ABSTRACTS

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

The abstracts selected for this Journal are divided into the following sections:

- Acute Rheumatism
- Rheumatoid Arthritis
- Still's Disease
- Osteo-Arthritis
- Spondylitis
- Inflammatory Arthritis
- Gout
- Bone Diseases
- Non-articular Rheumatism, including Disk Syndromes, Sciatica, etc.
- Pararheumatic (Collagen) Diseases
- Connective Tissue Studies
- Immunology and Serology
- Biochemical Studies
- Therapy
- Other General Subjects

At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.

ACUTE RHEUMATISM


The early diagnosis of acute rheumatic fever is usually easy, but there is often doubt whether the heart is affected. In this paper from the Université Libre and the Hôpital Universitaire St-Pierre, Brussels, the authors report a study of the value of the Q-T interval as a criterion. This interval represents electrically the duration of cardiac systole, and it is inversely proportional to the heart rate; the corrected Q-T interval (Q-Tc) may be calculated from Bazett's formula: Q-Tc = \( \frac{\sqrt{R-R}}{R} \) (sec), where R-R is the duration of the cardiac cycle. The normal value of Q-Tc, as proposed by Almirurg, is 0·404 sec. The present authors took the upper limit of normal to be 0·430 sec., although they believe that about 15 per cent. of normal children might have values slightly higher than this.

The investigation was carried out in two parts:

1. In 102 episodes of acute rheumatic fever affecting 91 children ECGs were recorded at the beginning of the illness and during treatment with corticosteroids and penicillin. The children's ages ranged from 4 to 16 years, and fifty were boys. Prolongation of Q-Tc was found before treatment in 45·1 per cent. of cases (to more than 0·430 sec in 35·3 per cent. and to more than 0·456 sec in 9·8 per cent.). Patients with a normal Q-Tc at this stage retained it throughout the study. In all but three (2·9 per cent.) of the cases Q-Tc reverted to normal during corticosteroid therapy, usually within a week; but corticosteroids were not given in some relapses, and in such circumstances Q-Tc took longer to become normal. Of nine children who still had an increased Q-Tc after their first or subsequent attack, three relapsed within a year and one developed mitral insufficiency 4 years later. (Certain apparent numerical discrepancies do not seem to be resolved.)

2. A study was also made of 110 children with a similar age and sex distribution to that of the first group; all had had rheumatic fever but none had shown clinical or laboratory evidence of active disease or cardiac involvement for at least a year. Only 10·9 per cent. of these had a slightly increased Q-Tc; this incidence is greater than that expected for normal children, but nevertheless greater than the 2·9 per cent. found in children treated with corticosteroids. This difference suggests that corticosteroids shorten the duration of cardiac systole. Again, no patient who escaped valvular damage showed lengthening of Q-Tc; thus corticosteroids may prevent cardiac damage.

The authors conclude that Q-Tc is of diagnostic importance. Prolongation of Q-Tc at the end of treatment was an unfavourable sign in half the cases studied, and patients showing this feature should therefore be followed up with particular care.

Joan Gomez


It is difficult to diagnose Bouillaud's disease in the presence of a febrile rheumatism syndrome in a child. In the present study the attacks of rheumatism occurring in a 5-year-old boy were accompanied by miscellaneous clinical symptoms—among them plastic iritis, polymorphous erythema, congestion of the lung and, later, abdominal pain. Corticosteroids were prescribed as treatment for Bouillaud's disease but failed, and antimalarials were given instead. After some months of treatment with Nivaquine the attacks grew less frequent and less severe and the plastic iritis improved.

Anita Edwards


Benzathine penicillin (Bicillin) was first used in the U.S.S.R. for the seasonal prophylaxis of rheumatic fever about 10 years ago. In 1963 a programme of continuous prophylaxis was initiated at the Institute of Rheumatism of the Academy of Medical Sciences, Moscow, in which bactericidal blood concentrations are maintained with intramuscular injections of 1·5 megaunits Bicillin-5 every 4 weeks.

In a group of 100 adult patients (12 male, 88 female) with a history of recurrent rheumatic carditis with valvular lesions who were undergoing continuous prophylaxis serial estimations of the antistreptolysin-O (ASO) (all patients), antistreptohyaluronidase (ASH) (46 patients), and antistreptokinase (ASK) (46 patients) titres were carried out at intervals of 3 to 4 months for 2 years. A high degree of correlation was found between the clinical course and changes in the ASO and ASK titres. Thus in patients whose rheumatism was inactive throughout the period of observation these titres remained normal; when treatment was started during an exacerbation the titres returned to normal in 3 to 6 months in patients whose attack followed an acute course and in 6 to 12 months when it was protracted; and in patients who had recurrent attacks despite prophylaxis the ASO and ASK titres remained high. In contrast the ASH titre showed considerable variation between normal and high levels without any correlation with other indices of rheumatic activity.

S. W. Waydenfeld


Over the past 3 years the authors of this paper from the Catholic University of Rio de Janeiro, Brazil, have been studying tricuspid stenosis, which they believe is fairly frequent in rheumatic heart disease. They have collected 41 cases; 23 of the patients were women, and the average age of the group was 28 years. All 41 had concomitant mitral valve disease, but only four had atrial fibrillation. As a result of investigations which included electrocardiography, phonocardiography (intracardiac as well as extracardiac), and haemodynamic measurements of the right atriioventricular gradient the patients were divided into three groups.

Group 1 (16 patients). These had very mild tricuspid stenosis with little or no pressure gradient between the right atrium and ventricle. Auscultation might reveal the stenosis, and the phonocardiogram showed the characteristic appearance. The authors emphasize the diagnostic value of Rivero-Carvalho's observation that during inspiration tricuspid murmurs are accentuated while those arising in the mitral valve diminish. Five of these patients were recatheterized 1 to 3 years later, when they were found to have developed a pressure gradient between the right atrium and ventricle.

Group 2 (22 patients). These had the characteristic murmur, and an atriioventricular pressure gradient was always present though it might be as small as 2 mm. Hg. There were no congestive changes.

Group 3 (3 patients). All these had congestive cardiac failure, with marked venous dilatation. They were subjected to mitral and tricuspid valvotomy, both valves being treated at the same operation. All three improved clinically.

The authors point out that radiography can also help in the diagnosis of tricuspid stenosis: the right atrium will be hypertrophied and there may be evidence of dilatation of the superior vena cava. Most authors stress that in tricuspid stenosis the jugular veins are congested, but in the present study this sign was only a late manifestation.

(The paper is illustrated by several ECGs and phonocardiograms.)

Paul B. Woolley


RHEUMATOID ARTHRITIS

Pulmonary Infections and Rheumatoid Arthritis. Walker, W. C. (1967). Quart. J. Med., 36, 239. 1 fig., 45 refs. Little attention has been paid to pulmonary infections occurring in patients with rheumatoid arthritis although...
an association has been suggested. The author of this paper has therefore investigated the incidence and significance of pulmonary infections in this disease. A total of 516 patients (140 male, 376 female) with definite or classic rheumatoid arthritis (ARA criteria) attending the Rheumatism Clinic at the General Infirmary at Leeds, Yorkshire, and 301 control patients (62 male, 239 female) with degenerative joint disease were studied. Respiratory symptoms were noted, inquiry was made regarding previous respiratory diseases and smoking history, and chest radiographs were taken in all cases.

Chronic bronchitis (defined as a cough productive of sputum on most days throughout periods of 6 months for at least 2 consecutive years) was present in 31 (22 per cent.) of 140 men and in seventeen (4.5 per cent.) of 376 women with rheumatoid arthritis, the incidence in the controls being six (10 per cent.) and sixteen (7 per cent.) respectively. In most cases the bronchitis preceded the rheumatoid arthritis. A history of pneumonia was given by 37 (28 per cent.) of the men and 77 (20 per cent.) of the women with rheumatoid arthritis, the corresponding figures for the controls being six (10 per cent.) and 36 (15 per cent.). The majority of attacks of pneumonia antedated the onset of the arthritis. The rheumatoid arthritis group contained sixteen cases of definite bronchiectasis (proven by bronchography or with a history of cough with purulent sputum, haemoptysis, positive physical signs, and abnormal chest radiograph), ten of probable (strongly suggestive radiograph or typical history without radiographic confirmation), and eight of possible (localized shrinkage on chest x-ray without suggestive symptoms) bronchiectasis. The control group contained one definite, one probable, and one possible cases of bronchiectasis. The lung disease preceded the rheumatoid arthritis in thirteen patients. The incidence of pulmonary tuberculosis (radiographic evidence) was the same in both groups and nonpulmonary infections were not more common in the rheumatoid arthritis group than in the controls. In the former group 60 per cent. of the women were nonsmokers and in the controls 65 per cent. were nonsmokers. However, only 7 per cent. of the men with rheumatoid arthritis were non-smokers compared with 19 per cent. of controls.

The author considers that pulmonary infections may play an aetiological role in some cases of rheumatoid arthritis and he discusses the possible mechanisms.

K. C. Robinson

Asymmetrical Rheumatoid Arthritis after Poliomyelitis.


This paper from the Metropolitan Hospital, London, describes findings which suggest that paralysis protects a limb from the effects of rheumatoid arthritis. Complete or partial absence of arthritic change was found in the paralysed limbs of twelve patients with rheumatoid arthritis who had paralysis owing to previous poliomyelitis. There was good correlation between the clinical and radiological findings. The more severe the paralysis, the greater was the degree of sparing; very little arthritis was found in flail limbs. Nodules, found in three cases, were confined to the non-paralysed limbs in two.

The author suggests that this sparing of joints is due to absence of the high intraarticular pressures that have been shown to occur during normal active movement. These pressures might force synovial fluid and—in rheumatoid disease—abnormal globulins into and through the synovial membrane. Such considerations may have relevance for decisions about rest and exercise in the management of patients with rheumatoid arthritis.

B. E. W. Mace


The authors of this paper from the Kivelä Hospital, Helsinki, Finland, record the effects of intra-articular administration of radioactive gold (198Au), their aim being to achieve the equivalent of a bloodless synovectomy in the affected joint. The radioactive gold was given in colloidal suspension, diluted in some cases with 0.9 per cent. saline solution. The dosage depended upon the area of synovium to be treated, ranging from 1 mCi for metacarpophalangeal joints to 2—5 mCi for shoulders and elbows and 5—10 mCi for knee joints. The region of the treated joint, the local lymph glands, liver, spleen, and heart were scanned for radioactivity 1 hr, 24 hrs, and several days after each injection. Scanning of the whole body was carried out in some cases and in two the radiation dose to the gonads was calculated after treatment of a knee joint. Radioactivity reached its maximum 24 hrs after injection and thereafter decreased with the decay of the 198Au.

Ninety patients (74 female, 16 male) were given a total of 165 intra-articular injections into various joints, but the present report is concerned chiefly with 85 of these patients. All suffered from synovitis of the knee joint, with effusion due to rheumatoid arthritis in 83 cases and to osteoarthrosis in two cases. These patients were treated by intra-articular injections into the knee joint only and remained under observation for periods of from 4 months to 2 years. Of the 85 patients treated, no benefit ensued in eighteen, effusion and tenderness were reduced in 39, and the effusion disappeared in 28; a second treatment improved the effect in six cases. In nine patients in whom osmium tetroxide was injected into the opposite knee joint the results appeared to be slightly better with radiogold. Scanning showed that some diffusion beyond the joint had occurred in 89 per cent. of cases; the diffusion was slight in about 50 per cent. but serious in 36 per cent. Calculated radiation dose to the liver was insignificant or small (up to 40 r) in all except one case—in this case it was 40—50 r (equivalent to that which might follow a thorough radiological examination of the abdomen). The radiation dose to the lymph nodes exceeded 5,000 r in five out of 27 studied and in one it was over 15,000 r, which carries a risk of radiation injury. In one case (illustrated) the scintigram showed an activity defect in a lymph node that persisted more than 8 days—this suggested necrosis in the centre of the
ABSTRACTS

STILL'S DISEASE


The authors of this paper from the University of Michigan, Ann Arbor, have seen 130 children aged less than 14 years with juvenile rheumatoid arthritis during the 5-year period 1961–65, and in forty of these (31 per cent.) the disease was initially monoarticular and remained confined to one joint for at least 4 months.  (The criteria for diagnosis are listed.)  In these forty cases girls were more often affected than boys (3:1), and the commonest age at onset was 2 to 3 years (thirteen children).  The disease remained monoarticular in nine children (for a median observation period of 6 years).  In nineteen children two to four joints later became affected, and in twelve children more than four joints; those who developed polyarthritis tended to do so relatively soon after the onset.  The joint most often affected initially was the knee (75 per cent.); the early symptoms were mild and only three children had spontaneous pain.  Only one child eventually developed rheumatoid nodules; synovial biopsies were performed in sixteen cases, but no histological evidence of rheumatoid nodules was found.  Uveitis and band keratopathy developed in six patients—a significantly higher incidence for the group with monoarticular disease than for the total 130 patients.  There were no other complications and no deaths.

Radiologically, there was temporary increase of bone growth near the affected joint, with acceleration of epiphyseal maturation.  Bone necrosis occurred late and was not serious.

John Lorber


node.  The radiation dose to the gonads was deemed equivalent to that which might occur with routine x-ray examination of the colon.

Discussing their findings, the authors express some concern about the diffusion of radioactivity from the treated area and consider that injections of 186Au should be reserved for patients over the age of 40.  As a further precaution a tracer dose of 0.5 mCi might be given initially to test for diffusion.  They conclude that so far as effusion in knee joints is concerned radioactive gold given by intra-articular injection is effective in most cases and at least as efficient as osmium tetroxide.

William Hughes


The genetics of rheumatoid arthritis (RA) and of the rheumatoid factor (RF) have been studied in two large Indian populations.  No evidence was found that genetic mechanisms play any important role in the etiology of RA and RF in these tribes.—[Authors' summary.]


Central Nervous System Involvement in Rheumatoid Disease.  OUYANG, R., MITCHELL, D. M., and ROZDILSKY, B. (1967).  Neurology (Minneap.), 17, 1099.  7 figs, 18 refs.


OSTEO-ARTHRITIS


SPONDYLITIS


INFLAMMATORY ARTHRITIDES


In the original description of this disease, Whipple emphasized the accumulation of fat within the intestinal mucosa and mesenteric lymphatics, although he also noticed rod-shaped organisms in the affected tissue. In 1949 Black-Schaffer found PAS-positive macrophages within the intestinal mucosa. More recently electron microscopy has confirmed the presence of organisms.

This paper from the Veterans Administration Hospital and Duke University Medical Center, Durham, North Carolina, reports an electron microscope study of small-bowel biopsy specimens from four patients with Whipple's disease who were either untreated or in relapse and of necropsy material from a further four patients who had died before the introduction of antibiotic therapy.

Many of the findings confirmed those of other authors. Thus bacteria were scattered throughout the lamina propria of all five biopsy specimens from patients with active disease and the lamina propria was packed with macrophages containing disintegrating bacteria, although plasma cells were scarce. Polymorphonuclear cells containing bacteria were also found within the lamina propria and in the spaces between absorptive cells. The epithelial cells were normal except that they contained many lysosome-like bodies in their apical third.
A hitherto unreported finding, however, was the presence of myriads of bacteria within intestinal absorptive cells at the villous tips. Many of the prominent lysosome-like bodies in the villous tips contained bacteria in the terminal stages of digestion. Organisms which seemed more viable were confined to the bases of absorptive cells and the intercellular spaces. Bacteria were not seen in specimens taken during antibiotic therapy. The lymphatic vessels appeared to contain precipitated protein, presumably of bacterial origin, and in one case a bacterial form was identified intact within an intestinal lactic.

Fat malabsorption in Whipple's disease has not been satisfactorily explained. One possibility is that bacterial invasion of the epithelial cells renders them functionally abnormal, and the authors also suggest that the large numbers of macrophages within the lamina propria physically impede the progression of chylomicrons to the central lacteal. Further obstruction to the lymphatic flow probably occurs because of enlargement of the mesenteric nodes. The original portal of entry of the bacteria is still unknown.

A. W. H. Foxell


GOUT


From the Veterans Administration Hospital and the University of California School of Medicine, Los Angeles, the authors report four cases in which symptoms and signs of median nerve compression in the carpal tunnel occurred in association with tophaceous gout. The diagnosis was confirmed by the finding of delay in motor nerve conduction time or of EMG evidence of denervation in the thenar muscles. Section of the anterior carpal ligament was performed in two cases with relief of symptoms; the presence of tophaceous deposits on the flexor tendons was confirmed in one of these cases. In another case the symptoms gradually decreased in severity after 3 to 4 years of uricosuric therapy, but delay in nerve conduction time has persisted. In the fourth case section of the carpal ligament has been postponed until the effect of more intensive uricosuric therapy can be seen. In addition to these cases a cadaver of unknown medical history, but with large tophi, was shown on dissection to have marked indentation of the left median nerve at the wrist with a tophus on the flexor tendons beneath it.

Only two cases of the carpal tunnel syndrome associated with gout appear to have been reported previously, but the authors suggest that it may be found more often if specifically looked for.

B. E. W. Mace


Some authors have suggested that serum uric acid levels are higher in men of greater aspirations or achievement. In this paper from the University of Michigan and the University of Michigan Medical Center, Ann Arbor, the authors compare the serum uric acid levels of a group of 167 normal healthy business executives aged 30 to 59 with the values in an age-matched general population; the Tecumseh population was chosen for this purpose because 88 per cent. of the total population of 9,500 had already been studied in detail. [For references the original paper should be consulted.]

The executives had a higher mean serum uric acid concentration than did the controls (P < 0.05); within the executive group the subgroup of bankers had the lowest mean uric acid concentration, but this value was still higher than the mean for the Tecumseh population. Uric acid levels did not appear to be related to age.

The executives tended to be taller and heavier than the controls, with a higher relative weight (observed weight divided by predicted weight), which suggests a greater degree of fatness. Although a low but significant correlation was found between uric acid level and body fatness, fatness was nevertheless sufficient to explain only a small percentage of the higher uric acid levels.

A correlation was noted between uric acid level and blood pressure, and the authors think that this correlation may be influenced by the known connection between fatness and blood pressure. They caution against attaching too much importance to this finding, because the blood pressures were measured by different technicians.

The executive group had higher serum cholesterol levels. No correlations were found between serum levels of uric acid and cholesterol in executives, nor were correlations found for the Tecumseh population except in the case of the lowest age group (30 to 39). The authors therefore feel that the higher mean serum uric acid of the executives is not the result of a rise in serum cholesterol levels.
The small number of executives studied and the many variables concerned did not allow the drawing of definite conclusions about the effect of smoking on uric acid levels. However, the executive group contained relatively more nonsmokers and ex-smokers than did the Tecumseh population; in the Tecumseh population ex-smokers tended to have higher uric acid levels.

The two populations showed a clear difference in the amount of physical activity taken. Only 6 per cent. of the executives were classed as moderately active, and none as active. Of the Tecumseh population about one-third was put in each group (sedentary, moderately active, and active). Serum uric acid levels were not related to activity in the Tecumseh group except for boys excelling in athletics, in whom they were higher; however, the more physically active executives had the highest uric acid levels.

The authors conclude that they cannot decide whether men with high uric acid levels also possess the attributes which lead to executive positions, or alternatively whether the executive way of life leads to a rise in uric acid levels. However, executives show the characteristics associated with coronary heart disease to a greater extent than does the general population.


Hyperuricaemia is known to exist more frequently in younger patients with cardiac infarction than in healthy control subjects. The authors of this paper from the University of Pittsburgh School of Medicine and the Veterans Administration Hospital, Pittsburgh, first review the literature on certain aspects of serum triglyceride levels, especially in relation to body size, and then report a study of the interrelationships among a group of factors—serum levels of uric acid, cholesterol, and triglyceride, and body size—in both healthy persons and those with a history of gout, myocardial infarction, or cerebral thrombosis.

The healthy control group contained 225 men and 135 women who were accepted or acceptable as blood donors. The upper level of normal for serum uric acid was taken as 6·5 mg./100 ml. in men and 5·5 mg./100 ml. in women; in 20 per cent. of the men and 14 per cent. of the women the levels exceeded this value. The uric acid level appeared to be unrelated to age. Serum cholesterol levels did rise with age, but were unaffected by sex or race; as with uric acid, levels were lower in women than in men of corresponding age. Serum triglyceride levels are known to vary widely from day to day and to be affected by a diet rich in fat and even more so by one rich in carbohydrate: the values were lower in women than in men and lower in negroes than in white subjects.

Body size, as reflected by the ponderal index, was larger in sixty gouty subjects than in age-matched controls: triglyceridaemia but not cholesterololaemia was found in this patient group, but the concentrations of both substances were lower in gouty negroes than in gouty white people. The levels of all three substances were not significantly different in 32 patients with a history of cerebral thrombosis from those in control subjects whose mean age was 12 years younger. On the other hand, all three substances were present in higher concentrations in 32 patients who had a history of myocardial infarction. Finally, the concentrations of the three substances appeared to be independent of one another in the healthy subjects and also in the gouty patients. The authors concludes that the metabolic basis of the disease process in cerebral arterial thrombosis is different from that underlying arteriosclerotic coronary disease.

H. Summers


There has been conflicting evidence on the relationship between obesity and the levels of lipids and other biochemical components in blood. This study concerned 104 men who had been psychiatric inpatients for at least 5 years in the Veterans Administration Hospital, Palo Alto, California. All were physically healthy and in the age range 36 to 78 years (median 49). Body fatness was assessed in four ways: by their absolute weight, ponderal index, skinfold thickness over the triceps, and by recent changes in weight. Three blood samples were taken at weekly intervals for estimation of serum cholesterol, triglycerides, and uric acid and plasma glucose levels, and the mean of these three weekly estimations was used for analysis.

Age showed a negative correlation with obesity (r = -0·32 for weight, -0·31 for ponderal index, and -0·40 for skinfold thickness). This suggests either that obesity causes early death or that men lose weight as they grow older. All indicators of body fatness correlated significantly with serum triglyceride (r = 0·43-0·45) and with uric acid (r = 0·40-0·43), but less with glucose and cholesterol levels (r = 0·14-0·31 and 0·07-0·26 respectively). Partial correlation coefficients, eliminating the relation of each biochemical component to obesity, showed that only cholesterol and triglyceride values were significantly linked with one another, and even this relationship was of a low order (r = 0·20; P < 0·05).

Multiple correlation analysis, using the ponderal index as a measure of obesity, showed that obesity had a significant independent relationship to triglyceride, glucose, and uric acid but not to cholesterol levels.

When the men were divided arbitrarily into obese and lean categories according to their ponderal index and triceps skinfolds, the obese showed significantly higher values for serum cholesterol, triglyceride, uric acid, and plasma glucose. All four biochemical components were also higher in the 46 men who had gained at least 10 per cent. of their body weight in hospital.

T. B. Beggs

Excluding diabetic and hypertensive retinopathy, 76 per cent. of 46 patients with “retinal vascular accidents” (retinal haemorrhages, vessel spasms, thrombosis, etc.) manifested an abnormally high urinary uric acid level.

*J. L. Baum*


**BONE DISEASE**


Osteomalacia is probably more common than is generally recognized amongst elderly people in Britain and the present paper analyses the findings in 37 patients presenting for the most part in South-East Scotland. Of these all but three were women and the mean age was 72 years.

Diagnosis was made on the basis of combined clinical, radiographic, and laboratory findings. Important presenting symptoms were skeletal pain and progressive muscular weakness. Fourteen patients presented with fractures and Looser’s zones were recognized in thirty. Radiographic translucency was most marked in the limbs, contrasting with the predominantly axial distribution of osteoporotic rarefaction. While plasma calcium and inorganic phosphorus levels were low in the majority, eight had calcium x phosphorus products greater than 27. Alkaline phosphatase levels were raised in 31 patients and urinary calcium excretion was diminished in most of the subjects tested. Subjective histological assessment of undecalcified bone sections (site not stated) was carried out in 25 cases and was the basis of diagnosis in those in whom other findings were equivocal; three patients with histological evidence of osteomalacia had normal biochemical and radiographic findings.

Evidence of mild intestinal malabsorption was found in some patients and was not confined to those who gave a history of previous gastric surgery. Other factors of possible aetiologic significance were lack of sunlight and inadequate dietary intake of vitamin D. Correction of the vitamin D deficient state was effective in treating the condition.

*A. Garner*


Sodium fluoride has a well-recognized osteosclerotic effect and because of this it has been suggested as a possible treatment for osteoporosis. The authors of this paper from Harvard Medical School and Robert Breck, and Peter Bent Brigham Hospitals, Boston, describe calcium and phosphate balance, x-ray crystallographic, and histological studies made on twenty out of thirty osteoporotic patients who were treated for 2 to 12 months with sodium fluoride; only those patients with idiopathic osteoporosis (except one patient with active thyrotoxicosis) were studied.

Calcium and phosphate balance was studied before and during fluoride therapy in a dosage of 22-66 mg./day. Bone biopsies were obtained from the mid-portion of the iliac crest either before or after 1 year of treatment (in three patients biopsies were obtained both before and after treatment). [For details of the tests performed the original should be consulted.]

In eighteen of the twenty patients a slightly positive calcium balance was obtained (mean increase in calcium balance 113 mg./day); this increase was statistically significant (*P < 0.001)*. The serum alkaline phosphatase level, usually normal in osteoporotic subjects, rose occasionally in three patients given 44 mg. or more fluoride daily. The results of all other blood tests and urine analyses remained unchanged during therapy. Eighteen patients reported a significant reduction in bone pain and an increase in mobility. Radiography of the lumbar spine revealed increased bone density in four patients receiving fluoride in a dosage of 44 mg./day. X-ray diffraction studies of bone, performed on some patients, showed that the incorporation of fluoride into the hydroxyapatite shell produced larger and more perfect bone crystals. Histological studies of bone biopsy material showed complex changes in lamellar
resorption, osteoid seam width, calcification, and osteon activity.

The authors suggest that fluoride may be useful as adjunctive therapy in various metabolic bone disorders, but stress that they make no claims as to its curative value. They found no evidence of an effect on any system except bone and calcium metabolism.

M. J. Tarlow


The authors of this paper from the Hôpital Tenon, Paris, have sought a relationship between the bony lesions of Paget's disease and changes in elastic tissue. They made histological studies of skin taken by biopsy from twelve patients with Paget's disease and also examined the appendicular vessels and the vessels of muscle from other patients with this condition, as well as the vessels associated with bone in material obtained at necropsy.

The skin showed some atrophy of the epidermis and some dermal abnormalities such as vascular hyperplasia with surrounding inflammatory cells. Superficially there was a loss of the fine elastic fibrils, while at deeper levels the elastic fibres assumed unusual prominence. Vessels from all the sites studied showed thickening, reduplication, and fragmentation of the internal elastic lamina, together with some calcification.

The authors feel that in Paget's disease there is an abnormal proliferation of elastic tissue, and though they cannot relate this directly to the bony lesions, they suggest that classification of Paget's disease with McKusick's mesodermal congenital dystrophies should be considered.

G. Loewi


The author describes a clinical case, which besides the known symptoms of Marfan's syndrome presents duplication of the lueta, atrophy of the optic nerve, and mitral stenosis. The frequency of congenital mitral stenosis is discussed as well as the classification of this case as Marfan's syndrome or as a new similar congenital syndrome.

P. Vancea


Acacutonuria and Ochronotic Arthropathy. (Acacutonurie et arthropathie ochronosique.) PHOCAS et al. (1967). Rev. Rhum., 34, 381.


NON-ARTICULAR RHEUMATISM


The authors of this paper from the Sanatorium des Éperons, St-Martin-du-Tetrc, Val-d'Oise, France, have seen 85 patients with periarthritis of the shoulder among an all-male population undergoing treatment for tuberculous spondylitis. The overall incidence was 2.3 per cent. In three cases a clearly local or traumatic cause was evident; in the remaining fifty the shoulder lesion was attributed either to tuberculosis itself or its drug treatment. Some of these patients also had a shoulder-hand syndrome. The periarthritis occurred particularly in men aged more than fifty, usually within a few months of the patients starting their first course of treatment. Half had symptoms in both shoulders. There was no correlation between the side of the affected (or worse) shoulder and...
the side of the affected lung. The lung lesions were usually severe.

The symptoms were pain and stiffness in the shoulder with (by definition) inability to abduct the arm beyond 90°. In no case did the shoulder joint proper seem to be affected. There was no increase in ESR attributable to the shoulder. Radiography showed osteoporosis of the humeral head without any specific abnormality in the shoulder joint.

The authors suspect that sensitivity to one or more of the anti tuberculous drugs used accounted for at least some of the fifty cases [though no evidence is produced for this view]. Psychological factors were evidently also of importance. Treatment consisted of repeated injections of corticosteroids; physiotherapy and manipulation were held in reserve until the worse of the initial painful phase was over.

J. A. Cosh


A case is presented of iritis with formation of nodules and raised ocular tension, preceding the appearance of erythema. The possibility of association with Behçet’s syndrome, Heerfordt’s disease, or the Stevens-Johnson syndrome is considered but the clinical course in this case did not establish this possibility.

Author’s Summary


PARARHEUMATIC (COLLAGEN) DISEASES


In this paper from the Johns Hopkins School of Medicine and the Johns Hopkins School of Hygiene, Baltimore, the authors report what they believe is the first recorded population study of systemic sclerosis. The hospital records, necropsy reports, and death certificates of all 53 persons known to have died with systemic sclerosis in Baltimore (population nearly a million) between 1949 and 1963 inclusive were reviewed, and each of these subjects was compared with two controls matched for decade of age, sex, and race who had died of "natural causes" (other than violence or suicide).

In each successive 5-year period, particularly the last, the number of cases of systemic sclerosis increased. Women outnumbered men (39 to 14), and 38 per cent. of the patients were negros. When Baltimore residents (as opposed to those who had died in Baltimore but were not residents there) were considered separately, the mortality risk for negro females was seen to be three times that for white females (6.6/million/year and 2.2/million/year respectively); similar findings have been reported for systemic lupus erythematosus in New York City. Negro and white males did not differ significantly in their mortality risks (1.0/million/year and 1.3/million/year respectively). Survival times for female and male patients were approximately equal, but were significantly shorter for negroes compared with whites.

No significant occupational or other environmental or personal factors distinguished the patients from the controls, even though special attention was paid to occupational exposure to silica dust, which has been reported as a possible contributory cause of the disease.

F. T. H. Wood


The author of this paper from the National Institutes of Health, Bethesda, points out that corneal and other ocular abnormalities are much commoner in systemic lupus erythematosus than is generally believed. Out of 24 patients with this disease (which was in clinical remission in fifteen) thirteen had symptoms of corneal...
abnormality (blurring of vision, photophobia, pain, sensation of a foreign body in the eye, or the appearance of flashing lights) and 21 showed corneal staining with fluorescein. This staining was usually punctate and only apparent with the biomicroscope; as a rule it lay just inside the limbus in the area covered by the upper lid. Only five out of 100 control subjects showed such staining, and this was slight.

The author also illustrates and discusses certain other lesions seen in these patients, including a previously undescribed retinal depigmentation. He is uncertain about the pathogenesis of the corneal lesions, although he feels able to exclude as possible causes corticosteroids and deficient tear formation.

J. S. Malpas


At the Kaiser Foundation Hospital, Oakland, California, the authors studied the ability of the kidneys to excrrete acid and concentrate the urine in twelve patients with systemic lupus erythematosus (SLE). Twenty-one healthy subjects of similar age served as controls. All the patients had some evidence of moderate renal involvement, mainly confined to mild proteinuria, microscopic haematuria, and cylindruria, but none was uraemic or acidaemic. Renal biopsy was performed on six patients and showed mild nonspecific changes only.

Mean baseline values for blood hydrogen ion concentration, urinary pH, urinary titratable acid and ammonium excretion rates, and creatinine clearance were similar in the two groups. In response to a loading dose of ammonium chloride (0.1 g./kg. body weight) the SLE group showed a mean rise in blood hydrogen ion concentration similar to that seen in the control group, but the mean minimum urinary pH was significantly higher and the mean excretion rates of titratable acidity and ammonium significantly lower (P < 0.001 in each case) than in the control group. Renal concentrating ability (as indicated by urine osmolality after 14 to 15 hours of fluid deprivation) was also significantly (P < 0.01) impaired in the SLE group.

These findings are taken to indicate that renal tubular acidosis, which has been shown to occur in certain rheumatic disorders such as Sjögren's syndrome and in various types of hypergammaglobulinaemic state, may also be present in subclinical form in patients with SLE.

M. Wilkinson


Corticosteroids were first used to treat periarteritis nodosa in 1950 and although the initial results have been very encouraging little is known about the long-term effects. The authors of this report from the Mayo Clinic and Foundation, Rochester, have assessed the results of treating 130 patients with histologically proven periarteritis nodosa seen in the Clinic from 1945 to 1962, comparing those who received corticosteroids with those who did not, in an attempt to define the effect of corticosteroid administration on prognosis. The patients ranged in age from 6 to 75 years and there were twice as many males as females. For both sexes the maximum incidence of the disease was in the middle aged. Symptoms of systemic disease occurred in over 70 per cent. of patients whilst involvement of the joints, skin, or nervous system was noted in about 50 per cent. of cases.

A total of 110 patients received treatment with corticosteroids or ACTH during or shortly after their initial examination. The remaining twenty patients were not given corticosteroids either because their disease was too mild or because the nature of the condition was not established until necropsy. In the treated group patients received corticosteroids (cortisone 200 mg./day or its equivalent) or ACTH for at least 6 weeks, and then either continuous or intermittent therapy was given to 24 patients for the next year; 33 patients received corticosteroids for 10 years because of recurrent manifestations.

Comparison of the treated with the control group revealed that the 5-year survival rate was 48 per cent. in the former and only 13 per cent. in the latter. [The control group is so small and poorly matched that caution must be advised on any interpretation] Pulmonary involvement did not imply a worse prognosis, but the presence of hypertension and/or renal disease was a bad prognostic feature. In both the treated and control groups the chief cause of early death was renal failure.

The authors note the value of preliminary electrocardiography to determine the affected muscle and hence the best site for biopsy. In this way they were able to obtain a positive muscle biopsy in nearly half the patients in their series. They conclude that early recognition of periarteritis nodosa and prompt and adequate corticosteroid therapy are of the utmost value in improving the prognosis. They believe that the chief value of long-term therapy is to prevent relapses and suppress symptoms.

J. S. Malpas


A case report of periarteritis nodosa in a 58-year-old white female. Ocular manifestations included recurrent scleritis, keratitis, and choroiditis as well as retinitis. The ocular manifestations occurred 4 years before systemic involvement.

Paul Henkind


A young woman aged 22 presented with an acute abdominal pain and routine tests showed a positive Wassermann reaction for which anti-syphilitic treatment was started. It became evident that the true diagnosis was polyarteritis but despite high doses of systemic steroids she developed bilateral choroiditis with secondary retinal detachment. The condition was fatal.

J. H. Kelsey
Takayasu's Arteritis. Clinical Report of 84 Cases and Immunological Studies of Seven. Nakao, K., Ikeda, M., Kimata, S., Nittani, H., Miyahara, M., Ishimi, Z., Hashiba, K., Takeda, Y., Ozawa, T., Matsushita, S., and Kuramochi, M. (1967). Circulation, 35, 1141. 84 cases of Takayasu's arteritis were studied retrospectively. The distribution of lesions was investigated by aortography in 54, and clinically in thirty. The aortic arch and branches were involved in 47, the thoracic and lumbar aorta in ten, and there was generalized involvement in 27. In the early stages of the disease, the majority had symptoms suggestive of generalized systemic involvement, or symptoms attributed to pulmonary or cardiac involvement. Local pain over involved arteries was common. Arthritis or arthralgia was present in twelve.

Using a haemaglutination test with tanned red cells, circulating anti-artery anti-bodies were found in five out of seven cases. Eight patients had a positive DAT or latex test, and eleven a raised antistreptolysin-O titre but none were thought to have rheumatoid arthritis or rheumatic fever. Corticosteroids given in the acute stage induced a remission in five, and improvement in thirteen out of 29 patients. A. B. Myles

Prognosis of Rheumatoid Purpura (Schoenlein-Henoch): a Study of 50 Cases. (Pronostic du purpura rhuma
toid de Schoenlein-Henoch: à propos de 50 observations.) Orsini, A., Pierron, H., and Perrimond, H. (1967). Pédiatrie, 22, 283. Bibl. Henoch-Schoenlein purpura has usually been thought to be benign, but recently stress has again been laid on the abdominal and renal manifestations. To evaluate the prognostic significance of these the authors of this paper from the Hôpital de la Conception, Marseilles, have reviewed the course of the disease in fifty patients aged from 6 months to 8 years.

Three forms of the disease were distinguished:
(1) Mild forms (60 per cent.). In about one-third of these there was microscopic haematuria often accompanied by proteinuria; however, the illness only lasted for an average of 3 weeks and the urinary abnormalities usually disappeared in 2 months.
(2) Severe forms (34 per cent.). These were divided into a group with predominantly abdominal symptoms (pain and persistent slight intestinal bleeding) and indeterminate physical signs, and a group in which serious urinary abnormalities (more marked haematuria and proteinuria) developed in either an apparently mild case or in a severe case characterized initially by abdominal symptoms. The urinary abnormalities persisted for up to 2 years but then disappeared.
(3) Complicated forms (16 per cent.). There were two cases of pseudo-appendicular symptoms which appeared before the cutaneous purpura, two of intussusception, and one of pseudoperitonitis. Other patients in this group had severe prolonged renal abnormalities: one child died with nephritis, uraemia, and hypertension after 20 months, another still had microscopic haematuria and albuminuria after 8 years, while two others had such signs after 6 years.

In the short term the abdominal symptoms were of greater prognostic importance: the appendicular pattern was the commonest and most favourable, and the peritoneal variety rare but serious, while the prognosis in intussusception depended on early recognition and operation. Renal involvement was more important in the long term, but to assess it accurately biopsy by renal puncture was necessary. [The authors briefly describe four typical histological appearances.] The question of therapy, including the possible use of immunodepressive drugs, remains to be decided. Joan R. Gomez

Ischaemic Optic Neuropathy in Raynaud’s Disease and in Arteriosclerosis. [In Japanese with English Summary.] Tsukahara, I., Fujii, I., and Shimizu, A. (1967). Rinsho Ganka, 21, 833. 4 figs, 14 refs.

Two cases are reported. One patient had sudden blindness and died after periarterial sympathectomy of the brachial artery. Histopathology of the eye showed ischaemic necrosis of the optic nerve in the lamina cribosa. J. Tsutsui


This paper from the Departments of Pathology and Radiology, Yale University School of Medicine, New-haven, Conn., describes the clinical, radiological, and pathological findings of oesophageal diverticulae in a patient who died with dermatomyositis and breast cancer. Careful search of the literature by the authors failed to find a previous description of oesophageal diverticulae in dermatomyositis, although erosions and ulcerations had been described. Histological examination of the diverticulae showed that these were true diverticulae in that all layers of the oesophageal wall were present, although most of the muscularis mucosa was replaced by fibrous tissue. The authors point out that abnormalities in the barium swallow produced by these diverticulae could easily be confused with the changes produced by ulceration. In the patient described in this report no mucosal ulceration was present in the post mortem examination of the oesophagus. The authors considered that the diverticulae were due to scarring and atrophy of the smooth muscle of the muscularis mucosa of the oesophagus. W. Watson Buchanan


This paper describes two patients with the classical syndrome of polymyalgia rheumatica who both had the classical features of temporal arteritis on biopsy of the temporal artery and who subsequently developed ocular complications with blindness. On the basis of their own observations and a review of the literature the authors came to the conclusion that polymyalgia rheumatica is a symptom complex in which temporal arteritis may be the underlying disease in up to half the patients.
consider that the importance of polymyalgia rheumatica is that in many cases it reflects giant cell arteritis with a consequent risk of blindness. The authors therefore recommend that temporal artery biopsies should be made in suspected cases of polymyalgia rheumatica, even if there is no clinical abnormality of the temporal artery. If arteritis is present, especially with giant cells, corticosteroids should be given in high dosage, 40 to 60 mg. prednisolone or equivalent, for 12 weeks. This recommendation is made since in classical temporal arteritis corticosteroids reduce the incidence of blindness and since the visual complications are most likely to occur within 12 weeks of onset of the general symptoms.

W. Watson Buchanan


Idiopathic thrombocytopenic purpura (ITP) can arise from a variety of causes. In some cases of disseminated lupus erythematosus (DLE), purpura is present before the disease can be diagnosed clinically. The present authors, from the Departments of Medicine and Pathology, Western Reserve University School of Medicine, and the University Hospitals of Cleveland, Ohio, studied in retrospect the records of all cases of thrombocytopenia in which splenectomy was performed at the University Hospitals of Cleveland over a period of 25 years (1940-65), and found that cellular alterations in the spleen could in a significant number of cases support a diagnosis of DLE before definite clinical symptoms of the disease appeared.

Records of 69 patients with thrombocytopenia were studied: six due to drug sensitivity, eight as a result of infectious disease, sixteen associated with DLE, and 39 in which ITP was the only possible diagnosis. The first two groups had an immediate response to splenectomy with an increase in platelet count which remained normal (defined as initial rise to >300,000 per mm.\(^3\) and subsequent level of >150,000 per mm.\(^3\)).

Of the patients with DLE, seven were diagnosed clinically before splenectomy. Cytological changes suggestive of DLE were present in the spleen of nine cases and of these only one had no clinical evidence of DLE 14 years after operation. Three changes were present in the spleens of fourteen out of the sixteen cases of DLE: the presence of large mononuclear cells with prominent nucleoli in the follicles and marginal zones; plasma cells in the nonfollicular white pulp; and nonphagocytic mononuclear cells in the walls and lumens of the sinusoids of the red pulp. The authors consider these, when all three are present, to be criteria for the diagnosis of DLE by histological examination of splenic tissue. Photographic illustrations of these abnormalities are given. Nine of the sixteen patients in this group had a permanent remission of their thrombocytopenia after surgery.

Histological and cytological changes (enlargement of the germinal centres, dilation of the sinusoids of the red pulp, and the presence of varying numbers of megakaryocytes, eosinophils, and neutrophils) found in the patients with ITP were not specific for thrombocytopenia. Of 39 patients studied, 24 responded to surgery with a rise in platelet count, and of these 22 were in complete remission for 1 to 15 years. No response was obtained in fifteen patients. No reliable criteria to predict which patients would benefit from splenectomy were found in either group. The authors note that, although the patients with ITP were drawn from a large Negro community, only two patients were of that race—a fact noted by others.

I. M. Nairn


CONNECTIVE TISSUE STUDIES


Leucocytes containing characteristic cytoplasmic inclusion bodies, presumably resulting from phagocytosis of material precipitated within the synovial cavity, have been seen in the synovial fluid from joints affected with rheumatoid arthritis, and there is evidence that these inclusions contain rheumatoid factor. It also appears that lysosomal enzymes play a part in the pathogenesis of some rheumatoid lesions of joints, especially by causing destruction of the cartilage.

If it be assumed that lysosomes normally participate in the digestion of foreign material ingested by the cell, such material, if immunogenic, should react immunologically with the lysosomes. The above considerations led the authors of this paper from the University of Chile, Valparaiso, and the University of Virginia, Charlottesville, to undertake the following study.

Methods. 1. Leucocytes isolated from two types of source were examined:
(a) fluid from the knee joints of seventy patients with rheumatoid arthritis and 71 with other types of arthropathy;
(b) peripheral blood from the above seventy patients with rheumatoid arthritis, 33 further patients with rheumatoid arthritis but without joint effusions, seventeen patients with other diseases but without serological evidence of rheumatoid factor (RF), and 38 patients with other forms of arthropathy. The total number of leucocytes and the percentage containing inclusions were determined in an aliquot of each sample. The samples were then homogenized and the homogenates were tested for RF by latex techniques.

2. (a) Inclusion-containing leucocytes similar to those found in synovial fluid were artificially produced in vivo by incubation of leucocytes from normal blood with precipitates formed by RF and y-globulin.
(b) Lysosomal enzymes (acid phosphatase, b-glucuronidase, and cathepsin) were assayed in normal leucocytes and their lysosome fraction after incubation of the cells with RF-containing precipitates (as described above).

Results. 1. (a) Inclusion-containing leucocytes were present in the synovial fluid of all seventy patients with rheumatoid arthritis, the percentage of cells carrying such inclusions ranging from three to 36. RF was found in homogenates in 66 of these cases; in the four in which RF was absent the percentage of inclusion-containing cells was less than five. In fifteen of these cases serological tests for RF gave negative results. Inclusion-containing cells were found in synovial fluid of fourteen of the 71 controls, while RF was found in three of these cases.

(b) Inclusion-containing cells were found in the blood of 46 of the patients with rheumatoid arthritis and RF in 32 of these cases. In the 33 cases of rheumatoid arthritis the corresponding figures were fourteen and eight; in the seventeen cases of other diseases associated with serological evidence of RF, nil and nil, in the 38 cases of other arthritic conditions, three and one.

2. The immunological and enzymatic studies of normal leucocytes in vitro supported the view that the inclusion bodies are formed as the result of an immunological reaction between the lysosomes and the ingested material containing RF.

Conclusion. In a given case, the presence of leucocytes containing inclusions in synovial fluid (and to a lesser degree in blood) is strong though not conclusive evidence in support of a diagnosis of rheumatoid arthritis.

C. M. Ottley


A lymph-node permeability factor (LNPF), which can increase vascular permeability to plasma protein, cause emigration of leucocytes, and lead to deposition of a material resembling connective tissue fibrinoid, has been found in human lymphoid tissue and circulating lymphocytes. It has been suggested that LNPF causes the inflammatory changes found in many types of delayed hypersensitivity reactions. In this paper from St Bartholomew's Hospital, London, the authors report their detection of LNPF in human synovial tissue and synovial fluid.

Synovial membrane was obtained from three patients with rheumatoid arthritis who were undergoing synovectomy and at necropsy from four patients who had not had arthritic disease. Thirty specimens of synovial fluid were taken from twenty patients with a variety of joint disorders. The active principle was extracted by centrifugation (after ultrasonic disintegration in the case of the synovial membrane specimens). Assessment of activity was performed by binding an azo dye (trypan blue) to plasma albumin by incubating leucocytes from normal blood with precipitates formed by RF and y-globulin.

(b) Lysosomes (enzymes (acid phosphatase, b-glucuronidase, and cathepsin) were assayed in normal leucocytes and their lysosome fraction after incubation of the cells with RF-containing precipitates (as described above).

The present study, reported from the Department of Orthopaedic Surgery and Pathology of the Columbia University College of Physicians and Surgeons, New York, confirms the light microscopic findings published in an earlier communication (Shaw and Bassett, Anat. Rec. (1964), 149, 57) and describes the ultrastructural observations on the osteogenesis in a tissue culture system.

In this system, explants of 11-day-old chick embryos were cultured for a period of 7 to 14 days. At 14 days, striking changes were observed near the cartilagenous ends and cut and exposed surfaces. Many chondrocytes near the ends showed advanced degenerative change; the majority of the lacunae contained either no cells or only fragments of necrotic cells. In this region many lacunae contained varying amounts of 640 Å banded collagen fibrils with greatly variable thickness (diameter 450-4,000 Å). Many collagen fibrils with more uniform thickness (500 Å average diameter) were also noted in the inter-lacunar space replacing fine non-banded filaments of the normal matrix. Intra and extra-lacunar collagen fibrils were more numerous near the distal ends. At the cut surface also numerous collagen fibrils with more uniform diameter (average 500 Å) were observed replacing most of the pre-existing thin non-banded filaments of the matrix. In the newly formed osteoid on the exposed surface of the explants the cells which morphologically resembled osteoblasts and osteocytes were found along with the matrix containing randomly arranged collagen fibrils and showing focal calcification. In this region the collagen-apatite and matrix-cell relationships were similar to that in embryonic bone. The authors believe that trophic collagen formed by osteoblasts in the region diffuse into the cartilage ends where they aggregate to form collagen fibrils.

In 7-day specimens, the only significant change was a disappearance of glycosaminoglycan from the chondrocytes of the explants and the presence of many osteoblasts with little matrix on the cut surface.

The authors have confirmed in this study that mineralisation of in vitro formed organic matrix can take place in tissue culture and most of the morphological features of embryonic bone can be re-duplicated in this system.

S. Roy


Metabolism of Collagen and its Hormonal Control in the Rat. Laitinen (1967). *Acta endocr. (Kbh.)*, Suppl. 120.

**IMMUNOLOGY AND SEROLOGY**


[At the Medical College of Virginia Hospitals, Richmond] serum immunoglobulin levels were determined in 45 patients with rheumatoid arthritis and in 25 control subjects of similar age and race. Total immunoglobulin, IgA and IgM levels were significantly, but not strikingly, elevated in the rheumatoid patients. Neither sex, age (in the 40 to 60 year span chosen for study), duration of disease, stage of disease nor rheumatoid factor titres was significantly correlated with serum immunoglobulin levels.—*Authors’ summary.*


In previous papers Najjar et al. have proposed that the serum γ-globulins consist not only of antibodies to specific antigens but also of a variety of specific (but nonantibody) fractions which coat cell membranes and are necessary for cell function and survival. To study this problem the authors devised a chromatographic method of fractionating γ-globulin which allows the separation of four fractions (I-IV). They then undertook further studies based on the assumption that deficiency of any one fraction might predispose the subject concerned to a particular disease, and in this paper from Vanderbilt University School of Medicine, Nashville, Tennessee, they report an association between complete absence of Fraction I and acute rheumatoid arthritis.

Sera from three children with rheumatoid arthritis and one child who had psychomotor retardation and whose maternal uncle had classic agammaglobulinemia were studied. [The authors state that the patient with psychomotor retardation “neither showed symptoms nor had a history of arthritis”, but this appears to be contradicted in one table.] In all four patients the γ-globulin was electrophoretically normal both in the γ-globulin preparations and in whole sera. No significant immunoelectrophoretic abnormalities were found in γM or γG, but γA was completely lacking. Ultracentrifugal studies showed the normal 7S and 19S characteristics of γ-globulin, and no 22S complex was seen. Chromatography [for details of which the original paper should be consulted] revealed a total absence of Fraction I, which is normally composed of γA and of some γG-globulin with the same elution characteristics as γA.

The relatives of one of the rheumatic patients were also studied. Although she had no history of arthritis, the mother showed alterations of γ-globulin similar to those of her child. This child, unlike the others, failed to respond to salicylates or prednisone; she was therefore treated with intramuscular injections of γ-globulin
(3.2 g. once a month) for 8 months and improved; her serum γ-globulin then contained near-normal levels of Fraction I. When γ-globulin injections were withdrawn her symptoms recurred but remained mild; apparently normally constituted Fraction-I γ-globulin continued to be found in her serum 6 months after the withdrawal of therapy, both γA and the type of γG belonging to Fraction I being present. The authors speculate that γA may actually be made from γG.

William H. S. George


Reactivity of Subunits of IgM and anti-B. ECONOMIDOU et al. (1967). *Immunology*, 13, 235.


**BIOCHEMICAL STUDIES**


This study based on fourteen patients with active rheumatoid arthritis and control groups consisting of fourteen healthy people and sixteen ill patients of whom four had inactive rheumatoid arthritis and the others other rheumatic disorders, or general medical conditions suggests that the cortisol metabolism of patients with rheumatoid arthritis differs from controls in three ways.

1. The excretion of cortisone relative to cortisol was increased;
2. 20-dihydrocortisol was excreted in excess while the ratio cortisol/20-dihydrocortisol was markedly decreased;
3. 6β-hydroxycortisol excretion was increased. Although no correlation could be found between the amount 6β-hydroxycortisol excreted and the drugs taken this possibility cannot be excluded. There appeared to be no correlation between the excretion of free cortisol metabolites and the urinary 17-hydroxycorticosteroids.

A hypothesis which could accomodate these findings was put forward suggesting that in the presence of inflammation, the rate at which cortisol is locally inactivated is enhanced with the effect of reducing the stability of lyozomes and of furthering the inflammatory process.

B. M. Ansell


In vitro Effect of Thyrocalticon on Bone Solubility. KHAN et al. (1967). Endocrinology, 81, 398.

Study on Calcium Metabolism, Thyroid Calcitonin Assay, and Effect of Thyroidectomy in Pseudohypoparathyroidism. MAZZUOLI et al. (1967). Israel J. med. Sci., 3, 627.


THERAPY


From the County Hospitals of Copenhagen in Gentofte and Glostrup, the authors of this paper describe their use of three cytostatic drugs—thiotepa, azetepa, and osmic acid—which were used intra-articularly in the treatment of various rheumatoid diseases. In all they treated 39 patients (thirty female, nine male, aged 18 to 75 years), 32 of whom had rheumatoid arthritis according to ARA criteria, three osteo-arthritis, two chronic traumatic synovitis, and one each lupus erythematosus and plasma cytoma. Azetepa was used in five cases, azetepa seven cases, and osmic acid in five. The last two drugs were injected into the knee joint only, whereas thiotepa was injected into the smaller joints as well, in a dosage ranging from 5 mg. for finger joints to up to 50 mg. for knee joints. Azetepa was given in a dosage of up to 50 mg. while osmic acid was given as a 1 per cent. solution (100 mg. in 10 ml.); 3 to 4 hours after injection as much as possible of the osmic was withdrawn from the joint. In six cases the injection of thiotepa was repeated after 2 weeks because the first injection had been ineffective, and in seven cases corticosteroids were injected into the opposite knee joint as a control. Patients were followed up for 2 to 2.5 years; leucocyte and thrombocyte counts were “rigidly controlled” and liver function tests and also synovial biopsy examinations were performed in some cases.

In ten cases (eight of rheumatoid arthritis and one each of osteo-arthritis and traumatic synovitis) there was either no obvious improvement or an improvement which lasted less than 2 weeks; in fourteen cases (eleven of rheumatoid arthritis, two osteo-arthritis, and one lupus erythematosus) improvement of from 2 weeks to 3 months’ duration was observed and in fifteen cases (thirteen of rheumatoid arthritis, one of traumatic synovitis, and one of plasmacytosis) improvement lasting more than 2 years was observed. Osmic acid, which was given to patients with rheumatoid arthritis only, produced lasting benefit in four out of five patients, while azetepa had a prolonged beneficial effect in four out of seven patients. Thiotepa gave temporary benefit to seventeen out of 27 patients, but only seven of these (five with rheumatoid arthritis) achieved permanent benefit. Side-effects included severe and painful local reactions for 1 to 3 days after each injection of osmic acid. There was a considerable fall in the leucocyte count in one patient after simultaneous injections of 75 mg. thiotepa into both knee joints. The patient recovered after treatment with blood transfusion, corticosteroids, and antibiotics.

The authors consider that azetepa and osmic acid give better therapeutic results than thiotepa, but that the painful local reaction after osmic acid will preclude its use except in the most refractory cases. [Cytostatic drugs are the most dangerous used so far for the treatment of rheumatoid arthritis. Much more detailed observation will be required before these remedies can be recommended for use outside hospitals or research institutions.]

William Hughes

Controlled Clinical Trial of Flufenamic Acid in Rheumatic Arthritis. [In English.] SYDNESE, O. A. (1967). Acta rheum. scand., 13, 55. 3 figs, 7 refs.

At Haugesund Sanitetsforenings Revmatismesykehus, Haugesund, Norway, the author has carried out a double-blind crossover trial of flufenamic acid in comparison with a placebo in the treatment of thirty patients—27 with “definite” rheumatoid arthritis (ARA criteria), two with spondylarthritis, and one with monarthrosis. The patients’ average age was about 50 years and the mean duration of the disease 80 months. Lansbury’s indices were used for clinical evaluation of the antirheumatic effect;
the system index is derived from the duration of morning stiffness, time of onset of fatigue, aspirin requirements, grip strength, and ESR; the articular index is based upon the number of joints involved and the activity in those joints. Before treatment each patient was observed for 1 or 2 weeks and the indices recorded. Treatment was then given for 2 weeks with either flufenamic acid 300-400 mg. daily or a placebo and the indices again recorded, after which the alternative treatment was given for a further 2 weeks and a final estimation of the indices made.

An improvement in both indices over the values recorded in the observation period was demonstrated with both flufenamic acid and placebo, but statistical analysis showed the drug to be significantly more active (P < 0.01 for articular, < 0.005 for systemic index). No side-effects or complications occurred.

C. E. Quin

Comparison of Duration of Activity of Corticotrophin-gelatin and Corticotrophin-carboxymethylcellulose.


Since corticotrophin is quickly destroyed in the blood stream a number of substances, notably gelatin, have been added in an attempt to prolong its action. A recent addition is carboxymethylcellulose, which is claimed to have a delayed-release action similar to that of gelatin. In order to test the validity of this claim the present author, at University College Hospital, London, examined the relative effectiveness of corticotrophin-gelatin and corticotrophin-carboxymethylcellulose. Ten normal subjects (two men and eight women aged 22 to 35 years) were studied without dietary restriction and while they continued their normal activities. A crossover method was used, each subject receiving one preparation 7 days after the other, the preparation used initially being selected at random. Endogenous corticotrophin release was minimized by 2 days' treatment with dexamethasone (2 mg. in four divided doses each day) and the dosage of each corticotrophin preparation was 40 IU by deep intramuscular injection. The indices of adrenal stimulation used were the plasma and urine levels of 11-hydroxycorticosteroids (11-OHCS) measured at various times after injection.

From 5 to 15 hours after injection corticotrophin-gelatin gave higher mean plasma levels of 11-OHCS and from 5 to 12 hours the excess was statistically significant (P < 0.05). From 7 to 12 hours after injection the urinary excretion of 11-OHCS was significantly greater with corticotrophin-gelatin whereas in the first 6 hours after injection the difference was not statistically significant.

It is concluded that corticotrophin-gelatin has more prolonged adrenal cortical stimulant action than corticotrophin-carboxymethylcellulose and therefore the claim that the latter has a similar delayed-release action to that of the gelatin preparation is not valid. Thus, caution is needed when changing from one preparation to another in equivalent doses.

W. L. Ashton

Treatment of Acute and Chronic Staphylococcal Osteomyelitis and Soft Tissue Infections with Lincomycin.


Lincomycin is an antibiotic which is active in vitro against Gram-positive cocci other than Enterococci but ineffective against Gram-positive and Gram-negative bacilli. Experimentally it has been shown to reach a high concentration in bone. In this paper from the Misericordia and Royal Alexandra Hospitals, Edmonton, Alberta, the author reviews the results of treatment with lincomycin in fifteen patients with staphylococcal osteomyelitis and eleven with soft-tissue infections.

Of the 26 patients (whose ages ranged from 5 to 60 years), 24 had previously been treated unsuccessfully with other antibiotics. Most patients were given 500 mg. of lincomycin 6-hrly by mouth for 4 to 7 days, followed by 500 mg. every 12 hours. Patients who were severely ill were given 600 mg. either in an intravenous infusion every 8 hrs or by intramuscular injection every 12 hrs. The duration of therapy varied from a few days to months depending upon the disease treated and the clinical response.

Oral lincomycin caused diarrhoea in three of the 26 patients, but only in one was this sufficiently severe to necessitate withdrawing the drug. All five patients with acute osteomyelitis and seven of the ten with chronic osteomyelitis recovered completely, while the remaining three improved slightly. All the patients with chronic osteomyelitis had previously had surgical treatment and only one successfully treated patient had had 32 operations. Seven of the eleven patients with soft-tissue infections (due mainly to Staphylococcus aureus and Streptococcus pyogenes) recovered completely, one improved, and three showed no benefit. Two of these last three were infected with organisms which were found to be resistant to lincomycin and treatment was withdrawn from the third because of severe diarrhoea.

The author is enthusiastic about these results and believes that the value of lincomycin may be due to its capacity to penetrate diseased bone and severely infected soft tissue—"whatever the explanation, certain clinical results of its use have been outstanding."

N. A. Simmons

Recovery of Hypothalamo-pituitary-adrenal Function after Corticosteroid Therapy.


The recovery was studied by measuring the plasma 11-OHCS concentration before and after IV insulin (0.1 unit/kg) using the technique of Landon et al. (1963). At the time of the test 31 patients had stopped taking corticosteroids for 24 or 48 hrs, fourteen for one month, and 26 for longer periods. All appeared to show some increment in 11-OHCS concentration in response to the induced hypoglycaemia, but at 48 hrs it was below normal in fifteen of thirty, at 1 month in two of three of fifteen, and after longer periods in one of 22. The defective responses occurred almost entirely in those
who had received 10 mg. or more of prednisolone daily and they could not all be forecast from the resting 11-OHCS concentrations. [That the adrenal must take some days to return to normal if it has been involuted by therapy is to be expected. The cause of delayed recovery—shown to occur in a small percentage of patients—has yet to be defined.] H. F. West

REFERENCE


Subtotal synovectomies were performed on the knee joints of rabbits, and 15 hours before being killed at daily intervals, 0.2 mc. 35S-labelled sodium sulphate was administered to each animal intravenously. Up to 15 days, the maximum period studied, the operated knees showed no decrease in the uptake by the articular cartilage of the labelled sulphate radical, as measured by autoradiography. Compared with the control knees, there was a suggestion that the superficial layers of cartilage in the synovectomized knees showed increased uptake of sulphate. This was considered to indicate that, during the period studied, synovectomy produced no impairment of the ability of the chondrocytes to absorb and utilize sulphate. The results also suggest that there exists an adequate pathway for supplying the articular cartilage with sulphate, which is unaffected by synovectomy.

In a further series of animals in which synovectomized knee joints were stained with toluidine blue after being killed at intervals up to 100 days, absence of metachromasia, in varying degree, was noted during the period of synovial regeneration. This is considered to be due to diffusion of a cathepsin or plasm in from the joint cavity into the cartilage, with subsequent enzymatic degradation of the protein-polysaccharide ground-substance, while the increased uptake of sulphate by the superficial layers is thought to represent an attempt by the chondrocytes to replace this ground substance. W. Wilson Downie


126 synovectomies were performed between 1965 and 1966 on a total of 64 patients with chronic rheumatoid arthritis. A short term follow-up, ranging from 6 months to 2 years was performed, to investigate the local effects of surgery on the operated joint, and the general effect of synovectomy on the rheumatic disease process itself. Of the 126 operations, 59 were performed on knees, four on hips, and 63 on hands, comprising 33 synovectomies of tendon sheaths and thirty on digital joints. The local effects were studied on knee joints using pre- and post-operative arthrography, post-operative biopsy of regenerating synovium, serial x rays of the joint, and the drying-up of effusions. The results indicate that following synovectomy, the regenerating synovium is diseased, but the articular cavity is enlarged, and the effusions are less abundant than before surgery. There is no evidence that synovectomy has any effect on the x-ray appearances of the bony outlines of the joint. The functional effect of synovectomy was measured by the subjective assessment of alteration in pain and mobility by the patient. It was found that pain was relieved in more than 90 per cent. of cases, at least within the period of follow-up, but stiffness was little altered. The authors' conclusion is that pain in the joint is a prime indication for synovectomy, but that stiffness in a pain-free joint is unlikely to be relieved by surgery.

The effect of synovectomy on the disease process itself in 31 cases was investigated objectively by comparison of pre- and post-operative laboratory parameters: erythrocyte sedimentation rate, RA Latex and Waaler-Rose tests, antinuclear factor, and L.E.-cells. Reduction in therapeutic requirements, e.g., steroids and salicylates, was regarded as an index of improvement. It was concluded that a small number of cases showed definite improvement in their general condition following synovectomy as judged by favourable alterations in the above criteria. The authors conclude that this aspect should be examined more closely, and also suggest that the application of synovectomy in early cases of the disease might have a prophylactic value.

W. Wilson Downie


At the Second Moscow Medical Institute and the Institute of Rheumatism of the Academy of Medical Sciences, Moscow, ophthalmological examinations were carried out on 100 patients (20 men, 80 women) aged 17 to 65 years with rheumatoid arthritis who had been under treatment with chloroquine phosphate (Resochin) for periods up to 4 years. Activity of the disease was maximal in only three cases and thirty patients were in remission. More than half the patients had been ill for less than 5 years.

Eye changes were demonstrated in 27 patients altogether. Deposits of chloroquine localized in the corneal epithelium and subepithelial tissue were found in ten patients. Retinal changes were quite common, but not always attributable to chloroquine. Constriction of the field of vision was demonstrated in fifteen cases. None of the patients showed evidence of optic atrophy. The dose of chloroquine used was low (125–250 mg. daily), which probably explains the relatively low incidence of ocular side-effects which, however, was shown to increase in direct proportion to the duration of uninterrupted therapy. It is claimed that the frequency of such side-effects can be reduced by half if chloroquine therapy is withdrawn for 1 to 2 months each year.

S. W. Waydenfeld

Report of the case of a 13-year-old boy who had received treatment for 3 years for chronic polyarthritis; after sudden suppression of the drug he presented a severe intracranial hypertension syndrome with papilloedema; recurrence of treatment was followed by total recovery; the drug was then gradually discontinued without any new damage.

S. Vallon


In a 5-year-old boy with rheumatic fever, β-methasone 2 mg. was given every day; 4 days later, it caused an increase in intraocular pressure. This acute rise in pressure was reproduced in this patient by the administration of β-methasone.

Y. Mitsui


A case report in which central serous retinopathy developed in a patient who was receiving large doses of corticosteroids for Reiter's syndrome. As the therapy was stepped up in total dosage a rise in the blood pressure occurred for which reason the dosage was again reduced. The retinopathy coincided with the sudden reduction of the dosage.

The pathogenesis in this case is considered to lie between angiospastic oedema of the sensitive macular region and intravascular clumping within the arterioles and capillaries as a thrombo-embolic phenomenon which is known in therapy with corticosteroids. S. N. Cooper


No evidence of the development of posterior subcapsular cataract should be found in 136 patients treated with Betnesol drops or ointment for periods exceeding two months to 3 years.

R. F. Fisher


Clinical Study of a New Corticosteroid Intra-articular Injection: Paramethasone Acetate (75 Cases Treated) (Etude clinique d'un nouveau corticostéroïde intra-articulaires: l'acetate de paramethasone (75 cas traités.) VINEL, P. (1967). Rhumatologie, 19, 126. 7 refs.


Results with Indomethacin Treatment. (Nos résultats dans le traitement à l'indométacine.) GASPARDY, G., and BALINT, G. (1967). Rhumatologie, 19, 287. 7 refs.


ABSTRACTS


Value of an Extract of Fresh Cartilage and Fresh Bone Marrow in Association with Physiotherapy and Thermal Therapy in Rheumatoid Arthritis. (Significato dell'associazione d'un estratto di cartilagine fresca e di midollo osseo fresco in trattamenti fisioterapici e termali nella poliartrosi.) LORENZINI, P. (1967). Riv. med., 81, 841.


Action of intra-articular Prednisolone, Tertiary Butyl Acetate (Codelcortone TBA), and Methylprednisolone Acetate (Depomedrone) in the Normal Rabbit Knee Joint. BRANEMARK et al. (1967). Acta orthop. scand., 38, 247.


Review of Flufenamic Acid in Rheumatoid Arthritis. HILL, A. G. S., p. 87. 3 figs. 7 refs.

Controlled Clinical Trial of Flufenamic Acid in Rheumatoid Arthritis. SYDNES, O. A., p. 93. 3 figs, 8 refs.

Clinical Trial of Flufenamic Acid in the Treatment of Rheumatoid Arthritis. CARDOE, N., p. 99. 6 refs.

Flufenamic Acid and Indomethacin in Rheumatoid Arthritis. BAIN, L. S., and MASHETER, H. C., p. 104. 1 fig., 2 refs.


Comparison of Flufenamic Acid and Phenylbutazone in Osteo-arthritis of the Hip. BROCKS, B. E., p. 114. 1 fig., 2 refs.

Mefenamic Acid compared with Indomethacin and Placebo in Osteo-arthritis. BUCHMANN, E., p. 119. 2 figs. 7 refs.


OTHER GENERAL SUBJECTS


Sjögren’s syndrome is sometimes complicated by lymphoma. Furthermore, in certain lymphoid disorders, such as Hodgkin’s disease and chronic lymphatic leukaemia, the peripheral blood lymphocytes lose the ability which they normally possess to transform themselves into large “blast” cells in vitro in the presence of various mitogenic agents. In this paper from the National Cancer Institute and the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, the authors report a study of lymphocyte transformation in 33 patients with Sjögren’s syndrome.

Blood lymphocytes from the patients and from 20 normal control subjects were incubated in vitro with phytohaemagglutinin (PHA) or streptolysin O (SLO). With PHA the percentage of lymphocytes undergoing transformation ranged from 6 to 81 (median 39) for the patients, compared with from 41 to 83 (median 65) for the controls. With SLO the respective percentage ranges were 0 to 45 (median 6) and 2 to 47 (median 16).

Transformation was impaired in about one-third of those patients in whom only the sicca syndrome of dry eyes and mouth was present, but in cases where the disease was complicated by rheumatoid arthritis, pseudolymphoma, or malignant lymphoma the proportion was higher. Essentially similar results were obtained when lymphocyte transformation was assessed by measuring the uptake of tritiated thymidine. That impairment of transformation was not due to a serum abnormality was shown by the fact that it could not be corrected by the use of normal human plasma or calf serum as a medium for resuspension in place of the patients’ own plasma.

Delayed skin hypersensitivity to contact stimulation with 2, 4-dinitrochlorobenzene (DNCB) could be induced in only eight of the 33 patients with Sjögren’s syndrome (24 per cent.) compared with sixteen out of seventeen normal subjects (94 per cent.). No correlation was found between the in vivo responsiveness to DNCB and in vitro lymphocyte transformation in the presence of either PHA or SLO.

The authors discuss their results in relation to the known existence of two types of lymphocyte and speculate that in Sjögren’s syndrome the lymphocytes in the parotid gland are of the “central” type (that is, similar to those in the thymus) as opposed to the “peripheral” type found in the spleen and lymph nodes. Lymphocytes from the parotid gland may appear in the circulation, and this, the authors believe, may explain the observed reduction in in vitro transformation, since “central” lymphocytes are known to transform poorly with PHA.

J. Gough


A female patient had Sjögren’s syndrome for 8 years. She showed positive L.E.-cells, positive Coombs’s test, hypergammaglobulinaemia, pacytopenia, and severe joint deformities. Post mortem examination disclosed atrophy of the lacrimal and salivary glands, as well as a general picture of necrotizing vasculitis and fibrinoid degeneration. The authors mention the possibility that this was an autoimmune disease with a wide lesion.

A. L. de Medeiros


A 45-year-old woman showed polymyositis, rheumatoid arthritis, parotitis, and lacrimal adenitis.

W. E. S. Bain


These authors from the National Institutes of Health, Bethesda, Maryland have reviewed roentgenograms of 52 patients (forty female and two male; age range 25 to 77 years) with proven Sjögren’s syndrome. Up to this time, the syndrome has been characterized roentgenographically by the features of polyarthritis and secretory sialo- graphic findings although it is now known that there is widespread systemic involvement—lung, peripheral lymph nodes, kidneys, and gastro-intestinal tract.

As well as the well known salivary and rheumatoid changes the authors found destructive juxta-articular changes similar to that found in psoriatic arthritis (illustrated). [The number involved is not clear from the text.] Fourteen patients had reticular or nodular changes similar to those seen in collagen vascular disease. Four patients had dense patchy infiltrates decreasing with corticosteroid therapy (illustrated). On biopsy of the lung specimen a non-encapsulated densely cellular lesion with lymphocytes, plasma cells, reticulum cells, and occasional giant cells which invaded the peribronchial and perivascular structure was found. Three patients with abnormal lymphograms, none with reticulum cell sarcoma, had a pattern identical to the lung lesion. Contrary to other reports in the literature a normal gastric mucosal pattern was found in 24 out of 25 cases. One case of nephrocalcinosis was seen.

From this study the authors note some roentgenographic features not commonly associated with Sjögren’s syndrome—juxta-articular bone description and abnormal pulmonary and lymphographic patterns.

I. M. Nairn

An up-to-date survey covering the ocular complications of ankylosing spondylitis, Reiter's syndrome, rheumatoid arthritis, and periarteritis. W. E. S. Bain


Differentiation by radiological means between specific rheumatic and nonspecific pneumonic infiltration of the lungs may prove very difficult. The authors found radiological changes in the lungs or pleura, or both, of 31 out of a series of 61 patients with connective tissue diseases (excluding rheumatoid arthritis) examined at the Essen Clinic of the University of Munster. Most of the 31 had systemic lupus erythematosus, but others had polyarteritis nodosa or scleroderma. In seven of these cases (which are described in detail) there was thrombosis of leg veins, and an initial diagnosis of acute pulmonary infarction was made on clinical, radiological, and partly even electrocardiographical grounds. From the subsequent course of the illness, however, it became clear that the pleuropulmonary phenomena were associated with an acute exacerbation of lupus erythematosus or polyarteritis and were not due to embolism.

It is suggested by the authors that the possibility of systemic collagen disease should be considered in any atypical case of suspected pulmonary embolism.

G. Loewi


This paper from Wayne State University School of Medicine and Detroit General Hospital reports an investigation of skin reactivity to intradermal challenge with nuclear antigens in 258 patients with various rheumatic and nonrheumatic diseases and 46 healthy controls.

Solutions of commercially purified calf thymus DNA (1 mg./ml.), histone (1 mg./ml.), and nucleoprotein (2-2 mg./ml.) were used. All preparations were sterile on culture and were administered intradermally into the volar aspect of the forearm in 0-1 ml. doses. Reactions were measured after 24 hours and were classed as weak if the diameter of induration was 0-4 mm., intermediate if 5-9 mm., and strong if 10 mm. or more. No adverse side-effects were noted. The technique requires accuracy in injecting the correct dose of antigen intradermally. With practice in measurement observer error was reduced to ±mm.

Most (84-92 per cent.) of the 46 controls gave weak reactions and the remainder intermediate reactions. All of 42 patients with systemic lupus erythematosus (SLE) gave strong reactions with one or more of the antigens, most of them reacting strongly to nucleoprotein and histone and 40 per cent. to DNA. Of 40 patients with discoid lupus only the 5 who had manifestations of dissemination (though without L.E. cells) reacted strongly to one or more of the antigens, about half of the remainder showing intermediate reactions. None of 41 patients with rheumatoid arthritis gave strong reactions, but 15 to 30 per cent. showed intermediate reactions. None of 38 patients with other inflammatory rheumatic diseases and only one of 97 with miscellaneous disorders gave strong reactions to any of the antigens, most of them giving weak reactions.

It is suggested that this increased skin reactivity to nuclear antigens could be used as a simple additional diagnostic test for SLE.

G. Blandford


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