steroid therapy.]

An "excellent" or "good" response was obtained to 32 of the 37 courses given to patients with rheumatoid arthritis, the remission in some three-quarters of these instances lasting more than 2 months. Of the 61 courses given to patients with osteo-arthritis "excellent" or "good" results were obtained in response to 58.

From a review of the literature the author found that these results were much better than those hitherto reported.

K. C. Robinson.


The results of phenylbutazone therapy in 590 adult patients (aged 19 to 75 years) suffering from various rheumatic disorders are reported. The daily dose ranged from 100 to 800 mg., the average daily maintenance dose being 200 mg. In 54 cases treatment was given for at least one year. Excellent or good results were obtained in 34 out of 78 cases of rheumatoid arthritis, in 95 out of 115 cases of osteo-arthritis, and in all ten cases of ankylosing spondylitis. It was necessary to discontinue treatment in thirty of the 55 cases in which undesirable reactions occurred. These reactions, which were observed more frequently in patients with rheumatoid arthritis than in those suffering from other forms of rheumatism, included rashes and gastro-intestinal distress. Leucopenia developed in two patients. For the most part, the reactions occurred within the first month of treatment and when the daily dose exceeded 300 mg.

In view of these results the author recommends that phenylbutazone should be administered with caution in cases of heart disease. Fluid retention must be avoided, especially in the elderly, and for this purpose the dosage of the drug must be low and any gain in weight must be checked. The drug must not be given on an empty stomach. Antacids may be of use if mild gastro-intestinal symptoms develop. The amount of salt in the diet should be restricted in all cases. Phenylbutazone therapy is contraindicated in patients with a history of peptic ulcer. During the early stages of treatment a complete blood count is performed weekly; later, the blood is examined at intervals of 4 to 6 weeks. The patient is warned to report immediately the occurrence of untoward signs and symptoms such as pruritus, rash, sore throat, fever, gastro-intestinal disturbances, and tarry stools. The author considers that when these precautions are observed long-term therapy with phenylbutazone is likely to prove both safe and effective in the management of rheumatoid arthritis, ankylosing spondylitis, and other chronic forms of rheumatism.

A. Garland.


This paper is based on a clinical and radiological study of sterno-clavicular arthritis, of which some ten cases are
seen annually at the Hôpital Lariboisière, Paris. Both sexes may be affected, but most often the patient is a post-menopausal woman engaged on manual work. The right side is more commonly attacked than the left and the condition is often preceded by scapulo-humeral peri-artitis on the same side. Examination reveals a swelling over the sterno-clavicular joint; radiologically this is shown to be due to ante-ro-medial subluxation of the sternal end of the clavicle, and when the shoulders are braced back the swelling disappears. There is usually no pain and there are no signs of inflammation. Radiographs show the presence of osteophytes. The condition is benign and the prognosis is good, the main interest of this trivial ailment being its correct diagnosis, since the pseudo-tumoral appearance of the lesion may occasionally give concern to both doctor and patient.

G. Loewi.


An investigation of the value of intra-articular injection of prednisolone trimethylacetate in the treatment of arthritis was undertaken at Glasgow Royal Infirmary, the injections being given into the knee-joints of 27 patients with active rheumatoid arthritis, six with osteo-arthritis, and two with recurrent hydrarthrosis. The knee-joint was entered from the lateral aspect at the level of the upper border of the patella. A small amount of fluid was removed for analysis, but no attempt was made to drain the joint. The standard dose of prednisolone trimethylacetate for injection into the knee was 20 mg., and initially the interval between injections was 7 days, until the effusion had resolved; thereafter the injections were gradually spaced out and eventually stopped. The average follow-up period after the last injection was 6.1 months. In rheumatoid arthritis the results at the end of the follow-up period were good in 23 cases, fair in two (regular maintenance injections being necessary), and poor in two. The results were good in two cases of osteo-arthritis, fair in two, and poor in two. Good results were obtained in both cases of hydrarthrosis.

In ten patients with bilateral effusions the effect of prednisolone trimethylacetate was compared with that of lignocaine, one knee being injected with prednisolone trimethylacetate and the other with an equal volume of lignocaine. Prednisolone trimethylacetate was more effective than lignocaine in reducing the amount of pain and swelling.

The authors conclude that prednisolone trimethylacetate is an effective agent for intra-articular therapy.

C. E. Quin.


At Glasgow Royal Infirmary the authors studied the cytological and biochemical changes in the synovial fluid from the knee-joints of patients with arthritis. Altogether 57 knee-joints were aspirated, suitable serial specimens being obtained from forty (rheumatoid arthritis in thirty, osteo-arthritis in six, and hydrarthrosis in four). Injections of prednisolone trimethylacetate were given at weekly intervals, and before each injection a small amount of fluid was withdrawn for study of the total and differential cell counts, total protein content, mucin content, viscosity, and electrophoretic pattern. During treatment with prednisolone trimethylacetate there was a fall in the cell count, due mostly to a sharp diminution in polymorphonuclear leucocytes, although there was also a real fall in lymphocytes and monocytes. Initially the average protein content was 4.4 g. per 100 ml.; after prednisolone treatment it fell to 3.4 g. per 100 ml. Electrophoresis showed a rise in the albumin content of the fluid in most cases. The changes in the cell count occurred after the first two injections, but the changes in the protein content occurred more gradually. The viscosity of the synovial fluid from 26 rheumatoid joints rose and the mucin content of fluid from 27 similar joints fell. The initial cell count and total protein were lower in the synovial fluid from osteo-arthritic joints, but the change after intra-articular therapy followed the same pattern as those observed in the fluid from joints affected by rheumatoid arthritis. In ten patients with bilateral effusions one knee was injected with lignocaine. No change in viscosity or mucin content of the fluid was observed; the cell count rose in six and was unchanged in four, while the protein content rose in four and was unchanged in six. An analysis of the electrophoretic pattern in this group showed no significant changes.

C. E. Quin.


In this paper the author has assembled the results of laboratory tests performed on the series of cases of Reiter’s syndrome previously reported. The tests were all carried out in London, at St. Mary’s Hospital, St. Mary’s, the Institute, and the London Hospital. For various reasons not all the tests were performed in every case and there was therefore a slight over-representation of severe cases of the disease.

Controlled bacteriological and serological tests for pleuro-pneumonia-like organisms showed that they were not a significant factor in Reiter’s syndrome. Nor is the gonococcus considered likely to be of primary aetiological significance for various reasons, in spite of the fact that this organism was isolated from 107 of 195 cases examined. The gonococcal complement-fixation test was of little practical value, but may occasionally draw attention to the presence of unsuspected venereal infection. Culture of the urine of patients without gonorrhoea revealed nothing of significance in the absence of complicating organic lesions, but examination of the prostatic secretion revealed that 55 per cent. of 1320 patients had prostatitis according to the generally accepted criteria: the full significance of this finding, however, cannot be assessed because of the lack of a control group. Moderate normocytic anaemia was present in 15·9 per cent. of 88 patients, and some degree...
of neutrophil leucocytosis was present in one-third of the patients tested. A raised erythrocyte sedimentation rate was usually associated with active disease, especially when active arthritis was present. Electrophoretic analysis of the serum protein pattern in thirty patients showed a decrease in the albumin fraction and an increase in the γ-globulin fractions; it is suggested that these changes, though not specific for Reiter’s syndrome, warrant further study. The differential agglutination test, the L.E.-cell test, the identification in the serum of C-reactive protein, and estimation of the serum uric acid level are of value only in the differential diagnosis.


This, with the preceding abstract and other articles in the same issue of the Brit. J. vener. Dis., comprises a comprehensive discussion on our present knowledge of Reiter’s disease—a disease characterized by non-gonococcal purulent urethritis, followed by arthritis, conjunctivitis, and anterior uveitis. The suggestion is made, particularly in male patients, that the primary lesion is a genito-urinary infection, usually a prostatovesiculitis which gives rise to various forms, the most common of which is spondylitis. The infective agent is unknown but it is suggested that the clinical variations may be due to such factors as genetic predisposition and the effect of repeated infections. [The final article has appended a select bibliography covering the years from 1916 to 1959.]

Stewart Duke-Elder.

Diagnostic Difficulties in a Case of Juvenile Chronic Ankylosing Polyrheumatoidarthritis with Blindness and Chondroarthrodisplasia associated with Scleroderma. (Difficoltà diagnostiche in un caso di poliartrite cronica anchilosante giovane con cieà e condro-atrodisplasia associata a sclerodermia.) DELLA CASA, R. (1958). Minerva pediat. (Torino), 10, 1234. 30 figs, 19 refs.


Reiter’s Syndrome. (Sindrome di Reiter.) LUCHERINI, T., and CECCHI, E. (1958). Reumaitismo, 10, 151. 10 figs, 17 refs.


Association of Multiple Arthritis with Carcinoma. PATHY, M. S. (1959). Rheumatism, 15, 73. 14 refs.


Disk Syndrome


The authors describe a pilot study of three commonly used physical methods of treatment of cervical spondylosis which they carried out at the London Hospital on 163 patients complaining of neck and/or shoulder pain, or peripheral paraesthesias attributable to this condition. The treatment regimens were:

1. heat, massage, and longitudinal neck traction given for one-hour periods three times a week for one month (42 patients);
2. the fitting of a felt collar reinforced with plastic, this to be worn as much as possible and especially during sleep (22);
3. neck and shoulder girdle exercise (six patients in each class), these being given for half an hour three times a week for one month (29).

A fourth smaller control group (seven patients, Group 0) was treated according to the physician's free choice of method.

Allocation to the various treatment groups was made by reference to the last digit of the patient's hospital registration number; by chance this method unfortunately resulted in a very uneven distribution, and the authors comment on the advisability of a truly random allocation. The age incidence was highest in the 10-year age group 40 to 49, and was reasonably consistent between the groups. All patients were reviewed after 2 and 4 weeks' treatment, and assessment of the result, being dependent mainly on relief of pain, was entirely subjective.

The results in 146 patients (seventeen having defaulted) showed that, after 4 weeks, the felt collar gave the best "improvement" rate (51-8 per cent.), this rate in Groups 0, 1, and 3 being 69-2, 70-5, and 71-8 per cent. respectively. Group 3 (the exercise group) showed the highest "cure" rate (15-4 per cent.), but also the highest defaulter rate (13-3 per cent.), and the highest aggravation rate (12-8 per cent.). Patients in Group 0 (the "physician's free choice" group) did not do particularly well, and the authors therefore consider that the method of arbitrary selection of treatment employed was quite justified. They also point out that the apparently most effective treatment, that is, the fitting of a collar, is the one most sparing of time for both patient and physiotherapist. They stress, however, that this was a pilot trial only, and much larger numbers of patients, including a placebo group, would have to be studied to provide definite results.

B. E. W. Mace.


From the University of California Medical Center, Los Angeles, the authors report nine cases in which inflammatory lesions appeared in the intervertebral space following surgery for herniation of a lumbar disk. Case histories are given and radiographs reproduced. In three cases there was acute and obvious suppuration in the operation wound, another patient developed meningitis, and in a fifth case there was some discharge from the wound, but no organisms could be cultured. The remaining four patients showed no evidence of frank suppuration, but had disabling lumbar pain. Such pain was the characteristic feature of the clinical picture; it often spread to the groin and lower abdomen and was sometimes associated with paravertebral muscle spasm. In the acute supplicative cases clinical evidence of infection was amply apparent. Radiological changes, which were first noted 2 months after operation and in some cases for up to 2 years, consisted in extensive destruction of adjacent vertebral bodies with, later, bony fusion between them.

In regard to treatment, the frankly suppurating lesions were treated along usual lines, including open drainage, later secondary closure, and appropriate antibiotic therapy. The non-suppurating cases were treated con-
servatively; in these cases immobilization of the spine and antibiotic treatment did not appear to affect the progress of the disease. Although bacterial agents were probably responsible for the majority of these cases, other processes may have been involved. In some, for example, it is possible that the naturally occurring progression of degenerative disease of the joint, aggravated by surgical trauma, might have accounted for the clinical and radiological changes observed. Brodie Hughes.


The authors describe the circumstances in which a surgeon may be compelled to perform further operations on the spine of a patient who has already had one or more operations for prolapsed intervertebral disk. These second (or even third) operations are always difficult and require considerable skill not only in performance but in the selection of cases. Among the reasons for re-operation are failure of the original operation to benefit the patient; true relapse (defined as recurrence of sciatica at the same level after a period of freedom following the first operation); or subsequent development of sciatica at another segmental level or on the opposite side. Myelography should be performed in all cases before deciding to operate. Definite radiological evidence of a localized protrusion strongly indicates operation, but a negative myelogram counsels caution.

In reviewing their own experience at the Hôpital Beaujon, Paris, of 87 re-operations (59 patients formerly operated by one of the authors and 28 initially operated on elsewhere) the authors conclude that these further explorations are negative in the majority of cases, apart from those in which a herniated intervertebral disk had been missed or incompletely removed on the previous occasion. Those patients do best in whom a new herniation is found and removed, but section of nerve roots sometimes brings benefit in cases in which the second exploration gives negative results. Early re-intervention produces better results (100 per cent. of sixteen cases cured) than do later re-operations (56 per cent. cured, 26 per cent. improved, and eighteen failures in 66 cases). A third operation was rarely of benefit. J. B. Stanton.


The condition first described by Forestier and Rotes-Querol (Ann. rheum. Dis., 1950, 9, 321; Abstr. Wild Med., 1951, 9, 641) as senile ankylosing hyperostosis of the spine, but which the present author prefers to call hyperostotic discosomatic vertebral arthrosis, has received little attention in the literature of rheumatism. In the opinion of the author many cases escape diagnosis even after radiological examination, so that errors occur both in diagnosis and in treatment, while some cases have even found their way into the literature labelled ankylosing spondylitis.

Figures are quoted to show that the condition is commoner than is generally supposed. It occurs especially in older patients, and occupational and family history have little bearing on the diagnosis, which is often made by chance on the basis of a radiograph taken for some other purpose. The level and extent of spinal involvement vary widely. The characteristic bony lesion occurs most commonly in the thoracic region, particularly on the right side. Peripheral joints and bony surfaces far from joints may also be affected. Because the disease so often attacks the aged, kyphosis is not necessarily significant. Local or generalized pain or stiffness are the commonest symptoms. Although the bony lesion is usually thoracic, yet it is in the lumbar region that the patient usually feels the pain, which is often aggravated by movement or prolonged standing, is most obvious first thing in the morning, and tends to pass off as the day wears on. Rest in the horizontal position reduces and may abolish it. Unlike that of inflammatory spinal disease the pain of this condition does not occur at night, and it is never referred remotely. Physical examination may be no more informative than the history. Forced movement of the spine sometimes increases the pain, but tenderness on pressure over the spinous processes or near the transverse processes is rare. There is often some stiffness in peripheral joints such as the hip and shoulder. In a series of more than twenty cases [exact number not stated] seen at the Turin Rheumatological Centre the author was unable to confirm the occurrence of psychiatric disturbance, such as depression, described by other authors. Haematological changes, such as raised erythrocyte sedimentation rate (E.S.R.), and circulatory disorders, such as hypertension, were notably absent. Diagnosis may be possible only by radiography. The characteristic appearance is of new bone formation which appears to have "dripped" down the right half of the thoracic spine. Protrusion of the intervertebral disks may enforce a convex, bridge-like appearance on the new bone as it crosses the intervertebral spaces. Arthritis may affect the various intervertebral joints and there may be osteophyte formation. The normality of the sacro-iliac joints is important in the differential diagnosis from ankylosing spondylitis, which also occurs at an earlier age and may be associated with systemic symptoms and a raised E.S.R.

The symptoms are frequently mild or absent and the outlook good. The organic changes show no regression, yet the symptoms are intermittent and intervals of freedom may last for months or even years. Rest is important in the relief of pain, as also are antirheumatic and analgesic drugs. The author gives first place in treatment to phenylbutazone, provided there are no contra-indications. Aspirin may also help, but steroids are useless. Any physiotherapy must be determined by the needs of the individual case.

The author sets out the various views as to the origin and nature of the disease: that it is a link between ankylosing spondylitis and rheumatoid arthritis; that it is due to metaplastic ossification of the anterior longitudinal ligament; that it is a normal component of the ageing process; and that it is a separate disease. He himself belongs to a school that sees it as a form of spinal
arthritis. He finds it difficult to account for the anatomical localization and examines various theories.

A. C. F. Green.


Cervical Whiplash Injury. HACKETT, G. S. (1959). Rheumatism, 15, 64. 3 figs, 7 refs.

Gout


The authors report, from the Hôtel Lariboisière, Paris, a study of the clinical manifestations, antecedent history, and sites affected in one hundred cases of gout in which the disorder was characterized by typical painful crises responding to colchicine. At the time of study the disease had been present in all cases for at least 10 years. Of the hundred patients, of whom only four were female, 37 gave a family history compatible with gout, while seventy described a prodromal symptom, in nine cases associated with calculus in the renal tract. The first attack usually involved the metatarsophalangeal joint of the big toe, and this joint was involved throughout the course of the disease in 96 per cent. of the cases. The joints next involved, in descending order of frequency, were the knee, ankle, other foot joints, elbow, and wrist. Polyarthritis occurred in six cases, while 59 patients had tophi and 22 had renal colic at some time in the course of their history. Of 75 patients investigated, eight had proteinuria, ten azotaemia, and nine a urea clearance of less than 50 per cent. Renal manifestations were commoner in cases of gout with tophi than in those without tophi. In 96 of the hundred cases the blood uric acid level exceeded 6 mg. per 100 ml. at some stage [method of determination not stated]. Out of eighty cases examined radiologically, osteo-cartilaginous lesions were observed in the feet in 66 and in the hands in 41. In discussing treatment the authors state that they favour the use of colchicine or phenylbutazone as therapeutic agents.

G. Loewi.


The author describes 32 cases in which pain was localized over a costo-chondral junction, the commonest site affected being the 3rd left junction. There were no superficial signs of inflammation, but in all except one case there was pain on local pressure. The author regards this as a manifestation of gout, since in eighteen cases the maximum blood uric acid levels ranged from 5-5 to 11-1 mg. per 100 ml. [a finding impossible to evaluate, since the method of determination and the normal range are not given]; it is further stated that some other manifestation of gout was present at some stage [but no details are offered]. Improvement followed treatment with colchicine, or local injection of procaine or hydrocortisone. The importance of differentiating this gouty condition involving a costo-vertebral articulation from the anginal pain associated with coronary arterial disease is stressed.

G. Loewi.


In nine patients undergoing long-term chlorothiazide therapy for various cardiovascular diseases at the Veterans Administration Hospital, West Roxburg, Massachusetts, the serum uric acid level and uric acid excretion were determined during treatment and 7 to 10 days after chlorothiazide was discontinued. The serum uric acid level was high in seven of the nine patients during treatment (average 7-8 mg. per 100 ml.; range 3-9 to 10-4 mg. per 100 ml.) and fell in every case at the second estimation 7 to 10 days after discontinuing the drug (average 6-0 mg. per 100 ml.; range 3-7 to 7-8 mg. per 100 ml.). Chlorothiazide administration was resumed, and 6 weeks later the serum uric acid level was again rising. The urinary excretion of uric acid behaved in the opposite manner. Since there was no rise in blood urea nitrogen level the glomerular filtration was not significantly reduced, and it is suggested that chlorothiazide (in these relatively low doses) blocked the tubular excretion of uric acid.

None of the patients had a gouty diathesis or symptoms attributable to the hyperuricaemia.

T. B. Begg.


Between 1951 and 1958 at the Lahey Clinic, Boston, probenecid was given in the treatment of 231 patients suffering from gout. The dosage of the drug was 0·5 to 1 g. daily, and with each 0·5 g. probenecid 0·5 mg.
colchicine were also administered. The dosages were adjusted so that the serum uric acid level did not exceed 6 mg. per 100 ml. In one patient given 0·25 g. of probenecid daily for more than 3 years the serum uric acid level was maintained at approximately 4 mg. per 100 ml. Two months after treatment was discontinued the level rose sharply to 7·5 mg. per 100 ml. Comparatively high serum levels of uric acid were detected in patients with renal disease.

Patients were advised to abstain from alcohol and to restrict the amount of purines and fat in the diet. In order to avoid precipitating an acute attack of gout no attempt was made to bring about a reduction in weight until the disease was under good control. In the first year the average number of acute attacks declined from 3·6 to 1·3 and in the second year to less than one. Probenecid with colchicine appeared to be more effective than probenecid alone. Untoward reactions to probenecid, which were recorded in 21 cases, included gastro-intestinal disturbances, rashes, headache, pruritus, and polyuria. In two of three cases in which urinary calculi were passed the calculi gave a positive reaction for urates. One patient experienced transient mental confusion. Radiological examination of the bones revealed arrest of the disease in eight cases, including four in which recalcification was observed in punched-out areas. Diminution in the size of the tophi was demonstrated in eighteen of 47 patients who received probenecid for at least 6 months. In three cases the disease failed to respond to treatment.

During the course of the investigation the authors studied the history and development of the disease. The age at onset was usually 35 to 39 years and the average weight of the patients was 37·3 lb. (17 kg.) higher than normal. It is concluded that tophaceous and non-tophaceous gout are clinical variants, and that the presence of renal disease is not essential for the development of tophi.


Since Garrod first demonstrated (Trans. med.-chir. Soc. Edinb., 1848, 31, 83) the great increase in the blood oxalic acid level in gouty patients, this finding has tended to dominate the picture. However, the present author, writing from Vittel, points out that the metabolism of oxalic acid may also be disturbed in gouty subjects. In such patients Looper and Guillain have reported an alteration in the ratio between the blood oxalic acid level and the urinary oxalic acid level to between 2:1 and 3·5:1, instead of the normal ratio of 1:2. In a study of 493 patients with hyperuricaemia the present author found hyperoxalaemia to be present in 395 cases (80 per cent.), a blood oxalic acid level of 0·5 mg. per 100 ml. being taken as the upper limit of normal. Of the 260 patients with obvious clinical gout, 86·5 per cent. had hyperoxalaemia, while in the 233 with hyperuricaemia (but no gout) the incidence was 73 per cent. This finding is considered to be of clinical importance, since a study of lithium in eighteen hyperuricaemic subjects (with normal blood levels of oxalic acid) revealed that 67 per cent. of the calculi contained oxalic acid and only 39 per cent. contained uric acid.

Two substances appear to be common to uricaemia and oxalaemia, namely, the aminoacetic acid glycocoll (glycine) and purines. The ingestion of the former has been shown to lead to increased excretion of oxalic acid in subjects prone to oxaluria (but not in normal subjects). Purines also have recently been shown to be associated with increased oxaluria. The author considers that in those cases in which hyperoxalaemia is found to be associated with hyperuricaemia the attacks of gout tend to be aggravated. This, he suggests, may explain the presence of an almost normal blood uric acid level in some gouty subjects in whom the blood oxalic acid level, were it estimated, might be found to be considerably raised.

D. Preiskel.


Salicylate administered to man in doses of 5 to 6 g. daily increases the urinary excretion of urate, whereas in doses of 1 to 2 g. daily it has the opposite effect. This phenomenon was investigated at the Mount Sinai Hospital (Columbia University College of Physicians and Surgeons), New York, in 23 male gouty subjects. Daily doses of 1, 2, 3, and 5·2 g. acetylsalicylic acid produced changes in the 24-hr urinary excretion of urate of −21, −14, +16, and +37 per cent. respectively. When 5·2 g. sodium bicarbonate was given daily in addition to 5·2 g. aspirin urate excretion was increased by 86 per cent.

Further studies showed that the paradoxical effect was determined at renal tubular level and depended on the concentration of free salicylate in the tubular urine. The conventional view is that urinary urate represents a small fraction of filtered urate that has escaped absorption by the tubules. The authors suggest, however, that the tubules absorb virtually all the urate from the glomerular filtrate and that the urate present in the urine is the product of tubular secretion. It is further postulated that a low concentration of salicylate in the tubular urine depresses the tubular secretion of urate, thus causing a reduction in its excretion. Intermediate concentrations of salicylate in the tubules depress tubular secretion and also, to some extent, tubular absorption of urate, so that the excretion of urate in the glomerular filtrate remains unaltered, while high tubular concentration of salicylate (produced by high dosage of salicylate or smaller doses plus an alkalizing agent) depress tubular absorption to such an extent that there is an increase in urate excretion over the normal value. The authors suggest that the uricosuric effect of probenecid, which is produced by inhibition of tubular absorption of urate, is counteracted by small doses of salicylate in part because of the suppression of tubular secretion of urate.

G. S. Crockett.

In this article from the University of Birmingham, the author discusses gout as a constitutional disorder. Whereas the diagnosis may be clear from the presence of tophi, and may be easy, even in their absence, from family and personal history, in some cases the signs and symptoms may lead to confusion with rheumatism. This is especially true when multiple joints are affected and no tophi are found. In such cases radiography, which frequently provides only confirmatory evidence of the diagnosis, may be of particular value.

Characteristically, radiographic changes occur in the extremities where tophi may cause bone dissolution on the joint surface, on the periphery or within the substance of a bone distal to a joint. These do not provoke reactive changes in the surrounding bone and occasionally calcification within these lesions occurs. Destruction may be so great that amputation becomes necessary.

In more proximal joints localized areas of bone destruction may similarly develop and one of these may be the site of presenting symptoms. The author illustrates this by quoting at length the case history of a man of 33 who suffered from sudden and multiple joint pain followed by swelling of the right knee. A false diagnosis of rheumatic fever was not corrected for nearly 2 years when the true diagnosis of gout was prompted by a similar attack affecting the feet. Observation over the subsequent 26 years showed the appearance of numerous destructive lesions, not only in the extremities but also in the knees, ankles, shoulders and elbows. Smaller cyst-like lesions were also noted in a greater trochanter.

[The author regards his report as being supplementary to previous writings on the subject.] R. O. Murray.


Pararheumatic (Collagen) Diseases


The trial herein reported of antimalarial drugs in the treatment of Sjögren’s syndrome was considered worth-while because there is evidence that this syndrome is a form of systemic lupus erythematosus, a disease in which antimalarial drugs have a beneficial effect. A total of 25 patients with Sjögren’s syndrome were treated at first with chloroquine and later with the reputedly less toxic hydroxychloroquine (“plaquenil”). All the patients had received treatment previously, some for many years, by orthodox methods, but usually there was only slight benefit. The dose of plaquenil was 800 mg. daily for 8 to 12 weeks; if there was improvement the dosage was then reduced to 400 mg. daily. The ocular irritation responded first and then photophobia. Altogether five patients were “greatly improved”, twelve were improved, and eight failed to benefit.

The author states that the period for which it is necessary to continue treatment is not known. In four patients the drug was stopped and the eyes became worse within a month, while in one case the eyes remained in a satisfactory state for 3 months after cessation of treatment.

Of 22 patients in the series who had plaquenil, six experienced side-effects; these were of a minor nature and resolved rapidly on reducing the dose or withdrawing the drug.

Kenneth Stone.


(1) The roentgen findings in systemic lupus erythematosus depend on the stage of the disease during which the roentgenograms are taken.

(2) Changes visible in the chest roentgenograms may suggest the correct diagnosis. These changes are:

Initial Acute Stage: Bilateral, moderate, or massive pleural effusion; subpleural inflammation; perivascular inflammation; small areas of interstitial pneumonitis at the lung bases; small areas of segmental pneumonitis at the lung bases.

Resolving Stage: Minimal unilateral or bilateral pleural effusion: minimal to moderate pericardial effusion with straightening of the left border of the heart silhouette but without widening of the heart base; small linear areas of “plate-like” atelectasis at the lung bases; areas of segmental atelectasis at the lung bases.

Chronic Stage: Unless the nephrotic syndrome is present, the cardiac contour returns to normal or cor pulmonale develops. In some instances the outline of the pulmonary conus remains partly obscured by fibrosis which fills in the pericardial spaces around the conus. The pleural effusion may completely disappear. Fine pulmonary scars may be seen at the lung bases repeatedly associated with “tenting” of the pleura, or the lungs may appear clear. Multiple pulmonary infections occur.

Exacerbation: Pleural and pericardial effusions are limited by adhesions; fine linear densities are intermingled with small areas of interstitial pneumonia at the lung bases; basal areas of segmental pneumonitis occur; subpleural and perivascular inflammation is present.
(3) Delayed renal function may be evident on intravenous pyelography.

(4) The relationship between systemic lupus erythematosus and destructive joint changes typical of rheumatoid arthritis is unproved. In the cases of this series, there were no instances of demonstrable joint changes other than soft tissue oedema and those changes attributable to Raynaud's syndrome.—[Authors' summary.]


Up to 1949 the prognosis in systemic lupus erythematosus was very poor, but the introduction of the L.E.-cell test in 1948 and the almost simultaneous introduction of steroid treatment in 1949 made it difficult to compare later series, even directly, with earlier series not treated with steroids because of probable differences in diagnostic criteria. In the present study of 77 cases of systemic lupus erythematosus seen at the New England Center Hospital, Boston, the authors set out to re-examine the course and prognosis of this disease in terms of sex, age, pregnancy, steroid therapy, and certain specific manifestations of the disease process. The analysis included fourteen fatal cases first diagnosed before 1949 on clinical evidence alone or with additional post-mortem evidence; the remaining 63 cases were diagnosed between 1949 and 1958, L.E.-cell test being performed in twenty fatal cases and on 39 patients still living; the results were not available in four (fatal) cases. The L.E.-cell test was positive in thirteen of the twenty fatal cases and in eleven of the 39 still living patients; in no case, however, was the diagnosis based solely on a positive L.E.-cell test.

There were only eight males in the series, and of these six died compared with 32 out of 69 females. Patients under the age of 21 years at the time of diagnosis did worse (nine out of fifteen died) than those over 45 (five out of fifteen). In some cases, however, symptoms may have been present for some years before the diagnosis was made. As other workers have found, the presence or absence of renal disease was the most important prognostic feature. Steroid treatment seemed to have no effect on renal involvement, but did suppress the rash, fever, serositis, myocarditis, pneumonia, and haematological and neurological complications. Pregnancy had little effect once the disease was established. The authors suggest that steroid therapy may have prevented the appearance of renal disease, since only one out of 29 patients so treated later developed renal trouble, compared with three out of ten not given steroids. In the untreated series death was due to "toxic" or cardiac causes or to uremia; in the steroid-treated patients ten out of eighteen died of renal failure and uremia, while six out of eight died of complications perhaps related to steroid therapy, including infections and gastrointestinal haemorrhage.

[There is a great deal of useful information in this paper which will repay detailed study.]

E. G. L. Bywaters.


The authors discuss the clinical, pathological, and radiological findings in 109 patients with collagen diseases admitted to the University of Minnesota Hospitals, Minneapolis, between 1942 and 1956. The aetiology is briefly discussed, and the symptoms at onset, laboratory data, electrocardiographic changes, and response to steroid therapy are analysed in a number of tables. The series included forty cases of polyarteritis nodosa, 37 of disseminated lupus erythematosus, twenty of scleroderma, seven of dermatomyositis, and five of rheumatic pneumonitis. There was pathological confirmation of the diagnosis in over two-thirds of the cases.

The radiological findings are described in some detail. The authors consider that abnormalities occur in the chest during the course of the disease in over 80 per cent. of cases. Interstitial pneumonitis, pleural effusion, and cardiac enlargement were common to all five diseases. Bilateral hilar vascular prominence was most often seen in polyarteritis, while interstitial pulmonary fibrosis and emphysema occurred mainly in scleroderma and dermatomyositis; a honeycomb appearance of the mid- and lower-lung fields was present in 20 per cent. of cases of scleroderma. Cardiac lesions were more common in disseminated lupus erythematosus and rheumatic pneumonitis and small pulmonary nodules in polyarteritis and scleroderma. Abnormal radiological findings in other systems are also briefly discussed and twelve cases illustrating the value of the x-ray findings in the differential diagnosis are described in detail.

B. Goldberg.


The results in forty cases of active systemic lupus erythematosus treated with methylprednisolone ("medrol") over 16 months are reported from the University of Southern California, Los Angeles. In fifteen of these cases antimalarial treatment was given concurrently.

The pattern of response was similar to that obtained with prednisone, triamcinolone, and other anti-inflammatory steroids, while the incidence of moon face, hirsutism, acne, and the formation of striae was about the same. The average daily dose of methylprednisolone for initial suppression was 29-2 mg. (range 8 to 96 mg.) and for maintenance 25-9 mg. per day. There was a high incidence of ecchymosis, which occurred in 27 per cent. of the patients, as compared with 14 per cent. with triamcinolone and 3 per cent. with prednisone. A new peptic ulcer appeared in only one case, which is described. Of the eighteen patients who had received other steroids, only two had better control and felt better while taking methylprednisolone. Nevertheless, this preparation is considered a relatively safe and potent anti-inflammatory agent for the treatment of systemic lupus erythematosus.

Oswald Savage.
Pseudo-Tumour of the Orbit and Polyarteritis Nodosa.
The report of a case of pseudo-tumour of the orbit which ended fatally. The post mortem examination showed evidence of polyarteritis nodosa. The relationship of pseudo-tumour with Wegener's granulomatosis is considered and the aetiology of necrotizing arteritis is discussed.
A. G. Cross.


Intemdiary Metabolism of Phenylalanine and Tyrosine in Diffuse Collagen Diseases. II. Influences of the Low Phenylalanine and Tyrosine Diet upon Patients with Collagen Disease. NISHIMURA, N., OKAMOTO, H., YASUI, M., MAEDA, K., and OGURA, K. (1959). A.M.A. Arch. Der., 80, 466. 3 figs, 49 refs.


General Pathology

Investigations are reported from the Institutum Divi Thomae and St. Mary's Hospital, Cincinnati, in which the authors sought to find an absolute correlation between the amounts of two acute-phase reactants in the serum—C-reactive protein (determined by the capillary precipitin method) and protein-bound sialic acid (determined by the method by Böhme and others; Klin. Wschr., 1954, 32, 289). Sera were examined for both factors from 58 subjects, including fifteen normal blood donors. No definite correlation was found between the levels of the two factors, although there was some degree of relationship [both being increased as a normal reaction to inflammatory processes]. The maximum sialic acid value of serum negative for C-reactive protein was 210 mg. per deciliter, and only four of 34 sera positive for C-reactive protein showed sialic acid values less than 210 mg. per deciliter. The mean value for sialic acid in normal serum was 130±7 mg., in sera negative for C-reactive protein 143±7 mg., and in sera positive for C-reactive protein 259±12 mg. per deciliter. It is considered “likely that different pathological processes may account for the appearance of C-reactive protein and an increase in the serum sialic acid level”.

The greater part of the serum hexosamine-pyruvate compound known as neuraminic or sialic acid is bound to the α-seromucoid fraction of the protein or the Winzler fraction soluble in 1·8 M perchloric acid. The C-reactive protein is generally held to be in the γ-globulin fraction, although it has been reported to be an α globulin. The normal values for serum sialic acid given in this paper are double those quoted by the authors of the method utilized. Considering the wide variations found in different diseases in both the γ-globulin and α-seromucoid fractions, it would seem unlikely to expect any absolute correlation between these two estimations in pathological sera.

Harry Coke.


Destruction of connective tissue leads to the accumulation in the blood of mucoproteins, which can be detected in the serum by means of the diphencylamine reaction. The author, using the colorimetric modification of this reaction described by Ayala and others (J. clin. Invest.,
ABSTRACTS


By careful statistical analysis of triplicate estimations the author, in an investigation at University College Hospital, London, has shown that when used alone the anticoagulant sequestrene, like heparin or oxalate, is unreliable for determining the erythrocyte sedimentation rate (E.S.R.). However, blood which has been collected into oxalate, heparin, or sequestrene and subsequently [maximum interval not determined] diluted with one-fourth its volume of 3-8 per cent. sodium citrate is suitable for determining the E.S.R. by the Westergen method.

M. Sandler.


The retardation of the erythrocyte sedimentation rate (E.S.R.) in blood which has been stored is believed to be related to the anticoagulant used and the temperature at which the blood is stored. If, however, 1 mg. sequestrene is used as the anticoagulant, blood stored at 5° to 10° C. for 24 hours can still be used for estimation of the E.S.R. by Westergen's method, provided it is then mixed with a 3-8 per cent. solution of sodium citrate in the proportion of four parts of blood to one of citrate. At Glasgow Royal Infirmary the E.S.R. (Westergen) of 25 samples of fresh blood-citrate mixture was compared with that of a similar number of samples of fresh blood-sequestrene-citrate mixture. No significant difference was observed between the E.S.R. of the two mixtures, nor was there any appreciable difference, with the blood-sequestrene-citrate technique, between the E.S.R.'s of 25 samples of fresh blood and 25 samples which had been stored for 24 hours.

[This finding promises to extend widely the use of the E.S.R. in clinical practice.] M. Sandler.


Specimens of serum from 3,652 patients were tested with p-toluensulphonic acid. There were 23 false positive reactions and one false negative, the latter in a patient with classic findings of systemic lupus erythematosus at necropsy. None of the patients in the false positive group had any clinical or pathologic findings of systemic lupus erythematosus.

The factor responsible for precipitation in the false positive reactions was observed to be in the beta globulin fraction. [From authors' summary.]


The F.II agglutination and the F.II precipitation reaction of Epstein and others (Proc. Soc. exp. Biol. (N.Y.), 1956, 91, 235) are based on the interaction between y globulin (Cohn Fraction II) and the rheumatoid factor macroglobulin. This reaction may be enhanced by preheating the F.II globulin reactant to 63° C. for 10 minutes. This paper from Roswell Park Memorial Institute, Buffalo, New York, records the estimation of the induced turbidity of this reaction by means of a photonreflectometer. The results were correlated with those of the alligator erythrocyte agglutination and the standard Rose-Waaler haemagglutination reactions.

A total of 58 sera were examined. All of fifteen cases of rheumatoid arthritis, in which the haemagglutination reactions were positive, showed increased precipitation activity (turbidity), whereas negative results were obtained in both tests with sera from 26 normal donors and from fifteen patients with various other rheumatic and allied diseases, which gave either or both of dermatomyositis (1) and lupus erythematosus (3), and from two with multiple myeloma. Sera from two cases of macroglobulinaemia gave negative turbidity reactions with positive haemagglutination reactions. Apart from these cases, representing 3-4 per cent., no false positive results were obtained.

Harry Coke.


The replacement of sheep erythrocytes in agglutination reactions based on the techniques of Rose and Waaler by polystyrene particles in the technique outlined by Singer and Plotz eliminated the need to heat the serum to destroy complement. In this paper from Harvard Medical School and the Massachusetts General Hospital, Boston, it is demonstrated that this preliminary heating to 56° C. for 30 minutes also destroys the action of a thermodabile inhibitor of the agglutination phenomenon. Thus, when a native unheated serum is used in the standard technique of Singer and Plotz (F.II L.P. test) a prozone will occur in the lower dilutions of the series, where agglutination is inhibited. In 25 of 177 "definite" cases of rheumatoid arthritis total inhibition was observed with native serum, whereas after preliminary heat inactivation titres as high as 1 : 5,120 were determined. The thermodabile inhibitor may be demonstrated in any serum that has agglutinating activity in the F.II L.P. test. Of the 177 sera from patients with "definite" rheumatoid arthritis, 118 (66-6 per cent.) gave positive results (1 : 160 or higher) after preliminary heat inactivation, whereas only 93 (52-5 per cent.) of the unheated aliquots gave positive results, 38 of the 93 showing the
prozone phenomenon. Tests were performed with heated and unheated serum from 418 patients from an arthritis clinic (including the 177 mentioned above), twenty patients with leprosy, and 360 patients (including normal subjects) from a general medical clinic and gave similar results. This thermolabile inhibitory factor has some of the characteristics of serum complement.

[It is to be remembered in considering this phenomenon that whether or not the serum is heat-inactivated before testing, the technique of the test involves heating the mixed reactants to 56° C. for 2 hours.] Harry C. C. Freisinger.


In this paper from the Medical Clinic of the University of Naples the authors first review the evolution of the various tests for the detection of the rheumatoid factor in human serum. They then report their own experience with the "R.A." test, a modification of the latex fixation test of Singer and Plotz, in thirty cases of rheumatoid arthritis three ofankylosing spondylitis, forty of painful osteo-arthritis, and 188 of non-rheumatic disease, including 133 cases of diabetes, and five of Addison's disease. The result of the test was positive in 96.7 per cent. of cases of rheumatoid arthritis, whereas in acute rheumatism it was positive in 2 per cent. of cases only. On the other hand positive results were obtained in 25 per cent. of the cases of painful osteo-arthritis, in 27.7 per cent. of the cases of diabetes, and in four of the five cases of Addison's disease. The authors conclude that the R.A. test is useful in the diagnosis of rheumatoid arthritis, though the possibility of false positive reactions has to be borne in mind, especially in cases of painful osteo-arthritis, in which the problem of differential diagnosis often arises. The R.A. test is slightly more sensitive and is easier to carry out than the Rose-Waaler test.

E. Forrai.


A reduction in the albumin fraction of the serum protein and an increase in the α- and γ-globulin fractions occur in cases of acute rheumatism. The increase in the γ globulins is most closely related to the activity of the rheumatic process, though in general the changes in the blood protein fractions seem to go parallel with the clinical symptoms. According to the author these changes depend not only on the activity of the rheumatic process, but also on the degree of circulatory disorder.

F. S. Freisinger.


A new method of estimating the polysaccharide content of the serum by digestion with pancreatic and extraction with toluene was used in the investigation of 54 patients suffering from acute rheumatism and sub-acute bacterial endocarditis. In both conditions a significant increase in the serum polysaccharide level was found which, it is claimed, provides an index of the activity of the rheumatic process and of the efficacy of treatment in cases such as these.

F. S. Freisinger.


The fibrin content of the plasma of 144 rheumatic subjects, including 78 suffering from an acute attack, was estimated by the method of Wohlisch (*Ergebn. Physiol.*, 1940, 43, 174). Healthy subjects and patients suffering from uncomplicated chronic tonsillitis served as controls. Most of the patients with acute rheumatism had an increased plasma fibrin level, the average value being 16.2 mg. per ml. compared with 6 to 11 mg. per ml. in the control group. It is claimed that this investigation is of diagnostic value.

F. S. Freisinger.


The authors used three serum tests:

1. Antistreptolysin reaction—an antigen-antibody reaction with streptolysin of *Streptococcus haemolyticus*.
2. Waaler-Rose test—agglutination of sensitized erythrocytes.
3. The latex test—a modification of the above, using a colloid suspension of latex rubber particles instead of erythrocytes.

82 clinically suspicious cases of rheumatic aetiology were studied. Only a small fraction of the results was positive. The slightness of the ocular lesions and the low virulence may explain those findings.

J. L. Reis.


**Characterization of Mucoprotein Level in the Serum of Patients with Rheumatoid Arthritis.** GIROUD, C. J. P. (1959). *Endocrinology*, 64, 730. 3 figs, 29 refs.

**ACTH, Cortisone, and Other Steroids**


tisol in the medium from glomerular tissue were attributable to contamination of the tissue slices with cells from the fascicular tissue.) Corticosterone was present in the medium from both types of tissue. Other unidentified steroids were present—one of these was probably 11-dehydrocorticosterone and was present in both media. The addition of progesterone, corticosterone, or deoxycorticosterone to the medium increased the production of aldosterone by glomerular tissue to an equal extent and in proportion to the amount of precursor added. Cortisol production by fascicular tissue was increased by the addition of progesterone or deoxycorticosterone, but not by the addition of corticosterone. Corticosterone production by both types of tissue was increased by the addition of progesterone or deoxycorticosterone. In the presence of 17-hydroxyprogesterone or 17-hydroxy-11-deoxycorticosterone cortisol production occurred in glomerular tissue and was increased in fascicular tissue; this shows that 17-hydroxy precursors can be 21- and 11-hydroxylated by glomerular tissue. On the basis of these findings the authors suggest that though there may be common precursors for different types of cortical steroid, the enzymic mechanisms may differ in the different zones. Thus 17-hydroxylase activity may be confined to the fascicular and reticular zones and 18-oxygenation activity to the glomerular zone. Other enzymic activities (such as 3β-dehydrogenase and 11- and 21-hydroxylation activities) appear to be common to all zones.

The addition of corticotrophin to the medium increased cortisol production by fascicular tissue, but did not affect aldosterone production by the glomerular tissue. Equivocal results were obtained in respect of corticosterone production, which was possibly increased in both types of tissue. However, in these experiments incubation was continued for 4 hours and there was evidence that corticosterone was disappearing from the medium in the later stages of this period. Similar results were obtained with various corticotrophin peptide preparations. Thus, while no evidence was obtained that corticotrophin influences aldosterone production in any way, it is still possible that it affects corticosterone production in all zones of the cortex.

Aldosterone production by glomerular tissue was increased in the presence of 21-hydroxyprogrenenolone or progesterone, but not in the presence of cholesterol; none of these effects was altered by the additional presence of corticotrophin. Cortisol production by the fascicular tissue was slightly enhanced in the presence of cholesterol, and very much enhanced in the presence of cholesterol plus corticotrophin; it was also greatly enhanced by the addition of progesterone, and this increase was uninfluenced by the further addition of corticotrophin.

Peter C. Williams.


In twenty confirmed cases of Cushing's syndrome occurring in sixteen female and four male patients studied at Georgetown University Hospital, Washington, D.C., the simple haematological tests carried out were evaluated by two standards:

1) By strict criteria, in which the test results were considered significantly abnormal if the proportion of neutrophil granulocytes exceeded 80 per cent., the total eosinophil granulocyte count was below 40 per c.mm., and the haematocrit value exceeded the normal by at least 5 per cent.; by this standard ten patients showed a significant rise in the number of neutrophils, ten had eosinopenia, and five polycythaemia, fifteen of the twenty patients having one or more of these abnormalities.

2) By the less strict standard—that is, proportion of neutrophils 70 per cent. or more, eosinophils 80 per c.mm. or less and haematocrit value 3 per cent. above normal—the number of positive test results increased, sixteen patients now showing elevation of neutrophils, seventeen eosinopenia, and twelve (all female) polycythaemia; all the patients showed at least one of these abnormalities and nineteen of them two or more.

Osteoporosis was present in twelve patients and a similar number had significant hypertension (blood pressure above 160/110 mm. Hg), while overt diabetes or carbohydrate intolerance was found in fourteen patients, all the patients showing one or more of these abnormalities. These findings are compared with those reported in the literature and with the effects of administering corticotrophin and corticosteroids. The authors conclude that careful evaluation of the results of these simple tests is a help in the diagnosis of Cushing's syndrome.

J. Warwick Buckler.


As Cushing's syndrome is a potentially fatal condition, and since recent advances in the management of the disease have considerably improved the prognosis, its early recognition is of great importance. The present authors have therefore re-examined the early symptoms and problems of diagnosis in a series of 34 cases seen at the Lahey Clinic, Boston. There were 27 female patients and seven males. In 27 cases the diagnosis was confirmed surgically and in seven it was based on characteristic clinical signs and laboratory findings. The clinical onset was rapid in 24 cases, five being of such clear-cut, remittent character that the onset might be termed "episodic"; in the remaining ten cases it was gradual. There were no aetiological differences between these two groups, both containing examples of adrenocortical hyperplasia, adrenocortical adenoma, and aberrant adrenal tissue in the pancreas. In those with a rapid onset the common initial symptoms were oedema of the face and legs, rapid gain of weight, amenorrhea (which might or might not be associated with either of the preceding features), renal colic, physical weakness, and
mental disturbances. The differential diagnoses that had been considered in these cases were hypothyroidism (7), hyperthyroidism (3), nephritis or nephrosis, cardiac oedema, allergy, simple obesity, idiopathic renal calculi, collagen disease, and psychosis. Facial oedema was present in fourteen cases and, it is suggested, is probably attributable to a combination of factors including the tendency to hypoproteinaemia, hypernatraemia, and vascular fragility. In the cases of gradual onset a more gradual weight gain, oligomenorrhea and hirsutism, diabetes mellitus, hypertension, mental disturbances, and osteoporosis were common presenting features which made the differential diagnosis from the other causes of such manifestations difficult. Among the helpful pointers to the diagnosis in such cases are the combined appearance of signs, high haemoglobin level, leucocytosis with relative lymphopenia and eosinopenia, severe fatigue and weakness, nervous complaints, and development of “moon face”.

The authors differentiate those features which should be regarded as signs—for example, hypertension (88 per cent.) and osteoporosis (53 per cent.)—from those which are complications, such as pathological fractures (32 per cent.), and renal calculi (30 per cent.). They discuss the cardiovascular complications which may result from the hypertension and the susceptibility of patients with Cushing’s syndrome to infection. Three of their patients developed duodenal ulceration, and three others peripheral neuritis of the Guillain-Barré type. They suggest that the latter may be a direct result of the disease process.

B.M. Ansell.


This paper from the Westminster Hospital, London, records a clinical comparison of the new steroid dexamethasone with its predecessors. In dexamethasone the hydroxy group of the triamcinolone molecule has been replaced by a methyl group, which appears to have much enhanced its glucocorticoid effect. Dexamethasone was compared with the steroid previously administered (prednisolone in all cases, but two) in thirty cases of rheumatoid arthritis, 1 mg. dexamethasone replacing 5 mg. prednisolone. The new steroid was given for periods varying from 1 to 24 weeks. The 1 : 5 ratio is probably slightly in favour of dexamethasone, the true ratio being perhaps 1 : 6 or 1 : 7. Dexamethasone was considered superior if improvement occurred on changing to it and deterioration on returning to the previous compound. Improvement was judged by the patient’s own assessment, strength of grip, and finger swelling as measured by jeweller’s rings.

Little difference was apparent: of the thirty patients twelve preferred dexamethasone, twelve prednisolone, and six were indifferent. Dyspeptic symptoms were no less common with dexamethasone than with prednisolone. There would seem to be no obvious advantage in changing to dexamethasone in the treatment of rheumatoid arthritis, though some patients seemed to prefer it. The fact that much the same clinical effect was obtained with a smaller dose is, the authors point out, of little practical importance unless the cost is reduced in the same ratio. One patient with ankylosing spondylitis who had received prednisolone for 16 months improved and became symptom-free when a change to dexamethasone was made. However, in three cases of systemic lupus erythematosus, two of scleroderma, one of ulcerative colitis, and one of status asthmaticus, little or no difference was noted.

Kenneth Stone.


From the Massachusetts General Hospital and Harvard Medical School, Boston, a histological study is reported of the adrenal cortex in eighteen female and two male patients aged 16 to 42 years with Cushing’s syndrome, biopsy specimens of the adrenal glands from fourteen patients without evidence of endocrine disease serving as controls. The tissue was placed in 10 per cent. buffered formalin and paraffin sections were stained with haematoxylin and eosin, while frozen sections were treated by several methods—for example, they were stained with Sudan IV or subjected to the Schultze, Windaus, Schiff, and naphthoic acid hydrazide tests. In four of the patients the glands were normal on gross examination, in twelve the cortex was hyperplastic, and in the remaining four the cortex was adenomatous. In the hyperplastic specimens there was a marked increase in width of the zona fasciculata, but no increase initially in the weight of the gland. Additional signs of overactivity were a depletion of sudanophilic material and cellular atypism.

A. Wynn Williams.


Writing from the University of Utah School of Medicine, Salt Lake City, the authors point out the several differential patterns of symptoms which may result from the too sudden withdrawal of steroid therapy as seen in young patients at their Pediatric Department, four cases illustrating these different patterns being described in detail. The first was in a girl aged 4 with juvenile rheumatoid arthritis who had been treated initially with cortisone and antibiotics with good results. When fever and joint pain recurred after the withdrawal of cortisone she was given ACTH and cortisone with fair response. When these were discontinued, however, the patient showed a fluctuating temperature, with joint involvement and adenopathy, and the dose of cortisone had to be pushed to 100 mg. daily if the recurrence of the fever was to be prevented. Her symptoms responded to 25 units of ACTH injected four times daily.

The second case was one of bullous exfoliative dermatitis (Stevens-Johnson syndrome) in a 3-year-old boy. The condition responded to intravenous injections of
300 mg. cortisone and 400 mg. tetracycline daily at first. When this was reduced on the 4th day the symptoms recurred and prednisolone, 12 mg. orally, was substituted. The patient collapsed and died within 24 hours of the change. The interesting finding post mortem was a massive haemorrhagic lesion in the left adrenal gland.

The third case, illustrating the symptoms of pseudo-rheumatism and Addisonian-like crisis, occurred in a boy aged 6 with juvenile rheumatoid arthritis who had been receiving corticosteroid therapy for 4 years with only occasional flare-ups. Before admission he had vomited and steroid therapy was withdrawn. In hospital he was restless and irritable, and any movement caused pain. The blood sodium and potassium levels were dangerously low and the electrocardiogram was typical of electrolyte deficiency. He recovered after the intravenous administration of cortisone and electrolytes.

The last case was one of juvenile rheumatoid arthritis in a child aged 3 in whom an intravenous dose of 1 mg. hydrocortisone per lb. (2-2 mg. per kg.) body weight was followed after 12 hours by acute symptoms, which were relieved by oral prednisolone.

In a special test twenty healthy adult volunteers were given hydrocortisone intravenously or prednisolone orally or intravenously and the blood steroid levels determined. In completing a questionnaire many of these subjects recorded "rheumatic" symptoms 4 to 72 hours afterwards. These were shown to occur when the plasma steroid levels were decreasing and were not dependent on the absolute steroid level. Discussing the origin of lesions in acute cases the authors compare the haemorrhagic necrosis of the adrenal gland to that of the uterine mucosa during menstruation, and suggest that both represent endocrine withdrawal phenomena of the same nature. In the treatment of withdrawal symptoms they consider that the dosage of steroids should be increased and not diminished in such cases.

William Hughes.


Other General Subjects


The diagnostic value in leukaemia in childhood of lesions of the long bones was studied in 140 cases seen at Johns Hopkins Hospital, Baltimore. Radiologically, bone changes were present in 89 (64 per cent.) of the patients, 74 of whom, predominantly males and white children, were between 2 and 10 years of age. Extensive destructive lesions were observed, which on the whole presented a characteristic pattern, with areas of rapid bone growth being peculiarly liable to involvement. Metaphysial bands of translucency were the most common finding (76 cases) and were usually seen at the knees and wrists. Of 740 consecutive radiographs of the long bones obtained over a period of one year 32 revealed this transverse translucent line of the metaphyses; none of the 32 patients had leukaemia and only four were over 2 years of age. The author therefore considers that this finding is non-specific below that age. In leukaemia, unlike scurvy, the lateral cortical margins and the metaphyseal plates are usually intact. In 53 cases osteolytic lesions were found in the spongiosa of the long bones, varying from punctate areas of increased translucency to zones of frank destruction. In some cases extensive areas of metaphysial decalcification may suggest that the metaphyseal band has expanded to include the spongiosa. In three cases infarctions of such areas were noted. Pathologically, these destructive lesions are attributed to interference with nutrition and pressure by the proliferating leukaemic tissue, with increased osteolysis. Periosteal elevation along the shafts of the long bones due to leukaemic infiltration between the cortex and the periosteum, was evident in 27 cases. Radiographs of the long bones in cases resembling leukaemia clinically, including 25 of rheumatoid arthritis and twenty of anaemia, did not show the transverse translucent line at the metaphysis, the osteolytic lesions, or the periosteal elevation seen in leukaemia. In metastatic neuroblastoma the radiological picture may be comparable, but without the transverse metaphysial band of translucency and with a greater tendency to central, rather than peripheral, bone involvement. The author concludes that radiographs of the long bones may be of value when leukaemia is suspected, especially in patients over the age of 2 years.

R. O. Murray.