ABSTRACTS

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

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

Acute Rheumatism
Rheumatoid Arthritis
Still's Disease
Osteo-Arthritis
Spondylitis
Inflammatory Arthritis
gout
Bone Diseases

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 authors contend that it is difficult to establish the diagnosis of active carditis in acute rheumatic fever in the absence of any of its five chief manifestations: mitral valvulitis, aortic valvulitis, partial heart block, pericardial effusion, and heart failure. Technical and laboratory procedures such as radiology, electrocardiography, and determination of the serum C-reactive protein content and erythrocyte sedimentation rate (ESR) are of little help in making an earlier diagnosis. Even the serum glutamic oxaloacetic transaminase (SGOT) level, which is fairly consistently increased in cases of myocar- dial infarction, was elevated in only 65 per cent. of a series of cases of clinically active carditis studied by Nydick and others (Circulation, 1955, 12, 754). As lactic dehydrogenase (LDH) is particular abundant in the myocardium and has been shown to be released from the tissues at an increased rate in other necrotic, degenerative, and inflammatory conditions, it was thought possible that the activity of this enzyme in the serum might be more consistently increased in the presence of rheumatic carditis. Accordingly its level was estimated at Cairo University Hospitals in thirty patients with acute rheumatic fever (according to Jones's criteria), 24 with inactive chronic rheumatic heart disease with or without heart block, eighty normal subjects, and ten patients with heart failure of non-rheumatic aetiology. [It is not stated whether any of the last group were suffering from coronary heart disease.]

The serum LDH level was 500 units per ml. or below in all the normal subjects and patients with non-rheumatic heart disease and also in all the 24 patients with inactive rheumatic heart disease. Of the thirty patients with active rheumatic fever, thirteen were considered to have active carditis on the basis of the presence of at least one of the five manifestations listed above. All these had extremely elevated serum LDH levels, ranging from 700 to 1,300 units per ml., before the beginning of salicylate treatment, whereas only three had electrocardiographic signs of active carditis. Of the seventeen without clinically active carditis, thirteen had a normal serum LDH level and in none was the level over 640 units per ml. In contrast, although the mean SGOT level in the patients with active rheumatism was higher than in normal subjects, neither the mean nor the individual values were helpful in distinguishing those with carditis from the rest.

There was a significant correlation between the degree of elevation of serum LDH activity and the degree of severity of carditis as assessed clinically. During the subsequent course of the illness the serum LDH level fell slowly in the patients with carditis (after a further rise in five cases) to reach normal values after a mean of 50 days. In eleven of the rheumatic patients without carditis the LDH level rose after the initial estimation (though in all but one it remained below 700 units per ml.) but in all it returned to normal more rapidly (mean 27 days) than in those with carditis. No correlation was found between changes in the serum LDH level during the illness and those in the SGOT level and the ESR, both of which returned to normal more rapidly than the LDH level.

The authors conclude from these findings that estimation of serum LDH activity is of value in establishing the presence and assessing the severity of carditis in the initial stages of rheumatic fever and in following the course of the disease, and that no patient should be regarded as cured until the LDH level has returned to normal. They consider that the serum LDH activity is the most sensitive available indicator of the progress of the rheumatic process.

[Although it is claimed that estimation of the serum LDH level is a sensitive diagnostic test for the presence of rheumatic carditis, its superiority in this respect over clinical methods has not in fact been shown. All the patients with really high LDH levels were those in whom the diagnosis was readily established by simple physical signs. The intermediate group with doubtful carditis had intermediate, doubtfully elevated LDH levels.]

John Lorber


Rheumatoid Arthritis


Skin lesions resulting from vasculitis in the course of rheumatoid arthritis are described in three patients. Vasculitis is common in rheumatoid arthritis but seldom causes skin manifestations. The latter, which range from purpura to gangrene, are frequently associated with severe arthritis, subcutaneous nodules, a high titre of circulating rheumatoid factor, and peripheral neuropathy. The relationship to other collagen disorders and to corticosteroid treatment is discussed. H. J. Wallace


The renal dysfunction which is commonly found in rheumatoid arthritis (RA) may have diverse causes. Thus amyloidosis is not uncommon in patients with RA, while the prolonged intake of large doses of analgesics for RA in these patients may be another cause of renal damage. Evidence for the existence of a primary rheumatoid renal lesion comes mainly from necropsy studies, glomerular hypercellularity (thought to indicate a specific form of glomerulitis) having been described by a number of authors. The three renal biopsy studies hitherto reported have given conflicting results.

In the study here reported from Kommunehospitalet, Copenhagen, the authors used a quantitative evaluation of nuclear distribution to assess glomerular cellularity in renal biopsy specimens from 32 patients with RA, of whom seventeen had proteinuria and an increased serum creatinine level. No confirmation was obtained of the increased cellularity of the glomeruli previously reported in patients with RA, though in some cases there were localized areas of hypercellularity within the glomeruli with no increase in the total number of nuclei. These could not be regarded as primary rheumatoid lesions as they were observed only in the presence of other lesions in the kidneys.

[The general histological findings in this series were very heterogeneous; eleven of the kidneys were normal, and in the rest the most frequent abnormalities were chronic interstitial nephritis (9 cases), amyloidosis (4 cases), and arteriosclerosis of the small renal arteries (6). The authors state that the question whether the frequent occurrence of chronic interstitial nephritis in RA represents a visceral rheumatoid affection, an increased susceptibility to pyelonephritis, or the result of toxic or ischaemic factors "must for the time being remain obscure".]

O. L. Meyers

Scintillation scanning techniques have shown that, if iodinated human serum albumin (IHSA) is injected intravenously into patients with active arthritis, the degree of localization in the joints is greater than that occurring in healthy individuals.

This paper which comes from the Ochsner Foundation Hospital, New Orleans, describes some preliminary observations on seven patients whose joints were clinically normal, forty with rheumatoid arthritis, six with osteoarthritis, and one with gout. These patients received radioactive IHSA intravenously [25 μc. per 10 lb. (4-5 kg.)], and 24 hours later scintillation scans were made of both hands, the knees, and the wrists. The synovial membrane was shown to be permeable to the IHSA, and the radioactive material in the synovial fluid was proved by strip electrophoresis to be limited to the albumin fraction. Aspiration of the synovial fluid caused only a minimal decrease in measured radioactivity, thus indicating that the significant amount was localized within the periarticular area, synovial membrane and the vascular bed.

Localization of the radioactive material was shown by the scanning process to be at those articular sites which clinically and radiographically seemed to be the most actively involved. This localization was not specific to rheumatoid arthritis because somewhat similar patterns were demonstrated in cases of osteo-arthritis and gout. Normal joints showed no localization above that amount expected to be in the adjacent soft tissues and vascular bed. The procedure may be valuable for measuring physiological alterations in joints. Harry Coke


The authors distinguish five types of rheumatoid lung, namely chronic fibrosing pneumonia, diffuse interstitial fibrosis, discrete nodules with or without cavitation, rheumatoid pneumoniosis, and pleurisy with effusion. They report one example of each. L. Hall


Still's Disease


In this study, reported from University Hospital, Lund, Sweden, the authors have attempted to correlate the clinical findings with the radiological changes in 63 cases of juvenile rheumatoid arthritis (JRA) involving the knee joints. The 63 patients (43 girls and 20 boys) were divided into three groups:

I (“definite JRA”). 14 girls and 8 boys with symmetrical involvement of other joints as well as the knees;
II (“probable JRA”). 22 girls and 4 boys with oligoarthritis running a more benign course;
III. 7 girls and 8 boys with “postinfectious RA”.

In the last group twelve patients had a focus of infection, eradication of which led to the subsidence of the knee arthritis, and in the remaining three this cleared up after immobilization and antibiotic treatment. A total of fifteen patients (3 in Group I, 11 in Group II, and 1 in Group III) had iridocyclitis which in each case had its onset after the arthritis; it was usually found in patients with oligoarthritis, and the presence of the iridocyclitis presaged a relatively favourable outcome of the arthritic process. The response to the sheep-cell agglutination test in all these cases was negative.

The degree of osteoporosis varied directly with the intensity of the disease, being most pronounced in Group I and absent in Group III; it was also more pronounced in those who already had or who later developed bilateral arthritis. It is considered that if the calcification is seen early it can be of prognostic significance indicating a more serious condition with a poorer prognosis. Prednisolone given for long periods in a dosage of less than 0-1 mg. per kg. body weight per day seemed to exert no influence on the calcium content of the bones but half the patients receiving a dosage of 0-18 mg. per kg. per day showed destruction of cartilage. The disease process often resulted in an increase in bone growth in the affected leg after 4 to 6 months with the consequent risk of flexion contracture. [No mention is made of the radiological appearances of the sacro-iliac joints.] D. Preiskel


In the previous paper the authors point out that 70 per cent. of the growth in length of the femur takes place in
the distal epiphysis, while in the tibia 55 per cent. of this growth is in the proximal epiphysis; also that ossification occurs more rapidly in girls than in boys. Radiological investigations included taking frontal and lateral films of both knee joints on two or more occasions, and in most cases orthodiagnostical measurement of the length of the femur and tibia on one or more occasions. As a control twelve healthy children were also examined. Planimetric measurements taken on the frontal films of the femoral epiphyses in patients with unilateral knee arthritis showed the epiphyses to be larger in the diseased limb than in the healthy one. The difference in bone length in these cases was usually found to be 2 to 4 per cent. In the younger children this difference was greater in the case of the femora than in that of the tibiae, the reason for this being unknown. The difference between the two limbs tends to disappear within 2 years of the arthritis healing or becoming bilateral. It is suggested that the basic cause of the increase in length of the bones and of the accelerated ossification, which also occur in other pathological conditions, is increased circulation in the growth zones.

D. Preiskel


Osteo-arthritis


The author's purpose in this paper is to suggest that minor anatomical variations in the hip predispose it to the development of osteo-arthritis and that this is an explanation for a high proportion of the so called primary or idiopathic cases. Critical inspection of radiographs will permit recognition of these minor variants leading to earlier diagnosis and treatment.

The investigation consisted of the comparison of radiographs from fifty "control" patients with 200 from patients thought to be suffering with primary osteo-arthritis of the hip joint.

Two variants were assessed radiographically:

1. Acetabular dysplasia: techniques for measuring the depth of the acetabulum and Wiberg's C.E. angle are given and from the control series criteria were established to delineate a shallow acetabulum, which is accepted as a forme fruste of congenital dislocation.

2. Tilt deformity of the femoral head: a geometrical method was used to measure what proportion of the femoral head lies medial to a line drawn through the axis of the femoral neck, a method open to technical difficulties. If this is greater than a specified figure, then a subclinical slipped epiphysis is thought likely to have occurred in youth.

The radiographs of patients with an initial diagnosis of primary osteo-arthritis were then re-examined using these criteria and highly significant differences from the control group were found. 65 per cent. were found to have these minor anatomical deformities and of the men only 15 per cent. were, thought to be unequivocally normal. 25 per cent. of the 200 cases had acetabular dysplasia with a female to male preponderance of 4:1. The deformity occurred in 40 per cent. with six males affected for every female. Osteo-arthritis developing in hips anatomically normal is four times commoner in females and has a later age of onset.

[The patients were attending a highly specialized orthopaedic hospital, and are presumably not a random sample of the total population with arthritic hips.]

I. P. Williams


Spondylitis


A case of fracture-dislocation of the cervical spine complicating advanced rheumatoid spondylitis is presented, and 22 other similar cases are reviewed. X-ray findings, later confirmed at autopsy revealed a fusion of the neural arches in the cervical region and a vertebra column obviously incapable of any significant degree of mobility. Fracture dislocation had occurred at the C6-C7 interspace, and the cervical cord was almost completely transected at this level.

F. N. Ghadially


Inflammatory Arthritis


This review article by a well-known authority is admirably concise yet comprehensive expanded version of the author's chapter in a recent text-book. There are sections dealing with the manifestations in various parts of the body, those describing the arthritis, skin and ocular lesions being particularly well done.

[The author states that corticosteroid therapy may be indicated in severe general disease; it is perhaps, a pity that in a journal of this sort, he gives no guide to the average duration of such treatment when required.]

Mary Corbett


Temporal arteritis is infrequently associated with ulceration of the scalp.

H. J. Wallace
Aetiology of Uveitis. (L'etiologie de l'uveite.) PERKINS, E. S. (1965). 

The most important causes of uveitis are spondylarthritides, Reiter's syndrome, sarcoidosis, Behçet's syndrome, tuberculosis, toxoplasmosis, and syphilis.

J. Rougier


A case of recurrent uveitis with hypopyon, retinal periphlebitis, mucous aphthosis and papillae'dema; the patient was treated by intradermo-reaction, cortico-therapy, and pyrotherapy without much success.

J. Rougier


Gout


Previous studies of glutamine metabolism in gout (Gutmann and Yü, Amer. J. Med., 1963, 35, 820) suggested to the authors that there was a deficient utilization of glutamine in the kidneys for the production of ammonia, leading to a surplus of glutamine being available to the liver for conversion to urea and uric acid. Working at the Mount Sinai Hospital, New York, they have therefore compared the urinary ammonia and acid excretion of 97 patients suffering from primary gout with that of 46 non-gouty control subjects. All the members of both groups were considered to be free of renal disorders. The patient with gout included some whose excretion of uric acid was normal and some in whom it was excessive. Urine was collected over a 2- or 3-hour period in the morning after the overnight urine had been discarded. No food was allowed, but some patients were allowed one or two glasses of water to facilitate diuresis. Estimations of the pH and the ammonia and titratable acid content of each sample were carried out without delay.

There was a wide scatter and considerable overlap of the values for ammonia and acid, but the pH tended to be lower in the gouty than in the non-gouty. When the groups were subdivided according to the pH value it was found that for the 83 gouty subjects who excreted urine of pH 4.8 to 5.7 the mean rate of excretion of ammonia was significantly less than that of their non-gouty counterparts. There was no significant difference in mean titratable acid excretion, so that there was a mean net deficit in elimination of metabolic acid in gouty subjects. When ammonia chloride was administered to 18 gouty and 6 non-gouty subjects for several days the urinary excretion of ammonia and titratable acid increased, but the increase was less in the gouty than in the non-gouty subjects. The deficiency in the excretion of ammonia in the gouty subjects did not appear to depend on age, duration of gout, presence or absence of uric acid calculi, or any overt manifestation of renal insufficiency. The authors suggest that the lower urinary excretion of ammonia in primary gout contributes to the acidity of the urine and predisposes to the formation of uric acid calculi, even when excretion of uric acid is not excessive. It may also be a factor in the overproduction of uric acid.

R. E. Tunbridge


The effects of diuretics on the circulation, blood viscosity, and blood clotting were studied in thirty patients [at the City Hospital, Bad Oeynhausen, Germany]. They were found to cause marked arterial constriction with an increase in total peripheral vascular resistance, a marked increase in blood viscosity, slowing of blood flow in the small and smallest vessels, and marked increase in blood clotting. These changes cause, in particular, a marked increase in cardiac work which may be harmful in heart failure. Decreased flow velocity and increased clotting tendency may increase the risk of thromboembolism. Counter-measures should therefore be taken in order to avoid fatal results.—[Translation of authors' summary.]


The authors of this paper suggest that over-rigidity in the use of two guidelines generally accepted in the diagnosis of acute gout—namely, that it is rare in Negroes and that the first attack is always monarticular—may be misleading and lead to delay in diagnosis. In support of this view they present the results of a retrospective study of the records of patients with arthritis seen at Jackson Memorial Hospital, Miami, Florida, between April, 1961, and April, 1964. Over this period 76 patients (54 males and 22 females) were considered to have acute gout. This diagnosis was based on the history and clinical appearance; the presence of hyperuricaemia; the finding of uric acid crystals in the synovial fluid in many of the patients;
the therapeutic response to colchicine; and, in the cases of multiple joint involvement, sustained remission on a regimen including probenecid and colchicine with a negative response to the FII latex test for rheumatoid factor and absence of radiological change at follow-up examination.

Of the 76 patients 38, including thirteen women, were Negroes—that is, 50 per cent. compared to the 25 per cent. of Negroes in the local hospital population. Eleven of the 76 patients, including four Negroes, had multiple joint involvement in their first recognized attack. In eight of these patients there was a family history of gout.

B. M. Ansell


The rise in serum uric acid concentration occurring during starvation, which has been attributed to various causes, has become of more clinical importance with the increasing use of starvation for long periods in the treatment of obesity. At Wadsworth Hospital, Veterans Administration Center, Los Angeles, the authors have studied uric acid metabolism in 36 male and seven female obese subjects in a metabolic ward before and during weight reduction by dietary means. Urine was collected daily for uric acid estimation, and serum uric acid levels were determined weekly. The various regimens employed were:

1. total starvation for up to 4 months,
2. a 500-calorie diet,
3. a 300-calorie diet. [It is not clear how many patients were treated with each regimen.]

Among the 36 males [all weighing more than 220 lb. (110 kg.)] the serum uric acid levels before treatment ranged from 5.4 to 10.2 (mean 8.7) mg. per 100 ml and among the seven females [all weighing more than 250 lb. (114 kg.)] from 3.6 to 8.1 (mean 5.2) mg per 100 ml. These values tended to be in the high normal range, but there was no correlation between the degree of obesity and the serum uric acid level. None of the patients had any history of gout, either personal or familial. Progressive hyperuricaemia accompanied by reduction in uric acid excretion occurred in all of fourteen patients not treated with probenecid who maintained a complete fast, although the rate of increase and the maximum concentration reached varied.

After the first 15 to 20 days the level reached 12 to 18 mg. per 100 ml.; it then rose more slowly, and after 2 months in one case a level of 21.8 mg per 100 ml. was reached. However, in a group of thirteen patients who were given 1 g. probenecid daily from the start of the fasting period the serum uric acid level remained near the initial value and urinary excretion of uric acid was at a higher level than in those not given probenecid. Nine patients who were given probenecid only after a long initial fasting period showed a "drastic" increase in uric acid excretion and a fall in serum levels. Semistarvation (300 or 500 calories) also led to increased serum uric acid levels (10 to 14 mg. per 100 ml.), and again this could be controlled with probenecid.

Four patients developed gout during starvation and had a total of seven acute attacks. In two cases colchicine was given with a good response. None of these patients had received probenecid from the beginning of their fast. After resumption of a normal diet the serum level and urinary excretion of uric acid remained normal and no further attacks of gout occurred. One patient who had had two episodes of gout developed symptoms and signs of a ureteral calculus; he had had two short courses of probenecid which had caused a marked increase in uric acid excretion. He subsequently passed a stone which was shown to be urate.

Ketonaemia and ketonuria accompanied the hyperuricaemia in patients receiving semi-starvation diets [and presumably also in those receiving no food, though this is not clearly stated]. In three patients who were given 250 g. glucose daily for a week at the end of the starvation period there was a prompt fall in serum uricacid and ketone levels. A similar though less marked response occurred in five patients who were given a milk powder containing 60 per cent. protein and only 7 per cent. carbohydrate.

Various possible mechanisms for the retention of uric acid during starvation are discussed. The case is men- tioned of an obese patient with known gout who developed hyperuricaemia during starvation despite the prophylactic administration of probenecid and colchicine from the first day and in whom, after 24 days fasting, there was a sudden increase in the serum creatinine level occurring suggesting renal insufficiency. It is therefore recommended that drastic reducing regimens be avoided in such cases.

B. M. Ansell


At the Hammersmith Hospital, London, in 1957 a family was observed to show a striking association of hyperuricaemia and hypertension. The possibility that this association may not be uncommon has now been investigated further (1) by observing the incidence of hyperuricaemia in patients attending the hospital hyper tension clinic, and (2) by studying the natural history of patients with hyperuricaemia and hypertension. For the purpose of the investigation hyperuricaemia was defined as a serum uric acid level in excess of 7 mg. per 100 ml. in males and above 6 mg. per 100 ml. in females.

Hyperuricaemia was found in 274 (58 per cent.) of 470 patients receiving treatment for hypertension and in ninety (27 per cent.) of 332 hypertensives who were not being treated; eleven of the latter had had gouty arthritis. There was no correlation between the severity of the
hypertension and the serum uric acid level, but the incidence of cerebrovascular disease, ischaemic heart disease, and hypercholesterolaemia was significantly greater in hypertensive patients with hyperuricaemia than in those without. Two of the hypertensive patients with hyperuricaemia became pregnant and both developed pre-eclamptic toxemia; three other hypertensive patients with normal serum uric acid levels had uneventful pregnancies.

The glomerular filtration rate and uric acid clearance were measured in eight patients with hypertension and hyperuricaemia. The results suggested that the mechanism of hyperuricaemia is one of renal tubular deficiency and that it does not depend on some glomerular lesion. Metabolic investigations on four patients provided no evidence of over-production of uric acid. The nature of the tubular abnormality is not clear. However the tubules are the first part of the kidney to be damaged in hypertension, and a raised serum uric acid level may therefore be an early manifestation of hypertensive renal disorder.

E. H. Johnson


The incidence of various conditions was compared in three groups of Polynesians over the age of 20 yrs, living in New Zealand itself, the Westernised capital town of the island of Rarotonga and the isolated, more primitive coral atoll of Pukapuka. The number of subjects in each group was 755, 471 and 379, the last being the entire population of the island.

Hyperuricaemia was considered present in males with over 7 mg. per cent. uric acid and in females with over 6 mg. per cent. More than 40 per cent. of all three groups came into this category. 10-2 per cent. of New Zealand males, 2.4 per cent. of Rarotongans, and 5.3 per cent. of Pukapukans had clinical gout.

Of the New Zealand gouty males, 56 per cent. were obese, 48 per cent. hypertensive, and 31 per cent. diabetic. There were no obese gouty subjects in the two islands and the incidence of hypertension and diabetes was low. The New Zealanders’ total calorie intake averaged 2,560, the Rarotongans ate 2,100, and the Pukapukans 1,800 calories. The average fat content of each was 44, 27, and 35 per cent. respectively.

The authors point out the striking similarity in the incidence of hyperuricaemia in the three groups studied. The different incidence of clinical gout, obesity, diabetes, and hypertension may well be due to the influence of environment on a genetic background of hyperuricaemia.

Mary Corbett


Bone Disease


A case report of a 34-year-old man with alkaptonuria, who presented at hospital with long-standing low-back pain with a recent history of sciatica.

The clinical and radiological findings were characteristic of the condition, but in addition there were neurological signs compatible with nerve root pressure from a lower lumbar disc protrusion.

At operation black gritty material extruded from the disc space when the posterior longitudinal ligament was incised. Microscopically the tissue was pigmented fibrocartilage with areas of fibrinoid necrosis. The pigment stained with melanin stains but not with those for iron. The operation was a complete success.

It has been said that back pain with disc protrusion are common in ochronosis, but the author of this case report was only able to find one other similar case in the literature (Eisenberg, 1950).

D. R. Sweetnam


Of about 20,000 autopsies during the period 1953-64, three cases of Marfan’s syndrome with aortic aneurysms could be observed; in two cases the aneurysms were ruptured.

K. Hruby


A report of a typical case in a female aged 30. The diffuse choroidal angiosclerosis which was found in this patient and in the youngest offspring, a daughter, is stressed. Two other children had dislocation of the lenses and arachnodactyly. Only one child (male) was completely normal.

S. N. Cooper


Non-Articular Rheumatism

This communication from Hope Hospital, Salford, reports the results of conservative therapy for carpal tunnel syndrome. Fifteen patients (4 males and 11 females) with the carpal tunnel syndrome were followed for from 2 to 18 months. In six patients, the onset of symptoms was related to unaccustomed manual activity; in nine patients there was associated systemic disease, including one each of myxoedema, motor neurone disease, and rheumatoid arthritis. Three patients were anaemic and two others later developed a polyneuropathy of which the carpal tunnel syndrome was the initial manifestation.

Treatment consisted of rest, weight reduction, correction of anaemia, and treatment of systemic disease. Seven patients received chlorthiazide on alternate days. One patient was treated surgically. Of the fourteen patients treated conservatively, ten improved and three deteriorated. It was noted that thenar wasting had been present initially in those patients who subsequently deteriorated.

The authors suggest that medical treatment for the carpal tunnel is justified in patients without thenar muscle wasting, but further suggest that surgery be advocated if there is no improvement after conservative therapy for 2 months. D. D. McCarthy


Disturbances of higher visual function are reported to have occurred in twenty out of a group of 110 patients with cervical spondylosis. The age range of these patients was from 30 to 57 years, and all twenty patients had evidence of pressure on nerve roots or the spinal cord. X ray examination showed degeneration of the intervertebral discs and osteophytes of neurocentral joints with encroachment upon the foramina transversaria. The visual disturbances which were paroxysmal included prosopagnosia, disorientation in space, seeing things apparently rose-coloured or yellow, and photopsy. The attacks were often precipitated by bending or rotating the head but they also occurred either in association with vertigo or occipital headache, or even without apparent cause.

The rheo-encephalogram is here described as being synchronous with the pulse, and it traces the phasic variations in electrical conductivity which are thought to reflect the alterations of the volume of blood and its flow through the brain. The recording usually takes the form of a curve with a fairly steep ascending phase, a sharp summit and gradual descending phase containing one or two well-developed supplementary waves. The duration of the ascending phase is thought to measure the speed of distention of the vessels while the duration of the descending phase, the number and prominence of supplementary waves and the ratio of ascending phase to total duration of the curve are taken as indices of vascular tone and elasticity. The amplitude of the curve measures the variation in blood volume in the region between the two electrodes. Bitemporal and bi-occipital electro-encephalograms may be used to assess the state of blood flow in the region of the brain supplied by the carotid and vertebral arteries respectively. Bilateral leads from frontotemporal region to styloid process may be used to gauge the state of the circulation in the ipsilateral cerebral hemisphere.

Rheo-encephalography was performed on eighteen patients. In twelve the bitemporal lead was normal when the patients were supine. The bi-occipital lead had a rounded summit and poorly developed supplementary waves in 14 patients, and in many of them the ascending phase showed both an absolute and relative increase in duration. Similar changes were usually seen when the fronto-styloid leads were used. Records were then made during rotation and extension of the head. The bi-occipital leads usually showed an exaggeration of the changes already described for the supine position, and it was particularly marked during extension of the head. The bitemporal and fronto-styloid leads showed little change. The electro-encephalogram (EEG) of most patients showed moderate diffuse changes which did not alter during head movements.

The authors postulate that the rheo-encephalographic changes and disturbances of higher visual function are due to a reduction in the size of the lumen of one or both vertebral arteries which occurs during rotation and extension respectively of the head; the lack of parallel EEG changes is thought to depend on the insensitivity of the circulatory disturbances.

G. P. McGovern


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Pararheumatic [Collagen] Disease

Vascular changes in the cutaneous lesions of lupus erythematosus and scleroderma were studied histologically (at the Institute of Post Graduate Medical Education and Research, Calcutta). While oedema of the superficial vessels was common to all, fibrinoid in systemic lupus erythematosus, dilatation in chronic discoid lupus erythematosus and compression with mild inflammatory infiltration in scleroderma were more frequently seen. Histochemical stains revealed patchy accumulations of hyaluronidase-labile, periodic-acid-Schiff- and alcian blue-positive, metachromatic material in and around the walls of the blood vessels signifying the accumulation of hyaluronic acid or chondroitin sulphate A or C.

In the deeper dermis, thrombosis was a rare but significant feature in the discoid group. Rupture, degenerative changes and destruction of the elastic lamina of the arterioles in the mid- and deep dermis both in lupus erythematosus and scleroderma without peri-arteriolar inflammatory changes were noted as a common and characteristic feature. [Authors' summary.]


Patients with chronic discoid lupus erythematosus may show clinical, haematological, or serological features similar to those which occur with the systemic disease, and a few cases have been recorded of transition from the cutaneous to the systemic disease and vice versa.

In a study carried out at the Western Infirmary, Glasgow, and the General Infirmary, Leeds, on 120 consecutive patients with discoid lupus erythematosus who showed no clinical evidence of visceral involvement, some manifestation of systemic abnormality was detected in 55 per cent. by means of extensive clinical and laboratory investigations. Antinuclear antibodies were detected in the sera of 42 of the patients but in only eleven sera of 120 matched control subjects. The “homogeneous” antinuclear antibody was the dominant antibody in 29 sera and the “speckled” antibody in 13 sera. Antibodies in older patients were most frequently detected in those for whom the disease was of long standing or very extensive, and in those showing evidence of low-grade systemic involvement such as chilblains, Raynaud’s phenomenon, joint pains, leucopenia, thrombocytopenia, and raised erythrocyte sedimentation rate or serum y-globulin level.

None of the 120 patients developed overt systemic lupus erythematosus within the subsequent 5 years, and the authors consider that the risk of the systemic disease supervening in cases of chronic discoid lupus erythematosus is less than 5 per cent. Associated immunological or biochemical abnormalities did not seem to increase the risk, nor did episodes of erythema-multiforme-like lesions which occurred in four cases. It has been suggested that inherited factors and somatic mutations may be implicated in the aetiology of lupus erythematosus, but that the chronic discoid type of disease seems genetically distinct so that no genuine transition from discoid to systemic type (or vice versa) can occur unless the individual is a genetic carrier for both.

E. W. Prosser Thomas


Bilateral papilloedema, narrowing of the retinal vessels, and dysoric retinitis with haemorrhages were seen.

J. Rouger


Acute papillitis with spasm of the central retinal artery on one side and narrowing of the arterial vessels on the other were noted.

J. Rouger


A report of a patient who had systemic lupus erythematosus associated with a band-shaped convex opacity extending diagonally across the eye in the deep stromal plane. Despite treatment with salicylates, ferrous sulphate, and topical steroids, the corneal condition gradually progressed.

E. W. G. Davies


Connective Tissue Studies Effects on the Bones of the Limbs of Prolonged Combined Action of Low Temperature and Humidity. [In Russian.] Orlov, G. A., and Gavrilova, K. M. (1965). Klin. Med. (Mosk.), 43, 15. 4 figs, 17 refs. The authors state that the ill-effects of prolonged exposure at work to conditions of cold and damp have not yet been thoroughly investigated, although they are more frequently met with than frostbite, which occurs in dry conditions. When humidity is high the degree of cold need not be very severe—not necessarily below zero—to produce such ill-effects, since damp conditions greatly increase the loss of heat from the extremities. This loss leads to neurovascular damage and to a condition of the extremities described as "cold vegetative polyneuritis". In mice and rats which had been kept in cages with a damp cloth floor at 2 to 7 °C. for a large part of each day, for periods of a week or more sections of the hind paws showed oedema of all tissues from the dermis inwards. In the early stages this oedema was patchy, but with longer exposure it became more generalized. There was also infiltration of all tissues as far as the periosteum with connective-tissue and lymphoid elements, particularly around the arteries; in one or two cases there was thrombosis of the nutrient vessels of the bones. It is stressed that these findings cannot be applied to the human subject, as the system of heat regulation in warm-blooded animals varies from species to species, but they may indicate the general nature of the changes in the soft tissues which occur as a result of chronic exposure to damp and cold.

A survey was then made of 562 workers in a timber works combine in Archangel whose work was carried on in the open, with frequent immersion of the extremities in water, throughout the year. X-ray examination of the bones of the hands and feet of 65 of these workers who had suggestive clinical signs showed a consistent pattern of changes in the structure of the bones. These changes consisted in:

(a) development of a spongy substance around and replacing the trabeculae;
(b) appearance of cysts in the bones;
(c) development of foci of sclerosis in the substance of the bones;
(d) periostitis and osteophytes in the diaphyses of the phalanges;
(e) moderately severe signs of arthritis deformans.

C. Nicholson


Viscose cellulose sponge implants stimulate connective tissue formation. The tensile strength of the granulation tissue produced was increased if the sponge was treated with hyaluronic acid before implantation. Pretreatment with chondroitin sulphate, paraffin, Tween 80, and a saline extract of connective tissue formed in a sponge implant had no effect.

J. Ball


Immunology and Serology

Reactivity of Rheumatoid Factor with Rabbit γ-Globulin.

A comparison was made between the action of rheumatoid factor and a sheep anti-rabbit γ-globulin antiserum in their capacity to agglutinate sheep cells sensitized with the subunits of rabbit-γ-globulin obtained by papain digestion. The specificity of the reactions was studied by inhibition tests with these various subunits.

The fractions I, II, and III were obtained according to the methods of R. R. Porter; the rheumatoid factor was a pool of eleven rheumatoid sera of high titre.

Three experiments were performed: in the first and third tanned sheep cells were coated with whole rabbit 7S γ-globulin or one of the three papain fractions; in the second the cells were not tanned but coated by a specific rabbit anti-sheep cell antiserum or fraction I obtained from it. In Experiments I and 3 the agglutinators was the rheumatoid serum pool, in Experiment 2 it was the sheep anti-rabbit antiserum.

The results were essentially the same with both agglutinators and with both types of sensitized cells insofar as the principal immunological determinant resides on fraction III, but with some minor reactions with the other fractions.

The similarity of the results provides further support for the view that rheumatoid factor is an antibody against determinants in human γ-globulin. L. E. Glynn


This investigation employed three methods for the detection of γ-globulin in the inclusion bodies of L.E.-cells. Unlike most other studies of this kind, the L.E.-cells were prepared as sections, not smears. The methods employed were:

(i) Autoradiography.—The γ-globulin from positive sera was labelled with 125I. In preparations exposed for 3 weeks more than 80 per cent. of the inclusions showed grain counts significantly higher than the background.

(ii) Immunofluorescence.—A sandwich technique was employed, since direct labelling of the L.E. globulin destroyed its serological activity. Here too the staining was confined to the inclusion bodies. The nuclei of the phagocytosing cells as well as other cells were consistently unstained.

(iii) Immuno-electron microscopy.—Here also the sandwich method was used. Staining was achieved by conjugation of the rabbit anti-human globulin antiserum by conjugation with ferritin. Sections cut at 1000 Å showed ferritin confined to the inclusions at a concentration of 20 to 50 particles per square micron.

The authors conclude that the γ-globulin in the L.E.-cell inclusion body is not confined to the surface, but diffusely distributed throughout the nucleus. L. E. Glynn


The authors of this paper, in common with other workers, have shown in a previous study (J. chron. Dis., 1962, 15, 131; Abstr. Wld Med., 1962, 32, 172) that the incidence and mortality of systemic lupus erythematosus in New York were highest in negroes, followed by Puerto Ricans and then other Caucasians. As the differences in incidence were unrelated to socio-economic factors the possibility that racial variations in serum γ-globulin levels may have been associated with the differences in incidence of systemic lupus erythematosus was investigated.

Serum γ-globulin levels were estimated in two samples of apparently healthy people living in New York City:

(1) 138 employees of Kings County Hospital, Brooklyn, consisting of 47 negroes, 46 Puerto Ricans, and 45 Caucasians;

(2) 175 family members of patients with malignant or other conditions unrelated to diseases characterized by abnormal serum protein values; these included 25 negroes, 45 Puerto Ricans, and 103 Caucasians.

Serum protein levels were determined by interferometry and fractionated by paper electrophoresis.

The results in the two samples were similar and the data were combined for a study of the frequency distribution of the serum γ-globulin levels within each ethnic group. Puerto Ricans were found to have serum γ-globulin levels intermediate in value between those of negroes, which were higher, and of Caucasians, which were lower. These differences could not be related to differences in environment, including duration of residence in New York, or other socio-economic factors. It is thought that genetic factors may be largely responsible for the ethnic differences in the serum γ-globulin levels.

M. J. Tarlow


The author, working at the University of Lodz, Poland, prepared antisera against γ-globulin obtained from six different species in rabbits and, by using immunoelectrophoresis, gel precipitation, and tests for the agglutination of red cells coated with γ-globulin, was able to show that cross-reactivity occurred between certain species. Bovine and sheep γ-globulins were very similar in their reactions, and this parallels the observation that rheumatoid factor reacts equally well with cells which have been coated with either of these two antigens. The fact that immunization of the rabbits with human γ-globulin caused the production of antibody against sheep and bovine γ-globulin is compatible with the view that the human rheumatoid factor is the result of antigenic stimulation by determinants present on the molecular surface of human γ-globulin.

G. L. Asherson


Inhibition of Methanol Metabolism in Mice with Acetyl Salicylic Acid. HASSAN, et al. (1966). Experientia (Basel), 22, 85.


Biochemical Studies


In an attempt to elucidate certain aspects of the metabolism of ACTH, commercial porcine ACTH was purified by column chromatography and labelled with tritium to a specific activity of 4,000 d.p.m./μg.

The ACTH-H3 was incubated in vitro with bovine adrenal cortical slices in Krebs-Ringer phosphate for varying time periods and the 17-OHCS produced estimated as Porter-Silber chromogens. The stimulation of steroidogenesis under these conditions was found to occur between 20 and 40 min. after ACTH-H3 was added to the adrenal slices.

The slices previously incubated with ACTH-H3 were then fractionated and the subcellular fractions obtained resuspended in Krebs-Ringer phosphate and assayed for ACTH activity by incubating them with fresh adrenal slices. The fractions were also counted for radioactivity.

No ACTH activity could be found in any of the subcellular fractions, although these fractions showed marked radioactivity. The distribution of radioactivity in the different fractions was tabulated. It was concluded that the adrenal cortex could bind and inactivate ACTH, but it remained uncertain whether this inactivation was due to the binding or enzymatic degradation. It could not be shown, however, that the adrenal was able to acetylate the N-terminal serine residue of ACTH.

All the experimental methods employed were described in detail. J. R. Daly

Medical Progress: The Mechanism of Action of ACTH.


Much interest was aroused by the hypothesis of Haynes and Berthet (1957) that ACTH promoted steroidogenesis in the adrenal by stimulating the formation of cyclic adenosine-3',5'-monophosphate (cyclic AMP). The cyclic AMP was thought to promote, through a series of enzymatic reactions, an increased production of NADPH (TPNH) which was known to be a co-factor for some of the hydroxylations in the synthesis of corticosteroid hormones. The hypothesis has led to much study of this and other possible mechanisms of ACTH action and this article is a detailed review of what has been done and includes some of the author’s contributions to the subject.

Its twelve tightly written pages and 84 references should provide an excellent introduction to the subject for interested biochemists. The author concludes that, of the seven proposed steps from ACTH to the newly synthesized corticosteroid hormone, only the first two or three are firmly established, so far as the early acute phase of ACTH action is concerned. How ACTH brings about its trophic effect is a further matter that still requires much study. H. F. West

REFERENCE


The method is given in detail; in summary it consists of the following steps, defattting, methylene chloride extraction, water/benzene partition, alkali wash, reaction with ethanol-sulphuric acid, and fluorescence measurement at 530 m$\mu_{}$. Recovery of added cortisol in the normal range was 72.4 ± 10.2 per cent. The mean 24-hr urinary excretion for normal individuals was 93 μg. (range of 60 to 159). The 24-hr excretion from subjects on long-term prednisolone therapy were all below the normal range but did not vary inversely with the dose given. [The 24-hr excretion of unconjugated cortisol is about double that found by more specific methods. The recoveries suggest that urine contains interfering substances and this may explain the unexpectedly high excretion rates for some of the prednisolone treated patients.]

*H. F. West*


This long review of 56 pages is not simply an abstract of published work. It is a lively account of some of the interesting recent developments in our knowledge of the metabolism, reversible conjugation and biosynthesis of steroid hormones that have a bearing on the determination of their secretion rates. This is preceded by a valuable discussion of the physiological significance to be attached to *in vivo* and *in vitro* steroid studies. The measurement of the secretion rates of aldosterone, progesterone, androgens and steroid sulphates are discussed as is the biosynthesis of progesterone and oestrogens in pregnancy. The review will be read and enjoyed by all medical endocrinologists.

*H. F. West*


**Therapy**


Previous studies have shown indomethacin to be somewhat more effective than a placebo, but not significantly superior to phenylbutazone in rheumatoid arthritis. However, in these earlier studies the drug was given in the form of tablets, and these were found to have variable dissolution rates and erratic absorption from the gastrointestinal tract. Indomethacin is now available in capsules, the use of which is stated to have "overcome these difficulties", and in this paper the authors report the results of treatment with capsules of 137 patients, mostly with rheumatoid arthritis and osteoarthritis, attending the out-patient department of the Royal Victoria Infirmary, Newcastle upon Tyne. The drug was administered orally in a progressive dosage starting with one 25-mg. capsule daily and increasing to a mean maintenance dosage of 75 mg. daily, the maximum dosage being 150 mg. daily. When the current therapy was with phenylbutazone this was stopped at once, but in cases receiving prednisolone and aspirin these were withdrawn gradually. Assessment of benefit was based on the patient's estimate of relief of pain and reduction of morning stiffness and on comparison with previous therapy.

Of seventy patients with rheumatoid arthritis treated for 1 to 82 (mean 33) weeks, three discontinued the treatment for reasons unrelated to indomethacin. Among the remaining 67 patients, the drug was withdrawn from 22 because of side-effects and from fifteen in whom there was no improvement. This left thirty (44 per cent.), including three who had a complete remission and 27 who continued to take indomethacin, in whom the treatment was "classed as completely or reasonably successful".

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Subjectively the results of therapy were rated "satisfactory" in eighteen (26 per cent.), "fairly good" in 28 (40 per cent.), and "doubtful or negative" in 24 (34 per cent.).

In fifty examples of osteo-arthritis treatment extended from 2 to 82 weeks (average 28 weeks). Of 49 patients who could be followed up, 31 continued treatment and three had a complete remission, making a total of 34 (69 per cent.) in whom the outcome was regarded as completely or reasonably successful. Subjectively 28 (56 per cent.) considered the treatment "satisfactory", fourteen (28 per cent.) found it "fairly good", and only eight (16 per cent.) regarded it as a failure.

A "miscellaneous" group of seventeen patients with other rheumatic manifestations received treatment with indomethacin for 1 to 55 (mean 13) weeks. There were three patients with gout, all of whom were relieved on a dosage of 75 to 125 mg. daily. Improvement was also noted in one of two cases of psoriatic arthritis, but three out of four patients with ankylosing spondylitis had to discontinue the drug because of side-effects.

Among the 137 patients, side-effects developed in 47 (34 per cent.); these included headache (19), vertigo (20), and nausea (14), and withdrawal of the drug was required in 39 cases. Depression developed in four cases, but this cleared when the drug was stopped. Three patients developed coma, epilepsy, and hallucinations respectively. In one case a duodenal ulcer perforated in a 67-year-old woman who had had no previous symptoms of dyspepsia. A macular rash developed in three cases.

The authors claim a satisfactory outcome in 71 (52 per cent.) of the 137 cases. Significantly better results were obtained for osteo-arthritis (69 per cent. of cases improved) than in the rest of the series (44 per cent.). They consider that, in general, the response to indomethacin can be predicted within the first few days of treatment. Attention is drawn to the common occurrence of dizziness as a side-effect of indomethacin treatment, and because this may occur at intervals patients should be warned of the hazard in modern traffic conditions.

**William Hughes**


This report from the University of Colorado School of Medicine, Denver, describes a comparative evaluation of indomethacin and corticosteroids for treating rheumatoid arthritis. The trial included 55 patients suffering from this disease, in whom clinical assessment was made as objective as possible by expressing the severity of arthritis in terms of an "inflammatory index", obtained by measuring the swelling of finger joints, strength of grip, walking time, shoe-tying time, hand and foot volume, and erythrocyte sedimentation rate. The drug was initially presented in the form of a compressed tablet and later as a capsule containing powder, which proved more effective. With a dosage between 100 and 300 mg. daily the drug was effective in less than one week, though 2 to 4 months were sometimes required for full benefit to be gained. Indomethacin was considerably less effective than corticosteroids but when the drug was used it was possible in sixteen out of thirty patients to stop giving corticosteroids. The commonest side-effects were headache, nausea and vertigo, though these symptoms were less frequent if the dose of indomethacin was gradually increased from an initial 50 or 75 mg. daily, and tended to recede if the drug was given for more than a month.

**J. A. Cosh**


Two double-blind crossover controlled trials were undertaken on patients with chronic rheumatoid arthritis attending the Lemuel Shattuck Hospital, Boston, Massachusetts. In one trial, in which 33 patients participated, two different daily dosages—0.75 and 1.5 mg.—of dexamethasone were compared, the patients receiving these in random order for one week each. The other trial (26 patients) was designed to compare the effects of 1.5 mg. dexamethasone daily with those of 0.75 mg. dexamethasone combined with 1.5 mg. aspirin daily, again given in random order for one week each.

In each of the trials the patients were asked to express their preferences between the two forms of treatment, thus regards the relief of pain and stiffness, improvement of well-being, and the development of side-effects, and the results were recorded by a method of sequential analysis. Nineteen patients took part in both trials.

In the first of these trials a daily dosage of 1.5 mg. dexamethasone was shown to be superior to one of 0.75 mg. for relieving symptoms. The results of the second trial suggest that the addition of 1.5 mg. aspirin to the lower dose of dexamethasone made it as effective in this respect as the higher dose. Side-effects were not severe, but were frequently in the first trial (twelve recorded side-effects in each week out of 33 patient-preferences).

The authors conclude that "the data suggest that the beneficial effects of corticosteroid and aspirin in their symptomatic relief of rheumatoid arthritis are additive, and that steroid-aspirin combinations may be useful in order to keep steroid dosage as low as practicable" [but the very short period during which the trials were carried out limits the validity of this assumption].

**B. E. W. Mace**


Dextrans are polyglucoses polymerized from sucrose by bacteria such as Leuconostoc mesenteroides, and their rheological properties depend mainly on their molecular weight. Thus while dextrans with an average molecular weight above 100,000 may cause aggregation of erythrocytes and interference with coagulation factors, dextrans...
with a low molecular weight (average 40,000) have been shown to reduce intravascular cell aggregation and lower blood viscosity, thus increasing capillary flow and tissue perfusion. Low-molecular-weight dextran has been used successfully in vascular surgery and in vascular insufficiency with and without occlusion, so that its trial in the severely impaired digital circulation of systemic sclerosis seemed to be indicated. The author therefore treated 23 patients with severely impaired digital circulation at the Royal Victoria Infirmary, Newcastle upon Tyne, by the intravenous infusion of low-molecular-weight dextran ("rheomacrodex") at intervals of 5 to 8 weeks during the winter and at longer intervals during the summer, 2 litres being given over 48 hours at each treatment. The changes in blood flow were measured by skin thermometry at reflex vasodilatation under standard conditions at varying intervals after courses of treatment. Out of twelve patients with advanced systemic sclerosis, ten showed considerable improvement for long periods with a readily demonstrable increase in blood flow, healing of ulcerated finger-tips, and disappearance of ischaemic pain. Of seven patients with Raynaud's phenomenon of late onset, six showed similar improvement. No undue side-effects were observed in these patients; however, the author points out that the toxic properties of dextran are not yet fully known. The rapid infusion of large quantities of dextran may increase excessively the circulatory volume and cause tissue injury as well as intravascular aggregation. Allergic sensitivity to low-molecular-weight dextran has not been reported. The author considers that it is probably safe to administer dextran slowly in the dosage used in this study to patients who do not have pulmonary oedema or thrombocytopenia. It does not seem possible to predict which patients will respond to treatment, since those with apparently irreversible digital lesions have been shown to benefit. It may be that repeated infusions will result in further improvement. As yet the optical and the minimal effective dosage of dextran have not been established, and will probably vary considerably in each patient. The results obtained in this small series are, however, considered to be sufficiently encouraging to justify further investigation.  E. W. Proser Thomas


Methyltrienolone is a new, wholly synthetic steroid which is reported to have an anabolic effect in animals. In clinical trials the drug was administered in a dose of 3 mg. a day by mouth for 8 days to nine patients suffering from severe malnutrition who were studied intensively in a metabolic unit. In eight of the nine there was a substantial gain in weight which could not be accounted for merely by an increased intake of food. The gain in weight was accompanied by retention of nitrogen and potassium and was attributed to a nitrogen-sparing effect and to increased utilization of fat. There was no evidence of retention of sodium. In a further series of 26 patients suffering from malnutrition administration of the steroid in a dose of 0.5 mg. per day for 8 to 14 days resulted in a mean weight gain of 185 g. per day, this gain being accompanied by an increased intake of food. Six of the twelve women in this latter series who were of reproductive age experienced menstrual disturbances during treatment. The anabolic effect of methyltrienolone exceeds that of any other compound known to the authors.  Bernard Isaacs


Experimental studies have shown that when radioactive colloidal gold (198Au) is injected into the knee joint most of it is concentrated in the synovium, and this prompted the present authors, at Malmö General Hospital, Sweden, to study the effect of intra-articular injection of colloidal 198Au in cases of persistent synovial effusion of the knee joint. A total of nineteen patients were treated, nine having rheumatoid arthritis and ten osteo-arthritis; in two cases the effusion was bilateral. The knee was first aspirated completely and then 20 ml. normal saline solution containing 5 millicuries colloidal 198Au was injected as a single dose. [The authors point out that this is only half the dose used by Makin et al. (Israel med. J., 1963, 22, 107).] The knee was immobilized with an elastic bandage for 24 hours, and then frontal and lateral scintigrams were taken to show the distribution of radioactive activity within the knee joint. At 3 weeks the knee was again completely aspirated. A test for leakage of the radioactive material on the day after the injection in fourteen patients showed only a trade of radioactivity in the inguinal lymph nodes or the liver in seven patients and none in the remaining seven, and the authors are satisfied that the isotope was almost entirely retained in the superficial synovial layer.

Although all 21 of the knee joints treated had previously needed repeated aspiration, the effusion subsided permanently within 2 months of the injection of 198Au in twelve and within 4 months in one, while in five a slight effusion persisted. Three joints did not respond and these received a second injection; in one the effusion subsided completely and in another partially, while the third (in a patient with advanced arthrosis who had not improved after synovectomy) again failed to respond. In three instances the effusion increased a few days after the injection of 198Au, necessitating aspiration for relief. Follow-up observations for periods of 6 months to 3 years revealed no ill effects of the treatment. The authors consider that intra-articular injection of radioactive colloidal gold should replace external irradiation in the treatment of persisting effusion of the knee joint. A single dose of 5 mc. is usually adequate, but in patients who do not respond a further injection may be given, 10 mc. being suggested as a suitable upper limit.  J. A. Cosh

Osteoporosis and fractured ribs are well known complications of prolonged corticosteroid therapy, but fractures of the vertebral bodies have been reported only rarely. Among 350 patients receiving long-term corticosteroid for asthma or other respiratory disorders at the Respiratory Clinic of the University of Aix, Marseilles, fifteen (4·2 per cent.) developed fractures of one or more of the vertebral bodies. Most of these patients had been under treatment for more than 2 years and had been taking up to 15 mg. prednisone (or the equivalent dose of other steroids) daily. The symptoms were severe lumbar pain and disability, usually starting spontaneously but occasionally initiated by trauma. Post-menopausal women seemed to be particularly liable to develop such fractures. The treatment recommended, both curative and preventive, is to give calcium-rich foods, vitamin D₂, and calcium salts by mouth.

A. W. Frankland


In a previous paper (J. Pediat., 1965, 67, 1089), the authors claimed that they could distinguish by histological means cases of glomerulonephritis with low levels of serum complement from those in which the serum complement is in the normal range. The principal differentiating features were pronounced lobulation of the tufts, thickening of the capillary walls and a poorly argyrophilic basement membrane in the hypocomplementaemic group.

Since complexes of antigen and specific antibody frequently fix complement, the extremely low level of complement found in many cases of glomerulonephritis has been widely accepted as evidence for an immunological basis for the disease, and forms the rationale for its treatment by immunosuppressive drugs.

The present paper reports the results of such treatment in six patients, four with glomerulonephritis and two with the nephritis of systemic lupus. Of the four patients with uncomplicated nephritis only one showed any obvious response to the treatment, but in this case the clinical improvement did closely match the progressive rise in serum complement. By contrast, the two patients with lupus responded well to the treatment, both clinically and serologically. The authors justifiably point out that this apparent difference in response could just as well be related to the shorter history of the disease in the patients with lupus as to any more fundamental difference in its nature.

L. E. Glynn


Nine patients were treated, all of whom had a facial rash, positive L.E.-cell preparations, and other manifestations. Three patients responded well to an intensive early course followed by weekly maintenance doses, for periods of 15 to 20 months. Three showed moderate improvement and three were not helped but developed severe alopecia and leucopaenia.

It is suggested that the drug may supplement or occasionally replace corticosteroids.

A. R. Jeffrey


This case report from Ashington General Hospital, Northumberland, concerns a 79-year-old woman with a 10-year history of pernicious anaemia well controlled by cyanocobalamin, who was admitted to hospital with purpura. In the 11 months before admission she had taken a total of approximately 10 g. phenylbutazone for "arthritic pain". Investigation on admission revealed a normochromic anaemia (Hb 5·6 g./100 ml.), leucopenia (WBC 2,100 with 8 per cent. neutrophils), and thrombocytopenia (platelets 45,000 cu. mm.). Sternal marrow sections were compatible with aplasia. Treatment consisted of blood transfusions and prednisone, 40 mg./day. She died on the 10th day with multiple haemorrhages of the meninges, stomach, and kidneys.

The authors emphasize the importance of close haematological review of patients receiving phenylbutazone.

D. D. McCarthy


The authors have compared serum concentrations of phenylbutazone in rats after ingestion of doses effective in various tests of antiphlogistic activity, with serum concentrations in patients under treatment with the drug. They report that the results after 25 and 50 mg./kg. doses in rats agree closely with figures obtained from patients under treatment, although on a mg./kg. basis the therapeutic dose in humans was considerably lower. It is concluded that the effect of phenylbutazone on different laboratory models of inflammation correlates well with the drug’s clinical anti-inflammatory activity.

T. M. Chalmers


Three case reports to illustrate that the onset of such glaucoma is insidious, without pain. The authors discourage indiscriminate and prolonged use of this drug after cataract and glaucoma surgery, and in those cases...
where it has to be used over a long period (spring catarrh)
there should be a frequent check on the ocular tension.

S. N. Cooper

Corticosteroid Glaucoma. NEMA, H. V., and BANSAL,

28 patients with allergic conjunctivitis were put on local corticosteroid therapy. A significant elevation of
tension was noted in 11 per cent. after 6 weeks' treatment.
On discontinuation of the drug it took 4 weeks for the
tension to return to normal. If a periodic check is kept
on the ocular tension during cortisone therapy, there
should be no hesitation in using this drug when indicated.

S. N. Cooper

Effect of Corticosteroids on Blood Salicylate Concentra-

In four cases the administration of salicylate to patients
on corticosteroid therapy resulted in a blood salicylate
concentration which was lower than expected. In all
cases the blood salicylate levels rose as the steroid dosage
was reduced. Studies of salicylate clearance (estimating
free urinary salicylate only) were carried out on five further
subjects during a control period and during a period of
hydrocortisone administration. Salicylate clearance
was increased after hydrocortisone in three of the subjects.
This was associated with a corresponding rise in
inulin clearance, suggesting that the effect was the result of
increased glomerular filtration rate.

The complexity of salicylate excretion makes the
clearance experiment rather difficult to evaluate, but the
clinical data are interesting and worthy of further
investigation.

J. T. Scott

Mortality from Cancer and Other Causes after Radio-
therapy for Ankylosing Spondylitis. COURT BROWN,

[Data concerning] a total of 14,554 patients with
ankylosing spondylitis, who were treated [in Great
Britain and Northern Ireland] with x rays during the
period 1935-54, have been studied. More than 98 per cent.
were traced on or after January 1, 1960, and less
complete follow-up information is available for a further
3 years.

The effects of irradiation have been assessed by com-
paring the numbers of deaths observed with the numbers
that would have been expected if the patients had suffered
the death rates recorded in the population of England and
Wales as a whole. The most important finding, apart
from the previously reported excess of deaths from
leukaemia and aplastic anaemia, relates to other cancers
originating in heavily irradiated tissues. Deaths attribu-
ted to these cancers were increased approximately two-
fold 6 or more years after first treatment, and 15 years
after first treatment the excess showed no sign of diminish-
ing. The excess was not limited to one or two types of
cancer, but many different types contributed to it,
approximately in proportion to their normal incidence.
In contrast to these findings the number of deaths from
cancer originating in lightly irradiated tissues was not
increased significantly.

It is estimated that in an average follow-up period of 13
years after first treatment the excess deaths from leukaemia
and from other cancers arising in heavily irradiated
tissues, which can be attributed to the effects of ionizing
radiations, were four per 1,000 patients and six per 1,000
patients respectively.

Deaths ascribed to spondylitis or rheumatism or to the
direct complications of spondylitis were increased, as were
to a less extent deaths due to a variety of other causes.
Many different factors probably contributed to this, but
their importance cannot be finally evaluated until results
are obtained from a similar study of spondylitic patients
reated by other means. [Authors' summary.]

Corneal and Vitréal Changes after Administration of
Synthetic Anti-malarial Drugs. (Altérations corn-
èennes et rétinennes dues aux anti-malariques de syn-
thèse.) CORDIER, J., BRETAGNE, A., SAUDAX, E.,
Small spotty corneal opacities and tiny black pigmen-
tations of the maculae have been observed after the use of
synthetic anti-malarials.

J. Rougier

Corneal Lesions during Treatment by Synthetic Anti-
malarial Drugs. (Complications cornèennes observées
au cours des traitements par antimalaréiques de syn-
thèse.) CALMETTES, L., DEODATI, F., BAC, K., FOUR-
65, 332.
Ten cases of keratopathy are reported in patients treated
by Nivaquine.

J. Rougier

Synovectomy of the Wrist for Rheumatoid Arthritis.
The author previously favoured osteotomy or early
arthrodasis for wrist joints involved by rheumatoid
arthritis, but during the past 3 years has instead been
performing synovectomy of the wrist after excision of the
ulna; 21 results from 28 operations were classified as
good. Full operative details are given. J. T. Scott

Arthrodasis of the Hip by Central Dislocation and Ilio-
Surg., 47-B, 694.
The operation consists of central dislocation of the hip
together with internal fixation using an intramedullary
nail passed from the ilium across the "hip" into the
femoral shaft. Obviously an extremely difficult opera-
tion, but one which the author has now performed thir-
teen times with only one failure.

The main advantage of the method over "conventional"
arthrodasis is that it is said that no plaster fixation is
necessary. Indeed, to quote, "Light athletic patients
will often discard their crutches or stick voluntarily about
5 weeks after operation". As a rule, however, such
support is advised for 3 months after operation.
This is an interesting attempt to rid hip arthrodesis of one of its major disadvantages—prolonged post-operative immobilization in a plaster spica. D. R. Sweetnam


In this paper based upon a lecture delivered at the Royal College of Surgeons of Edinburgh in 1963, Carl Semb, the well-known and respected Norwegian orthopaedic surgeon, describes his experience in the treatment of the osteo-arthritic hip by cup arthroplasty. His unit in Oslo has made a special study of this type of surgery during the past 17 years. The series he describes were all operated upon between 1946-58, and comprise 574 cup arthroplasties.

The two main theoretical reasons for preferring this operation are that the primary change was in the acetabulum in the majority of his patients (61 per cent.), and that following cup arthroplasty with deepening of the acetabulum the area of support for the head of the femur was increased, thus reducing the pressure per unit area.

Neither operative technic nor post-operative management are discussed in detail, but great stress is laid upon the feasibility of local bone grafting of cysts and necrotic areas to prevent further destruction of the remaining portion of the head within the vitallium cup.

His results are very good. In all types of osteo-arthritis, over 80 per cent. were better after operation. With a mean follow-up of over 10 years a quarter of his patients had an excellent result with almost no pain, and nearly normal mobility; 40 per cent. were “good”, with only little pain and hip flexion to 90°. None was apparently worse after operation, but 12 per cent. were said to be no better.

The paper represents a powerful and reasoned argument in favour of the old established procedure of cup arthroplasty, at present losing ground to other operations, which may or may not stand the test of time. D. R. Sweetnam


A very short paper which summarizes the author's view's upon the mechanism of deformity of the interphalangeal joints in rheumatoid arthritis. No new concept is presented, but emphasis is placed upon both the local destructive effect of "synovial granulation tissue", and disturbances of muscle balance. The latter, of course being commonly secondary to initial joint damage by the rheumatoid process, either in the joint concerned or others proximal to it.

Early synovectomy is strongly advocated and the indications are given as persistent pain and swelling, despite what is described as "a fair trial of conservative measures". The best results are said to follow operation before radiological evidence of destruction is present, and at this stage relief from arthritic pain can be virtually guaranteed. Restoration of full movement, however, is not so easy to predict, but manipulation of the joint under local anaesthetic three weeks after surgery is advised.

Arthrodesis is suggested for interphalangeal joints in which destruction has advanced to the stage where "restoration of useful movement is impossible", or when instability prevents a useful pinch grip. D. R. Sweetnam


CORRECTION
In the July issue of the Annals (1966), 25, 376, among the officers of the New York Rheumatism Association: for HARMER read DR. DAVID J. HAMERMAN (President), and for MANNHEIMER read DR. ROBERT H. MANHEIMER (Vice-President).