ABSTRACTS

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Acute Rheumatism


The numerous published reports on the relative merits of salicylate and corticosteroid therapy in suppressing rheumatic activity are reviewed, the authors concluding that the evidence that corticosteroids prevent or minimize heart disease is still inconclusive. They suggest that at the present time salicylates are the treatment of choice in patients with arthritis alone or associated with only mild carditis. Corticosteroids (usually for 7 to 10 days) may be of value if there is any significant carditis of recent onset and it may be necessary to give these drugs for a somewhat longer period in patients with marked carditis enlargement or heart failure at the onset of the illness. The complete failure of chorea to respond to either form of therapy is discussed. The place of rest in bed is critically appraised; the authors state that it would seem reasonable in rheumatic fever to allow rapid ambulation when there is little or no carditis, but patients with moderate or severe carditis are best treated by prolonged rest in bed followed by graded physical activity. There would appear to be no place for massive penicillin therapy, but an initial “10-day course of conventional therapeutic doses” should eradicate streptococci and this should be followed by prophylaxis with penicillin or sulphonamides.

The authors conclude that “it is fortunate”, in view of the many gaps in our knowledge, “that the incidence and severity of the initial attacks of rheumatic fever appear to be declining and that recurrences can be prevented by anti-streptococcal prophylaxis”. B. M. Ansell


The place of early treatment of rheumatic fever in the prevention of residual heart disease was studied in 264 patients admitted to Irvington House, Irvington-on-Hudson, New York, during a first attack of rheumatic fever. There were three treatment groups:

1. Salicylates only;
2. Corticosteroids with or without salicylates;
3. No anti-inflammatory drugs (the number of patients in the last group was very small).

Incidental comparison of the results of treatment showed that there was no appreciable difference between patients given salicylates and those given corticosteroids or combined treatment.

There was residual heart disease in 24 per cent. of the patients who started treatment in the first week of the illness and in 84 per cent. of those in whom treatment was delayed 4 weeks or longer. On further analysis it appeared that patients with arthritis (77 per cent. of the total) sought treatment early and that in this subgroup the incidence of carditis was low (29 per cent.). On the other hand, in the remaining patients who had no objective arthritis and sought treatment later the incidence of carditis was high (87 per cent.).

It was clear that all patients with severe carditis had residual lesions, while patients without carditis had none. In the group of 83 patients with mild carditis the incidence of residual lesions was 70 per cent. Of these 83 patients 53 had arthritis initially and the remaining thirty were non-arthritis. The pre-treatment interval had no effect on the frequency of residual cardiac effects.

The authors conclude that early treatment has not yet been shown to produce significant cardiac benefit in rheumatic fever. K. C. Robinson


There are conflicting views about the relation of psychological factors and the intelligence of the patient to the severity of the psychological sequelae, if any, of
Sydenham's chorea. The psychological aspects of the disease have never been investigated on a representative sample with adequate controls. The difficulty of obtaining a large enough number of patients who can be followed up over a long period has hampered previous studies and "has not been completely overcome in the present investigation". The present authors have studied four groups of children admitted to hospitals attached to the New York University School of Medicine.

I. Four girls and six boys studied during an attack of chorea.

II. Selected from 150 children with rheumatic fever but without chorea to match Group I for sex, age, race, religion, family composition, and cardiac diagnosis.

III. Four girls and six boys who, of sixty patients who had recovered from chorea, seemed to have had the most severe or prolonged attacks.

IV. Selected from 300 children who had recovered from rheumatic fever without chorea and who matched Group III.

There were no significant differences in the full scale scores or the scores in the verbal and performance scales of the Wechsler intelligence scale for children. The mean full scale I.Q.s for the four groups were 80-5, 88-6, 92-7, and 90-8 respectively. The subtest scores of patients in Group I were inversely related to the motor demands of the test. In response to the thematic apperception test the children in Group I chose a passive principal character who tended to be helpless and victimized more often than those in the other groups, but otherwise there was no significant difference between them. The scores of Group I in the Bender-Gestalt test were significantly lower than those of the other groups, the difficulty with the test being related to the degree of motor incoordination. Differences in responses to Rorschach tests were small, highly variable, and not significant. The drawings of people by Groups I and III differed significantly from those by the control groups in the frequency of absent or poorly-drawn hands. This was the only evidence of any residual psychological disability among the patients who had recovered from chorea. Other drawings by Group III showed more detail than those by Group IV.

The authors conclude that the psychological impairment in Sydenham's chorea is minimal and reversible and that most of the psychological difficulties are a direct consequence of the child's motor impairment or are the result of attitudes and reactions in other people who deal with the child, reactions evoked by the child's motor impairment (such as impatience and punishment). That the psychological disabilities demonstrated are not a direct consequence of the pathological process of the disease itself is also suggested by their positive relation to the motor impairment and their recovery when this subsides.

Christopher Wardle


From 1947 to 1960 a total of 4,264 children were referred to La Rabida Sanitarium, Chicago, with a diagnosis of suspected rheumatoid disease; but 455 (10.6 per cent.) of these were found to be suffering from some other condition such as acute pharyngitis, dental caries, or infection of the upper respiratory tract. In 455 patients with non-rheumatic disease it was such manifestations as low-grade persistent fever, heart murmurs, and polyarthritis which had led to a mistaken diagnosis of rheumatic fever. A history of streptococcal infection was obtained in fifteen cases, and 173 patients had an erythrocyte sedimentation rate (E.S.R.) of more than 20 mm. in the first hour (Wintrobe).

The authors point out that a number of minor ailments of children may be mistaken for rheumatic disease. Errors in diagnosis may be avoided by employing a modification of the Jones criteria for rheumatic fever as promulgated by the American Heart Association in 1955. Differentiation is required between arthritis and arthralgia, and between the murmurs of rheumatic heart disease and innocent murmurs or the murmur of aortic anatomic congenital heart disease. The presence of streptococcal infection should be confirmed by bacterial culture. An increase in antistreptolysin-O titre should not necessarily be regarded as an indication that the patient is suffering from rheumatic fever. Furthermore, the E.S.R. may be increased not only in rheumatic fever but also in pharyngitis, infection of the respiratory tract, and a number of other diseases. Establishment of the correct diagnosis determines the early use of corticosteroid therapy in the management of rheumatic endocarditis as well as the use of prophylactic measures against a recurrent attack of rheumatic fever.

A. Garland


The authors review their experiences at the General Rose Memorial Hospital, Denver, Colorado, with the percutaneous transthoracic route of left atrial puncture in the assessment of fifty patients with lesions of the mitral valve, and in particular its value in differentiating mitral stenosis from mitral regurgitation. The procedure induced some degree of pleural pain in all fifty patients, and there were individual cases of pericardial tamponade and pulmonary haemorrhage, two of pneumothorax, and one of pulmonary infarction and fever. However, no permanent disability resulted and no patient died. In five cases the left atrium could not be entered, and in a further ten the catheter could not be advanced from the atrium into the left ventricle.

In 25 patients left atrial pressure curves were obtained that were suitable for analysis and for comparison with the findings at operation. Various formulae derived from the v wave and the y descent were tested, but none gave a reliable indication of the nature of the mitral lesion as assessed by the surgeon's finger at operation. In the other 25 cases left atrial pressure curves could be compared with pulmonary wedge pressure curves obtained at right heart catheterization; all gave good correlation.

It is concluded that recordings derived from direct left
atrial puncture by this method add nothing that cannot be
obtained by safer means. In the authors’ view the best
assessment of the mitral lesion remains that obtained by
clinical evaluation, supplemented by right heart
catheterization and, if still necessary, left atrial puncture
at the time of operation. J. A. Cosh

Studies of the Role of Continuing or Recurrent Strep-
tococcal Infection in Rheumatic Valvular Heart Disease.
GUASCH, L. J., VIGNAU, I. A., MORTIMER, E. A., JR.,
Sci., 244, 290. 23 refs.
The serum antistreptolysin-O titre was determined in a
total of 260 children seen at the Manuel Arriarán and
Roberto del Rio Hospitals, Santiago, Chile, who had had
an attack of rheumatic fever between January, 1950, and
December, 1956. There was a suggestive but statistically
insignificant tendency for the titre to be higher in patients
with heart disease. A difference approaching significance
was observed in the titres in siblings of patients grouped
according to absence of valvular heart disease or severity
of cardiac involvement if present. The authors state that
“the most likely interpretation of this finding is that there
had been a higher incidence of relatively recent infections
in the homes of patients with valvular heart disease than
in the homes of patients without organic valvular
damage”. Thus there is probably a relationship between
the degree of valvular damage and prevalence of strepto-
coccal infection in family contacts.
The findings confirmed previous observations of an
association between recurring rheumatic fever and more
severe heart disease. There was no evidence indicating
whether recurrent infection leads to valvular disease or
whether valvular disease predisposes to further infection.
On the basis of their findings the authors emphasize the
importance of prophylaxis against streptococcal infection
in patients who have had an attack of rheumatic fever.
E. H. Johnson

Changes in Cardiac Status in the Course of Rheumatic
Carditis in Childhood. (Die Änderung der Herz-
tätigkeit im Verlauf der rheumatischen Karditis im
87, 2013. 7 figs, 11 refs.
At the University Paediatric Clinic, Leipzig, 89 cases of
rheumatic carditis were seen during the period 1957-60, of
which 81 were in children between 6 and 14 years of age;
the sexes were almost equally represented. In 61 cases it
was the first attack of rheumatic fever, but in the remain-
ing 28 it was a recurrence. Of the 89 children eight died,
21 recovered completely, and sixty were left with valvular
defects which in 41 cases affected the mitral valve, in five
the aortic valve, and in the remainder both these valves.
In eighteen of the 21 patients who made a complete
recovery the attack was the first one.
Serial study of phonocardiograms was found to be of
value since it showed either the progressive development
or reduction of cardiac murmurs. The electrocardio-
gram (ECG), however, had a more immediate prognostic
significance; thus of twenty children with normal ECG
tracings none died and sixteen made a complete recovery.
Radiographs showed cardiac enlargement in 81 of the 89
cases; all the eight patients with a normal heart size were
among those who recovered without cardiac damage. It
is of some interest that of the sixty children with residual
valve defects forty were thought to have mitral insuffi-
cency and only one mitral stenosis. [This unusual
finding is presumably due to the relatively short follow-up
period.] A. J. Karlish

Pulmonary Fibrosis in Rheumatic Heart Disease.
4 figs, bibl.
Occasional cases of advanced rheumatic heart disease
differ from the familiar picture of chronic passive con-
gestion complicating mitral valvular disease. Although
in these cases, as in the usual valvular type, the lungs are
infiltrated, they are relatively pale and dry and micro-
scopically show a distinctive type of interstitial fibrosis.
It seems more probable that in such circumstances right
ventricular failure is due to the abnormally high resistance
of the lung to perfusion because of the fibrosis, rather
than to obstruction by the mitral valve. The present
review from Middlesex General Hospital Laboratories,
New Brunswick, New Jersey, is based on the analysis of
the pulmonary findings in 166 selected cases out of 270 of
rheumatic heart disease coming to necropsy; these were
divided, according to the type and degree of fibrosis, into
disseminated or focal interstitial fibrosis.
(1) Disseminated interstitial fibrosis was found in 41
cases (25 per cent.). Of these patients the majority (28)
were under 50 years of age. Grossly, the lungs were firm
and the cut surface was mottled. Microscopically, there
was a patchy network of irregularly distributed fibrosis
within the lobules, generally most pronounced about the
bronchioles, blood vessels, and supporting septa. The
alveolar epithelium tended to be swollen, and the
capillaries were narrowed and relatively bloodless.
Dense scars had formed in a few areas. In general, the
fibrosis was most conspicuous in the lower parts of the
lungs. The lymphatic vessels, which were easily
demonstrated in lungs fixed in inflation, were excessively
wide (lymphangiectasia). A peculiar blanched appear-
ance, referred to as the “anaemic lung phenomenon”,
was observed in twelve of the 41 cases of disseminated
interstitial fibrosis. The blanched areas comprised one
or more pulmonary segments, and microscopically the
capillaries in the affected areas were empty. The fibrosis
in the arteriolar walls appeared to be severe, although the
alveolar walls themselves were normally thin and delicate.
(2) Focal interstitial fibrosis was encountered in 47
patients (28 per cent.), of whom all but five were aged 50
or over and thirty were males. Grossly there were widely
scattered, minute patches and dots of slight induration,
made visible by accumulation of anthracotic pigment.
Microscopically the fibrosis was mainly peribronchial and
pervascular and extended from these structures into
the surrounding alveoli. The affected alveoli were
contracted and showed adenomatoid metaplasia. Neigh-
bouring alveoli were occasionally hyperinflated. Some bronchi were widened, while others were constricted by peribronchial fibrosis which also affected the accompanying small arteries. In 64 cases there was no, or only minimal, evidence of pulmonary disease.

This study thus showed that in 88 of 166 cases of rheumatic heart disease there was interstitial fibrosis of the lung, which could be attributed to repeated episodes of inflammation. No causal relationship was found between mitral valvular disease and chronic passive congestion combined with interstitial fibrosis of the lung. Intractable right heart failure was a major feature in thirty cases and was invariably associated with disseminated pulmonary fibrosis and recurrent pulmonary infection. Signs of peripheral circulatory collapse had frequently occurred in these cases during attacks of acute pulmonary inflammation. The author concludes that these findings underline the vulnerability of these patients to secondary viral and bacterial infections of the lung.

In addition to the 166 cases under survey, fifteen cases of primary lung cancer were encountered among the 270 cases of the parent series, an incidence of over 5 per cent. Numerous cases of “scar cancer”, usually of alveolar-cell type, have been described in the literature. Among the fifteen cases in this series eight were classified as “alveolar-cell adenocarcinoma”. A. W. H. Foxell


Evidence has been presented by a number of workers that patients with rheumatic fever are more likely to be non-secretors of ABO(H) blood-group substances and also more likely to belong to blood Group A than normal subjects. This paper from the College of Medicine, State University of Iowa, reports studies of ABO blood-group frequencies in 771 patients with rheumatic fever. The ABO subgroup (A1, A2, A1B, A2B) and MN group frequencies were determined in 540 cases, the MNSs subgroup frequencies in 538, and the secretor status in 376. Control groups consisted of 49,979 blood donors, 157 unaffected siblings of the subjects, and a “random sample” of hospital staff, patients, and patients’ spouses (1,356 subjects). The differences in the incidence of the disease in patients of different blood groups were analysed by the method of Woolf (Ann. hum. Genet., 19, 251). The comparison between ABO group frequencies in patients with rheumatic fever and blood donors indicated a statistically significant deficiency of patients with Group O. Comparison with the “random sample” control group yielded no significant differences in the incidence of rheumatic fever between the ABO groups and subgroups. Comparison with the “random sample”, however, did indicate that the relative incidence of rheumatic fever is significantly increased in persons of non-O ABO blood group, of the rhesus phenotype included in the symbol (r' r'r)1, and of genotype R-s, and of blood group N, and in non-secretors of ABO(H) blood-group substances.

The authors conclude that their findings provide “a definite and affirmative answer to the question: Is there an association between the ABO blood groups and rheumatic fever?” In an appendix to the paper, J. H. Edwards of the Birmingham Medical School, discusses the statistical interpretation of the data and concludes that the association of rheumatic fever with both ABO and secretor systems seems clearly established.

E. J. Holborow


The plasma seromucoid level has been found by Kelley et al. (Pediatrics: 1953, 12, 607) to be directly correlated with the clinical severity of rheumatic fever. Moreover, unlike the erythrocyte sedimentation rate (E.S.R.) and the serum C-reactive protein (C.R.P.) levels the plasma seromucoid level is not directly affected by corticosteroid therapy. At the Institut de Cardiologie de Montréal plasma from 157 subjects, of whom 32 were healthy controls and 51 had miscellaneous diseases, 55 chronic rheumatic heart disease, and nineteen acute rheumatic fever with carditis, was examined, the concentration of the protein component of the seromucoids being estimated by the biuret method.

The mean normal value was 67±12 mg. per 100 ml., there being no significant difference in level between children and young adults. Raised mean levels were found in the nineteen cases of acute rheumatic fever with cardiac involvement (168 mg. per 100 ml.), three cases of mitral endocarditis (110 mg. per 100 ml.), five cases of rheumatoid arthritis (164 mg. per 100 ml.), three cases of nephrotic syndrome (194 mg. per 100 ml.), seven cases of malignant disease (153 mg. per 100 ml.), and five cases of ulcerative colitis (205 mg. per 100 ml.). Serial estimations were carried out during the treatment of the patients with acute rheumatic fever with bed rest, prednisone, and penicillin. The plasma seromucoid level remained elevated for a mean time of 66 days, whereas the E.S.R. and the serum C.R.P. level returned to normal in 12 to 16 days. In eight cases a sudden and transient increase in the plasma seromucoid level without any corresponding change in the E.S.R. or clinical condition appeared to be related to withdrawal of steroid therapy. The estimation of the plasma seromucoid level proved to be more reliable for the control of treatment than determination of the serum protein-bound hexose or C.R.P. levels or the E.S.R. and comparable to the E.S.R. for diagnostic purposes.

Harry Coke


Of the 221 confirmed cases of bacterial endocarditis encountered at the University of Minnesota Hospitals, Minneapolis, during the 21-year period January, 1939, to December, 1959, 54 were classified as acute on the basis
of a total course of illness of less than 50 days. All but two of these 54 patients died, and 48 came to necropsy. It was established that 34 of these patients had no acquired or congenital heart disease, while five had congenital and fifteen rheumatic heart disease (mainly mitral lesions). Necropsy showed that of the 34 without previous heart disease, twelve had mitral, five tricuspid, and six aortic valvular lesions, the remainder having combined lesions. The ages of these 34 males and twenty female patients ranged from 2 weeks to 84 years, 32 of them being over 50 years of age. In 31 cases the infection was initiated by surgical procedures, major or minor. The commonest manifestations of the infection were fever, tachycardia, and a heart murmur. Blood cultures were positive in 49 of the fifty patients tested during life, and in the remaining four so examined after death. The organism was a coagulase-positive staphylococcus in 82 per cent., sometimes associated with other organisms.

The increased incidence noted since 1955 is thought to be due to more vigorous surgical investigation and treatment, particularly in older patients. Therapy for infections with resistant staphylococci was mainly with methoxphenylpenicillin or vancomycin. The prophylaxis recommended for patients with rheumatic or congenital lesions is administration of penicillin for 5 days beginning 2 days before surgery, the dosage being 600,000 units procaine penicillin or 250 mg. methoxphenylpenicillin orally every 8 hours. Urogenital procedures should be "covered" in addition by streptomycin in a dosage of 1 g. daily. Erythromycin or tetracycline may be used for patients sensitive to penicillin.

J. A. Cosh


This is a retrospective investigation of the incidence of histological evidence of nephritis in 246 cases of rheumatic heart disease seen at necropsy at the London Hospital over a period of 48 years. Most of the patients had died in chronic heart failure, but the incidence of rheumatic activity could not be assessed. Some form of glomerulonephritis was found in 95 (36.6 per cent.) of the cases. Advanced glomerulonephritis was present in sixteen of these cases. In five of these the kidneys were contracted; in three there was a histological Type-I nephritis, associated with arteritis in one of them, and in two cases there was Type-2 nephritis; the remaining six cases did not fall into either histological category. In 76 cases proliferative glomerulitis was present, marked by endothelial proliferation and thickened basement membranes. Interstitial tissue changes were seen in twelve instances. In three cases no obvious proliferative glomerulitis was found, but scattered tufts showed adhesions and focal necroses.

Although no comparable figures for a series of routine necropsies are available, the author considers that the findings support the concept of an association between rheumatic heart disease and glomerulonephritis.

G. Loewi


Rheumatoid Arthritis


Blood volume studies were carried out on 51 controls and 88 patients with rheumatoid arthritis. The data were assessed in terms of the significance of haemodilution, the use of the body haematocrit/venous haematocrit ratio in calculations, the best index for comparing results, and the accuracy of routine haematologic criteria in demonstrating anaemia. These analyses led to the following conclusions. The appropriate body haematocrit/venous haematocrit ratio must be determined if this is to be used in the estimation of blood volumes in rheumatoid patients. The surface area index appears to be the best of those commonly used. In the presence of rheumatoid disease there is poor correlation between the relative and the absolute methods for demonstrating anaemia. Hemodilution is not a major mechanism in the anaemia of rheumatoid arthritis, but it participates frequently to a minor degree.

This study emphasizes the need for further standardization of methods and for further study of blood volume regulation with clarification of the matter of where plasma volume compensation for red cell mass reduction ends, and where changes that are not compensatory in nature begin.—[Authors’ summary].


Although a number of neuropathies may arise in rheumatoid arthritis, related or coincidental, what we have termed “rheumatoid neuropathy” appears to be a part of the rheumatoid disease itself, though usually precipitated by steroid therapy, particularly if interrupted or irregularly maintained. It occurs most frequently in the patient with a positive high titre sheep cell agglutination, with nodules and advanced and long-standing disease. In most cases it is a bad prognostic sign. It is considered by most workers a manifestation of rheumatoid polyarteritis. We have not found any form of therapy which has a definite beneficial effect.—[Author’s summary.]


Working at the Cantonal Hospital, Lucerne, the author has examined the menisci of the knee, temporomandibular and sternoclavicular joints in cases of rheumatoid arthritis. In three out of twelve knee joints, two out of twelve sternoclavicular joints, and one out of two temporomandibular joints complete destruction of the menisci was found, although a joint space had been maintained. In the other cases, in which there were severe arthritic changes, tears and fibrillation of the menisci were seen, with lesions ranging from superficial injury to break-up of the cartilage. Histologically, the central parts of the cartilage in the earlier stages showed proliferation of lining cells and some apparent rarefaction of the matrix. In a more advanced state there was fibrinoid necrosis followed by distintegration of the tissue. Near the junction with the joint capsule pannus covered the disc surface. Vascularization of the cartilaginous menisci was seen.


It has been reported by a number of workers that their patients have developed osteoporosis during the course of corticosteroid therapy in high or prolonged dosage. The presenting sign has in most cases been a fracture. At the Cardiff Royal Infirmary the present authors have endeavoured to assess the relative importance of corticosteroid treatment and pre-existing bone disease of any variety as factors contributing to the development of osteoporosis in a series of 97 patients with rheumatoid arthritis. The relationship of osteoporosis to purpura has also been studied, as a form of this is not infrequently seen to develop during the course of such treatment.

Of 36 patients who were not treated with corticosteroids, ten (27·8 per cent.) developed severe osteoporosis of the spine. Of 61 who were so treated, twenty (32·8 per cent.) developed similar lesions. The incidence of osteoporosis in these two groups did not, therefore, show any significant difference. A difference in the incidence of compression fractures of the vertebral bodies between these groups was also within the limits of chance. The amount of corticosteroid treatment given did not seem to be of importance for the development of osteoporosis, but the incidence tended to increase with the patient’s age, irrespective of treatment. There was an association between the presence of osteoporosis and the development of purpura, which was independent of age or of the amount of treatment with corticosteroids, but was related to the presence and duration of the rheumatoid disease.

The authors conclude that “osteoporosis and purpura in patients with rheumatoid disease may be the consequence of the same change in the collagen of bone and skin”.

W. S. C. Copeman


Hydroxychloroquine sulphate is now widely used in the treatment of rheumatoid arthritis, “but clinical trials of its efficacy have been few”. For this reason the authors, in a joint study at the Canadian Red Cross Hospital, Taplow, Bucks, and the Hammersmith Hospital, London, have given this drug to 47 patients suffering from rheumatoid arthritis who were not progressing satisfactorily on a conservative regimen. The trial was conducted under double-blind conditions and was of the cross-over type. No patient who had received corticosteroid therapy
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From the London Hospital the authors report three cases of interstitial fibrosis of the lung associated with rheumatoid arthritis. All three patients, two men and one woman, were between 50 and 60 years old and none had been exposed to any harmful dust.

The first patient was a man of 56 who had first noted clubbing of the fingers in 1952, when he was 47. Two years later he developed pain in the neck, wrists, ankles, and feet. He was dyspnoeic on exertion and had a persistent cough, and although there were no abnormal clinical findings in the chest at this time, there was radiological evidence of diffuse fibrosis. A year later his arthritis symptoms were worse, the erythrocyte sedimentation rate (E.S.R.) was increased to 30 mm. in the first hour and Rose's test gave a positive result at a titre of 1:32. Radiographs showed no joint changes beyond slight erosion of the styloid process of the left ulna. He developed carcinoma of oesophagus 3 years later. At this time the latex-fixation test gave a positive reaction at 1:160 and the radiological picture of the lungs was unchanged.

In the second case—that of a man aged 52—clubbing of the fingers was first noticed in 1936, when he was 27. At first asymptomatic, he developed dyspnoea and cough a year later and these progressively worsened. A radiograph of the chest revealed bilateral reticular shadowing at the age of 44 and these changes progressed gradually. In 1961 he complained of painful stiffness in the joints and had limitation of movement of the shoulders, elbows, wrists, and knees and spindle-shaped enlargement of two interphalangeal joints. He had a nodule on the dorsum of one wrist. Respiratory function studies gave results compatible with a diagnosis of diffuse fibrosis, but radiographs showed the presence, in addition, of a solid lesion in the left upper lobe which subsequently proved at operation to be a carcinoma and was removed by lobectomy. His E.S.R. was 60 mm. in one hour, the serum γ-globulin content was increased, and both the Rose and latex-fixation tests gave positive reactions (at 1:512 and 1:160 respectively).

The third patient, a woman of 59, had a recurrent winter cough of 4 years’ duration, with progressive dyspnoea and right heart failure. She had also had pain in the left wrist and hip. Clubbing of the fingers was present and reticular shadows were seen in the radiograph of the chest. Her E.S.R. was 43 mm. in one hour and the latex-fixation test gave a positive reaction at 1:640.

The authors discuss the relationship between chronic diffuse interstitial pulmonary fibrosis with rheumatoid arthritis supervening and rheumatoid lung, which has been reported only in cases in which the arthritis is well established. The same type of pulmonary fibrosis is seen in both forms of disease; however, clubbing of the fingers is a prominent feature of diffuse interstitial fibrosis, but is not observed in cases of rheumatoid lung. They suggest that the cases reported “support the hypothesis that some examples of chronic diffuse interstitial fibrosis are manifestations of rheumatoid disease”.

William Hughes


In this paper are reviewed 24 adult patients with chronic polyarthritis, splenomegaly, and leukopenia (less than 4,000 leucocytes per c.mm.) seen between 1931 and 1961 at the Ohio State University Hospital, Columbus. This represents an incidence of less than 0.5 per cent. among patients seen at the rheumatology clinic during the period. According to the criteria of the American Rheumatism Association rheumatoid arthritis was diagnosed in eighteen cases (three classic, twelve definite, and eight probable), while five patients were considered to have osteo-arthritis and one gout. Of the eighteen patients with a diagnosis of rheumatoid arthritis, subcutaneous nodules were present in eleven; nine were also deemed to be suffering from systemic lupus erythematosus (S.L.E.) on the basis of histological evidence of periarterial lamellar fibrosis of the spleen in eight and the finding of L.E. cells in the other. The arthritis tended to be severe and disabling; severe infections were noted in eight patients, and in those with a leucocyte count below 1,000 per c.mm. gave rise to serious problems. Drug sensitivity was also present in eight patients, in five to penicillin, a rash being the most common manifestation.

Splenectomy for hypersplenism was performed in eighteen cases, in nine of which (including the eight cases referred to above) periarterial lamellar fibrosis characteristic of S.L.E. was found. In one of these cases gout was diagnosed clinically, and in another sarcoid granuloma was found in the liver and a lymph node, while in four there were no significant changes. Additional causes for hypersplenism were Hodgkin’s disease, chronic lymphatic leukaemia, primary hypersplenism, and hypersplenism with hepatic cirrhosis.
The leucopenia occurring in this series of patients could not be attributed to bone-marrow failure, as thirteen of the 21 patients studied had a hyperplastic marrow, especially in the myeloid series; in six the marrow was normal, in one it contained sarcoid cells, and only one patient showed hypoplasia. This last patient had received gold therapy 11 years previously, but had had normal leucocyte counts for the next 9 years. Following splenectomy the leucocyte count tended to rise to normal or even high levels, but might fall again later. Of the three patients with associated thrombocytopenia, only one improved, and one patient passed into an acute phase of S.L.E. after splenectomy. There was no improvement in the arthritic state in any patient following splenectomy.

On the basis of their findings, the authors suggest that the combination of polyarthritis and splenomegaly with leucopenia represents two distinct disorders, the one causing the arthritic and the other the hypersplenism. The most common cause of the latter was systemic lupus erythematosus, but such conditions as Hodgkin's disease or leukaemia might also cause it. B. M. Ansell


In an investigation at St. Louis University Hospital, Missouri, thirty patients with undoubted rheumatoid arthritis were given colchicine, administration of which is said to help in differentiating gout from rheumatoid arthritis. The drug was given by mouth in a dosage of 0.6 mg. every hour for twelve doses or until improvement or toxicity occurred. Of the thirty patients, ten showed subjective improvement, and four of these were benefited objectively 18 to 24 hours after the start of the therapeutic trial. Colchicine was also given intravenously in doses of 2 or 3 mg. to fourteen patients, and seven of these had subjective improvement. Of twelve patients with rheumatoid arthritis given both oral and intravenous colchicine therapy, three had relief after both forms of administration, while two were improved with oral therapy only and three with intravenous therapy only. It was also noted that, of four patients who had improved when given colchicine intravenously, two had a good response to an intravenous placebo.

The improvement after the administration of colchicine was not maintained in the patients with rheumatoid arthritis, as contrasted with gouty patients, who continue to have relief until the next exacerbation. The author points out that, though the diagnostic significance of an immediate response is to be questioned, improvement maintained for a week may be significant, as the patient with rheumatoid arthritis will have relapsed while the patient with gout will not have done so. He also notes that the interpretations of the test is further complicated by the fact that half the improvement that occurred could be attributed to a placebo effect. J. S. Malpas


Still’s Disease


Osteo-Arthritis


Spondylitis


Writing from the Rhine Provincial Rheumatic Clinic, Aachen, the author suggests that it is wrong to think that ankylosis of the sacro-iliac joints is an early manifestation of ankylosing spondylitis. By the time ankylosis is established visible radiological changes in the spine are likely to be present also. The early clinical features are typical: the patient, generally a male aged 30 to 40, is woken after several hours of rest by sacral pain which is improved by getting up and walking about. The erythrocyte sedimentation rate is raised and phenylbutazone is particularly effective at this stage. Long before ankylosis of the sacro-iliac joints occurs finer radiological changes, which are not necessarily bilateral, may be detected. These consist in a widening of the joint space in the lower sector, atrophy near the cartilage, and cloudy sclerosis of the bone near the joint. Round sclerotic foci near the joint appear later. The sclerosis of osteitis condensans ili is more even in character and forms a typical triangle. The joint space in ankylosing spondylitis may assume a scalloped outline resembling a string of beads. Eventually ankylosis is seen, but by then the disease is fully established. In the author's opinion ankylosing spondylitis is not simply an ascending condition.

F. M. Abeles


At the University Polyclinic, Basel, the authors have studied the incidence of cardiac involvement in 44 patients with ankylosing spondylitis, of whom 38 were men and three gave a past history suggestive of Reiter's disease. It was found that one patient suffered from aortic insufficiency while ten showed electrocardiographic changes, indicative in one case of complete heart block and in nine of incomplete block, associated in one of the latter with right bundle-branch block; two of these patients had a history suggestive of Reiter's disease. From these observations and a review of the literature the authors conclude that aortic insufficiency and disturbance in auriculo-ventricular conduction are characteristically found in ankylosing spondylitis, and that this finding supports the view that ankylosing spondylitis differs from other forms of rheumatism.

G. L. Asherson


Chromosome studies have been done on 85 blood-cultures from 58 patients with ankylosing spondylitis, none of whom had had more than one course of x-ray
therapy to the spinal axis. These observations extend in time from immediately before x-ray therapy to up to 20 years later.

X-ray therapy produces extensive chromosome damage, and the resultant abnormal chromosomes can be classified into two general types—unstable and stable abnormalities. The proportion of cells with unstable abnormalities rises to a peak value 2 to 3 weeks after the end of treatment, and then it falls. But some of these cells persist 5 years and more after exposure. The proportion of cells with stable abnormalities does not change materially over the years from the level reached shortly after the end of treatment. Irradiation also causes a striking increase in the number of polyploid cells found in blood-cultures.

These findings are discussed in the light of the known leukaemogenic properties of therapeutic doses of x-rays.

[Authors' summary.]


Inflammatory Arthritis


In three patients with Reiter's disease there was evidence of a virus infection when the urethral secretions were examined by virological methods at the Hôpital Saint-Louis, Paris. Urethral scrapings were stained with Giemsa's stain and cytoplasmic inclusions were found to be present in the epithelial cells. Urethral secretions were inoculated into embryonated hens' eggs and these were opened six days later. Smears from the yolk material, when stained by Giemsa's technique, showed numerous minute red bodies with a purple centre and blue cytoplasm. After several such culture passages the quantity of the virus increased. Of twelve eggs inoculated with material from the three patients, eight showed chick-embryo malformations which were absent from the control eggs. Similar malformations are found in eggs inoculated with viruses of the psittacosis-trachoma group. Sections of the liver and heart of the chick embryos showed a few of the small bodies described. It is suggested that these findings favour a virus aetiology in the three cases studied.

G. W. Csonka


A retrospective study of 34 cases of Reiter's syndrome which had been observed at the University of Michigan Medical Center and Veterans Administration Hospital, Ann Arbor, was attempted. Follow-up contact was established with 26 of the 33 living patients, with seventeen by interview, and with nine by questionnaire alone, information concerning the remainder being obtained from the hospital records.

A close association between Reiter's syndrome and ankylosing spondylitis was confirmed. Acute lumbar or pelvic pain had been noted during the first attack in 27 cases (79 per cent.), and of 27 cases in which the history extended over more than 2 years, with an average of 2-6 attacks of Reiter's syndrome, pain in the back had been noted in 22. In thirteen of these 27 cases definite radiographic evidence of bilateral sacro-iliac disease had been found. Ankylosing spondylitis had been diagnosed in eight cases, and in several of these the course followed was typical of this condition. No evidence of the development of typical rheumatoid arthritis was found. A history of iritis was obtained in four (31 per cent.) of the patients with radiological evidence of sacro-iliitis but in one of the other cases.

Of the 23 patients followed up whose history exceeded 2 years, 21 were able to work regularly, although only two were free from symptoms of continuing rheumatic activity or from residual effects of previous bone or joint disease.

R. R. Willcox


Non-Articular Rheumatism


The volume of the cavity in an intervertebral disk can be determined by injecting fluid into the cavity for which purpose the disk itself is perforated. This technique reproduces the clinical syndrome while the liquid is being injected. Discography supplies additional information and for this a 50 per cent. solution of “sergosin” or of “cardiotast” is used. Anteroposterior and lateral radiographs are taken within 15 to 20 minutes of the injection. When the intervertebral disk is normal the contrast medium is distributed around the nucleus pulposus and somewhat posteriorly to it. The radiological shadow may be round, square, semilunar, angular, or in the shape of studs or parallel lines. The shadows usually measure “from 1 to 2.5 cm.” Degenerative changes in the disk result in the disappearance of the normal nuclear shadow, the contrast medium spreading and branching out or occupying the whole intervertebral space.

In all 74 disks were examined in 31 patients; of these sixteen were normal, 21 showed mild degenerative changes, seventeen marked degenerative changes, fifteen degenerative changes with prolapse of the disk, and five degenerative changes with rupture of the fibrous disk. In all the abnormal cases the radiological diagnosis was confirmed at a subsequent operation. *A. Orley*


Gout


Unfortunately hepatitis has been reported to have occurred in some cases during long-term administration of the drug, and although the hepatitis is indistinguishable from that of viral origin, the manufacturers have withdrawn zoxazolamine from the market. From the Veterans Administration Hospital, San Francisco, the author reviews her results in twenty cases of gout already treated with zoxazolamine. The patients’ ages ranged from 24 to 71 years and the duration of the disease from 2 months to 12 years. All were cases of primary gout except for one of myeloid metaplasia with secondary gout. Renal disease was present in seven cases and significant cardiovascular defect in eleven. Urinary lithiasis was recorded in seven cases. The dosage was 200 to 1,000 mg. daily in two to four doses and duration of treatment ranged from 1 to 28 months (mean 14 months).

Serum urate levels ranged from 6·4 to 12·9 (mean 8·8) mg. per 100 ml. before treatment and from 4·2 to 8·0 (mean 6·2) mg. per 100 ml. during treatment. In addition there was an improvement in the urate:creatinine clearance ratio, although creatinine clearance remained constant throughout. In fifteen cases the uricosuric effect of zoxazolamine persisted throughout the period of treatment, but in five it deteriorated without obvious cause after a few weeks to a few months. These five patients developed serious complications—myocardial infarction in three cases and congestive heart failure in two. In two of these patients who remained under observation in hospital the uricosuric effect of zoxazolamine returned during convalescence. Although the drug had no clinical effect on acute gouty arthritis, it produced excellent results in chronic cases and especially in those with tophi. All tophi regressed under treatment and many disappeared. The simultaneous administration of salicylate decreased the uricosuric effect of zoxazolamine, but the urate retention produced by chlorothiazide was reversed by zoxazolamine. Gravel or small stones were passed in the urine in several instances during treatment. One patient developed hepatitis without apparent cause during therapy. The drug was

The authors of this paper from Hahmann Medical College and Hospital, Philadelphia, have studied the serum uric acid level in eight consecutive patients with diabetic ketoacidosis. In four out of the eight patients the serum uric acid concentration was above normal, and in seven the level paralleled the degree of ketoacidosis, decreasing as the ketone level decreased. The authors contend that the raised serum uric acid level is not due to the diminished glomerular filtration rate resulting from dehydration, and discuss the relationship between uric acid and carbohydrate metabolism. They suggest that a depletion of liver glycogen and subsequent neoglucogenesis with the formation of purine breakdown products may explain the high serum uric acid level in diabetic ketoacidosis.

I. McLean Baird


It has been shown biochemically that 5-β-phosphoribosylamine, a unique and obligatory intermediate in the synthesis of urate, can be produced in the body from 5-α-phosphoribosyl-l-pyrophosphate (PRPP) and is thought to be involved in the regulatory feedback mechanism which normally limits the rate of synthesis of urate. Working at Duke University, Durham, North Carolina, the authors have therefore studied the production of PRPP in seven healthy males, six gouty males with normal urate production, and three gouty males with abnormally high urate production ("over-producers"), using imidazoleacetic acid (IAA) as an intravital marker for PRPP and isolating the reaction product, namely, imidazoleacetic acid ribonucleoside (IAAR). [The original paper should be consulted for details of the method used.]

It was shown that the incorporation of radioactive carbon (14C) into IAAR and the specific activity of IAAR were three times greater in the three gouty over-producers than in the remaining subjects, indicating an accelerated turnover of PRPP and thus suggesting an accelerated rate of renewal of PRPP from glucose-6-phosphate. Gouty subjects who produced normal amounts of urate did not differ from normal subjects in the amount of 14C incorporated into IAAR, suggesting either that the turnover of PRPP in these subjects is not accelerated, or that the method is inadequate for the detection of small increase in turnover.

Allan St. J. Dixon


Para-rheumatic (Collagen) Diseases


This paper from the Rockefeller Institute, New York, reviews various features of the antinuclear and anticytoplasmic antibodies found in systemic lupus erythematosus (S.L.E.). Tests on a series of 104 treated and untreated patients with the disease demonstrated the presence of I.E. cell factor in 87, and complement-fixing antibodies to nuclei in 79 and to cytoplasm in 39 patients. Thus I.E. cell factor or antinuclear antibody was demonstrated in all except two of these patients.

Estimations on serum from nine patients revealed marked depression of total serum complement and of its C1 and C3 component in all cases, with depression of C4 in six cases. The levels of the C1 and C3 component were normal. Estimation by a precipitin reaction with human aggregated γ-globulin showed a reduction of the 11s component (C1A) in all cases, while immuno-electrophoretic studies gave evidence of inactivated complement in the fresh serum from one patient. Steroid therapy caused a reduction in antibody titres and of serum γ-globulin levels, with a rise in serum complement towards normal. By fluorescein labelling it was possible to demonstrate the occurrence of one of the components of complement in the glomerular, splenic, and arterial lesions of S.L.E. and that the distribution of this component often paralleled that of fluorescent anti-7s γ-globulin.

The authors suggest that the low complement levels and
the apparent fixation of complement and γ-globulin at the sites of histological lesions in S.L.E. favour an immunological reaction in vivo which may possibly be responsible for some of these lesions.  

M. Wilkinson


Among 22 patients with disseminated lupus erythematosus studied at the Second Medical Clinic of the University of Munich, sixteen complained of myalgia though paresis was only rarely present. Electromyography was performed in fifteen cases, the main findings being a decrease in the mean potential duration to only 54 per cent. of normal, an increase in the mean phase frequency, and a corresponding decrease in the phase quotient. Only in one case were the findings normal. Histological examination of muscle biopsy specimens from sixteen patients and necropsy specimens from two others showed perimyositis with round-cell infiltration around small vessels in the connective tissue. An occasional small vessel was occluded by endarterial proliferation. Some degree of parenchymal muscle damage was seen in twelve cases, with partial or complete fibrillar dissolution, extending to necrosis of single fibres, and changes in the fibre nuclei. In one case the picture was that of acute polymyositis. With these changes in the muscle fibres there was a sparse interstitial infiltration by histiocytes and plasma cells.  

G. Loewi


The intraleisional injection of triamcinolone in the treatment of 28 cases of chronic discoid lupus erythematosus is reported from the University of Leeds. Many of the patients had had years of unsuccessful systemic therapy. Injections were usually given at 3-weekly intervals, from one to nine injections being required. In thirteen cases antimalarial drug therapy was continued. The injected lesions cleared in thirteen cases and there was improvement in thirteen; only two cases did not respond. The method was found suitable for scalp lesions, though hair did not regrow. In only one case was there a reaction, a sterile abscess developing after injections into a profunda type of lesion. After a slight discharge both the abscess and the lesion disappeared.  

E. W. Prosser Thomas


From the Department of Medicine, Veterans Administration, Washington, D.C., two cases of scleroderma are described which demonstrate the widespread changes in connective tissue throughout the body which may occur in this disease.

In the first patient, a man aged 65, in addition to the typical skin changes and finger deformities there were marked changes in the lungs, heart, and intestine, these consisting in septal fibrosis in the lungs, interstitial fibrosis in the myocardium, and collagenous fibrosis in the submucosa of the small intestine.

The second patient, a man of 46, showed marked changes in the kidneys and spleen, with considerable atrophy of the stomach and intestines. An additional case is described to demonstrate that rigorous classification of the various diseases of connective tissue may be misleading, and indeed may prevent better understanding of these conditions—hence, in the author's view, the value of a broad term such as diffuse systemic sclerosis. This third case had some features like those of lupus erythematosus disseminatus and others more like those of polyarteritis nodosa.

The paper ends with a short discussion of the varieties of palliative treatment which can be offered to these patients, including the use of vasodilator drugs, chelating agents, and serotonin inhibitors.  

E. H. Johnson


A study of the findings in 727 cases of systemic scleroderma seen at the Mayo Clinic between 1935 and 1958 suggests that there are two types of the disorder. By far the more common is acrosclerosis, which is nearly always preceded by Raynaud's phenomenon. There were, however, 39 patients in the series in whom the skin manifestation began on the central parts of the body as a yellowish, infiltrative, hyperpigmented sclerosis, without any Raynaud symptoms, which the authors term diffuse scleroderma.

Although the systemic features of the two types are similar, oesophageal, pulmonary, and other visceral involvement being recorded in about equal percentages, there was a marked difference in the general prognosis. It appeared that the diffuse sclerosis always ran an acute course, few of these patients surviving for 5 years, whereas the course of acrosclerosis was much more variable and on the average slower, 62 per cent. of patients being still alive 10 years after diagnosis. It is noted that laboratory tests and radiography are of no help in prognosis in these cases. The only method is to compare the condition of the individual patient and the degree of involvement when first seen with these same factors after a 6-month interval.  

E. H. Johnson


The frequency with which scleroderma produces signs and symptoms of obstruction of the small bowel was

Vascular disturbances in the hands or workmen using pneumatic drills have been described in many countries, particularly in those where the climate is cold. The condition, Raynaud's phenomenon, is characterized by numbness, weakness, and blanching of the hands, but not extending beyond the wrist. The condition once established persists even after the workman has ceased to use pneumatic tools. Affected hands become unusually sensitive to cold and this often "triggers off" an attack.

At a uranium mine in Northern Saskatchewan a group of eight cases were diagnosed among underground hardrock drillers. Observations made at the mine on these cases revealed two significant features additional to those usually described:

1. In men with this disorder, cooling the hands in ice water, even for 10 to 15 minutes, will not necessarily precipitate an attack, but whole-body cooling of even moderate degree will do so promptly.
2. While the warm hands look normal and are apparently normal to such neurological sensory tests as light-touch, pin-prick, vibration, heat, and cold, they are in fact abnormal in that they are not particularly painful after long exposure in ice water.

Of these eight patients two were admitted to the Ohio State University Hospital, Columbus, Ohio, for intensive study. This included clinical tests involving cooling of the hands and whole body by various means; arteriography of digital arteries after percutaneous needling of the brachial artery and after intra-arterial injection of vasodilator drugs; and arterial biopsy. A study of two cases, as acknowledged by the authors, does not permit any general conclusion to be drawn. However, the scheme of investigation and the results of the tests in each case are of considerable interest.

(The paper includes excellent reproductions of arteriograms of the hands, coloured photographs depicting the clinical appearances, and photomicrographs of the biopsy specimens.) **A. Meiklejohn**


The intralesional treatment with triamcinolone of thirteen cases of chronic discoid lupus erythematosus (lesions on nose, cheeks, ears, and chin) which had proved resistant to antimalarial drugs is described in this paper from the Western Infirmary, Glasgow. A solution of triamcinolone acetonide containing 10 mg. per ml. was injected into the upper dermis by means of a fine hypodermic needle fixed to a tuberculin syringe, 0·1 ml. being introduced at sites 1 cm. apart at weekly intervals for about six treatments, while at the same time antimalarial drug therapy was continued. Biopsy specimens were
examined before and after treatment. In all cases there was a diminution of follicular plugging and hyperkeratosis accompanied by some thinning of the epidermis, vascular dilatation and cellular infiltration having either disappeared or been reduced. Atrophy of the skin was not observed. There seemed to be deterioration of the lesions in two patients who stopped taking napcaine, suggesting a synergistic effect between the corticosteroid and the antimarial preparation. *E. W. Prasser Thomas*


Temporal arteritis and scleroderma were seen in a patient whose central retinal artery was occluded, but yielded to retrobulbar hydrocortisone.

**P. D. Trevor-Roper**


Scleroedema Adultorum—a Children's Disease. 

Primary Chronic Polyarthritis and Periarthritis Nodosa. 


Connective Tissue


Pathology of Rheumatic Diseases


An additional modification of the latex particle agglutination test has been developed at the Royal Northern Hospital, London, and is considered as being more convenient for handling large numbers of sera in a rapid, simple, and inexpensive manner. A "lacto latex 0.81 suspension" is employed, which is diluted and standardized by light transmission. The test method employs the patient’s own γ-globulin and is independent of the need for standardizing additional sensitizing globulin. The slide technique used requires only a simple mixture of diluted latex suspension and heated patient’s serum.

In a comparative study 508 sera were examined simultaneously with this test and the Rose-Waaler test as modified by Ball. Agreement in 96 per cent. was obtained. A further complete agreement was found in 38 cases with the Hyland R.A. test. It was found to be essential to heat the serum, 15 minutes at 56°C. being sufficient. Initial dilution of normal sera with borate buffer to 1:10 or greater then gave positive agglutination. Fractionation in a diethylaminoethylcellulose mixture by the method of Stanworth (Nature (Land.), 1960, 188, 156) isolated a single-strip electrophoresis fraction which retained the positive and negative capacities of individual sera [similar to the various euglobulin techniques].

Harry Coke


A serological investigation for the rheumatoid factor was carried out at the Hôpital Lariboisière, Paris, in 141 cases of polyarthritis of more than one year's duration, all of which were at least cases of "possible" rheumatoid arthritis, according to the classification of the American Rheumatism Association (A.R.A.). They were divided into "typical", that is, either "definite" or "classic" rheumatoid arthritis by the A.R.A. criteria, or with evidence of swelling, involvement of several joints including the wrist or fingers, or with radiological signs of cartilage destruction, or "atypical", that is, not conforming to the above.

Both the Rose-Waaler and the latex particle tests were performed, the latter being found to be the more sensitive; in only one case was this negative when the Rose-Waaler test was positive. Of the 84 "typical" cases at least one of the tests was positive in 72 (86 per cent.), whereas of the 57 "atypical" cases positivity was noted in only sixteen (28 per cent.). Among the twelve "atypical" sero-negative cases there were five in which the disease appeared to be inactive and one in which polyarthritis had started in childhood, but the remaining six appeared to be entirely typical in other respects, so there was no explanation for the negative serological findings in these cases.

In a discussion of the phenomenon of sero-negativity the authors point out that the frequency of negative reactions can be reduced by more sensitive techniques, at the cost, however, of a rise in the number of false positive reactions. Other conditions which mimic rheumatoid arthritis (a list of which is presented) are a further cause of negative reactions, and such reactions may also be found in cases in which the arthritis is of recent onset or is in remission, in young patients, or in patients with the condition of agammaglobulinaemia. But even after these exclusions a small number of cases remain for which no adequate explanation of the sero-negativity can be given.

B. E. W. Mace

Intra-articular Dissociation of the Rheumatoid Factor. 

It has been shown that the macroglobulins of Waldenström's macroglobulinaemia can be dissociated in vivo by
the oral administration of penicillamine. The author, working at the New York Medical College, Flower and Fifth Avenue Hospitals, has investigated the possibility of producing a similar in vivo dissociation of the rheumatoid factor, which is also a macroglobulin and which has already been shown to be dissociated in vitro by the action of sulphhydril-reducing substances with loss of its immunological activity. Preliminary studies in vitro showed that while both penicillamine and cysteamine were able to dissociate the rheumatoid factor in serum, the latter compound was approximately twice as potent as the former. When α-penicillamine was administered by mouth for 14 days in a daily dosage of 2 g. to two patients and 4 g. to two further patients with advanced rheumatoid arthritis no change in the serum level of the rheumatoid factor could be detected by quantitative precipitin and latex-fixation tests in either group. However, 400 mg. cysteamine injected into the knee-joints of six patients with active rheumatoid arthritis and synovitis caused a fall in the level of rheumatoid factor in the synovial fluid within 3 hours, the level beginning to return to the control value within 24 hours. When daily intra-articular injection of 400 mg. cysteamine were given for one week and the rheumatoid factor in the synovial fluid assayed daily it was found that the level gradually fell during the first three days of the study and then levelled off, with a slight rise on the 7th day despite continued injection of the drugs. Within 72 hours of the last injection the level had returned almost to the control values. Intra-articular injections of hydrocortisone in control subjects produced no significant change in the titre of the rheumatoid factor.

The results of intra-articular injection show that in vivo dissociation of the rheumatoid factor can be produced locally, and the failure of penicillamine given by mouth to produce any systemic dissociation may have been due to insufficient concentration in the blood, since the rheumatoid factor appears to be more resistant to dissociation by penicillamine than Waldenström’s macroglobulin. To obtain a systemic effect it may well be necessary to use more potent sulphhydril compounds. No clinical improvement was noted in the treated joints and no conclusion can be reached concerning the role of the rheumatoid factor in the pathogenesis of rheumatoid arthritis. However, it is pointed out that the duration of dissociation was probably too brief for any potential beneficial effect to become manifest, while the multiple joint punctures and introduction of a foreign chemical in themselves may have caused irritation of the joint.

B. M. Ansell


Complement-fixation reactions with human liver tissue were carried out with serum samples from 874 subjects. Positive reactions were found chiefly in patients with chronic active hepatitis, systemic lupus erythematosus, rheumatoid arthritis and in those with positive reactions to serologic tests for syphilis. Isolated instances of positive reactions were found in other disorders. It is concluded that these complement fixation reactions are of considerable interest in evaluating host response, but do not point specifically to any disease or pathologic process. They represent an immunologic phenomenon only in terms of in vitro test methods as far as can be determined at present.—[Authors’ summary.]


The author has investigated, at Johns Hopkins University Hospital, Baltimore, 192 patients who chronically showed biologically false positive reactions in the standard serological tests for syphilis (S.T.S.). Of this number 97 were detected when undergoing a routine medical examination as healthy subjects, 77 during the investigation of mild localized disease, and a further eighteen while being examined for some generalized disorder. In this last group were found two with frank systemic lupus erythematosus and one patient with Still’s disease. Syphilis was excluded by a negative result in the treponemal immobilization test. Follow-up for at least 2 years excluded the possibility of transient false positive reactions associated with infective hepatitis and other infectious diseases. It is pointed out that of the 192 patients 143 were women, a female predominance of 3:1.

Follow-up showed that fourteen patients (all female) had developed systemic lupus erythematosus, 43 had symptoms suggestive of connective-tissue disease, while 81 had raised serum globulin levels or some other abnormality of the serum proteins but no definite clinical evidence of connective-tissue disease. Three female patients developed Hashimoto’s thyroiditis and three other women patients (not in the series) with thyroiditis were observed to show false positive reactions in S.T.S. Of these six patients three had other diseases such as Sjögren’s syndrome, glomerulonephritis, haemolytic anaemia, or thrombocytopenia. Several of the patients with false positive reactions had relatives with various connective-tissue diseases. In his discussion the author postulates that the apparently separate disease entities reported above may in fact represent different manifestations in a particular host of a genetically transmitted abnormality of the immune apparatus of “variable penetrance and variable expressivity”, and draws an analogy with the situation in regard to syphilis before the introduction of the Wassermann reaction.

G. L. Asherson


In order to determine whether an autoimmune mechanism is involved in multiple (disseminated) sclerosis, the authors, working at the Royal Victoria Infirmary and King’s College, Newcastle upon Tyne, determined the serum levels of immuno-conglutinin in 27 patients with multiple sclerosis and compared them with
ABSTRACTS

those found in 43 normal subjects, fourteen patients with Hashimoto’s disease, and 22 patients with rheumatoid arthritis or other rheumatoid diseases. The method of titrating immuno-conglutinin was that of Coombs, Coombs, and Ingram (The Serology of Conglutination and Its Relation to Disease, Oxford, 1961) and the technical details are briefly outlined.

The results are presented diagrammatically. The immunoconglutinin titres and their distribution in both chronic and acute cases of multiple sclerosis showed no statistically significant difference from those found in the normal controls. On the other hand a markedly raised immuno-conglutinin titre was present in all cases of Hashimoto’s disease and in all cases of rheumatoid disease. In the latter group the immuno-conglutinin titres were independent of the result of the Rose-Waaler test. Tests on cerebrospinal fluid gave uniformly negative results.

F. Hillman


This is a study of the behaviour of the serum proteins and the erythrocyte sedimentation rate (E.S.R.) in 44 cases of idiopathic, postoperative, and pituitary hypothyroidism seen at Malmö General Hospital during the period 1954-60, in which the serum protein level had been determined before treatment started and there was no other condition capable of influencing the serum protein pattern.

The serum albumin concentration tended to be low and the \( \beta \)-globulin fraction to be increased, although the increase in the latter was less marked in the postoperative group. In twelve out of thirty cases of idiopathic hypothyroidism the \( \gamma \)-globulin level was raised, sometimes markedly. In postoperative hypothyroidism, on the other hand, the \( \gamma \)-globulin concentration was not increased. The possible reasons for this rise in \( \gamma \)-globulin level and its relationship to positive cephalin-cholesterol flocculation tests are discussed. Positive tanned erythrocyte tests did not correlate with the rise in \( \gamma \)-globulin concentration. In four out of five cases of pituitary hypothyroidism the reduction in the \( \beta \)-globulin fraction was the only finding in an otherwise normal serum protein pattern.

The E.S.R. was more than 15 mm. in one hour in 80 per cent. of all cases of hypothyroidism, and over 40 mm. in one hour in 21 per cent. It is suggested that hypothyroidism may be an obscure cause of a raised E.S.R.

I. McLean Baird


At the Second University Medical Clinic, Vienna, smears of sternal bone marrow from patients with rheumatoid arthritis and from non-rheumatic control subjects were investigated by the immunofluorescence technique of Coons et al. (J. exp. Med., 1955, 102, 49) to determine whether only plasma cells were responsible for the production of the rheumatoid factor. Bone-marrow smears from sixteen patients with rheumatoid arthritis in whom the later fixation reaction was positive (latex-positive cases), twelve patients with latex-negative rheumatoid arthritis, and eight control subjects were investigated. Bright fluorescent material was found in both mature and immature plasma cells in fifteen of the sixteen latex-positive cases and in nine of the twelve latex-negative cases of rheumatoid arthritis. In the material from the eight control subjects only an occasional fluorescent cell was seen. Fluorescence was confined to the plasma cells. It was estimated that in the marrow from latex-positive cases 10 to 30 per cent. of all plasma cells were fluorescent compared with 5 to 10 per cent. in the marrow from latex-negative cases. It was also noted


The low viscosity of synovial fluid in rheumatoid arthritis is believed to be due in part at least to decreased polymerization of the hyaluronic acid in the fluid and it has been shown that hyaluronic acid is rapidly depolymerized in the presence of certain inorganic ions. The authors, working at the Medical College of the University of Alabama, have studied the trace-metal composition of synovial fluid in rheumatoid arthritis to see whether any appreciable differences from the normal could be detected. Synovial fluid from thirteen patients with rheumatoid arthritis was compared by spectrophotographic analysis with that obtained post mortem from 33 subjects, none of whom had died from any disease involving the connective tissue disease. Blood from nine of the above patients with rheumatoid arthritis and five others who had no joint effusions was also examined. The technique of spectrophotographic analysis used is described in detail. Spectrophotographic standards were prepared to contain 43 individual metallic elements in ten concentrations ranging from 0.01 to 0.001 per cent.

Iron and chromium were found in all specimens of synovial fluid from patients with rheumatoid arthritis, but in only twelve and seventeen respectively of the 33 control specimens. Cobalt, cadmium, and nickel were absent from all specimens. Copper, aluminium, rubidium, lithium, and strontium were detected in every specimen of synovial fluid. The mean concentrations of copper, iron, and aluminium were elevated above the normal levels in the synovial fluid in rheumatoid arthritis. In addition to iron, measurable quantities of copper, aluminium and rubidium were found in all specimens of serum examined. In the blood from patients with rheumatoid arthritis the mean concentrations of copper and rubidium were 77 and 87 per cent. respectively higher, and those of iron, aluminium, and chromium about 50 per cent. lower, than those in normal control sera.

William Hughes
that a higher proportion of mature plasma cells were fluorescent in latex-positive than in latex-negative cases. Thus while no clear differentiation was found between latex-positive and latex-negative cases, there was a suggestion that the rheumatoid factor is released into the blood largely by mature plasma cells. The authors conclude that examination of the bone marrow by the immunofluorescence technique appears to be a practical diagnostic procedure, especially in latex-negative cases of rheumatic arthritis.

G. W. Csonka

Evaluation of Serum Mucoid Levels in Rheumatoid Disease.

In a study at the Royal Free Hospital, London, two "serum mucoid" fractions were estimated serially in 23 cases of rheumatoid arthritis with the objective of evaluating the results in relation to other acute-phase reactants and to the clinical and radiological findings. Serum mucoids (S.M.) were estimated by an electrophoretic separation previously described by Markham and others (J. Lab. clin. Med., 1956, 48, 559) with actual estimations of the polysaccharide by scanning the stained strip. Results were correlated (not statistically) with the erythrocyte sedimentation rate (Westergren), the quantitative C-reactive protein reaction, and the response to the sheep-cell agglutination test. High S.M. values were found in the more active and advanced cases, with no significant difference attributable to the presence of nodules or the type of joints affected. Reduction in S.M. level was recorded in three to six cases undergoing gold therapy, correlating with the erythrocyte sedimentation rate (E.S.R.), C-reactive protein level, and clinical condition. Six cases given corticosteroid therapy showed a pattern of an initial fall in S.M. level followed by a return to the previous values, which became reduced again only by an increase in dosage or a change in the nature of the corticosteroid employed. Prognostically, assessment after a 2-year period revealed that cases with the highest S.M. values initially tended to show the greater improvement clinically but not radiologically. It is suggested that this may be due to the selection of the advanced cases for a more intensive regimen and for corticosteroid therapy. "Serial readings of serum mucoid levels and E.S.R. were of equal though limited usefulness in reflecting minor variations in clinical activity, while the C-reactive protein level was less reliable." The S.M. did not return to normal values during suppressive therapy with corticosteroids.

Harry Coke


Bone Diseases


This paper is concerned only with primary osteoporosis, that is, osteoporosis which is not associated with any known predisposing condition. The orthodox teaching about osteoporosis has been that it is a disorder of the protein rather than the mineral component of bone, but the second-named author has challenged this view and has presented evidence (for example, Lancet, 1961, 1, 1011; Abstr. Wld. Med., 1961, 30, 202) indicating that clinical osteoporosis in man could be due to prolonged negative calcium balance. In the present study all the diet histories and the bone radiographs of patients seen by the authors at the Western Infirmary, Glasgow, between 1957 and 1960 have been reviewed for the purpose of testing the over-all relationship between dietary intake and the state of the skeleton as seen radiologically. The series consisted of 128 patients suffering from clinical osteoporosis and 103 other hospital patients of comparable age and sex but without evidence of osteoporosis who served as a control group; the majority of subjects in both groups were aged between 40 and 79 years. In recording the dietary histories particular attention was paid to calcium-containing foods such as milk, cheese, and bread (which in the United Kingdom is fortified with calcium carbonate). The standard radiographs comprised a lateral view of the lumbar spine and a postero-anterior view of the hands and femur, and these were assessed by the method of Barnett and Nordin (Clin. Radiol., 1960, 11, 166) in which a scale of “scores” for the measurement of cortical thickness (peripheral score) and vertebral biconcavity (spinal score) is used.

It was found that the mean calcium intake of the control group was 930 mg. per day and that of the patients with osteoporosis was 776 mg. per day. Since the mean body weight of the two groups was virtually the same the difference in calcium intake is highly significant whether considered in absolute terms or in relation to body weight. Taking both groups together, among 170 subjects whose calcium intake was less than 1 g. daily there were 107 cases of osteoporosis, whereas among 61 subjects with a calcium intake of over 1 g. daily there were only 21 cases of osteoporosis. The mean urinary calcium excretion was the same in the two groups. Again, if the minimum normal total “x-ray score” is taken as 169, then it is seen that only six patients with a total x-ray score below 169 had a calcium intake of over 1 g. daily, and also that subjects with a total x-ray score over 169 were more or less uniformly distributed over the whole range of dietary calcium intakes. The authors conclude that the distribution of the data is such as to suggest that osteoporosis does not develop in the presence of a high calcium intake, but that if calcium intake is low osteoporosis may or may not develop, presumably depending upon whether adaptation to the intake does or does not occur.

Joseph Parness


The aetiology and pathogenesis of eosinophilic granuloma of bone are still not finally established. It has been regarded by some authorities as a benign tumour,
but its simultaneous appearance in several bones and its spontaneous disappearance in some cases make this view unlikely. Others have considered it to be of inflammatory origin, while others again have regarded it as a reaction to trauma, or to some type of toxin, or virus infection, or even allergy. It is now classed among the granulomata, in some way related to xanthomatosis (Hand-Schüller-Christian disease). In view of the relative rarity of this latter disorder in comparison with eosinophil granuloma (a ratio of about 1:7) the author prefers to regard it as a special form of eosinophilic granuloma in which the base of the skull and the hypothalamus are involved. Both diseases tend to appear in the pre-school period of childhood, and all the 28 patients studied by the author were between 2 and 13 years of age, twenty being under 10, and the youngest 2 years old; in four cases of xanthomatosis the patients’ ages were 2, 3, 5, and 7 years respectively. Of the 28 children with eosinophilic granuloma, the cranial vault were involved in twelve, the upper part of the femur in eight, the pelvis in nine, the upper third of the humerus in two, the ribs in two, the vertebrae in two, and the scapula in one.

The radiological appearance of the lesions in the long bones is typical, namely, an oval form with “lace-like” edges and sclerosis of the surrounding bone. Laboratory findings are of little help in diagnosis; the erythrocyte sedimentation rate was slightly raised, and there was slight eosinophilia in only seven cases. Histological appearances were typical in nineteen cases, showing large areas of reticular cells, many with two or more nuclei, and localized nests of eosinophils, abundant leucocytes, plasma cells, histiocytes, and lymphocytes, together with numerous foam-cells containing neutral fats or, more rarely, cholesterol. In necrotic areas Charcot-Leyden crystals were numerous. Clinically, differential diagnosis must be from osteogenic sarcoma, Ewing’s sarcoma, chondrosarcoma, and tuberculous osteitis; radiological and histological examination of the contents of the bony lesions will establish the true nature of the disease. The treatment of choice is surgical curettage of the lesions if practicable; failing this, radiotherapy. The prognosis is favourable as compared with that of xanthomatosis. In this series there was no case of recurrence among the children surgically treated, but a fresh focus appeared in one child treated with radiotherapy, while in two other children similarly treated the lesions persisted but did not increase in size.

L. Firman-Edwards


The authors, who report from the Walter Reed Army Medical Center and the Georgetown University Hospital, Washington, D.C., compared the diagnostic value of serum calcium and phosphorus estimations with that of renal phosphate clearance in 36 patients with hyperparathyroidism, subsequently proven at operation.

Estimation of the serum calcium level proved the most valuable test of parathyroid hyperfunction, all 36 patients having serum calcium levels above 11.0 mg. per 100 ml. and 28 having values exceeding 11.5 mg. per 100 ml. Of the eight patients with calcium values between 11 and 11.5 mg. per 100 ml. (regarded as borderline) seven had a raised renal phosphate clearance (more than 16 ml. per minute). Serum phosphate levels were raised in only nineteen of the 36 patients; in the seventeen showing normal or near normal levels the renal phosphate clearance was raised in ten and normal in seven patients. Urinary calcium levels were normal in eleven of the 36 patients, and in ten of these the renal phosphate clearance was abnormally high. It is concluded that measurement of renal phosphate clearance is a reliable diagnostic aid, particularly when the serum calcium and phosphorus levels are only slightly abnormal. F. W. Chattaway


Other General Subjects


A 53-year-old woman, who had had signs of Sjögren’s syndrome from the age of 47 died of pneumonia. Histological examination showed atrophy of the glandular tissue in the lacrimal and salivary glands with slight fibrosis, and marked round-cell infiltration, chiefly mature lymphocytes and some plasma cells, in the interstitial connective tissue. In the parotid glands concentric hyaline rings were seen in the outer layers of the small arteries. Focal round-cell infiltration was demonstrated in the kidneys, suprarenal glands, pituitary gland, and bone marrow. G. von Bahr


On the Validity of the Concept of So-called "Malignant" Rheumatic Disease. (Sulla validita 'del concetto di malattia reumatoide cosiddetta "maligna"). LUCHERINI, T. (1962). Policlinico, Sez. prat., 69, 1637. 27 refs.


Therapy


Experimental modification of thyroid function is known to bring about changes in the pituitary-adrenal axis. The theories postulated by earlier workers are reviewed by the present authors working at the Warner-Lambert Research Institute, New Jersey. The present hypotheses assume that adrenocortical function is decreased by thyroid hormones. The subject is now re-examined and the findings give doubts on the validity of earlier assumptions.

The variables used in investigating thyroid influences on the pituitary-adrenal axis were adrenal weight; plasma free corticosterone levels; corticosterone production by adrenal incubates; pituitary ACTH content; and volume of distribution of corticosterone. Experimental hypothyroidism was induced in intact male rats by goitrogen administration; by surgical thyroidectomy and surgical hypophysectomy.

Hyperthyroidism induced an increased adrenal weight. However, this could be prevented by the injection of prednisolone tertiarybutylacetate; by hypophysectomy or when hypophysectomized rats were treated with constant small doses of ACTH. The findings indicate that the adrenal weight is influenced indirectly by the thyroid favouring ACTH release from the pituitary. The difficulty of interpreting the effects of hypothyroidism on the pituitary-adrenal axis is discussed in the light of the method used in inducing the hypothyroid state.

Plasma corticosterone levels were twice as high in thyroid-treated animals as in controls after ACTH injection. This increase is attributed to a 50 per cent. reduction in the volume of distribution of corticosterone in the thyroid-treated group. Adrenals of untreated or thyroid-treated intact rats produced similar amounts of Δ4,3-ketosteroids when incubated with ACTH in vitro compared with normal rats. Despite an increase in adrenal size, the actual production of corticosteroids was not significantly influenced by the thyroid. In view of the dissimilarities of distribution and initial concentration in the corticosterone volume studies, no significant conclusions were possible.

Thiouacil was found to be unsuitable as a drug for the study of thyroid-adrenal interactions because of its extrathyroidal and extrapituitary effect on adrenal cortical function.

The present evidence suggests that the functional life of ACTH may be decreased by thyroid. Some of the possible mechanisms which appear to counterbalance the increased ACTH output resulting from thyroid administration are discussed. The main conclusions suggest that the pituitary-adrenal axis is not impaired by hypothyroidism. Because hyperthyroidism was found to decrease the volume of distribution of corticosterone, it suggests the operation of a homeostatic mechanism to prevent hypercorticoidism. There is no indication that the thyroid hormone acts directly upon the adrenal cortex.

T. J. Hunt

Histologic Alterations in the Adrenal Cortex of Intact and Hypophysectomized Rats following ACTH, Pitressin, and Adrenal Steroids. WEXLER, B. C. (1963). Endocrinology, 72, 149. 18 figs.

The effects of the newer synthetic steroids (9-Alphafurohydrocortisone), with those of the older steroids (cortisone and deoxycorticosterone) on specific zones of the adrenal cortex were compared. Pitressin was included in the study because of its possible role in ACTH release.
ABSTRACTS

Intact and hypophysectomized male Sprague-Dawley rats were treated 24 hours after hypophysectomy. They were divided into three main groups and treated for 21, 42, and 63 days. Within each group there was further subdivision into groups receiving Pitressin, DCA, 9-Alpha-flurohydrocortisone, and ACTH, and another group received various combinations of the new and old steroids. At the end of the appropriate time interval the animals were killed by decapitation. Gross inspection was followed by a histological study.

The present results confirm the earlier finding that specific steroids are selective in their effects on specific zones in the adrenal cortex. These specific zonal alterations become more striking with prolonged treatment. The known effect of long-term ACTH administration in reversing the atrophy and zonal alterations produced by cortisone were also examined. It was found that, although ACTH can reverse atrophic and lipiddedepleting effects of cortisone on the zona fasciculata, it is unable to do so against the more potent new steroid 9-Alpha-flurohydrocortisone.

The differences in the effects of steroid treatment in intact and hypophysectomized animals are discussed. In most cases the results of steroid treatment of the hypophysectomized animals had many side-effects, including polyuria, polydypsia, and (in the case of the potent new steroid) hyperreactivity.

It is suggested that the zona glomerulosa is probably more essential for life maintenance than other zones of the adrenal cortex. The fact is stressed that 4 unit of ACTH when given alone, was sufficient to cause a significant increase in adrenal size in intact rats. But this dose was not sufficient to offset the atrophy induced by treatment with adrenal steroids. A gradual refractoriness towards ACTH developed with time. This might explain the lack of protection offered by 4 unit of ACTH against the zona atrophy induced by the lengthy administration of adrenal steroids.

The present long-term studies on the effect of hypophysectomy up to 63 days showed that the zona glomerulosa of the hypophysectomized rats remains filled with lipid and continues to increase in width.

It is advised that it is necessary to adjust the amount of ACTH to counterbalance the predicted physiologic effect of a given steroid, or the functional status of the adrenal gland. The importance of the dose of ACTH in affecting good adrenal zonal maintenance, and in offsetting the disease atrophy induced by steroids is mentioned.

Finally, it is recommended that the dose of ACTH be increased to prevent zonal changes when more potent steroids are used.

T. J. Hunt


The dangers to the foetus of the use of steroids during pregnancy have been widely reported in the literature. In an attempt to measure this risk, 33 women attending the subfertility clinic attached to L’École de Puériculture, Paris, who were given steroids during pregnancy were studied. Of the 33 patients, 27 were attending the clinic because of repeated miscarriages, and 25 of these were given steroids because the urinary 17-ketosteroid level was raised; the other two patients were already receiving steroids (for chronic polyarthritides and generalized eczema respectively) when they became pregnant. The remaining six patients in the series had attended the clinic because of sterility; the 17-ketosteroid level in the urine was high during the luteal phase and they were treated with steroids, which were continued when they became pregnant.

Hydrocortisone was given to five patients and its delta form to 28. The delta preparation was administered orally in doses which never exceeded 9 mg, a day initially for some 10 to 20 days and then in a dosage of 3 mg daily, corresponding doses of the hydrocortisone were given. Treatment was started at varying times. In all except three patients it was begun within the first 3 months of pregnancy (soon after conception in eight); twelve patients received steroids for almost the whole of the pregnancy and 8 received them from the end of the first trimester until term. There were 33 live infants (eighteen male and fifteen female), all of whom appeared normal; none showed any evidence of adrenal insufficiency. Nothing untoward occurred in any of the seventeen infants who were followed for periods up to 6 years.

The author contends that, although cortisone given during pregnancy may be dangerous to the infant, any resulting harm probably depends on the clinical condition of the mother at the time the treatment is given, the duration, and above all the dosage, which, in all 33 cases in this series was standard and moderate. Some workers have contended that the danger lies in delayed administration and others in too early treatment, but in this series thirteen and eight patients respectively were treated so without misadventure. The author could find no correlation or significance in the degree or rate of fall in the urinary 17-ketosteroid level resulting from the steroid treatment.

David Morris


It has often been stated that the majority of ulcers on the greater curvature of the stomach are malignant, but this view has recently been challenged. The author of this paper from the Radcliffe Infirmary, Oxford, describes four cases of benign gastric ulcer on the greater curvature in patients on long-term steroid therapy in moderately high dosage. The first patient, a male, was 24 years of age when admitted to hospital in 1953 with a 6-month history of polyarthritis and Raynaud’s phenomenon affecting all limbs; later the typical skin changes of scleroderma developed. In the second patient, a man aged 38 on first admission to hospital in 1958, collagen disease was provisionally diagnosed and later periarteritis nodosa. In the third patient, a girl aged 15 years on first admission to hospital in 1952, adrenal hyperplasia was diagnosed. The fourth patient, a female, was first
admitted to hospital in 1956 at the age of 63 for assessment of gross long-standing rheumatoid arthritis.

While the patients were receiving long-term steroid therapy gastric symptoms developed which called for treatment with an ulcer regimen of diet and antacids. Barium-meal examination showed an ulcer crater on the greater curvature in the first three patients. The dosage of steroid was thereafter reduced in one of these cases and ultimately in the other two (following haematemesis in one and perforation in one). Subsequent barium-meal examination revealed healing of the ulcer crater in these three cases. In the fourth case the initial barium-meal examination was negative, but a later examination after haematemesis and melaena demonstrated an ulcer crater on the greater curvature.

It is pointed out that the importance of recognizing the greater-curvature steroid ulcer is that it forms a group of ulcers in this situation which are without exception benign. Such ulcers characteristically lie in the antral portion of the stomach. In view of the tendency of barium to “pocket” between the coarser mucosal folds along the greater curvature an ulcer crater may be dismissed as such a “pocket”; this happened in the second case in this series, but retrospective examination of the radiographs showed an ulcer on the greater curvature. The ulcers are usually of moderate to large size with margins sharp and punched out. Healing tends to occur with minimal fibrosis.

The author has examined the case histories of all patients with gastric ulcer confirmed by barium-meal examination at the Radcliffe Infirmary in the 4 years 1957-61. During this period there were two cases of steroid ulcers of the lesser curvature as well as three of the cases described in the present paper. The evidence suggests that in patients receiving steroid therapy there is a greater tendency for ulcers to form on the greater curvature.


Prednisolone phosphate which if freely soluble in cold water was administered in the form of effervescent 5 mg. tablets dissolved in water to 27 patients at the London Hospital who had had dyspepsia during conventional oral steroid treatment for rheumatoid arthritis (25 cases) and polyarthritis nodosa (2 cases). Barium-meal examinations had been made in 21 patients fifteen of whom showed some abnormality radiographically.

Prednisolone phosphate was discontinued in three patients whose primary condition and dyspepsia deteriorated, and in two others who became free from dyspepsia and were able to revert to other oral steroids. One patient ceased attending for treatment but the remaining 21 were followed for a mean period of 17 months. The rheumatoid arthritis was well controlled by prednisolone phosphate and in only two cases was any deterioration reported. The severity of the dyspepsia decreased during the period of observation, dietary restrictions were needed in fewer patients and antacid consumption was reduced. Salicylate medication did not change appreciably in the group during the period of observation.

The authors regard prednisolone phosphate as the preparation of choice in the management of steroid-induced dyspepsia.


In this paper from the Paediatric Clinic of the Inner Mission, Garmisch-Partenkirchen, Germany, the treatment with methylprednisolone of six children aged 2 to 15 years with rheumatic fever and 42 with rheumatoid arthritis or Still’s disease is reported. The initial dosage for patients with rheumatic fever was 32 mg. per sq. m. body surface a day [but subsequent dosage is not stated]. The average duration of treatment was 122 days. In five cases the disease became inactive and in one it followed a chronic relapsing course. The patients with rheumatoid arthritis were treated on average for 276 days. The average initial dosage was 26 mg. per sq. m. daily and the maintenance dosage 4·7 to 8·5 mg. per sq. m. Treatment with salicylates, chloroquine, gold, and other agents was given at the same time. In addition, at intervals of 6 to 8 weeks a 10-day course of adrenocorticotropic hormone (ACTH) was given. While the activity of the disease and the function of the joints improved, no patient was symptom-free at the end of the course of treatment.

Three cases of iritis or iridocyclitis improved under treatment with methylprednisolone. While the initial dose of methylprednisolone was used was slightly lower than that recommended for prednisolone, the maintenance dose had to be as high or higher. The authors report, however, that side-effects were less frequent with methylprednisolone than with prednisolone.


Following the work of Maier in Liverpool and of Nathan and Scott at the National Hospital, Queen Square, London (Lancet, 1958, 1, 76; Abstr. Wild Med., 1958, 24, 15) the present authors, working at Massachusetts General Hospital, Boston, have investigated the value of intrathecal injections of phenol for intractable pain in 87 patients most of whom had advanced cancer. Two techniques were employed:

1. A 7·5 or 10 per cent. solution of phenol in “pantopaque” (iophendylate) was injected in volumes of 2 to 10 ml. under radiographic control on a tilting table in order that the solution might be accurately placed so as to reach the posterior roots which it was desired to impregnate;

2. A 5 per cent. solution of phenol in dehydrated glycerin was injected in amounts up to 1 ml. and the solution appropriately placed by noting the areas of paresthesiae or sensory reduction produced and tilting the table accordingly.
ABSTRACTS

In both techniques the patient lies on the affected side for 45 minutes after the injection, which is made as close as possible to the roots to be impregnated.

Of 57 patients treated with phenol in iophendylate fifteen obtained complete relief from pain and fourteen were benefited; 24 required more than one injection. The incidence of complications was small, only three developing disturbance of vesical control and three weakness of a leg. Initial analgesia was quickly lost, and there remained only a slight hypoalgesia. Of thirty patients treated with phenol in glycerin, nine had excellent or good relief from pain and twelve fair relief; in this group nine required more than one injection. Complications included weakness of a leg in four patients, loss of proprioception in a leg in one, and paraesthesia in four. Not only does this technique rarely disturb sphincter control, but it can relieve pain with the production of only minimal reduction of sensation, including awareness of a pinprick. It has been suggested that the phenol solution affects the small unmyelinated fibres in the posterior spinal roots, leaving the large myelinated fibres intact.

If there is as yet little information concerning the duration of the pain relief achieved by these techniques, since the majority of these patients are suffering from advanced malignant disease and the duration of life is short. There appears to be no doubt, however, of their usefulness in such cases.

J. E. A. O’Connell


The antifungal action of griseofulvin is of proven value in dermatology. Because of its apparently anti-inflammatory effect, Cohen and others (J. Amer. med. Ass., 1960, 173, 542) tried it, quite empirically, in certain rheumatic disorders and found it had a strikingly beneficial and unexpected effect on the “shoulder-hand syndrome”. This empirical observation led the authors to study the therapeutic action of griseofulvin in similar cases, and they now present this report, from the Rheumatology Clinic of the University of Montpellier.

In all, 94 patients have been treated with the drug in doses of 1 to 3 g. daily (divided into equal doses given three or four times daily) for 3 days to 3 weeks, with no sign of intolerance. In nineteen cases of the shoulder-hand syndrome, the observation of Cohen and others was fully confirmed. The duration of the malady varied from one week to 6 months. In all cases pain, in both the shoulder and hand, diminished or disappeared within 24 to 48 hours from the start of treatment. The effect on restricted movement at the shoulder was less striking, and the restriction of finger flexion was not benefited. The sympathetic signs in the hand, such as sweating, oedema, and local warmth, were favourably affected. In six cases of post-traumatic reflex sympathetic dystrophy of the extremities the same prompt relief of pain and trophic changes was noted.

In 31 cases of peri-arthritis of the shoulder the effect was variable. The more painful and more recent the condition, the more effective the medicament appeared to be, and this is the best indication for its use; considerable relief of pain is usually obtained in the first 48 hours and pain is entirely lost within a few more days. In cases of longer duration a beneficial effect is much less obvious and restriction of movement is largely unaffected. A good effect was also noted in fifteen cases of acute gout, but griseofulvin appears to be little, if at all, superior to treatments in common use. Lastly, in ten cases of pseudo-polyarthritis rhizomélique (the syndrome of Forestier and Certonciny, described in Great Britain under the inappropriate name of “polymyalgia rheumatica”) pain was relieved in seven, while in three there was an appreciable fall in the erythrocyte sedimentation rate.

No adequate reason can be given for the observed beneficial effect of griseofulvin in these cases. Its chief indication would seem to be the reflex sympathetic dystrophies of the upper limb, especially the shoulder-hand syndrome, and for relief of pain in recent and acute cases of peri-arthritis of the shoulder.

Kenneth Stone


Guervain’s Disease, and its Local Treatment with Corticosteroids. (La malattia di de Quervain e il suo trattamento locale con corticosteroidi). VIARA, M. (1962). Reumatismo, 14, 309. 1 fig, bibl.


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