ABSTRACTS

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

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

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

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 clinical and necropsy records of all adult patients with rheumatic heart disease who had died at the Mount Sinai Hospital, New York, between 1946 and 1959 and in whom fever had been a prominent feature of the terminal illness were studied to determine the relation between the febrile illness and the cardiac condition. Patients in whom rheumatic heart disease was a minor finding, those who had died immediately after admission, and those in whom subacute bacterial endocarditis had been diagnosed before death were excluded. The remaining sixty patients were divided into seven categories according to the cause of fever as revealed at necropsy:

1. Pulmonary infarction was the major finding in 31 patients, nine of whom also had systemic infarction. All but one of these patients were over 40 years old, and 27 had been in congestive failure for up to 5 years before death.

2. Rheumatic activity was responsible for the fever in twelve patients, five of whom were less than 40 and none more than 60 years old. All had died in congestive heart failure, and at necropsy the heart showed evidence of acute rheumatic inflammation, with typical Aschoff nodes in the myocardium in all cases and endocarditis in nine. Active rheumatic fever had been diagnosed before death in only three cases. The serum antistreptolysin-O titre was raised in four of the five cases in which it was determined.

3. Pneumonia was present in six patients, four of whom were over 50. Most had had cough and fever of recent origin, but the clinical and x-ray findings in the chest were not typical of pneumonia. At necropsy bronchopneumonia of one or both lungs was found, but no evidence of pulmonary or systemic infarction.

4. Congestive heart failure was the dominant feature in five cases. No evidence of infection, thromboembolism, or rheumatic activity could be found to account for the fever.

5. Subacute bacterial endocarditis was diagnosed post mortem in three cases, typical vegetations containing Gram-positive cocci being found, though cultures were sterile.

6. Pulmonary arteritis, with widespread acute, subacute, and chronic inflammatory changes in the medium-sized and smaller vessels, was present in two cases.

7. Systemic embolism, with acute infarction in one kidney, was considered to have been responsible for the fever in one case.

Haemoptysis, chest pain, and jaundice were more common clinical findings in Group 1 than in the rest, while a younger age and frequency of evidence of recent infection with β-haemolytic streptococci were distinctive features in Group 2. There were no distinguishing diagnostic features in the other groups. The authors suggest that when persistent unexplained fever occurs in a patient with rheumatic heart disease the possibility of pulmonary infarction should receive primary consideration in view of its high incidence. But the other possibilities should be kept in mind and it is emphasized that congestive heart failure alone may be responsible for fever.

E. H. Johnson


For 6 months all in-patients and out-patients with rheumatic heart disease seen in the cardiac department of the Stoke-on-Trent Hospital Group were studied with special reference to the incidence and type of neurological symptoms. A total of 323 patients were seen, 89 males and 234 females ranging in age from 13 to 69 (mean 42-5) years, of whom 199 had dominant mitral stenosis, 62 mitral stenosis with significant mitral regurgitation, and 62 a dominant aortic lesion. In 44 cases (14 per cent.) one or more classic cerebral embolic episodes had occurred. Of

In an attempt to increase the accuracy of the electrocardiographic assessment of left atrial enlargement the authors of this paper from New York University and Yale University Schools of Medicine have studied the standard electrocardiograms of 101 healthy children and 88 children with asymptomatic rheumatic heart disease and have correlated changes in the P waves with radiological evidence of left atrial enlargement. Abnormalities in the P wave were found to be more consistent in Lead VI than in Lead II, and the authors conclude that suspicion of left atrial enlargement should be aroused by either a broadly notched P wave in Lead II or an inverted or diphasic P wave in Lead VI. These changes alone are not diagnostic, but confirmatory evidence can be obtained from further analysis of Lead VI. Here the P-wave changes indicative of left atrial enlargement are that the downstroke has a depth of more than 1 mm. or a duration of more than 0-6 second. Not only are these changes in

Lead VI more consistent, they are also more easily discerned and measured than the corresponding changes in Lead II.

William A. R. Thomson


Rheumatoid Arthritis


A follow-up study is presented of 185 patients (52 male and 133 female) admitted to the Royal Bath Hospital, Harrogate, with rheumatoid arthritis which was sufficiently active or advanced for the patient’s admission to be sought by the general practitioner. Patients who lived too far away to attend the out-patient clinic after discharge were followed up by letter. During the period of follow-up, which ended in 1962, eighty of the patients (28 males and 52 females) died. The average duration of follow-up of the remaining 105 was 12 years 9 months. The degree of incapacity was considered to be mild when the patient’s normal activities were only slightly restricted, moderate when there was an appreciable impairment of ability to lead a normal life, and severe when the patient had become dependent upon others. On admission the degree of incapacity, in the 105 patients was mild in 64, moderate in 37, and severe in four; at the end of the follow-up period incapacity was mild in 25, moderate in 51, and severe in 29.

Death in 21 of the 28 males did not appear to be related to the arthritis, but in seven it was attributable to prolonged and increasing incapacity. In 27 of the females death appeared to be related to prolonged incapacity, while in 25 it was due to unrelated causes. Analysis of the age at onset of the disease in relation to mortality appeared to lend support to the findings of Cobb and others (New Engl. J. Med., 1953, 249, 553) that in rheumatoid arthritis the mortality rate is relatively higher in patients of both sexes in the younger age groups than in older patients and that patients over 50 years of age fare about as well as the general population. C. E. Quin


Of 279 consecutive patients attending the London Hospital with definite rheumatoid arthritis as defined by the American Rheumatism Association, 114 (41 per cent.) had evidence of hip involvement. Of these, 81 had symptoms referred to one or both hips, 69 had abnormal signs in the hip, and 71 had a definite radiological abnormality, while forty (14 per cent.) had both subjective clinical and x-ray evidence of hip involvement. In 33 (42 per cent.) of the 81 patients with symptoms these developed within 5 years of the onset of the arthritis, a tendency more marked in males than in females.

When the study was extended to include 79 cases from Chase Farm Hospital, Enfield, Middlesex (making a total of 358 cases), it was found that hip involvement was present in 168 cases. Both hips were involved in 67 (54 per cent.) of 124 cases with symptoms, 61 (57 per cent.) of 107 cases with clinical signs, and 70 (60 per cent.) of 116 cases with radiological abnormalities. Hip involvement increased with age and the duration of disease; it was also more common in patients with nodules and those giving a positive response to the latex fixation test.

The author emphasizes that his figures for involvement of the hip in rheumatoid arthritis are much higher than any previously reported, and suggests that the condition is frequently overlooked, especially in older patients with long-standing disease. E. D. Sever


Further experience of brachial arteriography in rheumatoid arthritis and some other disorders, including poliarteritis nodosa, is reported from Hammersmith Hospital, London. A short-bevelled needle (19 SWG) one inch (25-39 mm.) long is inserted into the brachial artery in the antecubital fossa. In 2 seconds or 10 ml. 45 per cent. "hypaque" (sodium diatrizoate is injected by hand and eight radiographs 15 × 12 in. (38 × 30.4 cm.) are exposed at a rate of one per second. Great care is taken to carry out the examination rapidly because of the tendency of this artery to go into spasm. General anaesthesia is given to patients with Raynoud’s phenomenon.

Satisfactory arteriograms were obtained in 38 cases of rheumatoid arthritis, and occlusive changes were present in 26, often accompanied by proximal narrowing and collateral circulation. Occlusive changes were often associated with clinical evidence of ischaemia, subcutaneous nodules, a positive D.A.T. (differential agglutination titre), peripheral neurarthropathy, bone erosions, and
pleural or pulmonary lesions. Hyperaemic lesions near bone erosions or sites of synovial proliferation were present in 22 cases.

A number of other patients were also subjected to brachial arteriography, including ten with primary Raynaud's phenomenon, many of whom had occlusive lesions. In three patients with polyarteritis nodosa there were occlusive lesions with a network of irregular tortuous arteries, which, the authors consider, may be characteristic.

D. E. Fletcher


More than 2,000 patients with silicosis and other forms of pneumoconiosis, most of them miners, were investigated clinically and radiologically for the presence of rheumatoid arthritis. Whereas pulmonary tuberculosis was a complication of the silicosis in 862 patients, rheumatoid arthritis was found in only 21, and the authors calculate that the incidence of this complication is between 0.6 and 1 per cent. Sometimes the onset of the arthritis preceded that of the silicosis, sometimes both developed together, but more often it appeared some time after the silicosis had been diagnosed. In some cases typical rheumatoid arthritis occurred; in others a mild form of polyarthritis without significant deformation of the joints was present. The latter syndrome requires further study.

In three of the 21 cases the typical radiological appearances of Caplan’s syndrome were observed, with multiple round shadows in the lung fields, while in another three large, asymmetrical, tumour-like shadows were present. Joint changes were found equally often in patients with and without pulmonary tuberculosis. The patients with rheumatoid arthritis were frequently observed to have a markedly progressive form of silicosis with characteristic radiological changes, and the authors suggest that the presence of rheumatoid arthritis may influence the development and progress of certain forms of silicosis.

Basil Hoagh


The object of this work [carried out at the Danish Red Cross Rehabilitation Centre, Hald, Denmark] is to evaluate kidney function in patients with rheumatoid arthritis in relation to the total drug consumption (phenacetin and phenylbutazone consumption as well as gold salt and corticosteroid therapy) compared with the kidney function of other groups of patients in relation to phenacetin consumption. The material consists of 790 patients:

1. 244 patients with rheumatoid arthritis (165 women and 79 men).
2. 546 patients with other diseases (328 women and 218 men).

All the patients have been questioned about previous treatment and drug consumption. The information obtained is compared with the kidney function, which has been examined with three single 24-hour creatine clearance tests. Clearance is corrected for surface. The material is statistically prepared. A short outline is given on the possible harmful effects of the medications mentioned on the basis of literature.

There has not been any relation between the kidney function expressed by clearance and the total drug consumption in patients with rheumatoid arthritis, just as there has not been any relation between kidney function and phenacetin consumption in patients without rheumatoid arthritis, whereas patients suffering severely from a rheumatoid arthritis of long duration have significantly lower kidney function than patients with a milder disease, and this seems to be connected with the disease itself, independent of medication.—[Author’s summary.]

Thomas Hunt


Out of 51 patients with ulcerative colitis treated at the Medical Clinic, Marburg, Germany, during the years 1956-62, seven (4 male, 3 female) also had arthritis. The arthritis was mostly mild, often flitting from joint to joint, and was associated with extensive colitis. In four of the patients joint involvement developed while taking sulphasalazine. In no case was the course typical of true rheumatic fever, and there was no evidence of psoriasis or of a collagen disease. The larger joints of the lower limbs were the most often affected. Periarticular reaction was minimal. The author terms the arthritis “colitis-rheumatoid”. He regards the flitting type of joint swellings, the minimal general reaction, and the occasional association with other allergic manifestations (rashes in five cases, asthma in one) as pointing to an allergic origin for the arthritis.

[No clear indication is given as to the relationship of the arthritis to specific treatment—none of the seven patients underwent colectomy—and it is not stated whether L.E. cells were found in the blood of any of the patients.]


During an epidemic of rubella in Norfolk, in the Spring of 1962, 21 cases of a transient arthritis were noted. All occurred in women whose ages ranged from 15 to 54 years. The arthritic symptoms usually appeared as a rash faded and the symptoms lasted for from 4 to 52 days. The joints involved were the fingers, wrists, knees, and ankles, in that order of frequency, and symmetrical involvement was more common than asymmetrical. Two short case reports are included. D. D. McCarthy
Pigmentation of Serum in Rheumatoid Arthritis.


The authors, writing from the General Infirmary, Leeds, have tried to explain their observation that the serum of some patients with rheumatic disorders often has a greenish tinge. They studied the sera of sixty cases of classical and definite rheumatoid arthritis and 32 had a greenish serum, whereas some coloration was found in only two of 27 sera from other patients attending the rheumatic clinic (with a variety of diagnoses other than rheumatoid arthritis) and two of fifty sera from normal subjects and patients with non-rheumatic disorders.

No chromobacteria were found in the specimens of green serum and nothing unusual could be detected on serum protein electrophoresis. Absorption spectra, however, were quite different for the two types of serum and this was particularly so after deproteinization with acetic acid and extraction with ether. Some of the differences could be accounted for by differing concentrations of bilirubin and porphyrin derivatives, but one peak at 362 mµ, found only in rheumatoid patients with greenish serum, could not be explained on pigmentary differences. This peak did not occur in any of the green sera from non-rheumatoid patients.

Further studies are being carried out in an attempt to characterize this substance.

D. J. Ward


Osteo-Arthritis


This paper from the department of orthopaedic surgery, Harvard Medical School, is the first part of a two-part article on “cervical osteo-artthritis”. Cervical spine changes of three grades of severity are described: “mild cervical-spine changes”, “moderate osteo-arthritis changes”, and “severe osteo-arthritis changes”.

Mild Changes: The author states that a large number of persons at 40 to 50 years of age will show some narrowing of the space between C5 and 6, with early or mild irregularities of the anterior borders of the vertebral spin. He suggests that perhaps the term “arthritis” should not be used in such cases; instead this condition may be referred to as “changes normal for the patient’s particular age group”. He believes that the majority of patients with mild changes in the cervical spine who complain of cervical stiffness, headaches, shoulder, and upper-extremity discomfort have a mechanical rather than an “arthritic” basis for their complaints. The mechanical factors which appear to be responsible for the symptoms are frequently associated with certain occupations, particularly those in which the patient’s head is repetitively used in a limited range of motion or in a position of strain.

Moderate Osteo-arthritis Changes: These involve the posterior articular and lateral interbody facets, with narrowing of the intervertebral spaces and the loss of, or reversal of, the normal anterior curve of the cervical spine. Spur formation of various degrees can occur along the anterior or posterior borders of the vertebral bodies. A moderate degree of cervical osteo-arthritis can produce a variety of symptoms, such as the chronic “stiff neck”, or the “foraminal syndrome” from compression or irritation of nerve roots.

Severe Osteo-arthritis Changes: Osteophyte formation in the cervical spine may become excessive, with resultant direct pressure posteriorly on the spinal cord or anteriorly on the oesophagus or trachea. Involvement of the Luschka joints by osteophytes can impinge on the vertebral arteries and the corresponding sympathetic nerves; this change may produce the “posterior cervical sympathetic syndrome”. Patients with cervical spondylosis who experience a severe hyperextension injury can develop spinal-cord damage without evidence of fracture or of dislocation; this injury has been termed the “central-spinal-cord syndrome”.

G. Meachim


**Spondyloitis**


An association between ankylosing spondyloitis and inflammatory disease of the bowel has been noted in a number of reports in the past, and with this in mind the present authors have reviewed 870 cases treated with irradiation for ankylosing spondylitis in Edinburgh between 1935 and 1960 (Group A) and 170 cases of ulcerative colitis or Crohn’s disease seen at the Western General Hospital, Edinburgh, between 1954 and 1960 (Group B). As a result twenty cases of definite ulcerative colitis or Crohn’s disease were found in Group A, and four cases showing the typical bilateral changes of ankylosing spondylitis in Group B. Furthermore, in the two groups of patients, eight families were found of which at least one member had ankylosing spondylitis and another member had ulcerative colitis or Crohn’s disease. The association between the two diseases was found more frequently in females than in males. The bowel lesion was diagnosed before the ankylosing spondylitis in eleven patients, in the same year in four, and some time later in nine, the interval between the two diagnoses where these were not concurrent ranging from 5 to 15 years. Only nine of the 24 cases had radiotherapy for ankylosing spondylitis before an intestinal lesion was diagnosed; it is therefore not considered likely that radiation plays a part in the causation of the latter.

The authors discuss possible explanations for the significant association between bowel disorders and ankylosing spondylitis. They consider that the familial occurrence of the two diseases "suggests either an inherited predisposition or the operation of an aetiological factor in the family environment". M. Wilkinson


Comparative Treatment of Sixty Cases of Ankylosing Spondylitis in Different Spas. (Traitement comparatif de 60 cas de spondylarthrite ankylosante dans différentes stations thermales.) Lenoch, F. (1963). *Rheumatologie*, 15, 209. 7 figs, 5 refs.


**Inflammatory Arthritis**


The first of these two cases concerns a 7-week premature male infant who developed a *Staph. aureus* infection of the hip joints at 15 days of age. Treatment consisted of appropriate antibiotics, whole blood transfusions, and skin traction to both legs. The infection was controlled, but pathological dislocation of the hips occurred, and this did not respond to manipulation and immobilization at 7 months of age. X-ray examinations at 15 months, 30 months, and 4½ years revealed gross dislocation of the hips, with absent femoral heads, stunted femoral necks, and shallow acetabula. The child walks with a symmetrical waddling gait but is fairly active.

The second case was that of a 3-year-old boy who had been born 4 weeks prematurely. Because of Rhesus incompatibility he had transfusions and a cutdown site became infected with *Staph. aureus*. He made reasonable progress with an appropriate antibiotic, but some months later, some asymmetry of the legs was noted, in addition to a delay in walking and a dragging of the left leg. Radiological examination revealed absence of the capital epiphysis and dislocation of the femur. Closed reduction was not possible and at operation the capsule was found to be densely adherent to the femoral neck, and the absence of the capital head was confirmed. After division of the tight structures about the femoral neck, reduction still could not be accomplished. At present he has 1 in. of leg shortening, but is painfree and able to run.

D. D. McCarthy

This is a review from the Western Reserve University, Cleveland, Ohio, of the anatomy of the bursae which occur on the medial side of the popliteal fossa, and of the pathology of the cysts which occur in that fossa.

A new series of 43 cysts in 39 patients is presented, amongst which only ten had other disease of the knee joint. All were treated surgically. 25 cysts were found to lie between the gastrocnemius and semimembranosus muscles, and the rest were unclassified. A communication with the joint cavity was found in 25: this was usually closed, but the cyst did not recur in those two cases in which it was not closed at operation. The histology of the lining was fibrous in 22 cysts, transitional in four, synovial in twelve, and inflammatory in five. Residual symptoms were seen only in those cases in which there was pre-existing joint disease; a cyst recurred in two cases. The authors believe that the cysts are usually bursae swollen as a result of repeated trauma, but that in a minority they arise as a herniation through the posterior part of the joint capsule.

A. J. Palfrey


This review article covers in detail the diagnostic features of the commoner causes of arthralgia-rheumatoid arthritis and conditions resembling it, including psoriatic arthropathy, ankylosing spondylitis, enteropathic arthritis, and palindromic rheumatism, psychogenic rheumatism, rheumatic fever, Reiter's syndrome, bursitis—and in less detail of many less common causes of this symptom, the rarer ones being listed very briefly.

E. G. L. Bywaters


Gout


This review article considers the subject under five headings:

1. Renal handling of uric acid in normal individuals. The evidence for tubular secretion, based largely on the work of Gutman, is summarized.

2. Renal handling of urate in patients with gout. The opposing views of Gutman and his colleagues, who find no evidence of a primary defect in tubular function, and of those who do are discussed.

3. Renal disease in gout.

4. Uric acid stones.
(5) Gout secondary to chronic renal disease. The rarity of this complication is emphasized and especially the possibility of its confusion with the pseudo-gout syndrome caused by deposits of microcrystalline calcium pyrophosphate.

This is an extremely useful review, brief but fully documented. L. E. Glyn


The metabolic defect in gout seems to be unaffected by diet or uricosuric drugs. A new approach to treatment was made by the authors of this paper from the Hôpital Cochin, Paris, who used uracil-6-carboxylic acid (orotic acid), a substance present as a growth factor in the milk of certain mammals. Orotic acid, which has also been tried in the treatment of cirrhosis of the liver and pernicious anaemia, appears to reduce the production of uric acid rather than increasing its excretion.

The drug was given to 34 patients in a daily dosage of 3 to 5 g. up to a total of 500 g. All the patients had established gout and a serum uric acid level usually in excess of 8 mg. per 100 ml. They were given a fixed diet and the serum uric acid level and urinary urate excretion were carefully measured during the administration of either a placebo or orotic acid. The latter consistently reduced the serum uric acid level by 20 to 25 per cent. Unlike probenecid, orotic acid caused no marked rise in urate excretion. It was extremely well tolerated and the authors consider that it can safely be given to patients for whom the commonly used uricosuric agents would be contraindicated (those with renal lithiasis, for example).

It is suggested that orotic acid and its derivatives cause a deviation in the cycle of uric acid synthesis at an early stage, as a result of which uridylic acid is produced at the expense of uric acid. The number of cases treated is still too small for definite conclusions to be drawn, but the complete absence of all side-effects should encourage trials on a larger scale.

[D. Preiskel]


Bone Diseases


"Anadur" is a long-acting ester of 19-nortestosterone (19-nortestosterone-p-hexoxyphenyl-propionate). The author, writing from the Rigshospitalet, Copenhagen, states that in animal experiments this substance has shown prolonged and powerful anabolic properties combined with a favourable anabolic/androgenic ratio. He has therefore studied the effect of a single intramuscular injection of "Anadur" in four patients with varying degrees of osteoporosis (two females aged 72 years and two males aged 45 and 60 years).

A definite anabolic effect, as shown by retention of nitrogen and calcium, was observed in two patients receiving a single dose of 150 mg. "Anadur" intramuscularly and in one patient receiving 50 mg. The fourth patient did not respond to a single dose of 50 mg. The balance data suggest that the single injection maintained a powerful anabolic effect for a period of at least 2 weeks in the subjects who responded. The rate of degradation of intravenously administered 131I-labelled albumin was studied in one patient, and was found to be unaffected by the "Anadur" injection.

One patient showed an undesirable side-reaction, developing "muscular restlessness", nervousness, tachycardia and a temperature of 39°C. 2 hours after the injection of 150 mg. "Anadur". No virilizing or progestational effects were noted in any of the subjects.

G. Meachim


This is a study, from the University of Siena, of the absorption of calcium from the alimentary tract in thirteen patients with senile osteoporosis and in five normal subjects. Three of the five normal subjects used were younger (31, 28, and 30 years) than any of the patients in the osteoporotic group (range 46 to 85 years).

Radioactive calcium (45Ca Cl2) was administered with carrier as a single oral dose to fasting subjects. Samples of venous blood were collected at intervals during the 4 hours after giving the isotope. Urine was collected every 2 hours during the 6 hours after the administration of the dose. Feces were studied as a pooled sample collected over 3 days (0 to 72 hours).
Radioactivity appeared in the plasma of all the normal subjects, both young or old, within 10 to 15 minutes of giving the radioisotope, and plasma radioactivity rose rapidly to a peak within 60 to 90 minutes. In the osteoporotic patients plasma radioactivity appeared later than in the normal subjects, increased more slowly, and did not attain a peak level until 120 minutes after administering the dose.

The peak level of plasma radioactivity attained was lower in the osteoporotic patients than in the normal subjects. The total urinary excretion of radioisotope over a 6-hour period was less in the osteoporotic group. The degree of radioactivity in the faeces taken over 3 days was greater in the osteoporotic patients than in the normal subjects.

The authors conclude that there is a defect in the intestinal absorption of calcium in senile osteoporosis.

G. Meachim


Calcium Therapy combined with Iodine and Vitamin C in Osteoporotic and Osteomalacic Arthritis. (La calcithérapie associée à l'iode et à la vitamine C dans les arthroses ostéoporotiques et ostéomécaliques.) Bernard, R. (1963). Rhumatologie, 15, 239.


Non-Articular Rheumatism


The authors, writing from the College of Medicine and the Children's Hospital, Cincinnati, record five cases of intervertebral disk calcification and review 48 others reported in the literature. More than one disk may be involved, although single disk calcification predominates, and the lesion occurs most frequently in the cervical spine. If the cervical disks are affected it is unusual to find the thoracic or lumbar regions similarly involved. Cervical disk calcification invariably gives rise to symptoms in contradistinction to that occurring elsewhere in the spine, patients complaining of pain, limited movement, tenderness, muscle spasm, and torticollis. The condition may appear at any time between birth and adolescence and is normally self-limiting. From the time of initial diagnosis the calcification tends to recede over a period of weeks or months, taking rather longer in the thoracic and lumbar regions where occasionally it may persist.

The cause is unknown. Some of the cases have associated systemic infections, others have a variety of congenital abnormalities, but there is no obvious causal relationship. Trauma is discussed as a possible contributory factor but, as the authors admit, this is extremely difficult to assess in young children.

Various therapeutic measures including immobilization, salicylates, and irradiation have proved ineffective and the authors recommend conservative treatment until spontaneous recovery occurs.

A. Garner


E. G. L. Bywaters


A study is reported in this paper from the University of Budapest School of Medicine, Hungary, of the incidence of Raynaud’s phenomenon in 434 men in the iron, steel, and engineering industry who had worked for over a year predominantly and continuously with pneumatic hand tools. Men with a previous history of Raynaud’s phenomenon, frost bite, or injuries to the hand were excluded. Special attention was paid to the way in which hand tools were used, the frequency of vibration, the duration of working time spent with each type of tool, and the duration of exposure.

Raynaud’s phenomenon usually developed 3 or more years after exposure and was related to the speed of vibration, duration of exposure in years, and the proportion of the working day spent in using vibratory tools. High-speed vibratory tools when used exclusively and frequently gave rise to Raynaud’s phenomenon; thus 79 per cent. of workers using fettling hammers for 3 or 4 years in a steel-casting cleaning room were affected. In workers using exclusively low-speed piston tools for ramming sand moulds Raynaud’s phenomenon never developed and it was seen only rarely in those operating exclusively low-speed rotary pneumatic tools. The high incidence of the condition resulting from continual handling of heavy piston-operated tools was moderated when these were used alternately with rotating pneumatic tools.

The authors conclude that a reduction in the incidence of Raynaud’s phenomenon can be achieved with longer rest periods and shorter exposure to heavy piston-operated tools or by an alternate change over from the latter to lighter rotatory tools.

Morris Greenberg


Role of Trauma in Painful (So-called Rheumatic) Affections of the Spine. (Rôle des traumatismes dans les affections douloureuses (dites rhumatismales) de la colonne vertébrale.) VERDAN, C. (1963). Rhumatologie, 15, 159. 2 figs, 8 refs.


Pararheumatic (Collagen) Diseases


The authors have found that the cryoprecipitation observed in the serum of some patients with systemic lupus erythematosus (S.L.E.) was always associated with active manifestations of the disease. The cryoprecipitate consisted in part of 7 and 19S material and on immunoelectrophoresis proved to be \( \gamma_{\omega} \) and \( \gamma_{M} \)-globulins. In serum from twelve patients with S.L.E. at the Presbyterian Hospital, New York, they found that a heat-labile component, readily supplied by the patient's serum or by serum from healthy subjects, was necessary for cryoprecipitation to occur. By adding normal serum fractions to heated S.L.E. serum it appeared that the C' fraction of complement was the heat-labile factor (except for a conflicting observation in one patient). Calcium, which is required for the interaction of C' with immune complexes, was not essential for cryoprecipitation. Another complement fraction (11 S component) usually associated with C' was therefore studied and appeared to be the heat-labile component. These observations suggest that the cryoprecipitation of S.L.E. sera depends on a reaction between the 11 S component of complement and soluble globulin components, possibly immune complexes. M. Wilkinson


A radiological investigation of the bones and joints was carried out at the Moscow Rheumatic Institute on 82 female patients aged 15 to 55 years with systemic lupus erythematosus (S.L.E.). The diagnosis was based on both clinical and laboratory findings, including the presence of L.E. cells in the peripheral blood. The length of the illness varied from 1 to 29 years (1 to 5 years in fifty cases) and the patients were under observation for a period of 1 to 14 years. Radiological examinations were carried out on one occasion only in 48 cases and more than once in 34. The patients were divided into four groups (I to IV) according to the severity of the clinical manifestations of joint disease, which were present in eighty cases (97 per cent.).

The most common radiological finding was osteoporosis (primarily in the epiphyses of the hands and feet), which was present in fifty patients (60 per cent.). While there appeared to be some relationship between the degree of osteoporosis and the severity of the joint symptoms, the authors do not consider it to be a direct one since other metabolic disturbances, including the effect of steroid therapy, have to be taken into consideration. Other changes were found in only twelve patients, all in Group III or IV. These were narrowing of the interphalangeal joint spaces of the hand (six cases), subluxation and deviation of these joints (eight, and single fine marginal lesions (seven). The authors consider that these changes were due to alterations in the periarticular tissue.

It is concluded that radiological changes in the osteoarticular system in S.L.E. are inconstant, minimal, and non-specific. This is an important difference from rheumatoid arthritis. Kathleen M. Jones


This paper from the Columbia-Presbyterian Medical Center, New York, reports the findings in 35 children with systemic lupus erythematosus (S.L.E.) seen between July, 1930, and June, 1961. The clinical findings were not different from those in adults with S.L.E., fever, arthritis, and rashes being the most common presenting features. A positive L.E.-cell preparation, raised erythrocyte sedimentation rate, leucopenia, and hypergammaglobulinaemia were the most common laboratory findings.

Before the introduction of steroid hormones and antibiotics in the treatment of S.L.E. the mean survival in affected children was 6 months, but more recently the average mean survival has been 4 years. The good prognosis in children whose illness would seem to have been a direct result of the administration of anticonvulsants is stressed; out of seven children who had received anticonvulsants, five were alive and in remission in June, 1961, while of 28 children with other modes of onset, three were alive with active disease, two were in remission, and 23 had died. Phenytoin, methoin, and toxidone in addition to hydrazine, sulphonamides, phenylbutazone, and p-aminosalicylic acid have been known to induce S.L.E. The case histories of nine children whose disease was induced by anticonvulsants or who survived for a long time are described.
The authors differ from some investigators in suggesting that steroid therapy sufficient to remove symptoms rather than maximum doses should be given, the only exception being when there is renal involvement. They consider that further therapeutic trials are required to decide the best regimen.

J. S. Malpas

Renal Disease in Systemic Lupus Erythematous.


The incidence and course of renal disease in systemic lupus erythematosus (S.L.E.) was studied in 52 patients seen at Bellevue and New York University Hospitals with proven S.L.E. Renal disease was considered to be present when persistent proteinuria or haematuria was observed. In 32 cases in the series renal tissue was examined histologically. There was clinical evidence of renal disease in 29 of the 52 patients. The authors state that the sex, age incidence, severity and duration of S.L.E., and the death rate were similar in those with and without renal disease. In none of the patients without renal disease when first seen was renal involvement subsequently observed. [This experience is not universal.]

Histological evidence of active glomerular damage seemed to correlate with disease activity; it was present in thirteen out of fourteen patients with active disease but in only one out of thirteen from whom renal tissue was examined during clinical remission (most of the latter group were receiving corticosteroids). In two cases serial biopsies demonstrated active glomerular damage during exacerbations which was not apparent during clinical remission.

Of the 29 patients with clinical evidence of renal disease, nine had proteinuria which subsided together with other systemic manifestations after periods up to 4 years; renal biopsy performed on two of these patients revealed only equivocal thickening of the glomerular basement membrane. In thirteen of the 29 patients proteinuria persisted in spite of disease remission, but biopsy again showed only thickening of the basement membrane. Urea retention was present in the remaining seven patients when first seen; of these, six died from uraemia or intercurrent infection while one continued to show mild urea retention. There were five patients in the series with urea retention initially in whom during steroid-induced remission there was either no evidence of renal disease (3) or only slight proteinuria (2). The nephrotic syndrome developed in seven patients, but three of these were alive 5, 7, and 9 years later respectively, although proteinuria persisted in two and biopsy examination revealed diffuse thickening of the glomerular basement membrane in one.

The authors consider that the prognosis in lupus nephropathy is better than previous reports have suggested, that in most cases the glomerular lesion is focal and subsides with administration of steroids in a dosage sufficient to control other features, and that in only the few cases of severe diffuse glomerular lesions does the condition progress to fatal renal insufficiency.

M. Wilkinson


Although the presence of a circulating anticoagulant may be demonstrated in patients with systemic lupus erythematosus (S.L.E.) serious bleeding is unusual. Of eleven patients with S.L.E. seen at the Mayo Clinic eight showed definite and three suggestive evidence of circulating anticoagulants, yet only one had significant haemorrhage and, paradoxically, four had thromboembolic complications. In six of the patients the plasma coagulation time was prolonged but the prothrombin time was normal, in four both values were abnormal, while in one there was prolongation of the prothrombin time only. In seven patients the abnormal coagulation time was not corrected by the addition of normal plasma, suggesting the presence of a circulating anticoagulant. All the patients had platelet counts above 50,000 per c.mm., but in ten there was abnormal prothrombin consumption; in seven this was corrected by adding a platelet substitute (“inosithin”), suggesting the presence of thrombasthenia, which in three cases may have been due to an associated uraemia. Of the four patients with a thromboembolic tendency three showed “an increased rate or yield of thromboplastin generated from the patient’s adsorbed plasma when mixed with normal serum and when inosithin replaced platelets as the source of phospholipid”.

The anticoagulant activity in four cases was studied further. In two of these activity was not reduced by dialysis through a “cellophane” membrane. The anticoagulant was present in serum and plasma, resisted heating to 56° C. for 30 minutes, and appeared to be associated with serum γ-globulin. Platelets from one patient and from a healthy control subject after incubation with patient’s plasma showed marked reduction in both the rate of generation and the yield of thromboplastin.

The authors speculate [inconclusively] on whether the varying clotting patterns indicate multiple anticoagulants or one anticoagulant acting at various points in the clotting mechanism. However, in at least six patients there was evidence of a platelet abnormality, possibly a consequence of their acquisition of a protein coating derived from a plasma factor.

[These observations include some borderline abnormalities.] M. Wilkinson


The authors, from the Royal Melbourne Hospital and the Walter and Eliza Hall Institute of Medical Research, Melbourne, describe thymic changes in four patients.

(1) The thymus of a 51-year-old woman with rheumatoid arthritis, examined at necropsy, showed structures resembling germinal centres.

(2) That of a woman aged 20 years with systemic lupus erythematosus (S.L.E.), removed at operation after the patient had been receiving corticosteroids for 7 months,
showed small epithelial-lymphocyte aggregations but no
germinal centres.

(3) In a patient who died at the age of 17 after cortico-
steroid treatment for severe S.L.E., the thymus showed
atypical germinal centres.

(4) A patient aged 14 years had a strong family history
of S.L.E. and the thymus was removed 10 weeks after the
onset of symptoms of the disease. She had not received
corticosteroids. The resected gland showed no cortex
whichever, while the medulla contained germinal centres
resembling those seen in the thymus in cases of myasthenia
grave; plasma cells were prominent. Fragments from
the thymus were incubated with tritiun-labelled thymi-
dine and uridine; the plasma cells were shown to be not
actively dividing, but were synthesizing ribonucleic acid.

The authors emphasize the gross thymic abnormality
found in an early untreated case of S.L.E. and suggest
that the aggregations of epithelial cells and lymphocytes
in the thymic medulla may be the significant lesion in
S.L.E. They suggest that autoimmune disease is due to
lymphoid cells which are able to react with the body's
own constituents and are unresponsive to the normal
homosteotic control. The finding of germinal centres
and plasma cells in the thymus is considered to indicate
that the thymus is important in the homosteotic control
and contains autoantigens which are capable of stimulat-
ing the abnormal cells involved in autoimmune disease.

G. L. Asherson

Procainimide-Induced Lupus Erythematous. LADD, A. T.

A man aged 49 was treated with procainimide for the
conversion of auricular fibrillation to sinus rhythm.
After 6 months' treatment he was admitted to hospital
with the following features of systemic lupus erythe-
matous: moderate fever, an extensive erythematous rash,
arthritis, bilateral pleurisy with effusion, and a strongly
positive test for L.E.-cells. The drug was immediately
withdrawn and within 9 weeks the symptoms and signs had
completely subsided. Owing to the return of the auri-
cular fibrillation an attempt was made 6 months later to
restart treatment with procainimide, but this was aban-
donned after the dramatic return of symptoms within a
few hours. These included flushing, rise in temperature,
and a pulse rate of 155, but no reappearance of pleurisy
or L.E.-cells; 9 months later there was no evidence of
systemic lupus.

This case raises but does not answer the question
whether sensitization to the drug is responsible for the
lupus-like picture or whether a subclinical case of lupus is
revealing itself by drug hypersensitivity. L. E. Glyn

Systemic Lupus Erythematous following Thymectomy for
Myasthenia Gravis. ALARCON-SEGÖVIA, D., GAL-
BRATH, R. F., MALDONADO, J. E., and HOWARD, F. M.,

From the Mayo Clinic the authors describe two patients
with myasthenia gravis treated by thymectomy who sub-
sequently developed systemic lupus erythematosus
(S.L.E.).

(1) Histological examination of the thymus gland of the
first patient showed germinal follicles. She developed
arthralgia 6 years after thymectomy, and the diagnosis
of S.L.E. was later made on the basis of arthritis, urticaria,
leucopenia, a false positive Wassermann reaction, and a
positive result of the L.E. clot test.

(2) The thymus of the second patient showed simple
hyperplasia. She became ill 3 years after thymectomy.
A diagnosis of ulcerative colitis was made, and after treat-
ment with "azopyrin" (salicylazosulphapyridine) she
developed S.L.E. with arthritis, pleuritis pain, lymphad-
enopathy, and a positive L.E.-cell phenomenon.
Biopsy showed cirrhosis of the liver and chronic
pyelonephritis with membranous involvement of the
glomeruli.

The authors found nine additional cases of myasthenia
gravis associated with S.L.E. in the literature. They con-
sider that this association suggests that a lupus diathesis
exists and that myasthenia gravis is an autoimmune
disease. The fact that S.L.E. developed in these two
patients following thymectomy, however, does not support
the view that thymectomy is of value when performed
early in cases of S.L.E.

G. L. Asherson

A Case of Disseminated Lupus Erythematous. [In
Chinese with English summary.] KIANG, S. W., and
4 figs, 6 refs.

A case in an 8-year-old girl with butterfly rash, cotton-
wool patches, and haemorrhages in the retina is reported.
L.E.-cells were not found. J. M. Chang

Discoid Lupus Erythematous: Correlation of Clinical
Features with Serum Auto-antibody Pattern. SHRANK,
1 fig., 31 refs.

The clinical, haematological, and immunological find-
ings in 82 patients with discoid lupus erythematous
(D.L.E.) seen at the Middlesex Hospital or St. John's
Hospital for Diseases of the Skin, London, are described
and compared with those in eighty healthy subjects
matched for age and sex. Of the 82 patients, two females
were found to have obvious systemic lupus erythematous
(S.L.E.) and 66 (45 females and 21 males) had localized
skin disease without haematological abnormality. Of
the remaining fourteen (11 females and 3 males), nine
had widespread disease and six had leucopenia; L.E.
cells were present in the blood of one patient in this group
without other evidence of systemic disease. These four-
teen patients were considered to be intermediate between
those with classic S.L.E. and those with chronic D.L.E.
The patients were followed up for 2 to 30 years and the
most striking clinical finding was that no patient pro-
gressed from D.L.E. to either the intermediate group or
to the group with systemic disease.

Of the 66 patients with uncomplicated D.L.E., 29 gave
a positive response to the test for antinuclear factor
(A.N.F.), although the reaction tended to be weaker than
in the patients in the intermediate group. The intensity
of the A.N.F. response, however, could not be correlated

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with pregnancy, age at onset, or the duration of the disease, or with the extent of the cutaneous lesions; there were, however, more positive reactions among patients with active skin lesions. A moderately high titre of thyroid antibodies was present in three times as many patients, chiefly female, with D.L.E. as in the control group. Although the incidence of thyroid antibodies was higher in patients giving a positive reaction to the A.N.F. test than in those giving a negative response the difference was not statistically significant.

Discussing the findings the authors suggest that from a practical point of view it would seem advisable to look for autoantibodies in all patients with L.E. and that the follow-up period should be prolonged if serological or haematological abnormalities are found. Patients with chronic D.L.E. and a normal blood picture need be seen only for so long as the skin lesions remain active.

Benjamin Schwartz

Exophthalmos Secondary to Periarteritis Nodosas.


The case is reported of periarteritis nodosa initially simulating an orbital tumour, diagnosed on biopsy. Death ensued after 14 years from renal and other involvement.

C. J. Maguire


The authors have reviewed all cases classified as polyarteritis nodosa at necropsy at the Mayo Clinic during a period of 30 years and selected 56 for detailed study. In 54 cases the disease process consisted of necrotizing arteritis of the systemic circulation but with few extravascular lesions; glomerulonephritis was a common finding. These cases were considered to represent true idiopathic polyarteritis nodosa. A further sixteen cases, in addition to systemic necrotizing arteritis, had pulmonary involvement and other extravascular lesions such as splenic involvement and lesions of muscles and lymph nodes; necrotizing glomerulitis was common in this group, which was considered to represent the allergic form of angiitis. The remaining six cases, which did not fit into either of the above two categories, showed only a few lesions of vasculitis and were associated with severe renal disease or hypertension, or both.

G. Loewi


A 42-year-old female carrier of systemic scleroderma from the age of 7 developed acute arterial hypertension with retinopathy and secondary retinal detachment 2 weeks before death. Histopathological studies showed some similarity in the renal and ophthalmic vascular changes.

K. Hruby


K. Hruby


From the Moscow Rheumatic Institute the author reports a study of systemic scleroderma in sixty patients (52 women and 8 men) ranging in age from 16 to 64 years (though most of them were between 30 to 50) from which it appeared that the course of the disease could be divided into three stages.

(1) Peripheral disease of gradual onset in 41 cases and of sudden onset in the remainder, and lasted from several months to several years. The most frequent early manifestations were vasomotor disturbances similar to those of Raynaud's disease (45 cases), joint pain (39), and brawny oedema (22). Trophic disturbances usually appeared later. Loss of weight was a comparatively early sign and was severe during the more active phases of the disease. Fever occurred in nine patients, all with acute onset. In eight cases there were early signs of visceral disease, but these were more characteristic of the second stage.

(2) The stage of generalization was observed in 38 cases. During this phase various symptoms developed, reflecting disease of most of the internal organs and systems. The most frequently involved were the cardiovascular system, the lungs, and the alimentary tract, while the kidney was rarely involved.

(3) A third terminal stage was observed in the twelve patients most severely affected with predominance either of visceral disease or of progressive general dystrophy.

Among the primary and contributory causes of death were disease of the heart and lungs (3), lungs alone (2), heart alone (1), kidney (1), and alimentary tract (8), severe dystrophy (2), cerebral haemorrhage (1), and sclerodermic disease of the lungs with adenocarcinoma (1). A study of the course of the disease enabled two basic forms to be distinguished. In the subacute form (18 patients) the onset was usually comparatively acute and the general and visceral signs predominated. The results of laboratory investigations indicated an active disease process, and there was a steadily progressive course leading to death in 1 to 2 years. In the chronic form (42 patients) there was a more gradual onset, usually with symptoms of the Raynaud type which persisted for several years before other peripheral signs appeared. The subsequent course was prolonged and comparatively benign, involvement of the internal organs being well compensated and relatively symptomless. Laboratory investigations did not provide evidence of active disease and there was only a gradual increase in the signs of progressive dystrophy. The distinction of these two forms of scleroderma is considered to be important as, in addition to general treatment, the administration of corticosteroids is indicated in the subacute type.

Kathleen M. Jones


Connective Tissue Studies


Immunology and Serology


The occurrence of globulins resembling rheumatoid factors in sera from persons over 65 years of age has been studied at Cornell University Medical College, New York. Samples of serum from 171 subjects without rheumatoid arthritis (121 over and fifty under 65 years of age) and eighteen with rheumatoid arthritis (ten over and eight under 65) were examined for the presence of rheumatoid factors by the Hyland R.A. slide test, the latex-fixation test (0-8-μ and 0-2-μ particles), and the sheep cell agglutination test. Of the sera from the over-65 subjects without rheumatoid arthritis, 46 per cent. reacted positively to the Hyland R.A. slide test and 42 per cent. to the latex-fixation test; only 2 per cent. gave a positive reaction to the sheep cell agglutination test.

When the nature of the serum constituent responsible for the serological activity was investigated it was found that the activity resided in a heat-stable euglobulin fraction and was destroyed by mercaptoethanol. Chromatography on diethylaminoethanol cellulose columns and precipitation reactions with various human γ-globulin preparations failed to distinguish the active serum constituents from the rheumatoid factors which appear in the serum of patients with rheumatoid arthritis. The authors compare the incidence of globulins resembling rheumatoid factors in the serum of the aged with that of such globulins in the serum of patients with diseases other than rheumatoid arthritis and discuss the possibility of a relationship between age and the incidence of these globulins.

J. E. Page

The latex agglutination test for the rheumatoid factor was carried out at the University of Pittsburgh School of Medicine on samples of synovial fluid and serum from 68 patients with possible, probable, or definite rheumatoid arthritis and fifteen with other forms of joint disease.

Among the 49 patients with rheumatoid arthritis whose serum gave a positive agglutination reaction there were 38 whose synovial fluid also gave a positive reaction. In some of the eleven remaining cases the negative reaction of the synovial fluid may have been due to recent intra-articular injection of steroids. In nine of the nineteen cases of suspected rheumatoid arthritis in which negative serum reactions were obtained the synovial fluid gave positive agglutination reactions. This observation, which might be of clinical value in the early diagnosis of rheumatoid arthritis, needs to be investigated further. Synovial fluid samples from the fifteen control patients gave negative reactions except in one case of ankylosing spondylitis and one of peripheral arthritis. Specimens of serum and synovial fluid giving strongly positive agglutination reactions were examined by immunoelectrophoresis and ultracentrifugation, and the effect of mercaptoethanol treatment on their reactivity was studied. The results of these tests indicated that the latex agglutination factor is a macroglobulin.

J. E. Page


ABSTRACTS


Biochemical Studies


The corticosteroid-binding globulin (CGB) of plasma was measured in terms of the amount of cortisol required to saturate it at 9°C and at 37.5°C, using diluted plasma and two or more simple dialyses. Cortisol in low concentrations was completely bound; above a certain concentration the proportion of unbound cortisol increased linearly with the log total concentration of cortisol, and the amount of cortisol required to saturate the protein under the conditions of the test was estimated by extrapolation of the straight line back to 0 per cent. unbound. Determinations of cortisol-binding capacity of CGB at 37.5°C were technically less satisfactory and consistently gave results which were 9 per cent. of those obtained at 9°C. In 24 healthy subjects the mean cortisol-binding capacity per 100 ml. plasma was 31.8 μG for men and 30.9 μG for women; in twelve men with various chronic diseases not affecting the endocrine system or liver the mean value was similar (33.5 μG). In twelve men with cirrhosis of the liver the mean value was significantly lower (24.3 μG). Treatment with oestrogen was followed by increase in the values to twice the previous levels in each group. The cortisol-binding capacity did not show a diurnal variation and was not influenced by treatment with corticotropin. Since determinations at 9°C are technically more satisfactory, even though less physiological, it is suggested that cortisol-binding capacity should be determined at this temperature and multiplied by a suitable factor to give the true value for circulating plasma at 37.5°C. Determination of cortisol-binding capacity of CGB was useful clinically in distinguishing between hepatic disease and adrenal hypofunction as causes of reduced plasma levels and urinary excretion of 17-hydroxy corticosteroids.

A. J. Popert


This supplement to the Acta Endocrinologica records the discussion which followed the morning session of the Fourth Acta Endocrinologica Congress at which the following papers were given:

"Investigation of corticosteroid biosynthesis and metabolism by the determination of urinary cortico-steroid patterns", by W. S. Cost.
"Conjugation of corticosteroids in man", by K. F. Stoa.
"Biogenesis and metabolism of oestrogens", by H. Breuer.

The discussion cannot adequately be summarized but some of the points raised may be mentioned.

Cost, amplifying his paper, pointed out that the ratios of the corticosteroids excreted in Addison's disease were abnormal in the early stages when the total cortisol excretion might still be normal; in Cushing's disease, however, an increase in cortisol excretion was the first change noted, whereas changes in the ratios were of value in distinguishing between benign and malignant causes of the disease.

Bush, discussing possible mechanisms by which one type of conjugating group might be replaced by another, pointed out that steroid conjugation with glucuronic acid was effectively irreversible, whereas sulphate conjugation might be reversible; it appeared doubtful whether sulphate conjugation of cortisol metabolites occurred to a significant extent under normal circumstances, although it did with oestrogens, which retained considerable biological activity in the conjugated form. Interconversion of cortisol to oestrogenic compounds was regarded as unproved. It was thought that the routes of conjugation and metabolism of the C19 steroids were incompletely known, while about 20 per cent of administered cortisol was excreted in the form of compounds which had not been identified.

A. J. Popert

Metabolism of Steroid Hormones in Hepatic Disease.


This paper summarizes some presently available data on the metabolism of various steroids and derangements occurring in liver disease.

Cortisol and corticosterone are rapidly taken up by the liver, the double bond of ring A becomes reduced, and the compound becomes physiologically inactive. The plasma disappearance rate of infused cortisol as half-life is 75 to 100 minutes. In cirrhosis, this disappearance rate is delayed, while that of the reduced metabolites is unaffected. Protein-binding is not apparently disturbed. Clinical effects arise only rarely, since hyperadrenocorticism is avoided by a reduction of cortisol synthesis. It is advisable, however, to administer smaller than normal doses of glucocorticoids, when this becomes necessary in cirrhosis.

In the case of aldosterone, the metabolic pathway is
reduction in ring A, followed by conjugation with glucuronic acid. The plasma disappearance rate is usually prolonged in cirrhosis, whilst in the presence of ascites there appears to be some hypersecretion.

There is often a reduction in 17-ketosteroid excretion in cirrhosis, probably reflecting a decrease in adrenocortical secretion of androgen. In thyrotoxicosis, the liver may be concerned in the increased production of androsterone. Impaired inactivation of endogenous oestrogens in cirrhosis may be the reason for feminizing features.

G. Loewi


The authors, writing from the Seton Hall Clinical Research Centre, Jersey City, point out that hydroxyproline, a non-essential amino acid, occurs in the body almost exclusively in collagen. Hydroxyproline is excreted in the urine in bound and free forms. The investigation reported was undertaken to determine if changes in urinary hydroxyproline could be found in conditions associated with altered bone metabolism.

24-hour urinary hydroxyproline excretion was measured in 52 subjects on a diet free of meat, meat products, fish, gelatin, ice cream, and soft candy. Free hydroxyproline was determined using unhydrolysed urine, and total hydroxyproline (bound plus free) after hydrolysis. In preliminary work it was found that free hydroxyproline did not contribute significantly to the changes observed in the present study; all subsequent determinations were therefore done for total hydroxyproline only.

The range of 24-hour urinary total hydroxyproline excretion in thirteen adults with various diseases not known to involve connective tissue was similar to that in seven normal adults. However, in six patients with hyperthyroidism and nine patients with Paget’s disease of bone, the urinary excretion of hydroxyproline was significantly raised. One patient with hyperparathyroidism and osteitis and another with active acromegalgy also excreted increased amounts of urinary hydroxyproline.

The administration of parathyroid extract was found to increase urinary hydroxyproline excretion in two patients with postoperative hypoparathyroidism. Human growth hormone increased the urinary hydroxyproline when administered to a 22-year-old hypopituitary dwarf and to a prepubertal achondroplastic dwarf. In seven normal prepubertal children the excretion of hydroxyproline was higher than in normal adults.

The authors suggest that urinary hydroxyproline may reflect bone collagen turnover, and that its estimation may be a useful guide to the metabolic activity of bone in various diseases.

G. Meachim


Mean maternal blood uric acid level (Folin method):

(a) 4.3 mg./100 ml. in 51 cases of late pregnancy,
(b) 3.8 in fourteen cases of early pregnancy,
(c) 3.5 in 100 non-pregnant controls.

The difference between (a) and (b) was significant.

In 51 cases of late pregnancy the mean uric acid level in the amniotic fluid was 6.7 mg./100 ml. as compared with 4.7 and 4.3 in foetal and maternal blood respectively. The relatively high level in the amniotic fluid is thought to be due to a contribution from foetal urine.

J. Ball


Previous experiments by these authors suggested that the amount of corticosteroid required to suppress pituitary-adrenal function during surgical stress was greater than the amount actually secreted. The findings were contrary to the view that corticotropin secretion under these conditions is regulated by corticosteroid levels, with the negative feedback mechanism reset at a higher level than under non-stressful conditions; this study was designed as a further examination of this view. 22 patients undergoing pelvic laparotomy and not receiving exogenous corticosteroids were used as controls: the experimental group consisted of 34 similar patients who received exogenous steroids or Metopirone. Blood was obtained during operation for corticotropin and corticosteroid estimations, and complete urine collections were obtained by means of indwelling catheters.

The plasma and urinary 17 (OH)CS levels rose to the same extent during and after operation in controls and in patients given very large doses of corticosteroids (10 mg. dexamethasone intravenously per hour). The secretion of corticotropin during massive corticosteroid infusion was investigated by direct estimation of plasma corticotropin levels, and by estimation of plasma 11-deoxycorticisol levels during infusion with metopirone with or without cortisol. The results showed that the plasma corticotropin level rose during laparotomy whether the plasma corticosteroid concentration was artificially raised to a very high level or not; the quantity of corticotropin secreted in response to surgery does not therefore appear to be closely governed by the plasma concentration of cortisol.

A. J. Popert


A study is reported in this paper from the University of Illinois, Chicago, of the activity of eight enzymes—lactic dehydrogenase, aldolase, phosphohexose isomerase, malic dehydrogenase, isocitric dehydrogenase, glutathione reductase, and glutamic-oxalacetic and glutamic-pyruvic transaminase—in the synovial fluid and serum of patients with rheumatic diseases. Of the sixty patients, 26 had rheumatoid arthritis, twelve gouty arthritis, three pyogenic arthritis, eighteen osteo-arthritis, and one Reiter’s syndrome. For control purposes synovial fluid from twelve cadavers in which there was no evidence of joint


Therapy

Adrenocortical Dysfunction: Reappraisal after 4 years' Therapy. Molnar, G. D., Mattax, V. R., and Maher, F. T. (1963). Metabolism, 12, 399. 15 refs. In 1959 these authors reported (J. clin. Endocr., 19, 1023) the case of a man aged 42 suffering from a salt-caving polydypsia and polyuria, the results of mineralocorticoid deficiency. His daily excretion of aldosterone was less than 0.5 µg. and was not increased by ACTH or salt restriction. He was treated with 0.1 mg. 9a-fluorochoridite daily and $20$ mg. cortisone 8-hrly. After 4 years of this treatment, during which he remained well, his general health and renal and adrenal functions were re-investigated. The most significant change was an increase in the daily urinary aldosterone to 5 µg/24 hrs., a figure within the normal range. The absence, however, of any further reserve was shown by failure to increase this despite salt restriction and omission of mineralocorticoid. The urinary excretion of more than 200 mEq. sodium per day when mineralo-corticoid treatment was stopped, despite the excretion of 5 µg. aldosterone suggests the presence of an aldosterone antagonist, probably $17a$-hydroxypregesterone, since its metabolite pregnanolone was being excreted in amounts of 8 to 19 mg. daily.

It is not possible to infer the exact nature of the lesion from the data available. The authors' diagnosis is partial adrenal insufficiency with acquired salt-losing adrenal hyperplasia. L. E. Glynn

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disease was examined. The authors state that since values for enzyme activity in cadaver synovial fluid were comparable with those in fluid from patients with osteoarthritis they were considered "a reflection of normal levels".

The serum activity of the eight enzymes was within the normal range in all except one of the patients in the series who had rheumatoid arthritis and "coincidental" liver disease. Synovial fluid from patients with osteoarthritis was normal except for aldolase activity, which was raised. The activity of the three oxidative enzymes, malic and isocitric dehydrogenase and glutathione reductase, and of the three glycolytic enzymes, lactic dehydrogenase, aldolase, and phosphohexose isomerase, was significantly raised in inflammatory conditions in which there was increase in the number of leucocytes in the fluid; it increased proportionately to the leucocyte count. The glutamic-oxaloacetic and glutamic-pyruvic transaminase values were not so increased, although that of the former was raised in a few patients. There was no correlation between enzyme activity and the diagnostic entity. The values for aldolase and phosphohexose isomerase activity were raised 40- to 50-fold in some of the patients.

The authors state that these findings are similar to those reported to occur in serositis. They suggest, on the basis of previous studies, that the leucocytes of synovial fluid contain similar enzymes to those of the blood, and further that the enzyme activity in synovial fluid is derived mainly from these cells.

E. G. L. Bywaters


The author of this paper from Columbia University College of Physicians and Surgeons and the Presbyterian Hospital, New York, has estimated the urinary excretion of a metabolic product of tryptophan metabolism, 3-hydroxyanthranilic acid (3-HAA), in 26 patients with rheumatoid arthritis, eighteen with other connective tissue diseases, and 23 controls with diseases and disorders of different types.

All except one of the controls excreted less than 500 µg. of 3-HAA in 24 hours. Of the 26 patients with rheumatoid arthritis, ten excreted more than 500 µg. in 24 hours and four excreted more than 1,000 µg. Of the eighteen patients with other connective tissue disorders, two with systemic lupus erythematosus and one with scleroderma excreted more than 500 µg. In the patients with rheumatoid arthritis the high excretion of 3-HAA could not be correlated with any other factor, such as severity or activity of the disease, titre of rheumatoid factor, deformity, or treatment.

These findings are considered to confirm those of other workers, and the author discusses their possible significance. Decreased activity of the enzyme "3-HAA oxidase", normally found in the liver, could be the factor responsible, but there is no evidence of this and nothing is known of the "renal handling of 3-HAA".

B. E. W. Mace

The author calls attention to the risk of failure in using corticosteroids. Frequently a disintegration of the corneal stroma and a severe lesion start so unexpectedly that even a tectonic corneal graft cannot repair the damage. The author presents the results of eight corneal transplantations required by perforation and fistulization of the cornea after corticosteroids. W. H. Melanowski


The aim of this study reported from Temple University School of Medicine and Jefferson Medical College, Philadelphia, was to compare the anti-rheumatic potency of amopyroquin hydrochloride with that of chloroquine phosphate. The 25 patients in the trial had definite rheumatoid arthritis which had been active for at least a year and had not recently been treated with antimalarial drugs. For the first 2 weeks the patients were given capsules containing a placebo and the index of disease activity at Weeks 0 and 2 was averaged to provide a baseline. At Week 2 administration of the test drugs was begun; drugs were in capsules of identical appearance and were given in a dosage which provided 250 mg. of active substance daily. The patients were allocated at random to treatment with amopyroquin or chloroquine and their condition was assessed monthly for at least 3 months (5 months in most cases). The decrease in the index of disease activity in the two groups at the end of the trial was considerable and almost identical.

The authors consider that the two drugs have "anti-rheumatoid" activity in about equal degree. Side-effects did not present any problem. In one patient receiving amopyroquin there was a transient rise in the serum glutamic-oxalacetic transaminase titre. B. E. W. Mace


At the Rackham Arthritis Research Unit, University of Michigan Medical School, Ann Arbor, eight patients with active classic or definite rheumatoid arthritis were given amopyroquin in a dosage of 150 mg. daily for 5 months and a placebo capsule for the following 5 months. In seven other comparable patients the same regimen was followed except that the placebo capsule was given first. The condition of the patients was assessed at monthly intervals. In all eight patients in the first group there was improvement in all disease and activity indices after 5 months of amopyroquin therapy; this was largely maintained in the next 5 months when they were receiving the placebo except that mean grip strength deteriorated and the erythrocyte sedimentation rate rose. In the seven patients in the second group there was improvement in joint tenderness and morning stiffness during administration of the placebo, but other indices were not significantly changed. Treatment with amopyroquin, however, resulted in improvement in all indices. In none of the patients was amopyroquin withdrawn because of unfavorable symptoms, for these were few and minor; more "toxic" symptoms occurred in patients during placebo therapy. The serum glutamic-oxalacetic transaminase (S.G.O.T.) titre was found to be raised in four patients on amopyroquin, and in three the drug was temporarily withdrawn, to be resumed when the S.G.O.T. level had fallen without further effect.

The authors consider that this controlled, double-blind trial demonstrates the anti-rheumatic potency of amopyroquin. B. E. W. Mace


During chloroquine therapy, corneal clouding and changes of the retina were observed in a few cases, and one was submitted to pathological anatomy. There were some changes in the retina and liver, apparently caused by the chloroquine. In another case, the ERG after light adaptation was delayed and the ascending part of the b-wave was disturbed. On the other hand, rabbits with experimental chloroquine intoxication were pathologically and electrophysiologically investigated and showed no significant retinal findings, but there was the same delay in reproducing the ERG as in the clinical case. These results show that diagnosis of irreversible changes is possible at an early stage. N. Kirisawa


A 54-year-old woman with polyarthritis was treated with chloroquine (1 tablet daily) for 20 months. She presented superficial corneal opacities, absence of foveolar reflexes, narrowing of the arteries, and paracentral annular scotoma, and colour vision was impaired. G. von Bahr

Corneal Changes with the Use of Chloroquine. An Examination of Twenty Patients with Chronic Polyarthritis treated with Chloroquine. [In Norwegian.] Sandvig, K. (1963). T. norske Laegeforen., 83, 1129. 6 figs, 8 refs.

In 22 of seventy patients with chronic polyarthritis treated with chloroquine, typical corneal changes were subepithelial slightly curved horizontal lines between the lower and the central third of the cornea. They disappeared when the treatment was stopped. The frequency was 46-1 per cent. among those who had had more than 75 g. of the drug and 30-8 per cent. among those who had had less. G. von Bahr


A 55-year-old woman who suffered from discoid lupus...


Other General Subjects


In a study of rheumatic granuloma the author, at the Pathological Institute of the University of Mainz, has examined various tissues from ten patients dying of rheumatic fever and specimens of the auricular appendage from 36 patients undergoing valvotomy for stenosis. He distinguished three separate types of lesions:

1. the productive type, consisting of the cellular Aschoff body and showing no fibrinoid substance;
2. the exudative type, consisting largely of fibrinoid and granulocytes;
3. the muscle fibre type. In this last type there was muscle fibre destruction in various stages, with giant forms of muscle cells as well as histiocytes. This lesion differs from the other varieties in its anatomical situation in the subendocardium and in the presence of muscle fibre remnants.

In three cases in which lesions were present in the cardiac muscle pharyngeal muscle was also found to be involved in a pathological process. There was some correlation between the clinical condition and the type of lesion present. Thus while the exudative and muscle fibre lesions were found in fatal cases, the productive type was frequently seen in the absence of overt clinical signs of activity. The author finally speculates on the resemblance between the exudative lesion and the Arthus reaction on the one hand, and between the Aschoff granuloma and the delayed hypersensitivity reaction on the other. G. Loewi

Contribution to the Study of the Oculo-Salivary Syndromes.

The Pavlovian concept of the body as a unity with a balance between theory and practice, has prompted the authors to investigate the oculo-salivary syndromes and to try to find a common denominator for various disorders known under different names. The syndromes bearing various denominations are held to be aspects of the same disease. To prove this concept, three case histories are reported, each belonging to a different group of oculo-salivary syndromes.

1. Heerfordt’s syndrome, viral uveo-meningo-potiditis. The patient had uveitis, peripheral paralysis of the facial nerve, and papilloedema, i.e. meningeal involvement.
2. Mikulicz disease, binocular tumefaction below the orbital margin, with slight ptosis. This was due to the largely hypertrophic lacrimal gland. The parotid, submaxillary, and sublingual glands were swollen. General examination showed pulmonary sclerosis with costodiaphragmatic sinus symphysis, and pachypleuritis; spasmodilia and endocrine disturbances were also noted.
3. Gougerot-Sjögren disease, deficient lacrimal secretion. Salivary secretion was equally diminished, there were vasomotor disturbances, and endocrine disorders (the old term was filamentary keratitis). The patient also had chronic polyarthritis. Ocular examination showed impairment of vision, photophobia, dryness, burning pains, lack of tears, and diffuse corneal infiltration.

In conclusion, the authors point out that the following-up of the ocular symptoms, together with all the other clinical findings, are valuable indications of the course and prognosis of the disease. The development of corneal lesions is indicative of severe prognosis, with irreversible degenerative lesions. N. Blatt


Arthritis and Arthrosis of the Hip.