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


Since the original description of dislocation of joints as a sequel of rheumatic fever by Lereboullet and Mouzon (Bull. Soc. méd. Hôp. Paris, 1920, 44, 86), the number of published cases has reached seventeen, to which the present authors contributed three (Rev. Lyon. Méd., 1956, 5, 18 and 849). They now report six further cases occurring in patients aged between 14 and 39 (mean 25) years, in whom the dislocations appeared 4 to 25 years after the first attack of rheumatic fever, during which time the patients had suffered a number of relapses. In twenty of the 23 published cases, cardiac lesions were also present. The authors state that the dislocations take up to 3 months to develop, are easily reducible, show no tendency to progress, and cause little inconvenience; they appear to be due to excessive laxity of the joint capsules and ligaments. The joint most commonly affected are the metacarpo- and metatarso-phalangeal; ulnar deviation of the hands and hallux valgus with hammer-toe of the adjoining toe are also often seen. Prophylactic treatment at an early stage by suitable splinting is advocated. D. Preiskel.


The authors of this paper, from the National Children's Cardiac Hospital, Miami, and the University of Miami, report the results obtained by swabbing the throats of 333 school children at monthly intervals during the 8-month period October, 1954, to May, 1955. A total of 533 isolations of Group-A β-haemolytic streptococci (Gp-A H.S.) were made. The isolations were grouped according to the number of colonies on the plate and analysed according to whether the child was at school at the time or absent from school for medical reasons. Similar analyses were made for the isolations of streptococci of various other groups. Gp-A H.S. were found in 38 (58.5 per cent.) of 65 children absent with upper respiratory infections as against 72 (37.1 per cent.) of 194 children not absent at the time of swabbing. When an "epidemic" of Gp-A H.S. (Type 6) occurred, there was no increase in the number of absences due to upper respiratory illness. No marked correlation could be established between absenteism and isolation of Gp-A H.S. The occurrence of a two-tube rise in serum antistreptolysin-O level, the number of colonies of Gp-A H.S. grown from the throat swabs, or the isolation of streptococci of other groups. The low rate of absence due to respiratory infection, combined with the finding that Gp-A H.S. isolations could be associated with an immunological reaction yet not cause absence from school, for medical reasons, suggested that the authors were dealing with relatively resistant hosts or relatively avirulent organisms. No cases of acute nephritis or rheumatic fever occurred among the children during the period of study.

Allan St. J. Dixon.


There is circumstantial evidence that improved diet particularly an increase in the number of eggs consumed lowers the incidence of attacks of rheumatic fever, and in animal experiments N-(2-hydroxyethyl)-palmitamide (HEP), a fraction of egg yolk, has been shown to have anti-allergenic properties in guinea-pigs. The study reported in this paper from New York Medical College was undertaken to determine if HEP could protect susceptible children against recurrent attacks of rheumatic fever and was carried out on 95 children from indigent New York families who had previously been in-patients for rheumatic fever, 152 siblings serving as controls. No antibacterial chemoprophylaxis was given to the patients. It had been previously estimated (from the known recurrence rate of rheumatic fever) that this number of subjects would be sufficient to detect a protective effect of HEP.

A placebo-controlled double-blind study was set up and arrangements made for periodic supervision, throat swabbing, and estimation of antistreptolysin-O titres.

In the event, no firm conclusions could be drawn from the study because the expected number of recurrences among the controls did not occur. The authors cite evidence for a considerable improvement in the diet of their subjects (including an increased consumption of eggs) during the period of observation, which may have interfered with the conditions of the study as originally planned. Despite the fact that nearly all subjects developed Group-A streptococcal infections at some time, only seven recurrences of rheumatic fever were seen, and only one (which occurred a few weeks after starting treatment) was in the HEP-treated group. Although the results of this investigation failed to reach significance at the 5 per cent. level, they are nevertheless regarded as promising.

Allan St. J. Dixon.


The study herein reported is based on the results of detailed clinical and serological studies in 31 children treated at the Second City Children's Hospital, Sofia, Bulgaria, for scarlet fever and followed up for more than 2 years. The serological factors studied included the response to the C-reactive protein test, the erythrocyte sedimentation rate, the plasma fibrinogen level, and the titres of antistreptolysin-O (ASO) and heterophil agglutinins. Evidence of autoimmunization was sought for in the response to the Coomb's test and the anti-human globulin consumption test of Steffen and in the Rose-Waaler reaction.

Although there was a remarkably high incidence of complications, such as recurrent sore throat and otitis media in 21 of the children, rheumatic fever did not develop in any of the patients. There was no instance of dysproteinaeinemia, of hyperfibrinogenaeinemia, or of an extremely high ASO titre, changes which the author accepts as characteristic of rheumatic fever. He therefore concluded that there "was no ground for considering that the post-scarlet fever period was immunobiologically identical with the acute phase of rheumatic fever".

L. E. Glynn.


The course of rheumatic fever in hospital in patients treated by bed rest alone and not given prophylaxis has been studied, and the degree of carditis related to other features of the attack. Prolonged raised temperature and sedimentation rate were more closely related to carditis than the sleeping pulse, but in severe attacks persistent tachycardia was a constant feature and carried a poor prognosis. Anaemia and loss of weight were uncommon and occurred only in the worst cases. Nodules were rare without heart disease, but were present in a quarter of those with slight carditis and in half of those with severe carditis.

The course in hospital in some patients treated by bed rest has been compared with that in others who were given 6-week courses of ACTH, cortisone, or aspirin, together with prophylactic sulphadiazine. The two groups were comparable in most respects, although (a) they were not run concurrently; (b) only the drug-treated series was given prophylaxis; and (c) the latter had less heart disease at the start. Arthritis, temperature, and sedimentation rate subsided more slowly in the bed-rest series, but temperature was similar in the two by the fourth week, arthritis by the sixth week, and sedimentation rate by the eighth week; the rapid subsidence of activity in some of the bed-rest cases was striking. There was little difference in changes in cardiac status in the two groups, except in the development or disappearance of soft (Grade I-2) murmurs, and this may have no important effect on the residual heart state 5 years later.

A third group of 47 cases was treated with 12-week courses of either cortisone or salicylate and did no better than those who had salicylate, cortisone, or ACTH for only 6 weeks.

Conclusions are drawn on the role of bed rest, salicylate, and steroids in the management of the disease. In many cases bed rest with salicylates to control fever and joint pain suffices, but in a few with severe attacks and cardiac enlargement delta-steroids are indicated and salicylates are potentially dangerous since they predispose to pulmonary complications.—[Authors' summary.]


In this investigation reported from the University of Miami School of Medicine, Florida, the recovery rate of β-haemolytic streptococci from throat cultures and the serological responses to these organisms were studied in three different age groups of apparently healthy subjects —800 elementary school children aged 6 to 9 years, 801 junior high school children aged 12 to 15 years, and 1,815 adults. Throat swabs were taken from all subjects and samples of blood from the adults. Streptococcal isolation rates were found to vary inversely with age. Group-A β-haemolytic streptococci were isolated from 14-4 per cent. of the children aged 6 to 9 years, from 7-9 per cent. of those aged 12 to 15, and from 2-2 per cent. of the adults. The pattern was similar for isolation of other β-haemolytic streptococci. There was no significant seasonal fluctuation. Group-C and Group-G β-haemolytic streptococci were found to be far commoner in the throats of children than in those of adults.

The average serum antistreptolysin-O (ASO) titre in the adults was between 71 and 74, but in those whose throat swabs were positive the average titre was 115 to 146. In an earlier study of other groups of children in Miami, the average ASO titre was found to be approximately 100. The lower average ASO titre in adults was considered to be due to a higher streptococcal carrier...
rate in the children. These results generally parallel the higher incidence of acute rheumatic fever in children.

John Lober.

Duration of Activity in Acute Rheumatic Fever. Feinstei

The duration of rheumatic activity was studied in 265 children and adolescents (aged 4 to 17 years) admitted to Irvington House, Irvington-on-Hudson, New York, with recent rheumatic fever. Rheumatic activity was considered to have ended when the temperature and sleeping pulse rate were normal, the erythrocyte sedimentation rate (uncorrected Wintrobe value) was 20 mm. per hour or less, and the response to the serum C-reactive protein test was negative. Abnormalities in temperature and pulse rate were regarded as significant only if they had been present for 3 consecutive days. Other clinical signs of rheumatic activity did not occur unless there were changes in temperature and pulse rate or in the results of laboratory investigations. Abnormalities in pulse rate or temperature usually subsided before the results of laboratory tests became normal. Therefore, cessation of rheumatic activity usually depended on the time when both the E.S.R. and the result of the C-reactive protein test became normal and remained normal after steroid and/or salicylate therapy was stopped.

The mean duration of activity in the entire group was 109 days; it was longer in patients with valvar involvement than in those without. In 31 patients originally treated with suppressive drugs, clinical rebounds occurred which were not treated; the mean duration of activity in this group was 79 days in patients with no valvar involvement and 112 days in those with valvar involvement, figures which were almost identical with those for similar patients whose entire attack had been untreated. The authors state that this was an unexpected finding which "suggests that the total duration of rheumatic activity remains essentially the same in most patients—rebound or no rebound, treatment or no treatment—so long as the original course of therapy is not given for a period of time longer than the natural course of the original inflammation".

C. E. Quin.

Rebound Phenomenon in Acute Rheumatic Fever.


These papers record observations on the incidence, significance, treatment, and prevention of the rebound phenomenon in acute rheumatic fever as observed in children admitted to Irvington House, Irvington-on-Hudson, New York, from July, 1956, to August, 1958, at various stages of an attack of rheumatic fever. Originally 265 consecutive patients with unequivocal attacks of rheumatic fever were studied. A rebound was defined as the reappearance of clinical or laboratory features of rheumatic activity after they had originally subsided in the absence of any intercurrent Group A streptococcal infection. The rebounds were subdivided into four groups:

1. Slight "laboratory" rebound with the appearance of C-reactive protein (C.R.P.) and/or an erythrocyte sedimentation rate (E.S.R.) of 21 to 30 mm. in one hour;
2. Significant "laboratory" rebound with a marked rise in titre of C.R.P. and/or an E.S.R. over 30 mm. in one hour;
3. Slight clinical rebound with laboratory indications of a rebound together with fever;
4. Significant clinical rebound with laboratory indications and one or more of the following clinical criteria—rise in sleeping pulse rate for three consecutive days, joint symptoms or signs, appearance of diastolic murmur of pericardial friction, development of congestive heart failure, and appearance of nodules or erythema marginatum.

The incidence of rebounds was studied with reference to the treatment the patient had received and the severity of the original attack. Of those receiving no specific therapy (34), no rebound occurred in 22 and a laboratory rebound (slight in six, significant in six) in twelve, but none developed clinical rebounds. Of the 106 patients treated with salicylates, 52 had no rebound, 44 had a laboratory rebound (slight in 15, significant in 29), and ten had a clinical rebound (slight in one, significant in nine). Of the 77 children treated with steroids alone, 25 had no rebound, 26 had a laboratory rebound (slight in 14, significant in 12), and 26 had a clinical rebound (slight in three, significant in 23). Of the 48 patients who received both salicylates and steroids, 21 had no rebound, fourteen had a laboratory rebound (slight in eight, significant in six), and thirteen had a clinical rebound (slight in four, significant in nine).

No patient without clinical involvement of the heart in the original attack showed signs of heart disease in the rebound, but evidence of new heart disease appeared in ten out of 35 clinical rebounds occurring in patients with valvar involvement in the initial attack. Clinical rebounds occurred more frequently in those with cardiac involvement in the initial attack. No rebounds occurred in patients treated with salicylates for more than 8 weeks. But, in those treated with steroids, the longer the drug was given, the more likely was a rebound to occur. To explain these findings it is suggested that suppressive medication (in which steroids are the most potent agent) "prevents the dispersion of rheumatic inflammation and that the accumulated residual inflammation thus appears in the form of a rebound when the suppression is reduced or stopped. The severity of the rebound will depend upon how much inflammation was present initially, how much of it was suppressed by the therapy, and how much remains afterwards".

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In an attempt to determine the best forms of treatment and prevention of rebounds, an additional 150 children admitted consecutively from September, 1958, to August, 1959, were added to the above group, making a total of 415 consecutive admissions with definite evidence of rheumatic fever. Of these, 64 developed one or more clinical rebounds, 100 rebounds occurring in all. Laboratory rebounds had no clinical effects, always subsided spontaneously, and needed no treatment. In patients with no initial valvular involvement, clinical rebounds did not produce cardiac manifestations. In patients with valvular involvement, but no significant cardiac enlargement, the rebounds sometimes resulted in the appearance of new murmurs but no more severe cardiac effects. In both these groups, when the rebound was treated with suppressive agents, it was often followed by an additional rebound when the therapy was stopped. This was less likely to happen if the rebound was treated with salicylates than if it was treated with steroids. Rebounds could be prevented by not using anti-inflammatory agents in the initial attack or by treating it with salicylates alone for more than 8 weeks. In patients initially treated with steroids the incidence and severity of rebounds could be reduced by adding salicylates and continuing these for several weeks after the steroid therapy was stopped. However, in the group of patients with severe cardiac involvement in the initial attack, as judged by significant cardiac enlargement, rebounds might be associated with pericarditis, further increase in heart size, or congestive failure. If there were no cardiac features in the rebound it subsided spontaneously, but it frequently recurred if treated. No specific therapy for the primary rebound in this group seemed to reduce the occurrence of secondary rebounds. In a few patients “chronic” rheumatic activity of prolonged duration appeared, characterized by clinical rebounds not subsiding spontaneously and apparently unrelated to previous suppressive treatment.

C. Bruce Perry.


Chronic Articular Rheumatism (Rheumatoid Arthritis)


The first part of this paper deals with the manifestations and complications of Still's disease in 100 patients (forty boys and sixty girls) followed up for 15 years at The Hospital for Sick Children, Great Ormond Street, and University College Hospital, London. The age at onset was most frequently “well below 5 years”. In eighteen of the children systemic manifestations preceded joint involvement for varying periods of time, the average being 4 months. Fever tended to persist for a long time, even for years, and might have a peculiar periodicity. A rash, which was observed in forty patients, was usually associated with leucocytosis and lymphadenopathy; a leucocytosis of 30,000 cells per c.mm. with 80 to 90 per cent. neutrophil polymorphonuclear leucocytes occurred in 44 of the patients. In fourteen, minor injury had preceded the onset of the disease. Of particular interest was the occurrence of laryngeal stridor in three patients, one of whom required tracheotomy, and of a sterile necrotic area in a biceps muscle—a previously unreported...
complication. Another unusual finding was that of osteocytic lesions of the skull in association with nodule formation; biopsy examination of subcutaneous tissue in the vicinity showed degeneration of collagen with fibrinoid changes. There was regression with steroid therapy. Dermatomyositis was present in three children, two of whom had subcutaneous nodules. In a further patient chorea with carditis developed 5 months after the onset of rheumatoid arthritis.

In the second part of the paper the management of patients with Still's disease and the long-term effect of steroid therapy are discussed. The basic regimen was rest followed by physiotherapy and graded activity. The authors state that with this regimen spontaneous remission may occur quite early, although it may not be maintained; there was a relapse in eleven such patients in the present series. Steroid therapy was instituted when simple measures failed; of 63 patients treated, sixty received steroids systemically and three by intra-articular injection. The initial dosage, which was high, was gradually reduced to a maintenance dose of 50 to 75 mg. daily, which was continued until it could be tapered off. The duration of treatment varied, but in the majority of patients 18 months was adequate, a finding which contrasts markedly with the duration of treatment of adults. More than one course of steroid therapy was necessary in some patients because of relapse. There were five deaths, two from the disease and three from intercurrent infections. Rapid improvement was observed with steroid therapy both in the acute phase of the disease and in the effect on the joints. Osteoporosis, particularly of the vertebral column, was seen in eight patients. This complication was likely to develop if the child was already osteoporotic at the start of therapy; however, no neurological complications were noted and calcification was observed when administration of steroids was discontinued.

The authors consider that steroid therapy should be instituted when systemic disease or severe joint disturbance persists after several weeks, since the best results and often complete recovery are most likely with early treatment.

B. M. Ansell.


Laryngeal complications developing in the course of rheumatoid arthritis are rarely diagnosed during the patient's lifetime, though extensive changes may be demonstrable in the crico-arytenoid joint at necropsy. At the Montreal General Hospital, 55 patients with rheumatoid arthritis were closely questioned and underwent examination of the larynx by the authors. Of these, seventeen had some symptoms referable to the larynx. On mirror examination eighteen patients showed some evidence of crico-arytenoid arthritis, but nine of these had no laryngeal symptoms. In five out of eleven consecutive patients with rheumatoid arthritis who were examined post mortem, there was evidence of rheumatoid involvement of the larynx, but only two of these patients had had any laryngeal symptoms during life.

The authors discuss the question why this complication is so often unrecognized. On examination of the larynx there may be redness and swelling of the mucosa over one or both crico-arytenoid joints, but in the authors' series this finding was noted only rarely. In some cases the joint becomes disorganized and ankylosed in a deformed position, while fixation of one or both true vocal cords may occur in the midline position. Fixation of one cord in the midline will not produce stridor or severe hoarseness and in a bedridden patient who has no need to exert himself, this may even be true with bilateral fixation. Vocal change is not a common finding in these cases. Other symptoms that might be expected to be present, but are more often absent, are persistent sore throat, a feeling of "something sticking in the throat" after swallowing, and dysphagia. Even when symptoms and signs of laryngeal disease are present in a case of rheumatoid arthritis, they may not necessarily be due to involvement of the crico-arytenoid joint. Darke and others (Brit. med. J., 1958, 1, 1279; Abstr. Wld. Med., 1958, 24, 441) reported that most of five cases of midline fixation of the cords clinically due to arthritis were proved at necropsy to be due to paralysis of the recurrent laryngeal nerve, while in one case the real cause was a laryngeal carcinoma. Other conditions to be excluded in differential diagnosis are the oedema of the area that may follow irradiation for carcinoma, laryngeal injury during endoscopy or endotracheal intubation for anaesthesia, prolonged feeding by nasal tube, and occasionally upper or lower respiratory tract infection with suppuration of or around the joint.

Stridor due to bilateral fixation of the vocal cords may necessitate surgical treatment in the form of tracheotomy or arytenoidectomy and cord lateralization. Some patients with rheumatoid arthritis have such deformity of the fingers that they may find it difficult to attend to a tracheotomy orifice; for these in particular lateralization of the cord or arytenoidectomy is useful. The authors point out that in some cases arthritic change can make indirect examination of the larynx impossible. [In such an event endoscopy must be considered.] The histories of the five cases which came to necropsy are given in full and a further case is mentioned in which routine post mortem examination of the crico-arytenoid joints in a patient who died of scleroderma revealed unsuspected non-suppurative arthritis. This suggests that such arthritis may occur in conditions other than rheumatoid arthritis.

[This is a valuable paper.] F. W. Watkyn-Thomas.


The rate of removal of radioactive sodium from a tissue is a quantitative measure of local circulation, and similarly the rate of clearance from the knee joint has...
been shown to be closely related to circulatory changes. At the Devonshire Royal Hospital, Buxton, the author has used this technique to study the knee-joint in normal subjects and patients with rheumatoid arthritis and reports the effect of short-wave diathermy. Rheumatoid knees were graded 0, 1, or 2 according to the degree of clinical activity of the joint.

There was an average increase in clearance rate of 97 per cent. in the normal knee-joint after 20 minutes' heating with short-wave diathermy. The rheumatoid joints showed initial clearance rates similar to normal joints for Grades 0 and 1, but for Grade 2 (major involvement) the average initial clearance rate was 100 per cent. greater than the normal, demonstrating the presence of hyperaemia. After 20 minutes' diathermy joints of Grades 0 and 1 showed an average increase in clearance of 60 per cent., but those of Grade 2 showed an average reduction of 25 per cent., though the individual results varied considerably. The latter effect is similar to the effect of intra-articular hydrocortisone. This reduction of the hyperaemia of an active rheumatoid joint provides some rationale for using diathermy.

J. B. Millard.


In five patients with rheumatoid disease, respiratory difficulty during anaesthesia or unexpected post-operative death occurred. It is emphasized that such patients may be difficult subjects for the induction of anaesthesia on account of arthritis and ankylosis of the small joints of the larynx, of the cervical spine, and of the temporomandibular joints. In the same way the maintenance of adequate respiratory excursions during anaesthesia may be impeded by ankylosis of the costovertebral joints. Because of these manifestations of rheumatoid disease grave respiratory complications may be precipitated in the post-operative period. Following operation, the occurrence of interstitial pneumonia in rheumatoid arthritis may delay recovery. Particularly careful and continuous observation of these patients is necessary.

In other cases with rheumatoid arthritis, apparently straightforward operative procedures are followed by unexpected death. The high incidence of severe amyloidosis may determine a poor response to anaesthetic and analgesic drugs and may in part account for these fatalities. Further, it is becoming increasingly evident that unsuspected and potentially dangerous infection may remain latent in joints which are the sites of rheumatoid arthritis. There is reason to suppose that such patients have an altered response to infections to which, in spite of their characteristically hyperplastic reticulo-endothelial systems, they exhibit abnormally low resistance.—[Authors' summary.]


In this investigation undertaken at the Western Infirmary, Glasgow, to determine if there was possibly a relationship between rheumatoid arthritis and Hashimoto's thyroiditis, the authors studied 31 female and three male patients with Hashimoto's thyroiditis, 73 patients with rheumatoid arthritis, and a large control group consisting of 179 women attending various clinics, 125 diabetics, and 54 patients with dyspepsia.

Of the 31 women with Hashimoto's thyroiditis, diagnosed on the basis of a goitre and a positive precipitin reaction, or histologically, five had arthritis resembling rheumatoid arthritis in that it was characterized by a positive Rose-Waaler reaction and radiological joint changes, while a further three patients had a positive Rose-Waaler reaction, but no other evidence of rheumatoid arthritis, and one with a negative Rose-Waaler reaction had equivocal signs of rheumatoid arthritis. One of the three male Hashimoto patients had rheumatoid arthritis and a positive L.E. test. In contrast, only two of the 179 female control patients had rheumatoid arthritis. Although the zinc sulphate turbidity was considerably raised in four of the six patients with Hashimoto's thyroiditis, the γ-globulin level was never above 1-4 g. per 100 ml. Of the 46 women with rheumatoid arthritis, the complement-fixation test with thyroid tissue was positive in twelve, of whom two were hypothyroid and also gave a positive precipitin reaction, but neither had a goitre. This incidence of positive complement-fixation reactions (26 per cent.) was significantly higher than the 27 found among the 244 female controls (11 per cent.). None of the 27 men with rheumatoid arthritis had clinical or serological evidence of thyroid disease, although six out of the 292 controls showed positive complement-fixation test results.

The authors conclude that there is a significant association between Hashimoto's thyroiditis and rheumatoid arthritis, and consider that this clinical association favours the view that autoimmunization may play a role in rheumatoid arthritis.

G. L. Asherson.


The author of this paper from Södersjukhuset, Stockholm, discusses the results of liver function tests carried out in 77 patients (22 male, 55 female), aged 18 to 64 years, suffering from rheumatoid arthritis. Analysis of the results did not reveal any apparent relationship between the activity of the disease and the serum level of either glutamic oxalacetic transaminase or ornithine carbamyl transferase. However, there was an increase in the serum level of the latter enzyme in seventeen cases, which was believed to constitute evidence of a slight degree of liver-cell injury. It was also considered that patients with increased enzyme activity gave a better response to treatment with gold compounds or phenylbutazone than did patients in whom the serum enzyme levels were normal. No side-effects of gold treatment were encountered. A correlation was established between the serum activity of the enzymes and a decrease in the erythrocyte sedimentation rate.

The author points out that liver injury may result
Electromyographic Changes in Rheumatoid Arthritis


This study was carried out at the Department of Physical Medicine, the London Hospital, on 93 patients with definite rheumatoid arthritis to determine whether electromyographic diagnostic investigations would throw any light on the cause of the muscular wasting which occurs in this condition. The disease activity was classified according to the method of Duthie and others (Ann. rheum. Dis., 1955, 14, 133; Abstr. Wild Med., 1956, 19, 64). The activity and range of movement of the neighbouring joint was noted, together with the degree of wasting and the power of the selected muscles, these being the small muscles of the hand, the deltoid, the biceps, and quadriceps. Intensity-duration curves were plotted for each muscle, an R.A.F. constant voltage stimulator being used, and electromyography, employing concentric needle electrodes and a GHS double-beam electromyograph, was then carried out on the same muscle. The electromyogram (EMG) was thought to give the most sensitive result, 79 (85 per cent.) of the patients showing electromyographic evidence of polymyositis in one or more muscles. The intensity-duration curves revealed partial denervation in 37 of the muscles showing electromyographic evidence of polymyositis and in two muscles with a normal EMG.

The authors discuss their findings in relation to previous work on biopsy specimens of wasted muscle in rheumatoid arthritis. They conclude that the changes are not caused by steroid therapy, that there is no constant relationship to wasting and weakness of the muscles and activity of the neighbouring joints, but that there is some relationship between the degree of disease activity and the present findings.

Kenneth Tyler.
ABSTRACTS


The authors report the results obtained with synthetic antimalarial drugs in the treatment of 191 cases of rheumatic disease, mostly (156) of rheumatoid arthritis. A course lasted 4 to 6 weeks and some of the patients were given eight to twelve such courses. Of the various drugs tried it was found that for practical purposes two chloroquine-type products and a diguanide were the only ones that were effective and well tolerated. The drugs were given in doses of from 100 to 900 mg. a day, either alone or in combination with other agents such as corticosteroids, gold, aspirin, and “butazolidin” (phenylbutazone); it was found that chloroquine often helped to reduce the maintenance dose of these drugs. No way was found of predicting which product or combination of products would suit a particular patient best.

Of the 156 cases of rheumatoid arthritis treated, 100 were regarded as having shown a very good or good response, and twelve out of nineteen cases of ankylosing spondylitis responded similarly. True idiosyncrasy to chloroquine was rarely observed. Side-effects, usually in the form of digestive disturbances, occurred, but none were serious and all appeared to be reversible. The problem of intolerance was often solved by changing the drug. There was no evidence of any acquired resistance to chloroquine. The authors consider that the use of these drugs in the treatment of rheumatoid arthritis is well worth while; they are safe, cheap, effective, and in many cases their use permits of the reduction of the dose of other more powerful and more toxic agents to a safer level.

B. E. W. Mace.


Osteo-Arthritis.


Among 23 cases of osteo-arthritis of the interphalangeal joints of the fingers recently investigated at Georgetown University Medical School, Washington, D.C., middle-aged women predominated, and in many cases a family history of the condition was elicited. In one family the changes in the hands were similar in mother and daughter; in another family two sisters presented almost identical manifestations.

The disease was characterized by acute episodes of pain associated with inflammation and eventual deformity of the proximal and distal joints. Redness, swelling, local heat, and tenderness on pressure were observed during the acute phase. When the swelling increased in size there was severe impairment of function, and radiographs showed osteophyte formation, progressive narrowing of the cartilage space, destruction of the epiphyseal bone, and subluxation of the digits. In fourteen cases the terminal interphalangeal articulations were primarily affected, but for the most part the disease soon extended to all the interphalangeal joints, including those of the thumbs. Osteo-arthritic changes were also observed in the cervical vertebrae. Other peripheral articulations remained free from the disease.

Differential diagnosis was required from the painless degenerative disease of the terminal interphalangeal joints and the painful inflammatory phase of rheumatoid arthritis of the proximal interphalangeal joints. Serological tests for the rheumatoid factor yielded negative results. As regards treatment, symptomatic relief was obtained from the intra-articular injection of hydrocortisone.

A. Garland.


(Osteo-Arthritis)


Over a recent 3-year period three cases of juvenile ankylosing spondylitis were seen at the University Hospital, Lund, Sweden. The patients, boys aged 5, 8, and 12 years respectively at the time the diagnosis was made, had pain in the back associated with pains in the hips, shoulders, or knees. X-ray examination revealed changes in the sacro-iliac joints typical of ankylosing spondylitis. The erythrocyte sedimentation rate was raised and the response to the sensitized sheep-cell test was negative in all three patients. The authors also describe nine cases of juvenile rheumatoid arthritis in which the cervical spine was involved. Of the nine patients, six had dislocation or subluxation between the atlas and the axis with erosions of the odontoid process; the remaining three had osseous fusion of the posterior vertebral segments of a varying number of cervical vertebrae which was associated in all three cases with narrowing of the intervertebral disks and in one with changes in the sacro-iliac joints.

The cases described are considered to show that morphologically and clinically there is no sharp dividing line between ankylosing spondylitis and rheumatoid arthritis.

C. E. Quin.


(Miscellaneous)


The clinical features in 86 cases of arthritis associated with psoriasis and the post mortem findings in sixteen of them are discussed in this paper from the University of Southern California School of Medicine, Los Angeles. Of the sixteen deaths, two were due to perforated peptic ulcers and one to coronary thrombosis, although a penetrating peptic ulcer was also present. Myocardial infarction was responsible for four further deaths, infection (pyleulcer, nephritis, bronchopneumonia, and septicaemia) for three, haemorrhage (pulmonary and oesophageal varices) for two, and adrenal insufficiency, secondary amyloidosis, and suicide (in a patient with a steroid-induced psychosis) for one each. Steroids were being administered to eight of the sixteen patients at the time of death and complications from this led to peptic perforation, psychosis, uncontrolled staphylococcal infection, increased hypertension, and acute adrenal insufficiency. All the patients continued to have exfoliative psoriasis in spite of a high dosage of steroids.

Discussing complications in the series as a whole the authors state that of the 86 patients peptic ulcers developed in ten, osteoporosis in two, and active tuberculosis in two. One gained 100 lb. (45-35 kg.) in weight in a year. Triamcinolone caused the greatest number of complications; during treatment with this drug diabetes...
mellitus developed in one patient, muscular weakness in three, and in one there was rupture of a pregnant uterus. The psoriasis exfoliated in five patients while they were receiving triamcinolone.

Electrocardiographic examination, which was carried out on 84 of the 86 patients, revealed abnormalities in fourteen patients under 50 years of age and in 22 of those over 50. Spondylitic heart disease was present in three patients and strongly suspected in two others. These patients apparently had more severe systemic disease, with iritis, urethritis, severe peripheral arthritis, and pustular psoriasis.

[The cases of spondylitis, pustular psoriasis, iritis, and urethritis would probably have been classified in Britain as cases of Reiter's disease; they indicate once more the possible interrelationship between this condition, psoriasis, and arthritis.] Benjamin Schwartz.


The author discusses some observations which suggest that primary osteoporosis may be due to a long-continued negative calcium balance. The work of Albright and the subsequent literature on the pathogenesis of osteoporosis are reviewed, and reference is made to reported experiments in animals which showed that calcium deprivation without deficiency of vitamin D produced osteoporosis. At the Western Infirmary, Glasgow, analysis of the dietary intake of 71 patients with primary osteoporosis and 96 healthy subjects revealed a significantly lower intake of calcium in the patients with osteoporosis than in the controls, an observation confirmed by workers in the United States. The author has found that whereas in healthy subjects 10 days on a low-calcium diet reduces the urinary excretion of calcium by at least 30 per cent., little or no fall in calcium excretion occurs in patients with osteoporosis. These and other observations emphasize his view that long-continued negative calcium balance is a factor in the aetiology of osteoporosis. Of a group of 46 osteoporotic patients given 6 g. calcium glycerol phosphate daily for 12 months, 22 were completely free from pain, although there was no convincing radiological improvement.

I. McLean Baird.


The acute arthritis which is an outstanding feature of Reiter's disease and thus suggests some resemblance to rheumatic fever has prompted several investigators to search for cardiac lesions. In this paper the authors describe, from St. Mary's Hospital, London, three cases of Reiter's disease, all in males, in which aortic incompetence subsequently developed. The first patient, a West Indian, having at the age of 29 contracted gonorrhoea, had his first attack of Reiter's disease at the age of 38, when he developed pericarditis and a harsh apical systolic murmur, the electrocardiogram (ECG) showing a prolonged P-R interval of 0.28 second. When he was seen 4 years later, there was evidence of aortic incompetence, the patient having, in the intervening period, had several attacks of polyarthritis (one of which was treated with corticosteroids) and one of gonorrhoea; the latter had responded to penicillin, but had been followed by a further attack of non-specific urethritis. The second patient also developed Reiter's disease after contracting gonorrhoea (in 1940 at the age of 27). When examined in 1959, having then been suffering from dyspnoea of effort for about one year, he was found to have aortic incompetence. The ECG showed the P-R interval to be 0.28 second. The third patient developed Reiter's disease 8 years after an attack (in 1927) of gonorrhoea, which was followed by recurrent attacks of iritis. In 1957, when he was 53, he was found to have aortic incompetence, the P-R interval being 0.24 second. He was observed for a further 3 years, during which time he has had two further attacks of iritis, but his cardiac condition remains unchanged.

The authors also describe the case of a woman aged 50 who died in cardiac failure due to aortic incompetence which had been first diagnosed 5 years previously. This patient had had transient arthritis, iritis, and cervicitis, but the diagnosis of Reiter's disease could not be definitely established. Post mortem examination revealed atheroma and thickening of the intima of the aorta and thickening of the adventitia with endarteritis, changes which are usually ascribed to the late effects of syphilis and rheumatic endocarditis. (The three male patients described were discovered as a result of a long-term study of 215 cases of Reiter's disease.)

H. F. Reichenfeld.

**Calcium Metabolism in Osteoporosis: Acute and Long-term Responses to Increased Calcium Intake.** Harrison, M., Fraser, R., and Mullan, B. (1961). *Lancet*, 1, 1015. 26 refs.

The cause of osteoporosis, or "simple" atrophy of bone, is not known. Recent studies of calcium metabolism do not support the widely accepted hypothesis that osteoporosis results from defective osteoblastic activity. Studies are reported here which suggest that calcium deficiency is an important factor in many cases of postmenopausal and senile osteoporosis. Many patients with these forms of osteoporosis absorb and retain calcium abnormally avidly when on a high calcium intake in the form of supplements (calcium gluconate), and, moreover, may continue to retain it avidly for at least 3½ years.

Symptoms of the disease are relieved, and no further fractures take place. Therapy with calcium supplements, therefore, seems to be of value for many patients with osteoporosis.—[Authors' summary.]


Hyperuricaemia may be an indication that chronic arthritis is gouty in origin, although there is not necessarily a history of acute gout and tophi may be absent.
If so, reduction of the blood uric acid level with a uricosuric drug might be expected to relieve symptoms by reducing tissue deposits of urates. This occurred in eight out of ten patients (eight males) who were treated for periods of at least 4 months with sulphinpyrazone in a dosage of 100 mg. four times daily. In all the patients the serum uric acid level was 6 mg. per 100 ml. or higher. Only two patients had had acute gout, but all had chronic joint symptoms. In two the response to the Rose test was positive. During treatment the serum uric acid level fell from a mean of 6.7 mg. per 100 ml. to 4.2 mg. per 100 ml., rising again after cessation of therapy. There was a dramatic relief of symptoms within a few weeks in two patients and more gradual but definite relief in six others. The only serious side-effect was diarrhoea, which necessitated withdrawal of the drug in one case.

J. A. Cosh.


This report from the University of California, San Francisco, confirms the value of contrast arthrography of the shoulder as a means of confirming the accuracy of a clinical diagnosis of soft tissue lesions around the joint which had been established by previous workers, and adds certain further observations. In addition to showing a high correlation with the clinical findings, the preoperative radiological diagnosis in a series of 125 arthograms was proved correct in the thirty shoulders subjected to operation. The technique as described may be performed on an out-patient basis with full aseptic precautions, using sodium diatrizoate as a contrast medium. The procedure is likely to be accompanied by mild discomfort following the injection, with soreness of the shoulder on the following day. In this series no infections of the joint occurred.

In a normal arthrogram the subscapularis bursa, with its prolongation beneath the coracoid process, is outlined. This communicates with the glenohumeral joint, where the articular cartilages on each side are seen as negative shadows between the medium and bone. The synovial reflection along the intrascapular portion of the long head of biceps fills inferiorly, to a level just below the transverse bicipital ligament, but no farther. The subacromial bursa, lying between the deltoid and the rotator cuff, does not fill unless the latter is torn. Such tearing was the most common lesion (seventy cases) seen in this study, being the result of either recent trauma or slow degenerative attrition. Radiographically the axillary view is particularly important, since abduction helps to force the medium through the defect. In four cases such tears were associated with tears of the long head of biceps, the contrast medium being seen to descend well down into the arm. Dislocation injuries cause ballooning of the capsule, and in cases of “frozen shoulder” the joint capacity is diminished. The authors consider the investigation to be of considerable value, and hope to enhance its value still further by the use of cineradiography.

R. O. Murray.


The first-named author with others described in 1946 (Arch. Rhum., 6, 129) a painful disorder of the upper limb which has since become known as the “shoulder hand syndrome”. The present report is based on a study of 52 cases of this disorder seen since 1952, of which 35 have been followed up for several years. The onset is usually marked by diffuse pain in one upper limb, the distribution of which does not suggest root pain. Several days later the hand of the painful limb becomes swollen and the shoulder stiff. Less usually the first sign may be a stiff painful shoulder, suggesting “scapulo-humeral peri-arthritis”, or a painful swollen hand, the condition occasionally being so severe as to suggest cellulitis or an attack of acute gout. At first the whole hand is moderately oedematous, the skin red, and there is palm sweating. Attempted movement of the fingers is extremely painful and the fingers cannot be fully flexed. At a later stage trophic changes in the hand are prominent, the skin is cold, often cyanotic, thin, and smooth, and the nails striated and brittle, while the intrinsic muscles are atrophied. Small indurations in the palmar aponeurosis suggestive of early Dupuytren’s contracture are common. A flexion deformity of the fingers follows, with greatly restricted interphalangeal and metacarpo phalangeal movements. The shoulder also shows severe restriction of all movements, resembling at times the almost complete immobility of “frozen shoulder”. The most common x-ray finding is osteoporosis, in some cases severe, affecting mainly the epiphyses of the fingers, the carpal bones, and the humeral head. This may be absent in the early stages, but is very marked in the stage of trophic changes. The joint spaces remain intact, and erosions never develop. As a rule the outcome is favourable, but recovery may be delayed for 6 months to one year, or even longer. Recovery may be complete, but quite often there are minor sequelae such as an inability to extend the fingers. Uncommonly, severe disabilities from a stiff shoulder and loss of grip persists.

The aetiology of the syndrome is unknown, but among the suspected factors are trauma, either of the shoulder or hand, coronary thrombosis, certain affections of the pleura and lungs, lesions of the central nervous system, such as hemiplegia or cerebral tumour, and cervical spondylosis. The pathogenesis is uncertain. The authors favour the theory of a reflex sympathetic dystrophy, as suggested by Leriche.

Of many suggested methods of treatment, three are especially important:

1. Immobilization, particularly if initial pain is very severe, when it may be permitted for a few days, but as soon as adequate relief is obtained active and passive movements must be begun.

2. Stellate ganglion block, in experienced hands may give a brilliantly successful result.

3. Systemic corticosteroid therapy often brings...
rapid relief, a short course of a few weeks being usually sufficient.

Some authorities hold that steroid therapy is not contraindicated in cases following myocardial infarction, but the authors' cardiological colleagues at Lyons do not consider that the risk, however slight, is justifiable.

[The paper contains a very full and useful bibliography.]

Kenneth Stone.


Studies of the Painful Shoulder (Scapulohumeral Periarthritis).


Gout


There is considerable variation in the severity of gout and although its familial nature is recognized the extreme severity of certain cases compared with the mild form of the disease with onset during middle age has remained unexplained. In the first type, in which symptoms develop during or soon after puberty, recurrent acute attacks occur and the disease progresses rapidly to death from renal failure before middle age. From the Medical Professoral Unit of the University of Queensland, Brisbane Hospital, the author reports two family pedigrees containing persons homozygous for the gouty trait. In the first family one member developed severe primary gout and secondary renal disease at the age of 18 years. Both parents had hyperuricaemia and this was present in both the paternal and maternal lines of descent. Overt gout, however, was present in only one other member of the family, a cousin of the patient's mother. In the second family pedigree gout or hyperuricaemia could be traced through five generations, and as a result of the union of one of the gouty males with a hyperuricaemic family, four hyperuricaemic and gouty children were produced; three of these also had hypertension and two had evidence of impaired renal function.

In the first family the patient's renal disease was due to gout in itself, but the second family illustrates the association of hyperuricaemia and primary hypertensive vascular disease resulting in renal disease in a gouty subject. It is to be expected that the occurrence of an elevated serum urate level in both parents will result in an increased tendency to hyperuricaemia in the children. If the inheritance is by a dominant gene the children produced by two hyperuricaemic parents could be homozygous for this trait and would probably tend to manifest gout both with a greater severity than others and at an earlier age. If the inheritance is polygenic, that is, similar to that of other bodily characteristics such as height, a similar state would still be expected in the children of two parents with elevated serum urate levels.

J. Warwick Buckler.


The relatively high frequency of gout in primary polycythaemia contrasts with the apparently low incidence in secondary polycythaemia, which the author regards as surprising. He has consequently investigated the incidence of gout in patients with polycythaemia secondary to congenital and acquired heart disease and to respiratory disease. During a survey at the Brompton Hospital for Diseases of the Chest, London, extending over 27 months there were 7,500 estimations of haemoglobin level, and only ninety patients were found to have a value of 120 per cent. or over (taking 100 per cent. as equal to 14-6 g. per 100 ml.). Gout was present in four of these patients, two of whom had congenital heart disease, one acquired heart disease, and one cor pulmonale. The author considers it important to recognize the association of gout with cyanotic heart disease, as otherwise the arthritis might be attributed to rheumatic
fever, vascular thromboses, or the embolic manifestations of bacterial endocarditis.

G. S. Crockett.


The treatment of five cases of primary gout with Anturan ( sulphipyrazone) is reported from the Royal Victoria Hospital, Belfast. There were four men and one woman aged between 33 and 72 years. The initial dose was 50 mg. (half a tablet) 6-hrly given with meals, increased where possible to 100 mg. 6-hrly after 4 or 5 days, the object being to lower the serum uric acid level to normal and to keep it there. To avoid renal lithiasis the urine was kept alkaline by the administration of sodium bicarbonate, 20 gr. (1-3 g.) 6-hrly. Except for a reduction in caloric intake for the obese patients no specific dietary regimen was followed. Acute attacks in the early weeks were treated with colchicine. One patient given hydrochlorothiazide for oedema of the ankles during treatment with Anturan showed a startling rise in serum uric acid level.

The mean reduction in serum uric acid level was 43 per cent. All five patients felt improvement within a few weeks of starting treatment, including one patient with impaired renal function. Acute attacks of gout developed in four cases during the first few weeks of treatment, but, as the author points out, this is liable to occur with any uricosuric agent. On the other hand the occurrence of oedema of the ankles in two cases was attributed to the Anturan or the high sodium intake.

The author suggests that Anturan is the most effective uricosuric agent at present available, and recommends its use for the routine treatment of gout.

G. S. Crockett.


Sulphinpyrazone (Anturan), a uricosuric analogue of phenylbutazone, was administered over an average period of 14 months to seventeen patients with gout, two of whom were in the chronic tophaceous stage of the disease, at the Medical Clinics of the Northwestern University Medical School, Chicago. The dosage was usually 400 mg. a day divided into four equal doses; colchicine was also given prophylactically in the initial months of treatment, but salicylates were prohibited.

Control serum uric acid values before treatment started averaged 8.7 mg. per 100 ml.; during therapy an average decrease of 37 per cent. to a mean value of 5.4 mg. per 100 ml. was obtained, the decrease ranging from 16 to 61 per cent. (A spectrophotometric uricase method was used for the serum analyses.) The frequency of acute attacks of arthritis fell after 5 months' treatment, and in the final 5 months no attacks at all occurred. The toxicity of the drug is stated to be low; two patients developed a maculopapular rash, one a mild leucopenia, and four had a dyspepsia which was relieved by taking the sulphinpyrazone with meals.

K. C. Robinson.


This paper, from the State University of New York College of Medicine, the Jewish Hospital, and King's County Hospital, Brooklyn, New York, describes the results of treatment with trimethylcolchicine acid (TMCA) in 34 cases of acute gout. Treatment consisted in the oral administration of 5 to 16 mg. of TMCA, usually in a single dose and within 4 to 3 weeks of the onset of the attack.

Response was complete or nearly complete in 26 cases (76 per cent.), partial in four (12 per cent.), and absent in four (12 per cent.). Four patients showing no response, and three showing partial response were later treated with colchicine and four proved to be resistant. There was a tendency for a poor response to occur in those cases in which treatment had been delayed. Prophylactic therapy with TMCA in doses of 1 to 3 mg. daily was exercised in seven cases. Although none of these patients developed an acute attack, it was considered that the period of observation (maximum 4 months) was too limited for an appraisal of the effectiveness of the drug as a prophylactic. Toxic effects were uncommon, and only occasional mild nausea (one) and mild diarrhoea (two), and it is considered that TMCA compares favourably with colchicine for the treatment of acute gout.

Hewett A. Ellis.


This article from the Rheumatological Clinic, Montpellier, describes the use of zoxazolamine in the treatment of 27 cases of gout. In most cases the drug was given in doses gradually increasing up to 600 mg. a day, and daily blood and urine urate estimations were made as long as the patient was in hospital. Twelve patients admitted for other conditions were similarly treated for control purposes.

It was found that administration of the drug caused a reduction in blood urate level to normal and an increase in urate excretion in all the gouty subjects except one whose blood urate level before treatment was normal.

In the control subjects, whose blood urate levels were also normal, the reduction under treatment was much less marked. In two gouty cases an appreciable reduction in the size of tophi was noted after 8 months of treatment. No side-effects of any significance were noted. Acute gouty attacks occurred in six cases during the early phase of treatment and in two of these the drug had to be withheld. Renal colic occurred in three cases after high dosage. Aspirin was shown to have an antagonistic effect on the uricosuric action of zoxazolamine but other uricosuric agents, such as phenylbutazone, probenecid, and "G 28315" [a phenylbutazone derivative], did not have this effect and can therefore be used in association with zoxazolamine with advantage, they may have a synergistic effect.
ABSTRACTS

The authors conclude that oxazolamine is a powerful uricosuric agent, of value in the treatment of chronic gout. Its effectiveness may lead to severe acute attacks at the beginning of treatment and for this reason dosage should be increased only gradually. B. E. W. Mace.


The authors draw attention to certain patients with a form of rheumatoid arthritis which resembles gout and described twelve such cases occurring among a series of 800 patients with rheumatoid arthritis. These cases showed large subcutaneous nodules on the elbows, ulnar borders, fingers, and Achilles tendon. In general, nodules superficially resembling the tophi of gout were found anywhere that such tophi occur, with the exception of the ear. On x-ray examination the patients showed punched out "cysts" in the ends of the bones, also resembling those of gout. [The French word for this lesion is géode, but this term has already been used in English to designate a dilated lymph space.] The remaining findings in these cases were those of rheumatoid arthritis. A. St. J. Dixon.


The state of the kidneys in 31 patients with gout has been studied at the Hôpital Necker, Paris. Of 27 patients with typical chronic gout eleven had interstitial nephropathy secondary to uric acid stones and, of these eleven, seven presented with acute anuria due to obstruction of the outflow of the one functioning kidney, the other having been destroyed by similar episodes, while four presented with renal failure following a history of renal colic and the passage of stones, these patients having proteinuria, pyuria, and acidosis. Biopsy and necropsy examination in four of this group of eleven showed ascending nephritis, with tubular atrophy, cellular inflammatory reaction, fibrosis, and patchy glomerular involvement. Prevention of these changes of "gouty kidney" lies in the prevention and treatment of the formation of uric acid stones.

Another twelve of those with chronic gout had glomerular nephropathy but no calculi; here proteinuria and haematuria were more frequent than pyuria. Histological examination showed glomerular changes similar to those of glomerulonephritis at various stages of their evolution. In the remaining four cases of chronic gout there was intercurrent renal disease which was unrelated to the gout.

In three patients with no previous history of gout who developed the typical joint involvement secondary to renal failure there was glomerulonephritis, cystic disease of the pyramids, and polycytic disease respectively. The remaining case of the 27 was one of acute renal failure due to acute leukaeic infiltration of the kidneys and here also secondary gout developed.

The study of the plasma levels and urinary excretion of uric acid, urea, and creatinine confirmed the established view that chronic gout is not due to a renal defect, and it is suggested that even in renal failure the secondary gout may be due to a mechanism other than failure of renal excretion of urates. T. B. Begg.

Identification of Urate Crystals in Gouty Synovial Fluid.


The nature of the crystals observed in synovial fluid from patients with gout and the frequency of their occurrence were studied at the University of Pennsylvania School of Medicine, Philadelphia. The fluid was examined by polarized light microscopy and a uricase digestion test was carried out on the crystals which were found to be negatively birefringent with extinction on the long axis. Urate crystals from a subcutaneous tophus were seen to behave similarly under polarized light microscopy.

Urate crystals were identified by polarizing microscopy in aspirated synovial fluid from fifteen out of eighteen patients with gout and by ordinary microscopy in fluid from only eleven of the eighteen patients. The crystals in fifteen positive samples and in two out of fourteen control samples from patients without evidence of tophi were specifically digested by uricase. On two occasions ordinary microscopy showed crystals that were not urate crystals. It is suggested that the concentration of urate in synovial fluid during an acute attack of gout is higher than that in the serum. In the authors' view examination of synovial fluid under a polarized light microscope should be a standard diagnostic procedure for gout. J. E. Page.


The association of renal disease with gout is well recognized, but the pathogenesis of the kidney disorder has not been clearly defined. This study of renal biopsy specimens, reported from the London Hospital, was designed to determine if very early lesions could be identified and if they could be correlated with the clinical state of the patients. Renal biopsy was performed on eleven men and one woman, aged 40 to 69 years, with a history of attacks of gouty arthritis ranging from 4 to 38 years. Renal function tests were also carried out. Only two of these patients were known to have evidence of renal impairment, but eight others were found to have proteinuria and/or impairment of renal function and six had disorders of renal structure.
The study provided no conclusive information about the production of gouty nephropathy. It is thought that possibly the earliest renal lesion is slowly progressive tubular damage accompanied by interstitial reaction. In time tubular atrophy would develop with or without coincidental infection and produce the final picture of “interstitial nephritis.” A. W. H. Foxell.


Pararheumatic (Collagen) Diseases


The authors, at the Medical College of Alabama, Birmingham, have studied the reaction of patients with systemic lupus erythematosus to intradermal injection of normal leukocytes. A positive reaction, maximal at 24 hours, occurred in fifteen out of seventeen cases of systemic lupus erythematosus, but in only two out of forty cases of rheumatoid arthritis and in one case of rheumatic fever out of 26 cases of other diseases tested as a control. Histological studies of the injection sites were made in a number [unstated] of cases of systemic lupus erythematosus and control cases. In the former area inflammatory exudate of polymorphs and mononuclear cells tending to localize around blood vessels, degenerative nuclear changes, and some fibrinous transudates were seen, whereas biopsies from the control subjects showed only mild oedema with little inflammatory reaction. M. Wilkinson.


This paper from the Mount Sinai Hospital, New York, describes the renal manifestations which occurred in 56 of ninety patients suffering from systemic lupus erythematosus (S.L.E.). All the patients had characteristic clinical and laboratory evidence of S.L.E., including a positive reaction to the L.E. cell test, and all those with renal involvement had persistent proteinuria, while 88 per cent. had haematuria, 63 per cent. pyuria, and 70 per cent. casts in the urinary sediment. Renal involvement was more frequent and severe in the younger patients, 35 instances occurring in those less than 30 years of age, while sixteen died and twelve others had azotaemia. Of 21 patients over 30 years, eight died, nine had minor renal damage, and four had azotaemia. The longer the disease continued without renal involvement, the less likely was this to occur. Clinical features in the patients with renal involvement included the nephrotic syndrome (37 per cent.), hypertension (44 per cent.), oedema (35 per cent.), and abnormal fundi (30 per cent.). Pathological examination of the kidney in nineteen cases showed that the degree of histological damage correlated with the severity of the clinical manifestations and the prognosis, but not with the blood urea level or 2-hr phenolsulphophthalein excretion values.

Treatment with various steroids (for example, cortisone, initial dose 200 to 300 mg., maintenance dose 50 to 100 mg. daily; prednisone, initial dose 40 to 60 mg.; maintenance dose 10 to 25 mg. daily) in doses sufficient to control other symptoms of the disease failed to control the renal manifestations. Thus, 26 of the 56 patients with renal involvement died, whereas none of the 24 patients without renal involvement who were followed up did so.
The study illustrates the serious prognosis in patients with renal involvement in S.L.E., even when treated with steroids. The authors suggest that more intensive and prolonged therapy might have favourably influenced the prognosis. 

Hewett A. Ellis.


In a previous paper (A.M.A. Arch. Derm., 1956, 73, 1; Abstr. Wild Med., 1956, 20, 62), the authors reported haematological abnormalities in just over half of 66 cases of chronic discoid lupus erythematosus, in five out of six cases of generalized discoid lupus erythematosus, and in all five systemic cases seen in the Sheffield area between 1948 and 1952. The present paper deals with the clinical and haematological states of the same patients after a further 5 years of observation. Of the original 77 patients, ten have died (but in only one case was death attributable to the lupus erythematosus), a further nine could not be traced, and one patient had moved from the area, leaving the 57 patients which are the subject of the present survey.

Of 51 chronic discoid cases (38 female, 13 male), in seventeen the disease was clinically inactive, seventeen showed active and scarred lesions, and seventeen active lesions only. Three of the four cases of generalized discoid disease and the two cases of subacute disseminated lupus erythematosus still showed active and scarred lesions. Haematological abnormalities were demonstrated in thirty cases of chronic discoid, two of generalized discoid, and two of subacute disseminated disease. These consisted of microcytic hypochromic anaemia (three), leucopenia (four), lymphopenia (four), leucocytosis (one), thrombocytopenia (six), raised erythrocyte sedimentation rate (25), and cold agglutinins (two). In addition, L.E. cells were found in the peripheral blood in four cases of chronic discoid, two of generalized discoid, and both cases of subacute disseminated lupus erythematosus. In all, thirty cases of chronic, two of generalized, and two of disseminated disease had some haematological abnormality.

In discussing their findings the authors comment on the increased number of chronic discoid cases which have become inactive, and they note again that there were no obvious clinical differences between the cases with abnormal and those with normal haematological findings. No cases of chronic discoid disease developed systemic lupus erythematosus, and only one case became generalized. In the period under review there was no evidence to suggest that cases of chronic discoid lupus erythematosus with haematological abnormalities are more likely to develop systemic manifestations.

Benjamin Schwartz.

Lymphadenoid Goitre and the Syndrome of Systemic Lupus Erythematosus. White, R. G., Bass, B. H., and Williams, E. (1961). Lancet, I, 368. 4 figs, 22 refs. The authors, at the London Hospital, have investigated the presence of antinuclear factor in the serum of forty patients with lymphadenoid goitre, using a histological technique with a fluorescent antibody. In 28 of these patients the diagnosis had been confirmed by histological examination of the thyroid gland. Positive control sera were obtained from cases of systemic lupus erythematosus, and negative controls from an antenatal clinic and from routine blood donors. Other tests performed were complement fixation and precipitin tests and haemagglutination of tanned sheep erythrocytes sensitized with purified thyroglobulin.

Of the forty cases, five gave a positive result for antinuclear factor; all five cases were in females aged from 48 to 82 years. In two of the cases no other disease was present; one had signs of systemic lupus erythematosus (S.L.E.) 2 years after a positive serum reaction for antinuclear factor had been elicited, while in another case there were features suggesting this disease; and one had rheumatoid arthritis and rheumatic heart disease.

It is suggested that, while these findings are not regarded as supporting the idea that lymphadenoid goitre is a direct manifestation of S.L.E., they may indicate that a small subgroup of cases of lymphadenoid goitre arises in patients with S.L.E. who have a special propensity to form antibodies generally.

B. M. Ansell.

Study of the Mechanism by which Quinacrine Inhibits L.E. Cell Formation. Neilson, N., and Lansbury, J. (1961). Amer. J. med. Sci., 241, 700. 2 figs, 13 refs. Working at the Temple University School of Medicine, Philadelphia, the authors have studied the inhibition of L.E. cell formation in cases of systemic lupus erythematosus (L.E.) by quinacrine (mepacrine) in the hope that this understanding of this mechanism might shed light on the antirheumatic action of the drug.

Electrophoretic studies on serum incubated with quinacrine suggested no firm binding of the drug by protein, and ultraviolet-light studies of blood films after exposure to quinacrine showed a considerable concentration of the drug in leucocyte cytoplasm, with little in the nuclei, and none in the erythrocytes. The addition of quinacrine to suspensions of normal leucocytes in normal plasma almost abolished pseudopod formation and phagocytosis by leucocytes when the drug concentration was 0-4 mg. per ml. or more.

Prior treatment of potent L.E. serum with quinacrine followed by dilution to below 0-4 mg. per ml. did not interfere with L.E. cell production, suggesting that quinacrine does not inactivate the L.E. serum factor. Nor did exposure of a suspension of leucocyte nuclei to quinacrine prevent their conversion to L.E. bodies and subsequent phagocytosis when potent L.E. serum and leucocytes were added. This suggests that quinacrine does not inhibit the union of L.E. serum factor and nucleoprotein. Only when the concentration of quinacrine reached 0-4 mg. per ml. was L.E. cell formation inhibited and the authors believe this to be due to inhibition of phagocytosis. This drug concentration is far above therapeutic levels and the study does not help to explain the antirheumatic action of quinacrine.

M. Wilkinson.

The authors have compared, at the Medical and Rheumatic Clinics of the University of Zürich, the clinical and serological features in 48 patients with systemic lupus erythematous (S.L.E.) with those in 48 cases of rheumatoid arthritis (R.A.) and five in which the diagnosis lay between these two conditions. The criteria for the diagnosis of the different disorders are described. Of the patients with S.L.E., 75 per cent. were female, compared with only 58 (4 per cent.) of those with R.A. There was some selection of the patients with rheumatoid arthritis, in that the more severe cases tended to be sent for examination.

Clinically, fever, tiredness, gastro-intestinal disturbances, cardiac symptoms, involvement of the lungs, kidneys, and serous membranes and enlargement of the liver, spleen, and lymph nodes were all more frequent in the patients with S.L.E.; a typical skin rash occurred in 35-2 per cent. of these patients, but joint deformity was noted in only about 27 per cent. Morning stiffness occurred in both groups. In the S.L.E. group there was a high incidence of mental symptoms which sometimes mimicked schizophrenia or severe depression. In some cases, however, the disease ran a very mild course and occasionally lesions histologically resembling those of Henoch-Schönlein purpura were seen; marked haemolytic anaemia was found in two cases. Although anaemia and leucopenia were commoner in the patients with S.L.E., 32 of them had leucocyte counts above 4,000 per c.mm. The L.E. test was positive in 75 per cent., as compared with 9-5 per cent. of the patients with R.A. Homogenization of the nucleus without phagocytosis was noted in 13-1 per cent. of the latter, but in only 2-5 per cent. of the former.

Performance of the very sensitive conglutinin modification of the complement fixation test showed that 42-5 per cent. of the patients with S.L.E. developed antibodies against histone, nucleoprotein, and notably deoxyribose nucleic acid (D.N.A.), but only 4-1 per cent. of those with R.A. did so; on the other hand, 32 per cent. of the latter reacted with one of these antigens as compared with 10 per cent. of the patients with S.L.E. Thus multiple autoantibody production was a feature of the lupus patients. The Coomb’s consumption test, using nuclei as antigens, was positive in 97-5 per cent. of the lupus patients, but in only 34-2 per cent. of the rheumatoid group; the figures for a positive latex fixation reaction were 42-5 and 89-6 per cent. respectively. Antibodies against thyroglobulin were found in 21 per cent. of the lupus patients. Although the formation of antibody against nucleoprotein and D.N.A. was characteristic of S.L.E. nearly all the known autoantibodies have been found in some cases of this disease, reflecting the loss of immunological self-recognition.

In the differential diagnosis of S.L.E. it is noted that septicaemia, disseminated malignant disease, Hodgkin’s disease, rheumatic fever, and scleroderma must be excluded. Difficulty arises when the typical rash is absent and the L.E. test is negative. When all tests for antibody against nuclei are negative the diagnosis of S.L.E. is rarely tenable. Differentiation from rheumatoid arthritis may be impossible in the absence of pathognomonic biopsy findings characteristic of S.L.E. Particularly puzzling are those cases in which withdrawal of cortisone leads to exacerbation of rheumatoid arthritis with visceral involvement.

The authors come to the conclusion that in spite of their apparent similarity, these two diseases are clearly distinct in their clinical picture and the pattern of their serology. They suggest, however, that rheumatoid arthritis may provide a favourable soil for the development of systemic lupus erythematous. G. L. Asherson.


Although haematoxylin bodies have frequently been described as occurring in necropsy and biopsy material from cases of disseminated lupus erythematous (D.L.E.), L.E. cells have apparently not previously been recorded in the naturally occurring lesions of D.L.E. They have, however, been found in the fluid of blisters artificially induced on the skin of patients with D.L.E. and in blood taken from a finger after constriction. The present work, communication from the Edward J. Meyer Memorial Hospital, Buffalo, New York, describes two cases. In the first case a woman with a confirmed diagnosis of D.L.E. had some cutaneous lesions at the elbow, one of which, on biopsy, showed many typical L.E. cells extra-vascularly, as well as haematoxylin bodies. The second case, of apparently uncertain diagnosis, showed, in a biopsy of clinically normal skin, some basophil bodies 10 to 33 μ in diameter. No other specific lesions were described in the biopsy specimen. The known factors required for the formation of L.E. cells are briefly discussed.

G. Loewi.


Collected by the author between the years 1950 and 1959, 170 cases of erythema nodosum, predominantly in adults, have been investigated with particular regard to aetiology. The general pattern demonstrated a spring incidence, a female preponderance (3 : 1), and a maximum frequency in the age group 20 to 29 years. Lesions on the arms were present in 7 per cent. of cases, while all the patients developed lesions on the legs. There was no deviation from the clinical description originally propounded by Willan in 1808, although many patients had constitutional signs such as fever for a few days before the eruption, and 62 per cent. had varying degrees of polyarthralgia. Radiographs, Mantoux and depot

A review of the reported cases of ocular lesions associated with erythema nodosum is given; the most common were scleral and conjunctival nodules and uveitis. A case of erythema nodosum and episcleral nodules is described. Biopsy of the latter showed a histological picture resembling the Aschoff body. The inflammatory reaction was considered to be an allergic response, probably excited by the streptococcus, and the author concludes that these reactions should not be classified among the collagen diseases. *M. C. Handscombe.*


A series of 54 patients (36 women and 18 men) attending or referred to the Whitechapel Clinic of the London Hospital were found to have persistent non-syphilitic reactions to the classic serological tests for syphilis. They had no past history or clinical evidence of syphilis, and the treponemal immobilization test gave negative results in all cases. These patients were observed for one to 5 years and were subjected repeatedly to haematological studies, estimation of the plasma total protein and albumin and globulin levels and of the serum cholesterol level, and investigation of their peripheral blood for the presence of L.E. cells.

During observations, six of the women developed systemic lupus erythematosus with L.E. cells in the peripheral blood, one dying, while one of the men died of periarteritis nodosa. In addition, nine women and five men developed discoid lupus erythematosus or other possible collagen diseases without L.E. cells, and twelve women and four men had various haematological abnormalities such as anaemia or a persistently raised erythrocyte sedimentation rate. The incidence of sensitivity to penicillin in the whole series was high (20 per cent.). As in other reported series, the chronic biological false positive reaction appeared to be of more serious prognostic importance in women than in men. The finding of such a reaction should lead to full clinical investigation and prolonged follow-up. *G. W. Csonka.*


Purpura is a frequent complication in patients suffering from rheumatoid arthritis who have been treated with high doses of adrenocortical steroids. The authors of this paper from the University of Colorado School of Medicine, Denver, describe the clinical and pathological findings in two such cases, and then speculate on the basis of the necrotizing angiitis, commenting on the fact that the lesion is perivascular as well as mural and intramural. Attention is drawn to the prevalence of mast cells in the neighbourhood of the blood vessels and in the loose connective tissues of certain structures and organs. There is evidence in the literature that the mast cell has been implicated in the production of heparin (Jorpes, 1936), hyaluronic acid (Asbee-Hansen, 1950), histamine (Riley, 1953), and serotonin (Benditt, 1955), and it is suggested that cells which produce such potent biological substances must have some important part to play in the chain of events known as the inflammatory reaction. *R. E. Tunbridge.*


Stating that it has been reported that “dietary deficiency of certain polyunsaturated fatty acids results in skin changes in rats not unlike those seen in human psoriasis” the authors describe a trial of these fatty acids in the treatment of six women with psoriasis, six others who received a placebo forming a control group. Most of the patients were given daily six capsules containing 320 mg. soya bean extract and 0-6 mg. pyridoxine, with 0-1 mg. vitamin A as an oxidant; for the control group the placebo capsule contained lactose and vitamin A. The serum lipid content and lipid fractions were fully investigated before treatment, after a fast of 12 hours, and periodically during 3 months’ observation. There was no significant difference between the two groups, no clinical response to the treatment, and the serum lipid levels, which were initially normal, did not change during or after the treatment. *S. T. Anning.*

This paper from King's County Hospital, Brooklyn, New York, presents a re-evaluation of the relationship of renal nodular sclerosis (intercapillary glomerulosclerosis of Kimmelstiel and Wilson) to the course of diabetic disease. The authors studied only cases showing the more severe histological signs—that is, more than half out of a series of twenty glomeruli showing at least one nodule each, the nodules being fibrous, slightly cellular, and located in the intercapillary space. Cases showing only diffuse intercapillary sclerosis and sudanophilic nodules were excluded. Clinically, patients were considered to have acidosi if there had been a history of diabetic coma, ketonuria, or diminished CO₂-combining power.

Of 525 diabetics examined post mortem between 1950 and 1959, forty had kidneys presenting the picture of severe nodular sclerosis. Of these, nineteen had had acidosi. Hypertension had been present in most, and proteinuria in all, of the forty cases. There was no positive correlation with the incidence of pathological changes in the islets. The authors consider their findings to be at variance with the conclusion reached by others (Zubrod and others, New Engl. J. Med., 1951, 245, 518; Abstr. Wld Med., 1952, 11, 52) that acidosi is rare in diabetics showing Kimmelstiel-Wilson renal lesion.

G. Loewi.


This report from King's College Hospital, London, and Stoke Mandeville Hospital, Aylesbury, describes the involvement of the heart in scleroderma in a personal series of 21 cases and in 28 cases found in the literature. There is a full review of previous work, which indicates that the heart is only rarely directly involved by the sclerodematous process. The cardiovascular system may be affected by cor pulmonale as the result of lung involvement, by hypertension secondary to renal scleroderma, or by direct involvement of the heart muscle.

In generalized scleroderma the cardiac symptoms do not appear until late in the disease. They presage early deterioration and death, the average survival being 30 months after the onset of cardiac symptoms. The progress of the cutaneous disease and its relation to cardiovascular symptoms are extremely variable. Dyspnoea, congestive cardiac failure, gallop rhythm, and mitral valvular incompetence occur commonly. Abnormality of rhythm is rare, though atrial fibrillation and flutter do occur. Pain in the chest is a common symptom, though there is no evidence of coronary vascular disease at necropsy. Extensive pulmonary fibrosis may occur with minimal x-ray changes. Pulmonary function may be impaired either as a result of reduced ventilation from involvement of the skin and muscles or of impaired diffusion through an alveolar-capillary block. The kidney may be infiltrated with scleroderma and if this is extensive death occurs from renal failure. Hypertension is unusual and when it occurs is pre-terminal. Death from this cause may be precipitated by steroid therapy.

Radiological investigation shows an enlarged cardiac silhouette; less frequently interstitial fibrosis and cyst formation are seen in the lower lung zones, and pulmonary calcification has been reported. Spontaneous pneumothorax and pleural effusions may complicate the course of the disease. The authors point out that the finding of deposits of calcium scattered throughout the body in any case of obscure cardiopathy is of obvious importance since they may occur in scleroderma unaccompanied by other evidence of the disease. The commonest site is the fingers, especially near the tips, and although such patients usually have severe and obvious sclerodactyly the calcinosis is occasionally an unexpected finding on routine radiology. Although the electrocardiogram may be normal in sclerodematous heart disease, non-specific changes were in fact found in 48 of the present 49 cases. The predominant changes were ventricular extrasystoles, prolonged P-R interval, right bundle-branch block, and T-wave changes. Changes typical of myocardial infarction in the absence of pain were considered to be suggestive of sclerodermal involvement.

The pathological changes in the heart, which, in about half the present cases, was increased in weight, are those of infiltration with collagenous tissue together with atrophy of the intervening heart muscle. The latter occurs without evidence of impairment of blood supply. Pericarditis is common and a verrucous endocarditis may occur. The lung shows fibrosis of the alveolar wall and obliteration of the capillaries. Changes secondary to spillover from the obstructed oesophagus may also be seen. Patchy changes are seen in the kidney, but opinion is divided as to whether involvement of the renal vessels is the prime cause for this as hyalinization of the glomeruli, with capsular thickening and the so-called wire-loop appearance, is also seen.

Treatment is unsatisfactory, though in the authors' experience life may be prolonged by the use of corticosteroids or steroids in high dosage. Care in their administration to patients with renal involvement is necessary, for while two of their patients improved, one died as a result of an exacerbation of renal failure.

J. S. Malpas.


Report of a case of linear scleroderma en coup de sabre of the face. Sectoral atrophy of the mesodermal layers of the iris appeared on the side of the skin lesions within a few months of onset of the disease. Their nature indicated a neurotrophic origin, suggesting a connection between scleroderma and the nervous system which is specially distinct in linear scleroderma. The authors do not believe that linear scleroderma en coup de sabre is identical with Romberg's idiopathic hemiatrophy.

M. H. T. Yuille.

This study, reported from the School of Medicine, Warsaw, was based on the electromyographic examination of fourteen cases of diffuse scleroderma (including acro scleroderma) and twelve cases of morphea. In the former group of patients, all females, 39 muscles, 28 in regions with sclerodermatous changes and eleven in apparently normal regions, were examined. In the four male and eight female patients with morphea electromyograms were recorded from 28 muscles, of which thirteen were in regions of sclerodermatous change and fifteen were in uninvolved areas.

All the patients were examined clinically, and other investigations included capillaryscopy, measurement of sensory chronax and of skin electrical resistance, recording of intramuscular temperatures, and histopathological examination. In recording the electromyograms concentric needle electrodes were used, three electrodes being inserted into each of the muscles investigated at different points and the position of the needle tips repeatedly changed by 5 to 10 mm.

The authors tabulate their findings as follows:
(1) Spontaneous activity;
(2) Reaction to passive movement;
(3) Type of effort pattern;
(4) Intensity of polyphasia;
(5) Peak to peak amplitude;
(6) Mean potential duration.

The results indicated that the features characteristic of myogenic inflammatory lesions comprise a complex interference pattern. Thus disturbances of effort gradation, and low potentials of short duration with a high percentage of polyphasic potentials can be observed in diffuse scleroderma both in muscles underlying involved skin and in muscles distant from such areas. The decrease in potential duration was not only statistically significant, but very marked. In cases of circumscribed scleroderma the abnormal features were noted in muscles underlying the skin lesion, but nine out of fifteen distant muscles examined gave normal electromyographic patterns.

Kenneth Tyler.


Scleroderma Heart Disease: Pathological and Clinical Observations. (La cardiopatia sclerodermica.) CURTARELLI, G., and PASQUARELLO, G. (1960). Reumatismo, 12, 260. 5 figs, 60 refs.


A 47-year-old man with a general disease, probably a generalized periarteritis nodosa, had bilateral central scotomata and acutely increased intra-ocular pressure. The eyes improved on treatment with corticosteroids, but the disease was fatal within 3 years. G. von Bahr.


General Pathology

The authors, working at the Hanusch Hospital, Vienna, have performed the latex-fixation test, the latex-drop test, and the antiglobulin-consumption test on the sera of patients with rheumatoid arthritis. The latex-fixation and the latex-drop tests showed good agreement; thus the sera of 35 of 49 patients with rheumatoid arthritis gave a positive result by both tests and those of seven a negative result by both, a concordance rate of 86 per cent. In the sera of 42 patients with miscellaneous conditions, including three with hepatic cirrhosis, four with Waldenström's macroglobulinaemia, and nine with osteo-arthritis, seven gave a positive result by the drop test. These seven patients were suffering variously from rheumatic fever, cirrhosis, uraemia, osteo-arthritis, or Henoch-Schönlein purpura. It is noted that none of the titres in these seven cases was above 1 : 40, whereas in the patients with rheumatoid arthritis the titres ranged from 1 : 80 to 1 : 1,280.

The antiglobulin-consumption test was performed by mixing the serum with lyophilized homogenate of human parietal and joint capsule tissue. After washing, the ability of the tissue to reduce the titre of an anti-human globulin serum was measured. Of 62 patients with rheumatoid arthritis, the serum of 41 gave a positive result, only 27 being positive in both the antiglobulin-consumption and the latex-fixation tests. It is pointed out that the factor responsible for the antiglobulin-consumption test could be absorbed by lyophilized joint tissue without altering the titre in the latex-fixation test. The authors had earlier shown that lyophilized brain tissue was inactive. In conclusion they stress the rapidity of the latex-drop test and its good correlation with the latex-fixation test. They conclude that two different serum factors occur in rheumatoid arthritis and raise the question whether the rheumatoid factor combines in vivo with the factor responsible for the antiglobulin-consumption test.


The authors have previously shown (J. exp. Med., 1959, 110, 875; Abstr. Wild Med., 1960, 28, 54) that a fluorescein-labelled aggregated human gamma-globulin (F.A.A.G.) was a sensitive reactant for the detection of the 19S macro-globulin complex known as "rheumatoid factor" in preparation of cells and tissue sections. They further report from the Hospital for Special Surgery in New York, describes similar observations utilizing another fluorescent immune complex (F.I.C.) (rabbit antibody to bovine albumin). In this test 127 specimens of synovial and lymph-node tissue from nine cases of rheumatoid arthritis and 83 from twelve control patients without rheumatoid arthritis were subjected to examination. The specificity of the fluorescent staining attributable to the rheumatoid factor was confirmed by inhibition of the reaction by previous exposure to similar complexes without the labelled fluorescein element.

It was shown that a small proportion of the cells in the richly cellular inflammatory exudate stained with F.I.C., these being plasma cells, both immature and mature and also those of the Russell-body type. (A greater number of cells stained with F.A.A.G., however, than with the F.I.C.) Similar differentiation was obtained by variation of the inhibiting reagents. Two categories of cells in lymph nodes were found to contain rheumatoid factor detectable with F.I.C., namely, the germinal centre cells and the plasma cells; the former may be numerous in hyperplastic lymph nodes. None of the control specimens showed positive staining with the single exception of a specimen from a patient with Waldenström's macroglobulinaemia, which reacted positively with F.A.A.G. and with a fluorescent antibody for macroglobulin, but did not react with F.I.C. It is therefore concluded that while there is much that is consistent with the hypothesis of the rheumatoid factor being an antibody directed to an altered human gammaglobulin and cross-reacting with rabbit gammaglobulin, the authors suggest an alternative explanation, namely, that there may be several rheumatoid factors directed against different antigenic components of aggregated human gammaglobulin, some of which are present also in the rabbit serum. F.I.C. In an addendum to this paper they announce...
the preparation of fluorescent reactants in contrasting colours by means of which differential staining of plasma cells can be produced, thus supporting at least a dual nature of cellular rheumatoid factor.  

Harry Coke.

Rapid Precipitation of the Rheumatoid Factor in a Solution of Boric Acid and Titration by the Agglutination Sensitized Human Erythrocytes.  
(Precipitation rapide du facteur rhumatoïde dans une solution d'acide borie et titrage par l'agglutination des hématies humaines sensibilisées.)  

A rapid and simple method of precipitating the rheumatoid factor from sera for testing by haemagglutination is described. It was found that if the serum was diluted in 20 volumes of 2 per cent. boric acid solution an adequate precipitate containing the rheumatoid factor could be obtained after 30 minutes. This fraction was shown to constitute, on average, 13.6 per cent. of the serum total protein content in sera from patients with rheumatoid arthritis. It is claimed that this method of separating the globulin fraction is superior to the use of citrate-phosphate buffer both by enabling a greater amount of precipitate to be obtained in a short time and also by giving a more clear-cut result in the subsequent haemagglutination test. It is suggested that this rapid and complete precipitation of the rheumatoid factor is due to a combination of boric acid with polysaccharides which are known to be present in quantity in the rheumatoid factor.  

G. W. Csonka.

Clinical Study of Serum Antinuclear Factor.  
Brit. med. J., 1, 933.  39 refs.

This paper from the MRC. Rheumatism Research Unit, Canadian Red Cross Memorial Hospital, Taplow, describes the application of Coon's fluorescent antibody technique to the demonstration of an antinuclear factor (A.N.F.) in the serum of patients with systemic lupus erythematosus (S.L.E.) and certain other disorders. Sections of human infant thyroid tissue were incubated with test serum at 37°C for 30 minutes and after careful washing were stained with a fluorescein isocyanate or isothiocyanate conjugate with anti-human-globulin serum. Under controlled conditions a nuclear fluorescence indicated a positive reaction for A.N.F. [It is stated that the positive nuclear fluorescence indicates an uptake of globulin from the test serum. Since some of the antisera used were directed against whole human serum, it is not clear which globulin component is being demonstrated.]

Positive A.N.F. reactions were obtained in 62 (98 per cent.) out of 63 cases of S.L.E., nineteen (14 per cent.) of 132 of rheumatoid arthritis, thirteen (13 per cent.) of 100 of Still's disease, and ten (13 per cent.) of 75 of discoid lupus erythematosus. Positive reactions were also obtained in 13 per cent. of 100 cases of thyroid disease and 39 cases of liver disease. The reaction was negative in 56 cases of rheumatic fever and in 131 of 133 normal subjects. It is concluded that, although in S.L.E. the A.N.F. reaction is persistently positive, a positive reaction is not in itself of diagnostic value.

The authors suggest that the A.N.F. in patients with S.L.E. may be the same as the factor responsible for the L.E.-cell phenomenon and they discuss the significance of the test from the diagnostic and aetiological points of view and in the light of Burnet's clonal theory.  

Hewett A. Ellis.

Latex-Fixation Test using British Latex and Bovine Gamma Globulin.  
J. clin. Path., 14, 309.  12 refs.

This paper from the Welsh National School of Medicine, Cardiff, records investigations into the use of bovine γ globulin and a British preparation of polystyrene latex particles in the latex-fixation test for rheumatoid arthritis. Initial investigations demonstrated that spontaneous agglutination occurred in a standard latex suspension with bovine γ globulin in two ranges of concentration—

\[3.1 \times 10^{-1} \text{ to } 9.8 \times 10^{-4} \text{ g. per 100 ml. and } 3.9 \times 10^{-4} \text{ to } 4.9 \times 10^{-5} \text{ g. per 100 ml.}\]

All concentrations from 2.5 g. per 100 ml. to nil were tested and, with the exception of these specified ranges, no agglutination occurred. In the presence of serum from patients with rheumatoid arthritis agglutination failed to occur with concentrations of bovine γ globulin of 6.3 \times 10^{-1} \text{ g. per 100 ml. and above. At concentrations between } 6 \times 10^{-3} \text{ and } 7 \times 10^{-4} \text{ g. per 100 ml., it was possible to obtain agglutination titres with a clear end-point. Prozoning did not occur as it did with concentrations of } 4 \times 10^{-3} \text{ g. per 100 ml. or below. A concentration of } 5 \text{ or } 0 \text{ mg. per 100 ml. was found to be the most satisfactory to give the highest titres with the majority of positive sera. Further experiments showed that the highest titres were evolved by bulk heating of the latex and γ globulin mixture and then adding it to the serum dilutions after cooling.}

Duplicate tests were made on 300 specimens of serum using a standard latex test based on these principles and the sensitized sheep cell test as modified by Greenbury and Ball, with plastic agglutination trays. Assuming the result of the latex test to be positive with agglutination to a titre of 1:80 or greater, there was agreement in 264 of the 300 tests (88 per cent.). Some analysis is made of the cases giving divergent results, which, it is noted, included a number of cases of rheumatoid pneumoconiosis. The technique of the standard test evolved is set out in detail and shown to be inexpensive, easy, and quick to perform. The titres obtained by this latex technique showed no correlation with those of the sensitized sheep cell test. In an addendum the results of a comparison of this latex test and the Hyland R.A. test, which utilizes human γ globulin as the reactant are reported. Agreement in 135 of 141 cases (95.7 per cent.) is recorded.  

Harry Coke.

The rheumatoid factor in serum has been shown to react with the agglutinate latex particles coated with polysaccharides such as heparin, chondroitin sulphate, and hyaluronic acid. The authors had shown also the binding of the rheumatoid factor with the polysaccharide dextran. This paper describes a study of the protein substance coating the erythrocytes of patients with rheumatoid arthritis and the removal of this substance by admixture with 3-6 per cent. dextran in physiological saline solution. After separation by centrifugation the supernatant was tested for agglutinating capacity by the standard latex-fixation test of Singer and Plotz. Initial saline washings of the erythrocytes never produced agglutinating capacity; the dextran washings, however, produced agglutination up to 1 : 64, with the majority at 1 : 4.

The erythrocytes of 196 patients out of 197 with classic rheumatoid arthritis produced positive agglutination. In further tests the number of positive results decreased with the grade of the disease, down to 65-2 per cent. in cases of "possible" rheumatoid arthritis. In 38 cases of definite rheumatoid arthritis in which the serum was negative with the latex and y-globulin latex-fixation tests, positive results were obtained by this method. Some positive results (35) were also obtained in a series of 92 cases of other "rheumatic disease syndromes", and nine positive results in a series of 141 non-rheumatic conditions. These results showed that the erythrocytes of patients with rheumatoid arthritis are coated with a protein substance which is similar in nature to the rheumatoid factor, and that this substance cannot be removed by saline, but is eluted by dextran solutions of Fraction II, sialic acid, or dextrrose.

Harry Coke.

Contribution to the Study of Sjögren's Syndrome.

In three cases of Sjögren's syndrome the author studied the histopathology of the glands and hairs of the axilla. Manifold rows of coiled apocrine glands showed atrophy and degeneration. Giant tubulae with amorphous and atonic walls were found. The cells showed degenerative mitochondria and a degenerate Golgi apparatus. The eccrine sweat glands showed a vacuolar granulation to a lesser degree. The sebaceous glands appeared to be atrophied and the hair follicles showed degeneration of the outer hair sheath. Iron was not found in the disordered apocrine glands.

G. von Bahr.


A serum agglutination test which is positive in rheumatoid arthritis proved to be negative in uveitis.

Paul W. Miles.

Current Concepts of Autoimmunization: An Interpretive Review.

Studies in the Laboratory Estimation of Rheumatoid Arthritis Serum Factor.
ABSTRACTS


ACTH and Other Steroids


At the Royal Victoria Infirmary, Newcastle upon Tyne, dexamethasone tertiary-butylacetate, in the form of “decadron T.B.A.”, was injected into the knees, ankles, and wrists of twelve patients suffering from rheumatoid arthritis. The compound was also administered to two patients with osteo-arthritis of the knees, one patient with gout, and one with systemic lupus erythematosus. In all cases the compound was used in a concentration of 4 mg. per ml. The results were compared with those obtained from the intra-articular injection of hydrocortisone acetate, 25 mg. per ml. The investigation was controlled by injecting decadron T.B.A. into one joint and hydrocortisone acetate into the contralateral joint. Assessments were made at weekly intervals until a relapse occurred. Criteria of assessment included assuagement of pain and tenderness, diminution of joint swelling, and increase in the range of movement. A similar study was also undertaken in a series of fifteen patients—thirteen with rheumatoid arthritis and two with osteo-arthritis—prednisolone acetate, 25 mg. per ml., being administered in place of hydrocortisone. Analysis of the data revealed that in both investigations decadron T.B.A. gave better results. No side-effects were observed in either series.

When the water-soluble phosphate ester of dexamethasone, in a concentration of 4 mg. per ml., was injected into extra-articular lesions such as pericapsulitis of the shoulder, subdeltoid bursitis, and tenosynovaginitis the outcome was again regarded as highly satisfactory, failure to obtain relief being recorded in only one of thirty cases. The dosage ranged from 1 mg. in a case of digital inflammation associated with Heberden's nodes to 12 mg. in cases of pericapsulitis of the shoulder. Local anaesthesia was not required. A satisfactory response was noted within 24 hours, and many patients experienced relief within 6 hours. As compared with hydrocortisone, dexamethasone phosphate produces a more rapid response with a minimal degree of local irritation. In one case, however, there was an exacerbation of the symptoms of duodenal ulcer 3 days after a substantial dose of the latter compound had been injected into the shoulder capsule.


This paper, from the Presbyterian-St. Lukes, Cook County, and Research and Educational Hospitals (University of Illinois College of Medicine), Chicago, describes the results of treating 26 patients with lupus glomerulonephritis with steroids. The diagnosis was based solely on the initial renal biopsy findings and two groups of patients were studied.

The first (low-steroid) group consisted of ten patients observed from 1953 to 1955 and treated with an average of 50 mg. cortisone daily to control symptoms. All of these patients died, five within 6 months, the longest and average survival being 42 and 13·8 months respectively.

The second (high-steroid) group consisted of sixteen patients observed from 1956 to 1958 and treated with a minimum dose of 40 mg. prednisone daily for 6 months. Seven died, three within one month and the others at 5, 22, 26, and 41 months respectively. Nine are still living after 34·2 months. Evidence was obtained by a comparison of the clinical features, renal function data, and histological findings to show that the two groups were comparable at the time of the initial renal biopsy. Renal biopsies were carefully assessed by grading the changes in the glomeruli, tubules, and interstitial tissue and vessels from 0 (normal) to 4 (extremely severe and affecting all or almost all of the particular structures). Features considered to be evidence of active and progressive lesions included fibrinoid change, local necrosis, karyorrhexis, haematoxyphil bodies, “wire-loop” lesions, and hyaline thrombi. Serial renal histological studies to a total of 25 were carried out on eight patients in the low-steroid group and 37 of nineteen in the high-steroid group. In the former histological evidence of activity persisted and increased in severity, whereas in the latter it was unchanged or diminished. In ten of the high-steroid group evidence of activity disappeared, although irreversible lesions such as thickening of the glomerular basement membrane and capsular adhesions persisted.

A number of complications were observed in the high-steroid group. Thus fifteen of the sixteen developed marked Cushing's syndrome, while four had miscellaneous infections, one a perforated peptic ulcer and sub-
Eye, Ear, Nose, Thr. Monthly, 40, 266. 2 refs.

An investigation of two series of cases revealed posterior subcapsular cataracts in ten of 260 cases not under treatment with steroids, and in five of 86 cases treated with steroids. In the latter group 23 patients were found to have lens changes.

It is suggested that steroids per se may not be the cause of cataracta complicata and that the causal role of rheumatoid arthritis is uncertain. J. R. Hudson.


Three groups of cases are considered, 45 rheumatoid arthritis patients of the author's own series, 206 rheumatoid arthritis cases of co-operating physicians, and 106 non-rheumatoid arthritis cases from the latter source. In these groups the incidence of posterior subcapsular cataracts was 9, 9, and 7 per cent. respectively.

There was no definite correlation between the occurrence of posterior subcapsular cataract and the size of the daily dose of corticosteroid or the duration of such treatment.

More extensive studies will be needed to determine what relation, if any, the occurrence of posterior subcapsular cataracts has to corticosteroid treatment in rheumatoid arthritics, or to the activity of the rheumatoid arthritis. J. R. Hudson.


This study of the effects of x-irradiation on adrenal cortical function was carried out at the Letterman Army Hospital, San Francisco, on nine patients with testicular tumour who were undergoing abdominal irradiation and in whom the adrenal glands were included in the treated volumes. Adrenal function was estimated before, during, and for 3 months after the period of irradiation by determining the urinary excretion of 17-ketosteroids and 17-hydroxycorticosteroids in 24-hour specimens of urine. The response to injections of ACTH was used as an additional more sensitive index of "adrenal reserve". The radiation was generated at 220 kV and was filtered to a H.V.L. of 1-35 mm. Cu. Portals of the order of 15 x 30 cm were used, usually as paired anterior and posterior fields, and the position of the adrenal glands was estimated with reference to the upper poles of the kidneys on a radiograph of the abdomen. The dose of radiation delivered to the adrenal glands varied between 1,569 and 3,526 r. delivered over 28 to 37 days.

Since the estimation of 17-hydrocortisone excretion was found to give less erratic results than that of 17-ketosteroid excretion most of the conclusions are based on the former. The following effects were seen:

1) There was usually an enhanced response to a 1-day injection of ACTH during the period of irradiation, this being in agreement with Selye's general adaptation syndrome and the accompanying adrenal response to stress.

2) There was also usually some reduction in the response to a 1-day injection of ACTH after completion of irradiation.

3) In some cases the 2-day ACTH injection test (the Thorn test) gave a lower response on the second day than on the first, this occurring especially towards the end of the period of irradiation. Normally the response on the second day is higher than on the first, so that the 2-day ACTH test may be a more sensitive gauge of the effect of irradiation.

It is concluded that to obtain more definitely significant data a similar trial should be instituted using, for example, mediastinal irradiation as a control, as it is not certain that the adrenal effect is necessarily due to direct irradiation of the adrenal glands. I. D. H. Todd.


Other General Subjects


Of the various products with an analgesic and antipyretic action, "pyramidon" (amidopyrine) and its derivatives are the most effective, but their use is strictly limited by their toxicity and tendency to provoke haematological changes. In this report from the Centro Traumatologico, Bologna, the author describes his experience with "Tomanol", a recently-introduced compound consisting of two parts of 4-isopropylamine-1-phenyl-2,3-dimethylpyrazolone and one part of phenylbutazone, in the treatment of 84 patients, of whom three were suffering from acute articular rheumatism, 32 from rheumatoid arthritis, two from ankylosing spondylitis, fifteen from deforming osteo-arthritis or spondylarthritis, ten from periarticular, epicondylitis, myositis or tendinitis, ten from various neuritic affections or root pain after intervention for disk hernia, and twelve from osteo-articular and muscular post-traumatic affections. The drug was administered preferably by intramuscular injection, but was also given orally as a suppository, the dosage varying for each individual case.

Therapeutic effects were rapid and noteworthy in acute and inflammatory cases and in the reactivation phases of chronic cases, but less so in mainly degenerative forms; post-traumatic and non-articular conditions responded particularly favourably to the treatment. The author found that carefully chosen patients tolerated the remedy well, provided a diet poor in salt was given. He stresses that frequent blood counts should be performed when treatment is protracted, and patients who have suffered previously from gastric or duodenal ulcers must be treated with circumcision; all patients with active ulceration of the gastro-intestinal tract or severe cardiovascular or hepatic insufficiency were excluded from the trial. The over-all therapeutic results were as follows: very good in 41 per cent., good in 34-5 per cent., and fair in 12 per cent., while no benefit was obtained in 9-5 per cent. Side-effects, which occurred in 16-5 per cent. of the cases, included nausea, hyperacidity, and vomiting in seven cases, oedema in four, and a rash and pruritus in three. No cardiac or renal complications occurred and no case of agranulocytosis was seen.

Robert E. Lister.

Phenylbutazone and Leukaemia: a Possible Association. Bean, R. H. D. (1960). Brit. med. J., 22, 1552. 4 figs, 5 refs. The author of this paper from the Repatriation General Hospital, Heidelberg, Victoria, Australia, describes six cases of leukaemia occurring in elderly males who had all recently been treated with phenylbutazone. The dosage and duration of treatment had varied from 10 g. given over a 3-week period to several hundred grammes given over 4 years. In one case there appeared to be a definite progression from an early toxic reaction to the development of myeloid leukaemia and death therefrom 18 months later. All the patients were rather poorly nourished and three had tuberculosis. Hypogammaglobulinaemia was found in two cases. In three of the more acute cases the morphology of the peripheral blood and bone marrow was atypical, aplasia and haemolysis being present. Lymphatic proliferation predominated in three. In all but one case the leukaemic phase was extremely short and treatment produced at best only transitory improvement.

A. Ackroyd.


Phenylbutazone has proved useful in the treatment of rheumatic disorders and toxic effects appear to be uncommon provided the dosage does not exceed 400 mg.
a day and it is not given to aged patients or those with dyspepsia or cardiac disease. Nevertheless, side-effects do occur from time to time and in the search for a nontoxic derivative with the same antirheumatic action two substances of interest have been synthesized, both of which are metabolites of phenylbutazone. One of these, oxyphenbutazone (G 27202; “Tanderil”), has been found to have, like phenylbutazone, antirheumatic properties, its effect on the inflammation of acute gout being especially striking, although it has no effect on the excretion of uric acid. The other drug, G 28315, has no clinical effect on acute gout, but it is powerfully uricosuric.

The purpose of the present communication is to record the author’s clinical observations with tanderil. He considers that its effect is so striking that rigidly controlled trials are unnecessary. In a daily dosage of 300 mg he found the substance to be less toxic, but also less effective, than phenylbutazone. A dosage of 800 mg daily for 3 consecutive days in every 6 was tried in 43 cases—thirteen of rheumatoid arthritis, two of osteoarthritis, seventeen of local fibrosis, and eleven of multiple fibrositis. Patients reported by telephone on their rheumatic symptoms and general well-being. In more than one-half of the group the effect was “striking” and in one-quarter it was as good as that of phenylbutazone. Nine patients reported toxic effects. A dosage of 600 mg daily for 5 days of each week was tried on fifty patients suffering from similar disorders. A rather smaller proportion gave a “striking” response than with the 800-mg. dosage, but toxic symptoms occurred in only six cases.

[The author’s reasons for not accepting the need for a controlled therapeutic trial are not convincing. His figures purporting to show a difference in toxic effects and in the proportion showing “striking” improvement between the 600-mg. and 800-mg. dosage schemes are not statistically significant.] Kenneth Stone.


Writing from Louisiana State and New York University Schools of Medicine, the authors briefly review the literature of rheumatic phlebitis. They then describe a type of lesion of the coronary sinuses found in cases of active rheumatic heart disease. The material used consisted of nineteen histological sections from eighteen cases of active rheumatic heart disease which included the coronary sinus. This was compared with comparable material from 35 individuals without evidence of rheumatic disease.

Of the eighteen cases of rheumatic disease, lesions were present in the coronary sinus in ten. An acute inflammatory reaction of the sinus was found in eight cases, in five of which Aschoff bodies were also present in the adventitia. Aschoff bodies were seen in the adventitia without other reaction in one case. In three cases there were bands of eosinophilic material in the intima and an acute inflammatory reaction with Aschoff bodies in the adventitia. The lesions involved only sectors of the sinus wall and in structure closely resembled those of rheumatic endocarditis. No thromboses were present. Healed lesions were seen in five cases, in four of which there were also acute lesions. The phlebitis apparently developed and healed rapidly and the presence of acute and healed lesions in the same sinus indicated that the vessel was being damaged repeatedly. None of the controls showed similar lesions. R. Wyburn-Mason.


The author describes his experience extending over a period of 9 years at the General Infirmary at Leeds of skin cooling by ethyl chloride spray in the treatment of various painful conditions. In acute lumbago 20 to 30 seconds spraying of the lumbar region causes the scoliosis and pain to disappear. Rest in bed for a number of days is advised before return to work, although some patients are able to return the same day. Chronic low backache does not respond quite so dramatically. Acute torticollis is relieved by this treatment, and it is claimed that a single application may relieve pain in patients with fibrosis, painful scars, and causalgia. In renal colic application of the spray from the renal angle to the pubes gives immediate relief, but the treatment may have to be repeated as the stone passes down the ureter. Similarly, dysmenorrhea can be relieved by spraying the hypogastrium for 15 to 20 seconds. In cases of fractured rib treated by local infiltration of procaine prolonged relief of residual pain is obtained by this method of skin cooling.

The author discusses the rationale of the treatment and suggests that there is a competitive inhibition between cold and pain impulses in the central pain receptor areas.

It is emphasized that the skin should be cooled and not frozen (the usual type of spray is not ideal for this) and that all the skin of the appropriate dermatome should be cooled for 15 to 30 seconds. Since ethyl chloride is inflammable, toxic, and anaesthetic, a new inert liquid in a spray pack “skefron” has been tried, with comparable results.

J. B. Millard.


The author reports two cases of rheumatic uveitis appearing after cataract extraction. The uveitis was torpid and in each case the patient had had polyarthritis some years before.

J. Rougier.


Rheumatism is an illness of the cardiovascular system and capillary-connective tissue and so is classified as a collagen disease. The author has performed ophthalmodynamometry on 32 rheumatic patients and discusses the significance of the findings. [It is not clear what the author means by “rheumatism”.] B. Jay.

Two cases of rheumatoid arthritis which show a combination of scleromalacia perforans and massive granuloma of the sclera are reported. Histological findings are given and both lesions are considered to be ocular manifestations of rheumatoid arthritis.

M. C. Handscombe.


