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 Arthritides
- 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


RHEUMATOID ARTHRITIS


Of 100 rheumatoid arthritics admitted to hospital, 25 were admitted to this study who fulfilled the following criteria:

1. Definitive or classical rheumatoid arthritis,
2. Flexion deformity of not less than 10° in one or both knees,
3. Some improvement could be expected.

All patients were given daily extensive physiotherapy. Serial plasters were used in eleven cases, being changed every week while improvement lasted (3 to 10 weeks). Skin traction was used in four. Thirteen patients were judged to have a good result, although only four achieved full correction. Range of flexion was unchanged in all patients. Age, duration and severity, and method of treatment did not appear to influence the result significantly.

A. B. Myles


OSTEOARTHRITIS


The role of the blood vascular system in the genesis of primary osteoarthritis is the subject of this communication from the Department of Anatomy, Guy's Hospital Medical School, and the Enfield Group of Hospitals, London. The authors observed:

1. On intraosseous phlebography done in 186 patients with primary osteoarthritis, there was distension of subchondral vessels and slowing of circulation. The subchondral vessels became normal with relief of pain after osteotomy, performed in 22 cases.

2. Experimental venous engorgement, produced by ligation of femoral and internal iliac veins in rats, resulted in (a) coarser traveculae of subchondral bone and increased thickness of calcified zone of the articular cartilage, (b) acceleration of fracture repair with early bony union.

3. The pH of blood in the microcirculation of growing rabbits was lower in the regions of rapid bone formation.

On the basis of these observations the authors feel that the venous engorgement of the subchondral bone causes, through reduced pH and “other physicochemical features”, defective cartilage and accelerated bone formation. Because venous engorgement is present in primary osteoarthritic joints and both defective cartilage and excessive bone formation are features of osteoarthritis, the authors suggest that “chronic venous stress in joints is a causal factor in primary osteoarthritis”.

S. Roy


Elimination of Na\(^{131}\)I from Knee Joints with Degenerative Changes. HERNBORG, J. (1968). *Arthr. and Rheum.*, 11, 618. 3 figs, 9 refs.

STILL'S DISEASE


INFLAMMATORY ARTHRITIDES


This report from the Case-Western Reserve University School of Medicine describes thirty patients with gonococcal arthritis seen over a 4-year period. The diagnosis of gonococcal arthritis was made in patients with acute arthritis not attributable to other conditions, in whom gonococci were demonstrated in joint fluid or blood or in the genito-urinary tract or skin lesions, and definite improvement occurred after antibiotic therapy. Of the thirty patients only one was male.

Four groups of patients were defined:
(1) Gonococci were demonstrated in joint effusion;
(2) Gonococci were grown in blood cultures;
(3) Gonococci were demonstrated only in the urogenital tract;
(4) Gonococci were found in a skin lesion only (1 patient).

In the first group (nine patients) none had positive blood cultures. Joint symptoms had been present for 4 or more days before admission. Six of the nine had monoarticular involvement.

The second group (six patients) had skin lesions as well as positive blood cultures. Joint symptoms had been present for 4 days or less and were accompanied by fever, chills, and multiple joint symptoms. In only one case was sufficient fluid present to allow aspiration and this was bacteriologically negative. Four of these patients had tenosynovitis about the wrist.

In the third group (14 patients) eight had skin lesions, and in them the duration of joint involvement was 4 days or less, and chills and fever were commonly seen. In the six patients without skin lesions there was wide variation in the duration of symptoms before admission.

No standard therapeutic schedule was followed, but most of these patients received liberal doses of penicillin. Others were given cephalothin, erythromycin, or tetracycline with good response. Two patients procaine penicillin, and one of them did not improve until the treatment was changed to aqueous penicillin G in high dosage. The response to treatment was excellent in all the others; the temperature fell within 72 hours and joint symptoms settled completely within a week. [In view of the rarity of gonococcal arthritis in Great Britain, this is an important study.] D. A. Pitkeathly


In 1868, Charcot described his well-known syndrome, but since that time little has been written about the acute neuropathic joint or its clinical and radiological appearances. A striking feature of such cases is the rapidity with which bone destruction can occur, so that early detection of such cases radiologically is of great importance.

The present authors, working in the Hospital for Joint Diseases in New York, present their observations upon a series of eight patients seen during the past 7 years, who developed such lesions. Joint destruction took place within 6 weeks in all cases but one, the shortest period being 9 days.

The patients were of both sexes and mostly within the fifth decade. In every case, the initial clinical diagnosis had been incorrect; the most common x-ray diagnosis was "mild osteoarthritis" or "trauma" where any radiological changes were reported, and "cellulitis" or "septic arthritis" was suspected in several instances. The authors consider that the most reliable early radiological sign of this disorder is the demonstration of bony detritus in the soft tissue swelling round the joint, whether or not effusion is present.

The underlying conditions which predisposed to acute neuropathic joint changes in this series were tabs dorsalis (6), multiple sclerosis (1), syringomyelia (1). Two of the patients showing neuropathic involvement of the feet also had changes complicating diabetes mellitus. W. S. C. Copeman


51Cr labelled chang cells (a cell strain derived from human liver) were incubated for 15 to 20 hours with human blood lymphocytes from 31 patients with inflammatory polyarthritis, including rheumatoid arthritis, Still's disease, ankylosing spondylitis, systemic lupus erythematosus, and erythema nodosum, and with blood from healthy volunteers. Damage to the chang cells was measured by release of 51Cr. There was no difference between the cytoxic effect on the lymphocytes of the control group and the patients. The addition of phythaemagglutinin enhanced the cytoxic effect to a similar degree in the two groups. A. B. Myles


This study records seven (mostly young) patients aged 14 to 47 years with polyarthritis lasting up to 35 days following (5 cases), simultaneous with (1 case), or preceding by one day (1 case) the onset of rubella rash. Five out of seven were female. The erythrocyte sedimentation rate ranged from 4 to 35 mm/hr (Westergren) and the latex fixation test was negative in all. The author stresses the involvement of the small joints of the hands and the severity of the pain in the presence of minimal objective findings. E. G. L. Bywaters
Major Vascular Complications in Behçet’s Syndrome.


The case histories of two patients with Behçet’s syndrome are described, one with bilateral popliteal aneurysms and the other with spontaneous thrombosis of the superior vena cava.

The literature on the association of Behçet’s syndrome with primary inflammation of large vessels, aneurysm formation, and thrombosis is discussed.

In one of the author’s patients an apparently acute arteritis was demonstrated. H. J. Wallace


GOAT

Short Trial Assessment of Uricosuric Therapy in Gout.


The short-term effects of sulphinpyrazone (0.1 g. four times daily) and probenecid (0.5 g. four times daily) were studied in twelve gouty patients. No significant difference in urate diuresis was found between the two drugs: in both the magnitude of this was related to glomerular filtration rate. When the latter was less than 80 ml per minute the increase in urate excretion was relatively small, a situation which was considered to be an indication for the use of allopurinol in preference to uricosuric agents. J. T. Scott


The authors find a 13 to 30 per cent. reduction of urate-binding capacity associated with the \( a_1 \) and \( a_2 \) globulins as compared with controls in all of nineteen cases of familial gout, in one case of hyperuricaemia, and six otherwise apparently normal members of a family.

The ratio of members with lowered binding capacity of a sibship of ten of this family was 1:25. These results suggest an autosomal trait for which affected individuals are heterozygous. The absence of hyperuricaemia in some individuals with lowered urate-binding capacity suggests that a multi-factorial inheritance is necessary for gout or the co-operation of certain physiological or environmental factors. G. D. Karsley


Benziodarone, originally developed as a coronary dilator, has been found effective in reducing blood uric acid levels in gouty subjects—even, according to some French authors, in the presence of severe renal insufficiency. This paper from the Jimenez Diaz Foundation, Madrid, reports a study in which benziodarone, in a daily dosage of 200 to 300 mg., was given to 25 patients with gout over period of 2 to 6 months. All the patients received a low-purine diet with increased water and alkali intake, and were also given colchicine in low dosage to prevent recurrence of joint symptoms. Measurements of blood uric acid level, creatinine and uric acid clearances, and urate elimination over a 24-hr period were made at the start and repeated at intervals.

Significant reduction of uricaemia was noted in 21 patients but not in the remaining four, who had marked renal insufficiency; in one of these four cases, however, there was an increase in the ratio of the clearance of urate to that of creatinine. Clinically, only one patient had a recurrence of symptoms in spite of a reduction in the blood uric acid level. Two patients had uric acid lithiasis. One patient with anginal pain gained relief from this. No skin eruptions, blood dyscrasias, or digestive disturbances were noted. Although benziodarone is chemically related to the dicoumarols, one patient who had a duodenal ulcer suffered no harm.

The authors conclude that their findings confirm the action of benziodarone as a uric acid eliminator which acts on the renal tubules; its use is indicated in gouty patients with intact or only slightly damaged renal tubules, especially if anginal pain is also present. G. K. Thornton


Uric Acid Levels in Full-Term and Low-Birth-Weight Infants. Marks et al. (1968). *J. Pediat.*, 73, 609.


**BONE DISEASE**


Paget’s disease of bone is found in 3 per cent. of necropsies on patients over the age of 50 years. To assess how common are the cardiac complications of the disease, the authors have reviewed 190 cases (114 men and 76 women). The mean age of the patients was 65 years.

Clinically, 44 patients (23 per cent.) had abnormal ascultatory findings (aortic or mitral murmurs). A blood pressure above 160/100 mm. Hg was found in 52 per cent. of patients. Twenty (10 per cent.) had evidence of heart failure, and this was commoner in those with extensive Paget's disease.

Chest radiographs were obtained in 117 cases: in 51 the heart was enlarged, again more commonly in those with extensive bony involvement. Arterial calcification was seen radiographically in 75 out of 168 cases and was commoner in male patients with widespread disease.

Electrocardiographic abnormalities were found in 95 patients (65 per cent.); atrial fibrillation and first-degree atrioventricular block were the commonest arrhythmias, while left ventricular hypertrophy and ischaemic changes were also common.

Histological examination of the arteries in patients on whom biopsy was performed (and in four cases which came to necropsy) showed calcified atheroma with, in some cases, medial calcification. No lesions of the elastic laminae of the vessels could be seen in either large arteries or arterioles of the skin.

The authors discuss how these findings relate to the biochemical and haemodynamic consequences of Paget's disease. *A. Breckenridge*


**Bone Density Studies in Primary Hyperparathyroidism. Forland et al. (1968). *Arch. intern. Med.*, 122, 236.**

**Normocalcemic Hyperparathyroidism culminating in Hypercalcemic Crisis. Eisenberg and Gotch (1968). *Arch. intern. Med.*, 122, 258.**

**NON-ARTICULAR RHEUMATISM**


Thirteen patients with a spinal condition of unknown cause have been seen at Geisinger Medical Center, Danville, Pennsylvania. In some cases it followed operation for prolapsed intervertebral disc, but in others this history was lacking. There was usually an insidious onset of backache, and the early films showed a small area of destruction in the end plate of a vertebral body; later, sclerosis and disc space narrowing appeared. The relative amounts of destruction and sclerosis varied. There was no clinical or pathological evidence of infection, and biopsy was unhelpful. In twelve cases the condition responded to rest and analgesics, though the time needed for recovery ranged from 5 months to 5 years; one patients required spinal fusion. *D. E. Fletcher*

**PARARHEUMATIC (COLLAGEN) DISEASES**


Percutaneous renal biopsies were studied from one male and twelve female patients, about one quarter of all the patients with systemic lupus erythematosus seen during a 3-year period. All had arthritis or arthralgia, butterfly rash or serositis, and positive L.E.-cell tests; renal involvement was diagnosed clinically and assessed as either minimal or definite. The clinical findings are tabulated; detailed case histories are given for all patients. Optical microscope findings based on the study of at least seven glomeruli showed four to have minimal changes, two with a membranous pattern, two with membranous patterns and fibrinoid deposits, and six with severe changes including wire loops, fibrinoid, and necrosis.

Electron microscope findings were generally based on the study of three glomeruli: Group I (5 biopsies) had a basement membrane of variable thickness and an increase in mesangial cells; Group II (5 biopsies) showed patchy fusion of the foot processes, subepithelial dense deposits, nodular basement membranes, reticulation of the endothelium, and a thickened mesangium; Group III (4 biopsies) showed focal foot process fusion, epithelial proliferation, thinned basement membranes, marked reticulation of the endothelium, dense deposits beneath both endothelium and epithelium, and an infiltration of the mesangium with dense material.
Historical review of the findings by optical microscopy revealed a change in emphasis as studies came to use biopsy rather than post mortem material. Early electron microscope findings emphasized endothelial changes; these are related to the findings of the present study. A sequential arrangement of the three groups is suggested but not thought to be proven. The nature of the dense deposit is discussed as is the relation of these lesions to those occurring in other diseases. The clinical correlations of the microscopic findings are thought to be closer with the electron microscope.

A. J. Palfrey


The clinical and histological features of six cases of lupus erythematosus profundus are described. Characteristic features include crops of subcutaneous nodules, usually on the head and arms, accompanied by deep scarring but with few, if any, signs of discoid lupus erythematosus. Histologically, necrobiosis was seen in the lower dermis and subcutis with some vasculitis.

Clinically lupus erythematosus profundus may closely mimic other forms of panniculitis from which, however, it may usually be differentiated by histological appearances.

H. J. Wallace


Histological and histochemical examination (including the Coons direct and indirect immunofluorescence techniques and the Goldwasser-Shepard test for complement) of ten biopsy and fourteen necropsy specimens of kidneys from patients with systemic lupus erythematosus (SLE) in various stages enabled the authors, at the First Moscow Medical Institute, to characterize two morphological types of lupus nephropathy—namely, glomerulonephritis (membranous or membranous-proliferative; focal or diffuse) with no morphological changes characteristic of lupus (and very few clinical signs of renal disease); and true nephritis (focal or diffuse) with specific lupoid changes and typical polymorphism.

In SLE γ-globulins and complement can be demonstrated in the basal membranes of the glomerular capillaries and in the foci of destruction, pointing to the autoimmune character of those changes. In the present study a direct relationship was demonstrated between the degree of destructive change in the renal glomeruli and (1) the amount of γ-globulin and complement fixation in them, and (2) the "clinicoinmunological" activity of the disease (as indicated by reduced serum complement titre, hypergammaglobulinaemia, high titre of antinuclear factor, and large number of LE cells. The authors therefore conclude that the renal lesions of SLE are of autoimmune nature.

S. W. Waydenfeld


This is an electron-microscopic study of the capillaries in biopsy specimens of the quadriceps femoris in pulmonary tuberculosis, rheumatoid arthritis, scleroderma, systemic lupus erythematosus (SLE) and suitable controls. Except for pulmonary tuberculosis, all showed a significant reduction in the number of capillaries. The mean diameter of the vessels was increased in SLE and scleroderma but not in the other disease groups. In SLE there was thickening of the basement membrane. This was also seen in scleroderma, but more commonly the basement membrane in this disease presented a laminated appearance. Swelling of endothelial cells was also a feature of the vessels in scleroderma. The dense deposits described in the glomerular basement membrane in SLE were not seen in the capillaries in the quadriceps muscle though all but three of the patients with SLE had clinical and/or biopsy evidence of renal disease. Although the vascular changes were largely limited to SLE and scleroderma they are regarded as non-specific. The degree of capillary abnormality in SLE was inversely related to steroid dosage. It is concluded that widespread injury to the capillary bed may be important to SLE and scleroderma.

J. Ball


The main point of interest in this paper, from the Lome Linda University School of Medicine, is the high pregnancy wastage in scleroderma. 45 of 66 patients admitted to hospital with scleroderma over a 13-year period had been pregnant. The mean age at onset of disease in those patients who developed it before or during pregnancy was 26 years. The age at onset in those developing the disease after all their pregnancies was 44.5 years.

145 pregnancies had occurred in the group as a whole, but only ninety had a successful outcome. The 26 pregnancies occurring in the six patients whose disease became apparent either before or during pregnancy, were particularly unfortunate. The outcome in this group included seventeen abortions, one premature stillbirth, and five premature live-born babies.

Practical measures recommended include the prevention of oesophageal reflux during pregnancy and the avoidance of general anaesthesia during delivery to prevent pneumonia. It is pointed out that healing of skin and other tissues is unaffected by scleroderma.

M. Corbett

The evaluation of any treatment in this condition with its different grades and manifestations, its relative rarity, and the lack of objective measurements available for assessment, is difficult.

There is some evidence that this disease is associated with a disturbance of immunological tolerance. It was therefore decided to try the effects of Azathioprine in patients attending the Department of Dermatology at the University of Arkansas.

21 patients were treated for an average of 14 months. All had positive biopsies and the mean duration of disease was 40 months. A starting dose of 150 mg. daily was arbitrarily selected.

Histology, pulmonary function tests, oesophageal motility, blood picture, serology, and tests of liver and kidney function did not correlate with the clinical picture and functional grading, although clinical photography was found to be of value.

Eight patients improved, seven remained the same, two became worse, and one was lost to follow-up. Three patients had to be withdrawn from the study because of recurrent high fever on each occasion the drug was given.

Other side-effects included leucopenia in four and thrombocytopenia in two patients. Dosage adjustment resolved these problems.

M. Corbett


This is a review of skin biopsy specimens from 55 patients with dermatomyositis seen at the Mayo Clinic between 1926 and 1967; 53 patients had muscle biopsy or electromyography (or both) compatible with dermatomyositis.

It was found that the chance of obtaining characteristic histological changes of dermatomyositis is remote unless the biopsy is taken from clinically involved skin.

There has been some doubt regarding the specificity of any of the histological changes in the skin in dermatomyositis. However, the authors of this paper conclude that poikilodermia in dermatomyositis has features that differentiate it from the poikilodermatous state seen in other conditions and that this finding, coupled with a comparable clinical picture, could be diagnostic.

The presence of mucin deposits was noted in 29 of the 55 biopsies and even in the absence of poikilodermia this may be suggestive of dermatomyositis.

Despite these findings, the histological changes in skin alone did not entirely exclude systemic lupus erythematosus in seven cases, but it was thought that there was little trouble in differentiating between dermatomyositis and scleroderma.

D. J. Ward

Results of Treatment with Vasodilators in Scleroderma (Risultati terapeutici con vasodilatatori nella scleroderma). Randazzo, S. D., and Guarneri, B. (1968). Rif. med., 82, 1166. 6 refs.


CONNECTIVE TISSUE STUDIES


Using a Weisssenberg rheogoniometer, the steady shear flow properties of a series of synovial fluids from patients suffering from various forms of arthritis were examined. Clear differences in flow behaviour were detected. In certain cases peak stresses were encountered in both the tangential and normal directions at the onset of shearing. Joint stiffness in any one patient and hyaluronic acid/protein complex concentration were found to correlate with viscosity. Rheumatoid factors and antinuclear factors did not. Synovial fluid flow behaviour showed no sign of circadian changes. [Author’s summary]


The case is reported from St. Bartholomew’s Hospital, London of a 38-year-old man who presented with an
irregular swelling of the wrist joint invading the scaphoid and lower end of the radius which was subsequently shown to be due to pigmented villonodular synovitis. Histologically there was no sign of malignancy and progress following resection of the lesion was uneventful.

A. Garner


The authors' method for obtaining muscle samples by needle biopsy is described in detail, and shown to be reproducible, representative, and adequate for studying muscle chemistry. In a preliminary study in normal children it was shown that muscle potassium increases with age from 1 to 2,000 days.

J. Ball


The nature of the pigment that appears in ageing cartilage and tendon is obscure, and in this report from the National Institutes of Health, Bethesda, an attempt has been made to resolve the problem.

Histological examination, chemical analysis, and enzyme digestion studies have shown that the pigment is neither a mucopolysaccharide derivative nor a lipofuscin, but that it is probably a high molecular weight substance closely bound to non-collagenous protein. Analysis of the amino-acid composition of this protein shows it to contain relatively large amounts of aspartic and glutamic acids, serine, and leucine, but no hydroxyproline. The pigment itself gave negative staining reactions for melanin and haemosiderin.

Pigmentation was more pronounced in costal cartilage and tendon than in articular cartilage, and apart from the fact that it increased with age as does osteoarthritis there was no correlation between these two disorders. This latter finding, together with the failure to demonstrate and relationship between the pigment and collagen, is taken to weigh heavily again the hypothesis that senescent pigmentation is equivalent to a physiological ochronosis.

A. Garner


This paper describes a series of 167 experiments on young adult rabbits conducted at the National Institute for Medical Research, London. Pieces of cartilage from freshly-killed animals were grafted either immediately or after treatment with papain, dimethyl sulphoxide, collagenase, and pronase in various combinations; isolated chondrocytes were prepared by the use of all three enzymes. Some preparations were stored for periods up to 2 weeks at -76° C. Grafts were placed into the cancellous bone of the ilium or the articular surface of the humerus after removal of an area of cartilage. Control experiments were performed. Recipients were killed between 2 and 26 weeks after operation and examined by optical or fluorescence microscopy.

No evidence for a homograft reaction was seen in any experiment. Isolated chondrocytes grafted to the ilium produced a new matrix by 2 weeks, but by 6 weeks this was invaded by host tissues and by 26 weeks had been transformed into cancellous bone. The chondrocytes were not affected by the enzyme treatments, nor by freezing, provided dimethyl sulphoxide was present; they did not survive so frequently when grafted in donor matrix, which was removed by the host tissues. Grafts on the articular surface were largely replaced by fibrous tissue but after 6 weeks some new formation of matrix was seen; these experiments were not continued for longer survival times.

A. J. Palfrey


This paper from Research Centre for osteo-articular disease and the Rheumatology Clinic of the Hôpital Cochin, Paris, reports an investigation of the levels of various components of complement (C') in the synovial fluid in 48 cases of rheumatoid arthritis (RA) and in forty non-rheumatoid arthritides. The overall level of the first four components of C' were determined by estimation of the titre by immune adherence which is determined by the fixation of C'3 to antigen antibody complexes. In this instance the complexes were provided by a suspension of S. typhi coated with a specific antiserum and the adherence was revealed by human O-Rh-positive red cells.

The results showed a clear cut difference between the RA fluids, which contained 0 to 25 units of C' as measured by immune adherence, and the non-rheumatoid fluids with a content of 25 to 80 units. The correlation between non-haemolytic complement as measured by immune adherence, and haemolytic complement was good in both series, thus showing no excessive deficiency of the complement components 5 to 9.

Although individual complement components were not measured the parallel deficiency of the haemolytic and non-haemolytic components in RA fluids is compatible with their removal by fixation to complexes of antigen with antibody in the affected joints.

L. E. Glynn


IMMUNOLOGY AND SEROLOGY


This is a combined study from the Department of Medicine, University of Cape Town, and the Department of Bacteriology, London Hospital Medical College. It is based on the investigation of 21 patients with the pulseless syndrome (Takayasu’s disease), and eighteen controls suffering from functional disorders and matched for age, sex and ethnic groups.

A statistically significant increase was found in the mean levels of the immunoglobulins G, A, and M, which were 1586, 396, and 159 mg./100 ml. respectively, whereas the corresponding control values were 1260, 276, and 111 mg./100 ml. Although complement-fixing antibodies were occasionally found against liver, aorta, and thyroid gland, they were not significantly different from similar antibodies in the control subjects. Nor were antibodies to aortic tissue demonstrable, either by fluorescent conjugates or by immuno-diffusion.

L. E. GLYNN


A characteristic feature of the L.E.-cell factor from patients with systemic lupus is its lack of species specificity. This note from the Wellcome Medical Research Institute of the University of Otago, New Zealand, reports that the similar factor in NZB mice and in NZB × NZW F1 hybrids also lacks species specificity, as shown by positive reactions with leucocytes from man, rat, and guinea-pig.

L. E. GLYNN


Sarcoidosis may be regarded as a disease characterized by an abnormal immune response. However, no clear correlation between the abnormalities found in the serum immunoglobulins and the activity of the disease has been established, although in the chronic state there appears to be a constant and significant increase in the levels of both total serum protein and serum globulins. Much controversy centres round the part played by the individual immunoglobulins in the active stages of the disease. This paper from the University Institute of Pathological Anatomy and Statens Serumistitut, ANF Laboratory, Copenhagen, reports a study of the tissue from the paratracheal lymph nodes of ten patients with sarcoidosis of varying activity. The direct and indirect fluorescent antibody techniques were used with rabbit antisera containing precipitating antibodies against human albumin, fibrinogen, IgA, IgG, IgM, and fractions of complement, and with human sera containing antimitochondrial antibodies. [For details the original should be consulted.] Appropriate control studies were also performed.
In the material taken from the patients an increase in immunoglobulins (especially IgA and IgM) was found in the areas where the normal morphology was most altered. The degree of activity could not be correlated with the presence of individual immunoglobulins, but increased amounts of complement were present in the more extensive lesions. These last also contained much mitochondrial material.

The findings support the view that sarcoidosis is a disease whose basic features resemble those of the collagen diseases. William H. S. George


This careful study from the Research Laboratories of the Hôpital Cochin, Paris, concern the ability of serum antinuclear factor to fix complement. Rat liver sections were layered with a dilution of the test serum, washed, layered again with a 1:10 dilution of complement (fresh normal human serum), washed, and finally layered with a 1:10 dilution of fluorescein-labelled rabbit anti-human gamma globulin. Serum complement levels, antinuclear factor titre and L.E.-cell formation were also studied. Eighteen out of 44 sera containing antinuclear factors were positive: they were derived from systemic lupus erythematosus (SLE) patients with three exceptions (cases of scleroderma, rheumatoid arthritis, and “polyarthritis”), whereas the 27 cases providing negative complement-fixing sera showed a miscellany of diagnoses—rheumatoid arthritis eight cases, SLE with or without additional diagnosis eight cases, and scleroderma, leucopenia, Sjögren’s syndrome, etc. The antinuclear factors in the first (complement-fixing) group showed a significantly higher titre than those in the latter (non-complement-fixing) group. However, serum giving a positive L.E.-cell test might be non-complement-fixing according to this technique. E. G. L. Bywaters


Effects in Changes
Hopkins Hospital, Johns tissues and Metabolism of
Increase Tissue and Plasma Cortisol by the cortisone released or a
ently of the average specific activity of the tetrahydro-derivatives of cortisol and cortisone released by hydrolysis. An important assumption made in calculating the rate is that the derivatives are unique metabolites of cortisol, e.g. if cortisol is produced other than from secreted cortisol the rate of cortisol production will be over estimated. [This report does not negate the hypothesis that pregnancy affords some relief to rheumatoid arthritic subjects through a raised effective concentration of cortisol in connective tissues as the effective concentration can vary independently of the production rate].

H. F. West

ABSTRACTS


BIOCHEMICAL STUDIES


This excellent report, emanating primarily from the Johns Hopkins Hospital, shows unequivocally that the cortisol production rate is slightly reduced during pregnancy. The technique used measures the quantity of cortisol entering the systemic circulation and is based on the intravenous injection of a trace dose of 4-14C-cortisol and the determination of the average specific activity of the tetrahydro-derivatives of cortisol and cortisone released by hydrolysis. An important assumption made in calculating the rate is that the derivatives are unique metabolites of cortisol, e.g. if cortisol is produced other than from secreted cortisol the rate of cortisol production will be over estimated. [This report does not negate the hypothesis that pregnancy affords some relief to rheumatoid arthritic subjects through a raised effective concentration of cortisol in connective tissues as the effective concentration can vary independently of the production rate].

H. F. West


THERAPY


The anti-inflammatory effect of indomethacin on joint disorders is well known, but its effect on soft-tissue lesions has received less attention. The present trial was conducted at the North Middlesex Hospital, London, and involved 110 patients under the age of 60 years with acute or chronic lumbar pain due to musculoskeletal origin. Patients were placed in one of two diagnostic groups—those with and those without sciatica or root pain—and were then given either indomethacin (25 mg in capsules) or a placebo, in a dosage of one capsule three or four times daily for a week. Progress was followed by noting changes in spinal flexion (measured as the distance between the spines of T 12 and S 1 vertebræ in full flexion), straight leg raising, pain, and restriction of movement. Separate analyses were made for the first two of these criteria (objective) and the second two (subjective), and sequential graphs were made by pairing successive patients in each treatment group according to their entry number in the trial. Not all the fifty patients in the group with nerve root involvement completed the trial but twenty pairs were available for sequential analysis. The upper boundary was reached in the analyses of both the subjective and objective criteria, indicating the superiority of indomethacin on both counts (P < 0.05). Sixty patients were treated in the group without nerve root involvement. Several of these withdrew from the trial because of side-effects, leaving 25 pairs for analysis. A middle boundary line was reached in both graphs, indicating that there was no significant difference in effect between indomethacin and placebo.

In their discussion, the authors note that there is surgical and histological evidence of an inflammatory neuritis in some disc lesions, and this should be helped by an anti-inflammatory drug like indomethacin. On

At the Institute of General Medicine and Therapeutics of the University of Siena the authors have evaluated gastric function in ten patients with rheumatoid arthritis and ten healthy subjects before and after 25 days’ treatment with indomethacin in a divided dosage of 200 to 300 mg daily. To test gastric function the effect of histamine [dose not stated] on volume, free acid content, and total acidity of the gastric juice was determined over a period of 80 min., samples being taken at 20-min. intervals.

Even before treatment the two groups differed, the mean basal values and response curve being normal in the healthy subjects whereas the patients had a tendency to basal hyposecretion and showed little or no response to histamine, the curve being flat. After indomethacin the healthy subjects showed a slight depression of basal secretion but a much increased response to histamine, the mean values at each interval being significantly higher than before treatment, though the shape of the curve was normal. The patients also showed a slight reduction in the basal values, but histamine now produced significant increases in volume, free acidity, and total acidity which were maintained at approximately the same levels throughout the period of the test, producing a plateau-like curve.

The action of indomethacin on the gastric mucosa is discussed and it is suggested that it would be desirable to investigate the patient’s gastrointestinal function before embarking on a prolonged course of treatment with the drug.

J. S. Cohen


In this paper from the Prince of Wales Hospital, Randwick, New South Wales, Australia, the author reports the results of prolonged treatment of 19 patients suffering from chronic staphylococcal osteomyelitis with large doses of either cloxacillin or phenoxyethylpenicillin combined with probenecid.

One patient was aged 8 and the others 15 to 62 years, and they had had osteomyelitis for between 1 month and 30 years. All had been treated unsuccessfully with a variety of antibiotics, and all but one had surgery. Three had developed a rash while receiving penicillin. *Staphylococcus aureus* was isolated from seventeen patients and the sensitivity was determined in fifteen cases. Only two strains were penicillin-sensitive and these were inhibited by less than 0-1 µg./ml. phenoxyethylpenicillin. The thirteen penicillin-resistant strains were all inhibited by 0-5 µg./ml. cloxacillin. The two patients with infections caused by sensitive organisms were treated with phenoxyethylpenicillin, the others with cloxacillin. The antibiotics were given to the adults in a dosage of 1 g. five times daily by mouth; the child received half the adult dosage of cloxacillin. Each dose was preceded by at least 3 hours’ fasting, and all the patients were given 2 g. probenecid daily to promote higher serum levels. In the case of five patients with significant systemic disturbances, which included nausea and vomiting, oral therapy was preceded by a week’s intravenous therapy at the same dosage. Antibiotics were given in the high dosage until well after the disappearance of clinical signs of the disease—that is, for longer than 6 months in all but four cases; thereafter, eight patients received a maintenance dosage of 1 g. antibiotic and 0·5 g. probenecid daily. Antibiotic serum levels were measured repeatedly in each patient, and at 1 hr after a 1-g. dose given with 0·5 g. probenecid were 22 to 50 µg./ml. for cloxacillin and 18 to 25 µg./ml. for phenoxyethylpenicillin. After 3 hrs they were 5 to 25 µg./ml. for cloxacillin and 2 to 5 µg./ml. for phenoxyethylpenicillin. Abscesses were drained or retained sequestra removed in sixteen cases.

The patients were followed up for between 7 months and 2½ years; fourteen were free of infection within 6 months and one within 12 months. In another all the sinuses healed within 3 months, but a small sequestrum was spontaneously discharged at 12 months. In two patients, who otherwise recovered, a sinus associated with a retained sequestrum persisted for twelve months; one declined surgical treatment and the other was unfit for surgery for reasons not related to the osteomyelitis. One patient died from an unrelated malignancy during the course of treatment. The only patient to show any side-effects from the treatment was a man with a previous history of penicillin allergy who developed an urticarial rash after 2 months’ treatment with cloxacillin.

N. A. Simmons


Three patients [at the West London Hospital, London] developed autoimmune haemolytic anaemia while being treated with mefenamic acid. In each case the autoimmune haemolytic anaemia was of the warm antibody γG type, and the antibodies had some rhesus specificity. All three patients recovered when the drug was withdrawn. Attempts to inhibit or enhance the activity of the antibody in vitro were unsuccessful.

Direct antihuman globulin tests were made in the red cells of 36 patients receiving long-term mefenamic acid therapy, but only one was found to be transitorily positive.—[Authors’ summary.]


In this study from the University of Vermont College of Medicine, five preparations containing acetylsalicylic acid were tested. The subjects, normal volunteers aged
22 to 63 years, were given $^{51}$Cr-labelled blood. Three or more days later, allowed for the clearance of free isotope, a 7-day course of placebo was given, with complete stool collections for the last 4 days with blood samples taken at the beginning and end of such collections. Next, a 7-day salicylate course was started, with collections again for 4 days.

Of fifty subjects, 48 showed increased gastrointestinal blood loss when receiving salicylate, mean losses all being greater than 2.5 × mean losses on placebo. The greatest loss was 3.80 ml/day, equivalent to 8.48 ml whole blood. In two subjects with relatively high losses, microhaematocrit values and occult blood tests were normal. There appeared to be no difference between the various salicylate-containing compounds.  

G. Loewi

Osteotomy in Osteo-Arthritis of the Hip Joint.  


Prof. Carl Hirsch, head of the Department of Orthopaedic Surgery at Göteborg University, together with his co-author, reviews their experience with osteotomy of the hip for arthritis; 123 such operations were performed between 1961 and 1965, and all are reviewed although only 102 cases were re-examined.

Displacement varus intertrochanteric osteotomy was performed, but there is variation throughout the series in methods of fixation and the duration of subsequent immobilization.

81 per cent. of their patients expressed satisfaction with their operation, the main advantage being loss of spontaneous rest pain. However, only about one-third thought that the range of hip movement was better and a similar number thought it was worse. Indeed, on examination, 38 per cent. were worse off in terms of hip mobility.

No less than sixteen patients developed a pseudarthrosis at the osteotomy site and in seven the internal fixation device broke. Infection of the wound occurred in twelve patients, one of whom died as a result of "general sepsis". The authors point out that improvement was most pronounced in those patients who had suffered constant pain at rest. It is interesting that in their experience the joint-space rarely increased after osteotomy and likewise sclerosis and cysts seldom disappeared.

Rodney Sweetnam

Adrenocorticotropin Action of a Natural and a Synthetic Preparation of ACTH with Added Gelatine by Intramuscular Injection (Adrenocorticotrope Wirkung eines natürlichen und synthetischen ACTH-Präparates mit Gelantinezusatz bei intramuskulärer Injektion).  


It has previously been found that biologically-obtained ACTH given intramuscularly, has a longer-lasting activity than the synthetic compound. The authors have embarked on a comparative study of the two products with added 15 per cent. gelatine to obtain slower absorption. The parameter chosen to assay activity was level and duration of plasma 11-hydroxy-cortisol (11-OHCS). The patients in the trial were seven males and five females, aged 21 to 74 years. The two compounds were injected with one week intervening, half the patients receiving the material first, and the other half the synthetic compound. Up to 2 hours after injection there was no difference in 11-OHCS levels resulting from the two types of ACTH, but after 8 and 12 hours the level achieved with natural ACTH was significantly higher than that with synthetic ACTH. Addition of gelatine prolonged the effectiveness of synthetic ACTH.  

G. Loewi


From the Institute of Experimental and Clinical Oncology, Moscow, and the First Moscow Medical Institute the author reports the necropsy findings in 26 fatal cases of pemphigus. Seven of the patients had been treated without ACTH or corticosteroids, three had been given small doses of ACTH only, and sixteen had been treated with large doses of corticosteroids over considerable periods. The appearances of the skin and mucous membrane lesions were practically the same in the three treatment groups except for increased neutrophil content of the infiltrates under the influence of steroids. Changes in the viscera were nonspecific, but visceral complications of steroid therapy were the cause of death or a contributory factor in seven cases, while in four cases of associated tuberculosis steroid therapy had resulted in exacerbations and haematogenous spread. Toxic encephalopathy was demonstrated in all cases, but oedema of the ganglion cells, proliferative changes in the glia, and alterations of capillary permeability were more evident in patients treated with steroids. Partial loss of structure and narrowing of the glomerular permeability were demonstrated independently of steroid therapy. Similarly, dystrophic changes in the fuscicular zone were attributed to the wasting nature of the disease itself, though prolonged steroid therapy led in sixteen cases to atrophy of the fuscicular zone and compensatory adenomatous hyperplasia of the cortex.

S. W. Waydenfeld


[At the Royal and Victoria Infirmary, Glasgow] 21 patients with "definite" or "classical" rheumatoid arthritis who had received long-term oral corticosteroid therapy were treated by anterior synovectomy of the knee. The rise in plasma 11-OHCS [hydroxycorticosteroid] levels induced by this operation was correlated with the results given by four procedures which assess the functional integrity of the hypothalamo-pituitary-adrenal (HPA) axis: the Synacthen (β 1-24 corticotrophin) test, the lysine-induced vasopressin test, the insulin hypoglycaemia test, and the metyrapone (SU 4885) test.
Twenty patients with “definite” or “classical” rheumatoid arthritis who had never received corticosteroid drugs and who were submitted to the same preoperative procedure served as controls. The plasma 11-OHCS response to this surgical stress has been shown to be reproducible in five subjects.

The rise in plasma 11-OHCS induced by the operation was graded and correlated with the HPA stimulation techniques. Patients who had a subnormal response to Synacthen demonstrated the lowest rises in plasma 11-OHCS followed by patients with a normal response to Synacthen, but a subnormal response to one or more of the other three procedures. Corticosteroid-treated patients who had a normal response to all of the four HPA stimulatory procedures showed the highest mean plasma 11-OHCS levels throughout operation. One of the nine patients with a subnormal response to Synacthen developed hypotension at the end of the operation. These results demonstrate the need for corticosteroid-treated patients with a subnormal adrenal response to Synacthen to have corticosteroid “cover” during operation.

Moreover, the findings suggest that the development of hypotension during stress (such as operation) in corticosteroid-treated patients is not merely a function of the inability of the hypothalamo-pituitary-adrenal axis to raise circulating plasma 11-OHCS levels. That other factors must be of importance is suggested by the observation that many of the corticosteroid-treated patients who failed to respond to the stress of surgery with an appreciable rise in plasma 11-OHCS levels did not develop hypotension.—[Authors’ summary.]


