ABSTRACTS

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

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

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

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 results of chlorpromazine therapy in 27 children with Sydenham's chorea treated at the Cincinnati Children's Hospital, Ohio, during the 7 years ending in November, 1963, have been compared with those of barbiturate therapy in 24 such children treated during the previous 7 years. The average age of the children in both groups was 10 years. Those receiving chlorpromazine had an average stay in hospital of 19.8 days compared with 32.4 days in the case of the barbiturate-treated children. The mean interval before improvement was noted was 6.6 and 17 days respectively in the two groups, and the mean time to recovery 32.4 and 59 days. Recovery rates, estimated by a life-table technique relating the recovery rate at any given stage of the disease to the number of patients under observation at that time, also were better with chlorpromazine than with barbiturates.

The dosages of chlorpromazine given were "comparable to those used in psychiatric therapy in children". The average dosage was 300 mg. per day (range 140 to 1,000 mg.). Starting doses averaged 25 mg. every 6 or 8 hours, and this was increased by 10 to 25 mg. per dose per day until improvement was noticed. The dosage was continued at this level until symptoms disappeared and then gradually reduced over 4 to 6 weeks. No toxic effects were observed with these large doses. Four patients had tremor and masked facies, which disappeared when the dosage was reduced or the drug discontinued. There was no jaundice or granulocytopenia.

The results of this study are considered to suggest that chlorpromazine is an effective agent in alleviating the motor symptoms of chorea and shortening the course of the disease. Patients were less somnolent and showed less lability of mood with chlorpromazine than with barbiturate therapy. The children were all able to dress and feed themselves and to attend school while in hospital. The authors consider that the evidence favouring a rheumatic aetiology is strong enough to support the use of antistreptococcal prophylaxis in all cases of chorea.

E. H. Johnson

Cases of Behçet's Disease which started as Acute Rheumatic Fever. [In Turkish.] YİĞITBAŞI, O., and YENICE, O. (1965). Ege Univ. Tip. Fak. Mec., 4, 60. 30 figs, 46 refs.

The authors present two cases of Behçet's disease which started with pain and swelling in several joints, the diagnosis being acute rheumatic fever. According to the authors approximately sixty cases of Behçet's disease have so far been reported in the Turkish medical literature.

C. Örge


Rheumatoid Arthritis


Eight cases of rheumatoid arthritis of long standing in which laryngeal stridor with dyspnoea developed are described. Dysphagia was a prominent symptom in the remaining case.

A detailed histological examination of the larynx in all these cases revealed a wide range of pathological changes. Severe chronic inflammation of the cricoarytenoid joints occurred in four cases with erosion of the articular surface of the cartilage in one. The mobility of the joints was still present although reduced. A polymositis of the laryngeal muscles was present in four cases. All eight cases showed evidence of neural atrophy of these muscles associated with degenerative changes in the recurrent laryngeal, superior laryngeal, and vagus nerves. The neuropathy appeared to be of ischaemic origin as arteritis of the vasa nervorum was found in two cases whilst another two showed obliterator endarteritis with calcification of the intima of these vessels due to metastatic calcification in necrotic inflamed tissue. Amyloid deposits were found in the vasa nervorum in one case whilst three showed lymphocytic cuffing of these vessels. One case showed ulceration of the pharynx and necrosis of the cricoid cartilage due to arteritis.

It is concluded that the laryngeal stridor occurring in rheumatoid arthritis is due mainly to rheumatoid...

After discussing the difficulties of neurological examination in patients with rheumatoid arthritis, the authors of this paper from the Postgraduate Medical School (Hammersmith Hospital), London, report their findings in thirty patients with rheumatoid arthritis and peripheral neuropathy. In 26 of these the result of the Waaler-Rose test was positive; 23 had rheumatoid nodules and ten had digital vascular lesions.

Five patterns of neurological involvement were encountered and though most patients showed signs of more than one type of involvement each pattern is considered separately. A distal sensory neuropathy confined to the lower limbs was present in nineteen patients. This was associated with lesions of the major peripheral nerves of the legs in five patients and with a "digital neuropathy" (see below) in nine. Complete recovery was unusual, but this type of neuropathy did not presage serious systemic disease. Major peripheral nerve involvement in the upper limbs (10 patients) and lower limbs (10 patients) was usually related to swelling or damage in a neighbouring joint and improved after relief of pressure where this was possible. Most of these patients (11 out of 16) had evidence of neuropathy elsewhere, and the implication of this finding is discussed. Digital neuropathy was present in twelve patients, being bilateral in ten. Symptoms were purely sensory and the patient complained of numbness in one or more fingers. Sensory loss was demonstrable in seven and progressed to involve the whole of one or both hands in two. As a rule disability was minimal, and some patients recovered completely; eleven however, had additional neurological disease, and in nine this was a distal sensory neuropathy. The fifth pattern, a motor and sensory peripheral neuropathy (3 patients), was preceded by a mononeuritis multiplex in two and associated with a widespread necrotizing arteritis; all three patients died within a few months with extensive visceral involvement.

Neuropathy in rheumatoid arthritis is usually attributed to an arteritis of the vasa nervorum, and the authors discuss the evidence for this and the possible aetiological role of corticosteroids. **E. D. Sever**


A review of the case records of 702 patients with rheumatoid arthritis attending the University of Arkansas Medical Center and the Veterans Administration Hospital, Little Rock, during the years 1950-63 revealed eight patients with diffuse pulmonary fibrosis having no apparent aetiology apart from the rheumatoid disease. The arthritis usually preceded the lung lesions, but there was no correlation between the severity of the arthritis and that of the pulmonary fibrosis. The course of the lung disease was variable; three patients eventually developed cor pulmonale and died. The chest radiographs showed no evidence of regression of the lesions, but in some cases these remained static.

The histological changes in the lungs are reported in five cases. All showed a diffuse fibrosis, two with lymphocytic infiltration and one with nodules having
central fibrinoid necrosis. The authors review the published reports of lung disease in rheumatoid arthritis and note that pleuritis with or without effusion is the commonest abnormality. The interstitial pneumonitis which also occurs may be diffuse or localized; it progresses to a fibrosis which may be diffuse or coarsely nodular. Arteritis has also been reported. It is concluded that the lung tissue in rheumatoid arthritis is unusually reactive, and that the pathological changes are caused by an exceptional tissue response to ordinary pathogenic stimuli.

K. C. Robinson


The authors describe 27 cases of chronic leg ulceration complicating rheumatoid arthritis and not associated with pressure or venous stagnation. One ulcer was tuberculous, and four occurred in patients with dermal atrophy due to prolonged steroid therapy, the ulceration being precipitated by minor trauma; ten patients had associated vascular lesions and in twelve there was no obvious cause.

Of the four ulcers attributable to minor injury and hypercorticism, two healed fairly well on conservative treatment and the remaining two, which were larger, healed after skin grafting. The ten patients with lesions suggestive of arteritis were mostly elderly males with nodular rheumatoid disease and strongly positive tests for rheumatoid factor. The ulcers were difficult to heal unless the patients were treated with high dosage steroids with or without skin grafting. The last group contained a preponderance of females and there was a fairly high incidence of subcutaneous nodules. The appearance of the ulcers and the best means of treating them were similar to the previous group. D. A. Pitkeathly


This is a single case report of fatal amyloidosis developing in the course of rheumatoid arthritis. Joint symptoms and signs disappeared and the Waaler-Rose and latex tests became negative during treatment for the nephritic syndrome. E. G. L. Bywaters


The effect of incomplete penetrance of a monofactorial recessive trait on the frequencies of sib-pair types in a random mating population is examined. A method of estimating the gene frequency and the penetrance percentage from sib-pair data is illustrated by two numerical examples. The difficulty in interpreting the sib-pair data on rheumatoid arthritis in the Blackfeet Indians is discussed. J. T. Scott


This article is one in an excellent symposium on diffuse interstitial pulmonary fibrosis and many of the other papers would repay study. It comes from the Hôpital Laennec, Paris, and consists essentially of a review of the literature of pulmonary lesions in rheumatoid arthritis. It cites two original cases (one with post-mortem, published previously, and one unpublished). These do not add a great deal, but in the autopsied case it is noted that the honeycombing was cortical. In the second case honeycombing was most marked in the lower lobes. E. G. L. Bywaters


Osteo-arthritis


A report from the Mayo Clinic concerning the history, technique, indications, and value of upper tibial osteotomy in the treatment of the osteo-arthritic knee in 22 patients.

The indication for this type of operation is said to be a little uncertain at present, but the combination of disabling pain, valgus or varus deformity, with unilateral joint narrowing and minimal generalized joint degenerative changes is ideal, the rationale being the correction of deformity in order to relieve the worn side of the joint from continuing to take an excessive share of the weight transmitted through the joint.

The osteotomy is performed above the tibial tubercle and the necessary wedge of bone excised to correct either valgus or varus. One or two staples across the bone are used for fixation, and the external support of a plaster of paris back-slab, and later a cylinder plaster is advised for 4 to 6 weeks. Partial weight-bearing is begun within a few days of operation, and knee exercises started when the plaster is removed.

Thirty knees in 22 patients were operated upon, the majority being with valgus deformity. Eighteen knees had a satisfactory result at the end of a year; three were unsatisfactory; nine were for one reason or another not included in the follow-up. These results are described as encouraging. D. R. Sweetnam


18 years ago the senior author described a technique for arthrodesis of the hip. This consisted of a combination of internal fixation with a trifin nail across the joint and a bone graft. At the time of his first report no more than ten patients had been operated upon.

The present short paper concerns the follow-up of
ABSTRACTS

Inflammatory Arthritis


Adult patients with bacterial arthritis of the hip treated at the Mayo Clinic between 1942 and 1962 are reviewed. Of the 26 infections only four were acute, and in 22 the age at onset was over 40 years.

Pain was the predominant symptom and almost all patients were febrile on admission. In all but four patients there was a delay in diagnosis of more than 3 weeks. Staphylococcus aureus was the infecting agent in sixteen, and many had a focus of infection elsewhere in the body. The earliest x-ray changes were joint narrowing and osteoporosis; destructive changes developed later.

In three patients the x rays remained normal.

The treatment advised is open surgical drainage from the front and back, together with rest in a hip spica and the appropriate antibiotics. Rather surprisingly, however, no patient with a staphylococcal infection developed bony ankylosis.

Final disability in most patients was severe; only nine out of 26 were able to return to work, or to the level of activity they had enjoyed before their illness. Almost all had severe limitation of hip movements. Firm bony ankylosis when it occurred, either spontaneously, or as a result of subsequent arthrodesis, gave the best final result.

D. R. Sweetnam


The relationship between ulcerative colitis, ankylosing spondylitis, and uveitis has been studied at the Radcliffe Infirmary and the Eye Hospital, Oxford, the incidence of these complications being estimated in 144 patients with ulcerative colitis and 100 controls of similar age and sex distribution who were either healthy volunteers or were suffering from the “irritable colon” syndrome. The presence or absence of ankylosing spondylitis was determined by the appearance of the sacro-iliac joints on a barium-enema radiograph, the criteria of sacro-iliac abnormality being loss of definition of the joint outlines, sclerosis of bone in the vicinity of the joints, and obliteration, fusion, or bony ankylosis of the joints. Both patients and controls were examined by an ophthalmologist who was unaware of the diagnosis. Uveitis was identified by the presence of cells in the anterior chamber, keratic precipitates, posterior synchiae, and a red eye in active attacks of colitis or other similar change indicating previous attacks.

Of the patients with ulcerative colitis, 11.8 per cent. had evidence of present or past uveitis compared with only 2 per cent. of the controls, while 17.4 per cent. of the former had sacro-iliac abnormalities compared with only one of the 100 controls. The two complications were markedly associated in the patients with ulcerative colitis, since thirteen of the 25 patients with sacro-iliac involvement also had uveitis, suggesting some common aetiological factor. There appeared to be no relationship [rather surprisingly] between the incidence of these complications and the extent of the disease, but the former increased steadily with the duration of a history of ulcerative colitis. Of other systemic complications of ulcerative colitis, aphthous ulcers and arthritis were positively associated with sacro-iliac involvement and/or uveitis.

It is concluded that the evidence strongly supports the view that uveitis and ankylosing spondylitis are true complications of ulcerative colitis rather than associated diseases.

T. D. Kellock


A short review of the genito-urinary, musculo-skeletal, and muco-cutaneous manifestation of this disease, with a sketchy description of the ocular changes.

M. A. Bedford

Gout


The brief report of a man who had renal stones and attacks of acutely painful joint swelling. Biochemical findings pointed to hyperparathyroidism, and an adenoma was removed surgically; afterwards the serum calcium fell to normal.

Renal function was virtually normal, but serum uric acid levels ranged up to 11 mg./100 ml. Fluid from a knee contained birefringent crystals, most of which dissolved when the pH was made alkaline. Chemically, neither urate nor calcium concentration was raised in the fluid.

The authors consider that both uric acid and calcium pyrophosphate crystals were present. [No other tests to identify the crystals are recorded, nor are we told if parathyroidectomy affected the subsequent occurrence of “gouty” attacks.]

M. R. Jeffrey


This study was undertaken because of the possible implication of glutamine metabolism in the cause of primary hyperuricaemia. Fourteen male controls with another 35 patients, and out of the total of 45 patients thus reviewed, sound arthrodesis is said to have occurred in 36 within 3 to 6 months of surgery.

The point is made that this is an effective method of arthrodesis and that the operation of arthrodesis should be considered in patients with degenerative arthritis. The method described has the advantage of a relatively short stay in bed, and the avoidance of a plaster spica, which the authors consider unnecessary in the presence of internal fixation.

D. R. Sweetnam
glomerular cells showed Henle's loops (serum creatinine level below 6 mg. per cent. (four healthy volunteers and ten recovering from acute infections or injury)) and fifteen ambulatory males (fourteen of whom had a serum uric acid above 7 mg. per cent. and a fifteenth who had been hyperuricaemic previously) were reviewed. No medication was given for 72 hours. After an overnight fast renal clearance measurements, using either endogenous creatinine or inulin, were performed to check renal function. While this was in progress, blood and urine samples were obtained for amino acid content. The serum amino acids included aspartic acid, threonine, serine, glutamic acid, glycine, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine, ornithine, lysine, histidine. Ten of the hyperuricaemic subjects had a rise in the serum free amino acids; the mean level for total amino acids was significantly higher in the hyperuricaemic subjects than in the controls; nine of the fourteen amino acids measured were significantly elevated. This could not be explained by renal rejections, as renal clearances were similar in both groups.

B. M. Ansell


According to published figures renal failure accounts for 22 to 25 per cent. of deaths in gout. The pathological characteristics of the gouty kidney have been studied by the authors of this paper from the Wadsworth Veterans Administration Hospital, Los Angeles, California, and the Francis Delafield Hospital, New York, in material obtained from seventy patients either by renal biopsy (28) or at necropsy (42). The patients, all men, were aged between 27 and 83 (mean 58) years. The duration of clinical gout ranged from 1 month to 46 years (mean 12 years). A history of urinary-tract infection was present in seventeen cases and 24 patients had received uricosuric therapy. Clinical signs included diastolic hypertension (43 patients), tophi (26), and joint deformity (29). Laboratory findings included a serum creatine level above 1-5 mg. per 100 ml. in 34 patients, a serum uric acid level above 6-5 mg. per 100 ml. in 63, positive urine cultures in nineteen (of 59 cases examined), proteinuria in 43, abnormal sediment in 38, and an abnormal intravenous pyelogram in ten (of 42 patients examined).

Of the 28 patients from whom a biopsy was taken, sixteen had previously recognized evidence of renal disease (proteinuria, azotemia). To distinguish early from later cases the biopsy series was divided into non-azotemic (serum creatinine level below 1-5 mg. per 100 ml.) and azotemic.

Completely normal renal tissue was found in only seven of the 28 biopsy cases and three of the necropsy cases. Tophaceous deposits were rare, occurring in only one of the biopsy and four of the necropsy series. Glomerulosclerosis was found in seventeen biopsy and 21 necropsy cases. The basement membrane of the glomerular capillaries was uniformly thickened and the number of nuclei was increased. Both endothelial and epithelial cells showed more abundant cytoplasm than usual. Henle's loops consistently showed dilatation with cellular atrophy and regeneration, and sometimes brown pigmentation. In a few cases the columnar cells lining the collecting tubules were hypertrophied.

Chronic inflammatory changes in the interstitial tissue, with colloid casts typical of chronic pyelonephritis, were observed in six of the biopsies and twelve of the necropsy cases. When medullary tophi were present the chronic inflammatory changes occurred in the peripheral medulla and overlying cortex. In kidneys free from tophi the lesions appeared chiefly in an area proximal to Henle's loops, and the peripheral medulla and cortex were little affected. The walls of both arteries and veins showed degenerative changes (hyalinization and/or thickening) out of all proportion to the severity of the parenchymatous changes.

Sections from selected cases were stained for deoxyribonucleic acid and ribonucleic acid with methyl-green pyronine and subsequently incubated with ribonuclease to remove ribonucleic acid. The chief abnormal finding was increased pyroninophilia of the cells of Henle's loop. The green staining was consistently removed by ribonuclease, showing that it was associated with ribonucleic acid, present in abnormally large quantity.

The authors draw the following conclusions:

(1) The high incidence of pathological changes in the gouty kidney, even in clinically early cases, suggests that the kidney is attacked very early in the disease.

(2) The low incidence of tophi suggests that deposition of urate in the tubules is not the cause of gouty nephropathy.

(3) Atrophy, pigmentation, and increased cytoplasm of ribonucleic acid of the cells of Henle's loop were a conspicuous feature of early cases, the other changes described above appearing in later stages of the disease.

(4) The changes found in Henle's loop may represent a reaction to increased concentration of uric acid (or of some precursor) in the glomerular filtrate and may resemble those associated with hyperuricemia.

(5) The chronic inflammatory changes in the interstitial tissue, accompanied by polymorphonuclear infiltration, are probably due to infection, but to degenerative changes.

C. M. Otley


One possible means of controlling gout is by decreasing purine biosynthesis and in this paper from the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, the effect of allopurinol (4-hydroxyprazolone 3, 4-D-pyrimidine) which is a non-toxic inhibitor of xanthine oxidase has been evaluated in eight gouty patients, three normal volunteer subjects, and one patient with xanthinuria.

All subjects were maintained for 5 days and throughout the study on a 2,600 calorie diet with protein 70 g. and virtually purine free. As well as balance studies, a comparison of renal clearance of uric acid with that of the uric acid.

These workers who write from the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, have already shown that the injection of microcrystals of uric acid into joints can produce an attack of arthritis indistinguishable from a spontaneous attack of gout, and that the intensity of the attack appears to depend on the physical characteristics of the crystals; these attacks also respond to the administration of colchicine.

In the present study ten patients with gouty arthritis and one normal subject were maintained on a low purine diet and were given injections of suitably prepared crystals of monosodium urate monohydrate and sodium orotate into the knee joints and the flexor surface of the forearm. Clinical assessment of inflammation was made at a time up to 4 hours before injection, 6 to 8 hours afterwards, and, when the response persisted in the knees, at 24 and 48 hours. The response in the flexor surface of the forearm was measured at 24 hours. Control studies and those following pre-treatment were performed within several weeks of each other. The pre-treatment consisted of colchicine 4 to 5 mg. injected intravenously during the preceding 24 hours and another 2 mg. 1 hour before the test injection, hydrocortisone 200 to 400 mg. daily in divided doses beginning 2 days before the injection and continuing for 2 days afterwards, and phenylbutazone 400 mg. 18 hours before the test injection and 100 mg. 6-hourly during the observation period.

It was found that pre-treatment with colchicine resulted in a decrease in the magnitude of the inflammatory response in eight of the ten patients who received intra-articular injections, and in six of the eight who received subcutaneous injections. This effect was most evident in those patients who showed the greatest inflammatory response in the control study. Similarly, hydrocortisone in three patients and phenylbutazone in two patients also produced a diminished inflammatory response. The serum urate concentration was raised by giving a high purine dietary supplement of ribonucleic acid 1 g. orally four times daily, or was lowered by giving probenecid or sufipyrazone. The authors also found that the magnitude of the response in the skin was not consistently related to the concentration of serum urate.

B. M. Ansell


Diseases of Bone


The authors report the age, sex, and race of patients with "minimal trauma" fractures of the hip in the population of Charlottesville, Virginia, during the 3-year period, 1960-62. Fracture of the femoral neck due to "minimal trauma" was defined as a fracture above the level of the lesser trochanter occurring without outside force. If the patient had fallen, the fall had started with the patient's feet on the ground or floor; the few instances in which the patient had fallen out of bed at home were also included. If any concomitant disease which could cause pathological fractures was diagnosed, the case was excluded.

The authors assume that osteoporosis is the basis predisposing to "minimal trauma" hip fractures, as defined by the above criteria. They quote evidence from the literature in support of this assumption.

The incidence of hip fractures due to "minimal trauma" was analysed, using coded hospital and operating room records and the population figures for Charlottesville. The fracture rate was much higher in white than Negro in women or in men of either race. The fracture rate also showed a distinct increase with increasing age. The authors point out that their findings are in keeping with reported observations on bone density in relation to age, sex, and race.

G. Meachim


A report of hydroxyproline elimination and calcium balance in a case of Marfan's syndrome. Total urine hydroxyproline was increased to 106 mg. per 24 hours; after ingestion of proline this was reduced to 63 mg. per 24 hours. Calcium balance was slightly negative (−20 mg. per 24 hours) and studies with 48[Ca] showed only mild departures from normal. The turnover rate increased to 1,305 mg. per 24 hours and the rate of Ca absorption from bone (990 mg. per 24 hours) exceeded the rate of deposition (97 mg. per 24 hours).

D. F. Cole


A case of Marfan's syndrome is reported, which had the ocular abnormalities of absence of the zonule and a

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small lens. The authors postulate that the defect in the eye is one of ectodermal rather than mesodermal dysplasia.

G. Davies


Characteristic stigmata of the Marfan syndrome are reported from seven members of a Queensland family extending over three generations. Clinical data and necropsy studies of four are presented. Ronald Lowe


Immuno-electrophoresis of serum from a patient with Marfan's syndrome revealed the presence of glycoproteins which stained with Schiiff's reagent. Glycoprotein was identified as the seromucoid and hapto-globulin fractions.

D. F. Cole


This paper from University College Hospital, London, describes six examples of juvenile osteoporosis in which the primary cause was unknown. The authors believe that these cases form a homogeneous group and represent a new disease entity.

All the children were apparently well until just before puberty, when the disease started with fractures of one or more bones after minimal trauma. In some of the children the initial complaint was pain in the region of joints, often leading to a mistaken diagnosis of arthritis. Radiologically the bones showed the changes characteristic of osteoporosis. The vertebrae were predominantly involved in all six patients, with multiple compression fractures of vertebral bodies, variable degrees of anterior wedging, and extended disk spaces; rib fractures, and osteoporosis of the long bones with fractures occurred very commonly around the knee-, hip-, and ankle-joints. These fractures often started as hairline cracks, as at the medial border of the femur where continued weight bearing was followed by collapse of the bone around the fracture site. The fractures nevertheless healed extremely well.

The plasma levels of calcium, phosphorus, and alkaline phosphatase were all normal, although two children became hypercalcaemic twice after immobilization, an adverse effect common to all types of osteoporosis. The urinary calcium level was raised in three children when first seen. In all those treated with vitamin D the urinary calcium level rose, often above 500 mg. excreted per 24 hours, but in none was there any evidence of nephrocalcinosis or nephrolithiasis.

Although none of the children had clinical evidence of Cushing's syndrome, adrenal function was fully investigated. Two patients had plasma cortisol levels above the upper limit of normal, but both were taking stilboestrol, which is known to increase the protein-binding power of cortisol and thus to raise the total level of circulating hormone. The diurnal rhythms and the dexamethasone suppression tests were normal. After ACTH stimulation, two children had an excretion of 17-ketogenic steroids above the upper limit of normal.

In spite of the overall normality of adrenal function tests, the authors consider that the osteoporosis may have been caused or initiated by a temporarily excessive production of adrenal steroids at the time of puberty. The calcium balance studies showed a characteristic pattern of a high faecal calcium level, almost equal to and in some cases greater than the dietary intake, so that there was gastrointestinal malabsorption of calcium. Dihydrotestosterone (DHT) was used effectively to restore calcium balance by increasing the absorption of calcium from the gut. However, two children were unduly sensitive to DHT and they became hypercalcaemic; it was only after the use of testosterone and stilboestrol that they were able to tolerate DHT. The use of sex hormones alone, without DHT produced a fall in urinary calcium level but did not produce a positive calcium balance.

In this series two children recovered without receiving any treatment. One deteriorated over a period of 5 years until he was given a combination of DHT and sex hormones; another treated with oral calcium and DHT, continued to deteriorate over a further 3½ years; both of these children ended up grossly deformed, dwarfed, and disabled. Another child, who was treated with a combination of sex hormones and DHT, suffered a number of fractures of the long bones, but remained in positive calcium balance throughout the period of observation and the bones returned almost completely to normal.

On the basis of unpublished observations by these authors, they suggest that congenital marble bone disease is the result of a metabolic defect which is the reverse of that in juvenile osteoporosis, the patient over absorbing calcium from the gut and depositing excess calcium in the skeleton. Therefore, one girl of this series with osteoporosis was given infusions of plasma obtained from such a case, and this treatment produced a positive balance of 100 mg. per day. There may well be a factor in this plasma or in normal plasma, which has a beneficial effect in juvenile osteoporosis.

[This is a most important paper which must be read by all interested in bone diseases.]

A. Gordon Beckett


Described in the present paper from the University of Newcastle upon Tyne are the results of a retrospective study of a series of 38 selected children who were suffering from acute haematogenous osteitis. These children were selected by the following criteria: the age-group of 2 to 12 years, a severe grade of disease, all the symptoms developing fully within 72 hours of the onset of pain, the duration of the illness at the time of admission being not more than 1 week, and a major long bone being infected.
while the joints were not. The children were treated with antibiotics, such as penicillin G, tetracycline and, latterly, cloxacillin, in high dosage for a minimum of 3 weeks. Any pus which formed in the periostea was removed by aspiration through a wide bore needle while the patient was under general anaesthesia. Splinting was not used as a routine. There were two patients (5 per cent.) whose illness was complicated by sequestrum formation and the other 36 (95 per cent.) were clinically cured. These results compare with a complication rate of 30 per cent. among similar cases reported recently in the literature. The importance of early diagnosis and of admission to hospital for effective treatment is stressed.

Winston Turner

Varioius Osteomyelitis. (Osteomyelitis variolosa.)

Pararheumatic (Collagen) Diseases
Gastrointestinal Complications of Collagen Diseases.
Arch. Surg., 89, 695. 19 refs.

This analysis concerns severe gastrointestinal complications seen over a period of 10 years at the Henry Ford Hospital, Detroit, in 342 patients with collagen disease. "Strict criteria" are mentioned but not explicitly stated. This group comprises 52 cases of essential polyangitis, 52 of dermatomyositis, and 231 of systemic lupus erythematosus, as well as seven patients who were not classifiable. Twenty developed gastrointestinal complications requiring either operation or "aggressive medical treatment" (none non-classifiable). The incidence was highest in essential polyangitis (21 per cent.), and lowest in dermatomyositis (10 per cent.), and systemic lupus erythematosus cases (2 per cent.). The ages of the twenty affected cases ranged from 6 months to 77 years. Perforation occurred in eleven patients, ten of whom were on steroid therapy. Haemorrhage occurred in eight patients (four on steroids), infarction in five (two on steroids), and a fistula developed in one; a total of 25 complications in twenty patients. In those with polyangitis, perforation occurred four times, haemorrhage three times, and infarction once. Patients with systemic lupus erythematosus suffered much less frequently from such complications (perforation three times and haemorrhage once).

The authors conclude that the administration of steroids facilitated the development of gastrointestinal complications, but that the latter occurred in a significant number of patients who had not received steroid therapy. The total mortality was high (25 per cent.), even with early diagnosis and "aggressive" treatment.

E. G. L. Bywaters

Respiratory Function Studies in Patients with Certain Connective Tissue Diseases.
Brit. J. Derm., 77, 221.

Respiratory function in certain connective tissue disorders was studied in 69 patients at the General Infirmary at Leeds. The two largest groups of patients comprised 31 with systemic sclerosis and twelve with systemic lupus erythematosus (SLE). A wide range of standard lung function tests was carried out, but only vital capacity and the carbon monoxide diffusing capacity are discussed, since abnormal findings were mainly confined to these values.

Of the patients with systemic sclerosis, vital capacity was reduced (less than 75 per cent. of the predicted normal value) in fifteen (49 per cent.) and diffusing capacity (less than 80 per cent. of the predicted normal value) was reduced in 22 (76 per cent.).

Of the patients with SLE, four showed reduced vital capacity and five a low diffusing capacity, although all lung fields were normal radiologically.

In patients with other conditions, such as morphoea, cutaneous vasculitis, Raynaud's phenomenon, and Sjögren's syndrome, impaired diffusing capacity was often found, but vital capacity was generally normal.

The authors conclude that diffusing capacity is a sensitive index of lung parenchyma involvement and impaired diffusing capacity is often the first sign of systemic involvement in skin disease. It is not possible, at present, to correlate abnormal results with pathological change in, for instance, capillary wall, interstitial tissue, or alveoli.

Eric Beck

Prognosis in Raynaud's Phenomenon after Sympathectomy.
Brit. med. J., 1, 962. 15 refs.

A follow-up study is reported of 75 patients who had undergone upper thoracic sympathectomy for severe Raynaud's phenomenon at St Bartholomew's and St. Thomas's Hospitals, London, between 1939 and 1960. This long follow-up period permitted subdivision of the cases into:

1. Primary Raynaud's phenomenon.
2. Digital artery thrombosis.
4. Miscellaneous.

The difficulty of recognizing systemic scleroderma is demonstrated by the follow-up findings. Of the 43 patients in whom the initial diagnosis was primary Raynaud's phenomenon, systemic scleroderma had developed in eight (19 per cent.) 6 to 24 years later. The authors state that oesophageal manometry was helpful in detecting systemic scleroderma and that mucosal telangiectases on the hands and finger-tip necrosis were also suggestive of the incipient stages of this condition.

Sympathectomy was successful in 58 per cent. of the cases of primary Raynaud's phenomenon and in 71 per cent. (15 out of 21) of the cases of digital artery thrombosis. None of the three patients in the miscellaneous group (systemic lupus erythematosus and dermatomyositis) was helped by operation. Of the eight patients with systemic scleroderma, only two were improved, suggesting that sympathectomy was of very little benefit in this condition although there was no evidence that it caused deterioration. Sympathectomy seems clearly indicated in cases of digital artery thrombosis and of primary Raynaud's phenomenon.

I. McLean Baird

The viscosity of the blood was studied at the University Department of Surgery, Newcastle upon Tyne, in 22 patients with Raynaud’s disease and twenty healthy controls. Viscosity was measured in vivo by Pirofsky’s technique in a temperature-controlled room at 20°C, three readings being taken in each case. In all the patients with Raynaud’s disease the blood viscosity was raised, compared with the controls. The plasma fibrinogen level was also consistently higher in the patients than in the controls. Slit-lamp microscopy of the conjunctival vessels was carried out in seventeen patients and six controls. In nine patients there was well-marked “sludging”, in seven and one control a minor degree of sludging, and in one patient and five controls no sludging.

This new observation on Raynaud’s disease has important therapeutic implications; the extent to which anticoagulants or low-molecular weight dextran may bring about improvement in patients with this disease remains to be determined. I. McLean Baird


The peripheral vascular manifestations of systemic lupus erythematosus (SLE) were studied in eleven patients with SLE seen at the Mayo Clinic between 1956 and 1962. Raynaud’s phenomenon was present in three of the patients, peripheral arterial occlusion in seven, chronic leg ulceration in seven, livedo reticularis in three, and thrombophlebitis in five. In six of the eleven patients, two or more manifestations of SLE were present in the peripheral vascular system, and in seven peripheral vascular disease was the presenting symptom. A striking feature of the cases was the long latent interval between the initial manifestation and the development of the full syndrome. The authors state that it is well-recognized that Raynaud’s phenomenon may precede the onset of other manifestations of SLE by many years, but it is not so well-realized that the same may also be true of other vascular complications.

Only three of the patients had received steroids before the peripheral vascular manifestations appeared, but in two these were signs of mild hypercortisonism. Definite improvement in the vascular lesions were observed in four patients, after treatment with adrenal steroids. Cryoglobulinaemia in one patient was not related to the presence of leg ulcers. The authors draw attention to the reported suggestion that thrombosis in SLE is an over-compensation against possible haemorrhage, but they note that of the patients studied by these workers the only one who had haemorrhagic manifestations had a low titre of circulating anticoagulants, while the patient with a very high titre had had vascular occlusion. It is concluded that various peripheral vascular syndromes are part of the natural history of systemic lupus erythematosus. J. S. Malpas


Promising results in the treatment of systemic lupus erythematosus (SLE) by the use of large doses of steroids given intermittently are reported in this paper from the New York Medical College. The dose was regulated according to the degree of immunological abnormality which was assessed by serial estimations of the level of serum complement (this was much reduced in all of the fifteen patients studied) and serum globulin levels, and by testing for DNA antibodies in the skin and in serum. Renal function tests were performed and in biopsy material taken from each patient immuno-fluorescent staining showed the presence of globulin attached to the glomerular basement membrane. Prednisone was given in daily doses of 60 to 100 mg. In most cases complement levels rose and globulin levels fell to normal in 8 weeks, and lupus erythematosus (LE) cell tests became negative, but if necessary the dose of prednisone was increased even to 180 mg. daily. After this, maintenance therapy was continued with triamcinolone 48 to 64 mg. per day on 4 days in each week. This intermittent regime was better tolerated than the continuous daily dosage.

Two patients died (from possible suicide and subdural haematomata respectively), but the remainder were symptomatically greatly improved and they returned to their previous occupations. Renal function improved and proteinuria either became reduced or disappeared. The duration of treatment averaged 21 months with a maximum of 57 months, and as had been expected certain side effects occurred, including temporary psychosis in seven patients and reactivation of healed tuberculosis in three.

J. A. Cosh


Changes in the respiratory system in systemic lupus erythematosus (SLE) were studied in the records of 26 cases of the disease seen at University College Hospital, London. Of the 24 patients, ten were seen personally by the authors, and the results of lung function studies in these ten patients are reported in detail. In six of these nine fatal cases in the whole series, well-documented necropsy records were available.

Respiratory involvement attributable to SLE was noted in sixteen patients, one or more of the following three clinical patterns being observed at varying times in their illness:

1. Pleurisy;
2. Recurrent febrile attacks;
3. Unexplained dyspnoea.

In eight cases dyspnoea was a prominent symptom and details of these are given. Lung-function tests revealed...
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reduced chest expansion, slow-moving raised diaphragms, very low vital capacity, and a restrictive defect of ventilation with reduced compliance. A good therapeutic response to corticosteroids was often obtained.

The authors discuss the differential diagnosis from thrombo-embolic pulmonary hypertension, and also the pathological process which may underlie the dyspnoea and the small stiff lungs. They consider that pleural thickening and pulmonary fibrosis are an inadequate explanation and suggest that a possible cause is alveolar atelectasis associated with the development of a hyaline membrane.

K. C. Robinson

Significance of the Lupus Erythematosus Cell Phenomenon in Older Women with Chronic Hepatic Disease.


The significance of the lupus erythematosus (LE) cell phenomenon in elderly female patients with liver disease is considered in this paper from the Departments of Rheumatology, Medicine, and Pathology of the Mayo Clinic.

Seven patients, all of them over 45 years of age and with chronic liver disease, were investigated. Systemic symptoms occurred in five patients (they occurred less commonly than in younger women) and in four the initial symptoms were attributable to the liver lesion. Four of the patients had recurrent fever, four had pleuro-pulmonary disease, and four arthralgia; one had a transient skin rash, one a diffuse sclerosis and Sjögren's syndrome, and two pericarditis; four patients died within 3 years of the onset of the disease. Mild anaemia, a raised sedimentation rate, a false positive serological reaction for syphilis, and raised level of serum γ-globulins were found whilst the final histological picture in three patients followed to necropsy was a post-necrotic cirrhosis.

The authors stress that the LE cell phenomenon is not limited to young women; in young patients systemic manifestations of the disease were not only more frequent but their appearance often antedated that of the hepatic disorder.

A. E. Read


Two cases of scleroderma are described, both showing retinal changes and one having also changes in the sclera, cornea, and uvea. It is considered that this condition may involve the eye directly, and not merely secondarily due to renal involvement.

J. H. Kelsey


A man aged 70 had a right central retinal artery occlusion, and while in hospital the left vision blurred. He was given systemic steroids, and CO₂ inhalations when the episodes of blurring occurred. These became less frequent, the erythrocyte sedimentation rate became normal in 3 weeks, and normal vision was retained in the left eye.

J. H. Kelsey

Connective Tissue Studies


In 1961 the author started an investigation of patients with rheumatoid arthritis (RA), systemic lupus erythematosus, and Reiter's syndrome, and tried to isolate viruses from various tissue fluids. Although no virus was isolated mycoplasmas or pleuropneumonia-like organisms (PPLO) appeared in several cultures which had been inoculated with synovial fluid from patients with RA. The present paper from the University of Michigan Medical School, Ann Arbor, describes similar experiments in which two cell lines which are normally free of PPLO have been used for culture media.

African green monkey kidney cells in Melnick's media and human embryonic lung fibroblasts in Eagles's medium were inoculated with biopsy specimens of synovial fluid, pleural fluid, bone marrow, urine, and serum, and post-mortem extracts of spleen and kidney obtained from patients with RA, systemic lupus erythematosus, or Reiter's syndrome. A total of fifty specimens were used, and cultures were passaged up to ten times. Similar specimens obtained from patients with traumatic or osteo-arthritis, acute viral infection, gout, and leukaemia served as controls.

D. D. McCarthy

Lengthy Survival in Systemic Lupus Erythematosus.


This case report from Cape Town describes a Cape coloured woman, in whom systemic lupus erythematosus was diagnosed in 1952 when she was aged 35 years. There had been a history of intermittent joint pains for 2 years, and the preceding year she had developed a left pleural effusion which resolved spontaneously. At the time of diagnosis, she was acutely ill with fever, weight loss, alopecia, and a rash in the "butterfly" area. Investigation revealed a marked anaemia, raised sedimentation rate, normal leucocyte count, and raised blood urea. Albuminuria, but not haematuria, was present. LE-cells were found. She responded well to cortisone, the albuminuria ceased, and she was discharged from hospital on 50 mg. cortisone daily; 5 years later prednisone, 7.5 to 10 mg., was substituted for cortisone, and she has been maintained on this medication since. The latest follow-up was in 1964 at which time she was well. LE-cells were still demonstrable, but the haemoglobin, and the sedimentation rate were normal. It is interesting to note that, while on steroid therapy, she had a normal pregnancy and delivered a normal full term child.
PPLO were isolated from fourteen of seventeen patients in the test group, but none was isolated from the control cultures. Antibiotic sensitivity tests showed that the PPLO were sensitive to tetracycline. There was some evidence that different strains shared common antigens but one strain was antigenically distinct.

The possibility that the cultures had become contaminated with PPLO is thought to be unlikely as the strains were not identical. The author considers that the isolated strains are closely related to each other and their isolation may provide a further link in the chain of evidence suggesting that some of the rheumatic diseases, especially Reiter's syndrome, may be caused by PPLO. [The distribution of the positive cultures obtained in this series is also described.]

Allene Scott

Immunology and Serology

**Macroglobulin Rheumatoid Factors directed towards Buried Antigenic Sites of Human \( \gamma \)-Globulins.**


In this communication from the University of California School of Medicine, the authors report their results after examining fifty rheumatoid sera with high FII haemagglutination titres for the presence of agglutinating factors directed towards an antigenic site revealed by pepsin digestion of human \( \gamma \)-globulins. Nineteen sera (38 per cent.) contained such factors. In twelve of thirteen sera the agglutinating factor was a 19S protein, as characterized by sulphhydryl reduction, column chromatography, and density gradient ultracentrifugation experiments. 7S agglutinators were present in two sera. Methods employed are detailed.

Haemagglutination inhibition studies are also reported, by which it was shown that proteolysis of human \( \gamma \)-globulins with pepsin reveals an antigenic site not available in intact molecules. This buried site was present only in the electrophoretic fractions of human sera which contain \( \gamma \)-globulins. Pepsin treatment of bovine and rabbit \( \gamma \)-globulins failed to reveal a similar determinant.

This present study provides further evidence for heterogeneity in combining specificities of the different anti-\( \gamma \)-globulin factors demonstrable in rheumatoid sera.

T. M. Chalmers

**Shwartzman Phenomenon Mechanism:** Newer Concepts.


The role of bradykinin and serotonin in the local Shwartzman reaction was investigated in rabbits by measuring the effects of inhibitory compounds. MAPTC (anti-serotonin) alone had only a slight inhibitory effect on the reaction, but combined with aminopyrine (anti-bradykinin) the inhibition was greater than the sum of the individual effects. PPBP (anti-serotonin and anti-bradykinin) had a greater inhibitory effect than aminopyrine. The inhibitory agents reduced haemorrhage, congestion, and oedema, but did not influence leucocyte infiltration or thrombosis. It was concluded that bradykinin and serotonin are among several agents involved in the Shwartzman phenomenon.

J. Ball

**Immunological Studies on Adrenal Glands. V. Chemical Studies on the Rabbit Adrenal-Specific Autoantigen.**

Shulman, S., Centeno, E., Milgrom, F., and Witebsky, E. (1965). Immunology, 8, 531. 5 figs, 8 refs.

Extracts of rabbit adrenal tissue, containing an adrenal-specific antigen able to elicit the formation of an autoantibody, have been characterized physicochemically. The extinction coefficient was shown to be 0.1. Ultracentrifugal analysis revealed a group of components; the predominant one was a 3-9S boundary. Additional components had sedimentation coefficients of 6-6S, 10-0S, 11-8S, and 18-1S. Starch block electrophoresis was unsuccessful in providing significantly purified antigen. There was a suggestion of a possible occurrence of two antigens. Some degree of fractionation was achieved by salting-out with ammonium sulphate. The antigenic material was associated with the fraction precipitating between 0·00 and 1·50S of this salt. These studies also provided some evidence that this antigen was associated with the 6-6S sedimenting component. Enzymic digestion with chymotrypsin readily caused destruction of the activity, indicating that this antigen is essentially a protein.

W. R. Alexander

**Anti-nuclear-factors (ANF) as determined by the Immuno-fluorescent Antibody Technique.**


The sera from patients with disseminated lupus erythematosus contain several antibodies directed against widely differing antigens. One of these antibodies is directed against nuclear substance and it forms the basis of the lupus erythematosus (LE) cell test. It is believed that the LE factor is a 7S \( \gamma \)-globulin and the LE-cell test merely demonstrates the existence of one of several antibodies. The present authors, from the Streptococcal Department, Statens Seruminstitut and Medical Department Sundby Hospital, Copenhagen, have used the indirect fluorescent antibody technique for demonstrating antinuclear globulin in sera. The substitute used was the nuclei from the thyroid glands of thyrotoxic patients. The anti-human \( \gamma \)-globulin was prepared by intramuscular injections of purified human \( \gamma \)-globulin into albino rabbits, the antiserum being checked by immuno-electrophoresis before use. The fluorochrom used was fluorescein isothiocyanate.

In all 194 sera from normal blood donors (controls) and 1,129 sera from patients were examined. It was found that 4·6 per cent. of tests for antinuclear factors were positive in normal individuals. Also, in 97 per cent. of patients with clinical and pathological evidence of disseminated lupus erythematosus 53 per cent. of patients with less definite evidence of lupus, 60 per cent. of patients with dermatomyositis, 42 per cent. of patients with Sjögren's disease, 38 per cent. of cases of hepatitis.
Serum Factors Gm (a), Gm (b), Gm (x), and Gm-like in Patients with Chronic Rheumatic Affections. [In English.] Podlachouk, L., Jacqueline, F., and Evque, A. (1965). Vox Sang. (Basel), 10, 188.


The authors tried using latex particles of different sizes which were coated with γ-globulin by suspension in solutions of varying concentrations, and they finally selected Lytron 615 particles of 2,500 Å diameter which were coated with Squibb 2015 γ-globulin in a concentration of 1.5 mg. per ml. [For full technical details the original paper should be consulted.] It was found that by the addition of albumin the stability of the coated latex suspension could be maintained for 1 year, and that when the new test was compared with the standard procedure in a trial which included the sera of 120 patients with rheumatoid arthritis, 343 patients with other diseases, and 250 controls, the results were very similar.

Harry Coke


The injection of an oily suspension of dead tubercle bacilli (Freund's adjuvant) into one footpad of a rat results in a local inflammatory reaction followed about 10 days later by widespread secondary lesions in other joints. This is known as adjuvant arthritis. Many anti-inflammatory drugs, such as phenylbutazone, can suppress the initial local response but have little effect on the secondary lesions. Even the corticosteroids only suppress these temporaril; their withdrawal being followed by the appearance of the lesions at the usual secondary sites. The prophylactic effect of 2-butoxy carbonylmethylene-4-oxothiazidine (I.C.I.43,823) differs fundamentally in that permanent suppression of the secondary lesions is achieved, even when it is administered for only 3 days, starting the day before the injection of adjuvant.

Asbestos, 30 per cent. of cases of rheumatoid arthritis, and 25 per cent. of cases of ulcerative colitis, the antinuclear test was positive. The fact that the antinuclear test is positive in diseases other than disseminated lupus proves that the finding of antinuclear fluorescence cannot be taken as diagnostic for one disease only, and shows that antibodies are frequently found in the auto-allergic diseases. Positive results were obtained in patients with Hashimoto's thyroiditis, pernicious anaemia, carcinoma, sarcoma, and myelomatosis. William H. S. George


The incidence of rheumatoid factor many small changes in technique have resulted in lack of standardization, so that the results obtained in different laboratories are no longer comparable. The authors of this paper from the Montefiore Hospital and Downstate Medical Center, New York, therefore propose a modified latex test which they claim is capable of giving results which are more constant.

The authors tried using latex particles of different sizes which were coated with γ-globulin by suspension in solutions of varying concentrations, and they finally selected Lytron 615 particles of 2,500 Å diameter which were coated with Squibb 2015 γ-globulin in a concentration of 1.5 mg. per ml. [For full technical details the original paper should be consulted.] It was found that by the addition of albumin the stability of the coated latex suspension could be maintained for 1 year, and that when the new test was compared with the standard procedure in a trial which included the sera of 120 patients with rheumatoid arthritis, 343 patients with other diseases, and 250 controls, the results were very similar.

Harry Coke


Biochemical Studies


The fluorochrome thioflavin-T has been described as a useful stain for demonstrating amyloid. The results of this staining procedure were compared with those obtained by using Congo red and the sections were also observed for dichroic birefringence with a polarizing microscope.

48 consecutive surgical specimens were studied. In addition three known amyloid controls and six rectal biopsies (one positive) were stained. There were no false positives using thioflavin-T, but several false positives were found. In particular arterial elastic laminae and intestinal mucus proved troublesome. However, it is concluded that the new method is useful for rapid screening of tissue sections for amyloidosis. If a positive result is obtained it must be confirmed by the more usual procedures. D. J. Ward


Organs affected with amyloidosis were extracted with saline, phosphate (pH 8.0), and 0.01 M acetic acid. The tissues were dialysed, dried, and then repeatedly extracted with 6M urea and then 8M urea. The proteinous extracts were characterized by starch gel electrophoresis. The liver, spleen, and kidneys of six patients with amyloidosis secondary to various diseases and the amyloid kidney from a case of familial Mediterranean fever yielded urea extracts having common major electrophoretic components which were not detectable in control organs unaffected by amyloidosis.

In hearts affected by primary amyloidosis, the amyloid material was more difficult to dissolve and did not regularly exhibit the same electrophoretic component as the secondary amyloid. Several alternative explanations for this difference between primary and secondary amyloidosis are discussed. J. Ball


Comparatively few reports have appeared about the effect of acute bacterial infections on the cortisol secretion rate. In this paper, secretion rates, using $^{14}C$ cortisol, have been determined in five patients during the acute stage of their illness, values found ranging from 24.7 to 89.8 mg./24 hours, and in three of these patients during convalescence when the rate varied from 10.9 to 17.2 mg./24 hours. Total 24-hour urinary OHCS determined at the same time as the secretion rates in four patients lay between 23.7 and 34.0 mg./24 hours in the acute phase and between 2.2 and 8.9 mg./24 hours during convalescence. One patient had erysipelas, one had pneumonia, and three had meningitis, one of whom developed transient hypotension and oliguria. In two patients the pattern of cumulative excretion of radioactive metabolites was identical during the acute stage and during convalescence, in the patient with oliguria, there was some delay during the acute phase. Between 40 and 50 per cent. of the cortisol secretion was recovered as 17 OHCS in 24 hours during both the phase of severe illness and in convalescence. It is suggested that these values for the cortisol secretion rates found may give some guidance to the dose of steroid needed during acute infections by patients with adrenal insufficiency, iatrogenic or otherwise induced, and that determination of total 24-hour 17 OHCS excretion may give valuable information on adrenocortical function in acute severe infection. The authors point out, however, that these results may be invalidated by impairment of liver or kidney function. C. J. Beardwell


This paper reports the results of a study of iron metabolism in 29 patients with rheumatoid arthritis at Bryn Mawr Hospital, Pennsylvania. The authors found that anaemia was pronounced in the eighteen patients who had the most active grade of arthritis. The anaemia...


Therapy


For this investigation, ten healthy subjects took 1 g. aspirin in solution or as three enteric-coated tablets with 200 ml. water after an overnight fast. One half of the group received tablets-solution-tablets-solution, and the other half received solution-tablets-solution-tablets, the study being repeated at weekly intervals. Nothing was taken for 2 hours after ingestion; blood samples were obtained at 0, 1, 2, 4, 6, and 8 hours after ingestion for salicylate level by Brodie's method; urine was obtained at 0, 1, 3, 5, 7, and 9 hours and at known intervals up to a total of 60 hours for estimations of total salicylate, free salicylate, salicylate and salicyl acid glucuronides by Smith's method modified by the authors.

The average maximum serum concentration after the enteric-coated preparation was lower than after the aspirin in solution at any time. In addition, while aspirin in solution yielded well reproducible plasma salicylate levels there was marked variation in the absorption pattern of the enteric-coated aspirin both in the different subjects and at the different times of administration in any one subject. However, despite this variable rate, absorption of enteric-coated tablets was complete. This variation in absorption appears to be due to the rate of gastric emptying which is, of course, affected by many factors. There was no real difference in the metabolic fate of aspirin when given either as a solution or as the enteric coated tablets.

The authors suggest that the variable rate of absorption constitutes a limitation in the value of all enteric coated tablets.

B. M. Ansell


Dimethyl sulphoxide (DMSO) is a versatile commercial solvent which, it is claimed, is rapidly absorbed through the intact skin, has local analgesic activity, lessens swelling, and promotes the healing of injured tissue. Its use has therefore been proposed for the treatment of many acute and chronic lesions of the soft tissues—rheumatic, traumatic, or inflammatory. This paper from the University of Oregon Medical School, Portland, briefly reports the results of its use in a series of 548 patients with acute musculoskeletal injuries (210) acute and chronic subacromial bursitis (63), rheumatoid arthritis (150), osteo-arthritis (110), gout (5), scleroderma (5), and Dupuytren's contracture (3). Treatment was by topical application of about 30 ml. of 60 to 90 per cent. DMSO one or more times daily for periods as long as 10 months. No evidence of serious toxicity was seen throughout. It is claimed that in most cases DMSO exerted a rapid and definite anti-inflammatory effect, with relief of pain and muscle spasm and increased range of motion in the affected area. The authors report that in this series 437 patients were "unequivocally improved".

W. S. C. Copeman


The "pseudo-rheumatism" syndrome is one side effect of corticosteroid medication which may be mistaken for a relapse so that the dosage of hormone, instead of being progressively decreased, may actually be increased to the point of danger. The syndrome comprises pain in joints and muscles accompanied by tenderness, extreme physical exhaustion and marked psychological liability. It occurs in those who have received treatment for many months (though the total quantity of hormone received may vary considerably) and who already show such recognizable side effects as moon face, oedema, and...

Based upon a paper read to the orthopaedic section of the Royal Society of Medicine, this short review of the surgery of the rheumatoid hand is a clear and concise description of the indications and techniques of surgery.

The indication for metacarpophalangeal synovectomy is given as radiological evidence of bone destruction or loss of joint space. Synovectomy is contraindicated in the presence of long-standing deformity with dislocation; at this stage the author advises arthroplasty and the method he recommends is a simple excision of the metacarpal head together with joint capsule, collateral ligaments and synovium.

In cases of swan-neck deformity, the Littler release by excising the oblique fibres of the extensor hood is recommended. Other procedures advocated are synovectomy of the proximal interphalangeal joints, arthrodesis of interphalangeal joints of fingers and thumb, release of trigger fingers and carpal tunnel decompression.

The author is an advocate of early surgery to prevent deformity.

D. R. Sweetnam


In normal man, the excretion of hexahydrated cortisone derivatives is twice as great of that of the tetrahydrated derivatives. In this paper the influence of ACTH on this ratio is examined. The method consists of hydrolysis followed by ether extraction, evaporation and resolution in methanol. This is followed by chromatography and measurement of constituents. Under the influence of ACTH, cortisol excretion is increased about twelve-fold, whereas cortisone excretion is increased only about four-fold. The tetrahydrated derivatives are increased similarly. The hexahydrated derivatives of cortisol are influenced less strongly by ACTH rising to 10·31 ± 4·18 mg./24 hours while the tetrahydrated metabolites are excreted at a rate of 14·93 ± 4·61 mg./24 hours. It is proposed that the reason for the difference may be that the enzymes which reduce C₉₀ of the hexahydroderivatives are only available to a limited extent.

G. Loewi


Indomethacin, a new antirheumatic drug, is an indole compound chemically unrelated to either corticosteroids or other anti-inflammatory drugs. Controlled clinical trials have shown that indomethacin relieves the symptoms of various arthritic disorders, though other parameters of inflammation such as the erythrocyte sedimentation rate remain unaltered. The tablets which were used originally frequently caused gastrointestinal irritation, including peptic ulceration, while other side-effects involving the central nervous system were also reported. The introduction of gelatin capsules containing the powdered drug and the use of smaller doses have reduced the incidence of side-effects, but the present authors, at the United Birmingham Hospitals, have studied the possibility of reducing it further by rectal administration, especially for patients with peptic ulceration, those who develop gastric intolerance, and those who require unusually large doses. Of the 40 patients studied, 34 suffered from rheumatoid arthritis, three from osteoarthritis, two from ankylosing spondylitis, and one from gout. Many were severely ill or resistant to other drugs or had developed complications of steroid therapy.

Initially the effects of single doses of 100 mg. of indomethacin given in capsules and suppositories on the symptoms and the serum level of the drug were compared in ten patients. (For details of the method of estimation of indomethacin in the serum the original paper should be consulted.) The drug was absorbed satisfactorily from the rectum, the peak serum levels ranging from 1·1 to 3·5 μg. per ml. compared with a range of 1·4 to 6·2 μg. per ml. after oral administration. Absorption invariably started shortly after insertion of the suppository, but was delayed to a varying extent, up to 2 hours, after ingestion of a capsule. Symptomatic relief showed a similar pattern, starting 20 to 30 minutes after a suppository and 40 to 60 minutes after a capsule.

The clinical effectiveness of indomethacin administration by each route was assessed in all 40 patients by reference to the relief of pain and tenderness in the joints, improvement in function, and the reduction of other therapy such as steroids. No patient was considered to have responded unless relapse occurred when dummy capsules or suppositories were substituted without his knowledge. (The usual daily dosage was apparently 100 to 150 mg., but details are not given, nor is the duration of treatment stated.) In 30 cases "a good result" was obtained with suppositories, and the effects were similar whichever way the drug was administered. Most patients preferred to use the suppositories at night, and in some cases a 100-mg. suppository given at night relieved early morning stiffness and relieved pain for up to 16 hours. In three cases local effects occurred from the suppositories, but there were no dyspeptic symptoms and systemic side-effects were negligible. (There is no mention of the frequency of side-effects noted during oral administration in this series.) Isolated measurements of the serum indomethacin level were found to be of no practical value in controlling treatment.

It is concluded that rectal suppositories provide a satisfactory means of administration of indomethacin and may be used either to supplement oral dosage or where oral administration is contraindicated.

Ann F. Tuxford

A boy suffering from a severe nephrotic syndrome twice developed lid-lag, lid-retraction, and apparent proptosis during the course of corticosteroid therapy. On each occasion the eye-signs regressed after steroid withdrawal. The steroids concerned were methyl prednisolone and triamcinolone. Thyroid function tests during the second episode of ocular signs included an elevated thyroid radio-iodine uptake and a high basal metabolic rate. The authors believe that their case sustains the possibility that hyperthyroidism may be a rare side-effect of steroid therapy.

S. Etzine


The development of posterior subcapsular cataract as a result of long-term systemic corticosteroid therapy is still in dispute. This study was confined to children wherein the development of this type of cataract is not seen as a normal ageing process. In these circumstances no definite relationship was proved.

R. F. Fisher


An account of the ocular manifestations of rheumatic arthritis, ankylosing spondylitis, and systemic lupus erythematosus is followed by a description of iatrogenic ocular complications resulting from their treatment. Salicylates in severe overdosage can cause optic atrophy. Gold therapy can result in deposition of gold in the cornea. Steroid-induced cataracts and glaucoma are mentioned. Antimalarial drugs such as chloroquine can cause extra-ocular palsies, decreased corneal sensitivity, corneal deposits, and retinopathy giving rise to symptoms of blurred vision, haloes, glare, diplopia, loss of vision, and decreased night vision.

G. Davies


From Letterman General Hospital and the University of California Hospitals, San Francisco, four cases are reported in which treatment of cardiac arrhythmia with procainamide for periods of 1 to 9 months was followed by an illness resembling lupus erythematosus (LE) and characterized by arthropathy, skin lesions, pleurisy, and the demonstration of LE cells (in three cases) and antinuclear factor in the blood. Withdrawal of the drug led to clinical but not serological improvement. The blood of six relatives of two of the patients was tested for antinuclear factor with negative results. Three previously reported cases of precipitation of a lupus-like syndrome by the administration of procainamide are also reviewed.

M. Wilkinson


This study from Bucharest concerns the anti-inflammatory effect of chloroquine given in both rabbits and guinea-pigs in doses between 15-40 mg./kg. body weight by various routes over a period of 4 days.

The inflammatory effects of a 24-hour croton oil peritoneal exudate from such treated animals was greatly reduced compared with those not so treated. These effects were tested by intradermal injection of the exudate in rabbits and measured using intravenous 1 per cent. trypan blue staining. The fact that diminution of the inflammatory response was greater if the chloroquine was given intraperitoneally leads the authors to suggest the possibility of a direct neutralization by chloroquine of inflammatory factors.

E. G. L. Bywaters


A 37-year-old man with lupus erythematosus was treated for 5 to 6 years (with interruptions) with daily doses of 250 to 750 mg. chloroquine and developed ocular complications in the form of deposits in the cornea, epithelium and fundus changes in the form of pigmentary foci in the macular area. While his central vision was unaffected, ring scotomata caused difficulty in reading.

L. Wittels


Of 408 patients taking a chloroquine derivative, two developed retinopathy possibly related to the drug. Of 333 who never received chloroquine, there were three with bilateral pigmented degeneration similar to the changes seen in the two treated patients.

Paul Henkind


A case of unilateral optic neuritis in a 16-year-old goldsmith is reported, after the use of chloroquine for fever. The onset was gradual and not acute as after quinine. The affected fundus had haemorrhages all over it with oedema of the retina and resembled the picture of central vein thrombosis. Vision was reduced to light perception. Although the condition appears to have improved to complete recovery after Depropanex (de-proteinated pancreatic extract), with other supporting therapy, it
should be noted that before this therapy vision had improved to 6/18 and again dropped to 6/60 with a recurrence of fever. The rationale of the therapy is not explained.

S. N. Cooper

Retinopathy following the Use of Chloroquine and Allied Substances. BUTLER, I. (1965). Ophthalmologica (Basel), 149, 204.

In 82 patients who had received chloroquine therapy for 2 to 3 years, 83 per cent. had corneal changes. There was no correlation between corneal and retinal changes. 25 per cent. of these patients had suspicious or definitely pathological pigmentation of the peripheral retina, while out of nineteen patients who had been receiving chloroquine for 4 to 5 years, 65 per cent. had retinal changes. A subnormal b-wave in the ERG is an early sign of retinal damage, as is a subnormal EOG.

Barrie Jay


Ocular complications of long-term chloroquine therapy were observed in eighteen of 95 patients so treated. This therapy was used in patients with rheumatoid arthritis, lupus erythematosus, sarcoidosis, discoid lupus, and other chronic collagen disease. Thirteen patients had curable corneal opacifications, seven had incurable retinal changes with visual loss and visual field defects. A pathological study was done on one patient.

C. McCulloch


The main aspects discussed are:

(1) General symptoms of intoxication: these include gastro-intestinal tract disturbances, nervous symptoms, and especially skin lesions: depigmentation, alopecia, pigmentation of skin and mucosae, and macular or papular eruptions.

(2) Subjective ocular symptoms: accommodative troubles, mistiness, haloes, photophobia, diplopia, and night-blindness.

(3) Corneal lesions: oedema, the well-known diverse opacities, thickening of the corneal nerves.

(4) Retinal lesions: macular (of several types, including disciform degeneration), and peripheral (usually of retinitis pigmentosa type), narrowing of the retinal arteries and pallor of the disc.

(5) Visual functions: depression of central visual acuity, scotomata (central, annular, pericentral, or peripheral), dyschromatopsia (occasionally of the red-green axis, suggesting an optic nerve lesion).

(6) Dark adaptation: normal. ERG and EOG: both depressed or absent in severe cases.

(7) Histopathology: generalized loss of rods and cones over most of the retina (except the fovea), and loss of pigment of the pigment epithelium and its phagocytosis in large round cells.

John Romano


The author examined the eyes of fifteen patients who had been taking chloroquine or a derivative. In two retinal pigmentation with field defects were found, which had developed keratopathy.

If possible, the daily dose should not exceed 250 mg, and the maximum period of continuous treatment is 18 months; after a spell, the treatment may be resumed, but ophthalmological supervision is obligatory.

G. Fenwick


Intravenous administration of sublethal doses of chloroquine to rabbits did not give rise acutely to alterations of ERG or EOG. The predominating feature of the experiments was the cardiotaxic action of chloroquine which caused paroxysmal tachycardia. Local application of chloroquine to frog or rabbit retinae caused rapid and profound alterations of the ERG.

D. F. Cole


Albino and pigmented animals were given 42 to 84 mg chloroquine phosphate per day per kg bodyweight. The ophthalmoscopic appearance, ERG, and ocular pathological changes were observed after 11 months.

Alterations of ERG were few and inconsistent but pigmented animals in the fundus were observed in pigmented rabbits given chloroquine. Albino and untreated pigmented animals did not show fundus changes or pigment deposits.

D. F. Cole


The ocular complications of anti-malarial drugs (chloroquine, hydroxychloroquine, amodiaquine) are reviewed. The now well-known manifestations: accommodative difficulties and keratopathy (reversible), and retinopathy (irreversible) are discussed, and nine cases are presented. Among the investigations leading to possible early diagnosis of the retinopathy before the irreversible stage the authors stress perimetry (papacentral, or periperal scotoma, with or without peripheral contraction), colour sense studies (tritanopia is a common early finding, all the more interesting because of its rarity as a congenital or acquired defect), dark-adaptometry, the ERG and, especially, the EOG. Any, or all of these should be performed in all patients taking large doses of these drugs for long periods.

John Romano