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**

The left atrial distensibility curves (volume-pressure relationships) in fifteen normal subjects without myocardial infarction and without left-sided heart failure were studied post mortem [at Los Angeles County Harbor General Hospital, Torrance, California]. The initial mean volume was 28.6 ml at zero pressure, and the mean volumes were 50.6 ml and 62.5 ml at 5 and 10 mm Hg, respectively. The curves were exponentially concave upward. The left atrium in normal subjects was less distensible at higher pressures. In patients above the age of eighty the volume-pressure curves were significantly shifted to the right, that is, the left atria of older subjects were more distensible from pressures of 0 to 5 mm Hg.

The left atrial volume-pressure curves studied post mortem in three patients with mitral valve lesions of pure or combined stenosis and insufficiency were different and presented an upward convexity. The initial volumes at zero pressure, 32.5, 125, and 180 ml, respectively, were four to twelve times greater than those of normal subjects, demonstrating left atrial dilatation which is to be expected in mitral valvar disease. In addition, these atria accommodated an even greater volume without the marked pressure rise seen in normal atria, thus demonstrating a property of greater distensibility not possessed by normal left atria. This ability of the atria of these patients to accommodate greater volume with little increase of pressure may be life saving because it protects against episodes of pulmonary oedema.

The left atrial volume-pressure curve in one patient with mitral stenosis and mild insufficiency in another patient with mitral stenosis, post-commissurotomy, which admitted two fingers, were concave upward similar to that in normal persons. The left atrial distensibility was also somewhat less than normal.

This study demonstrates that a quantitative estimation of mitral regurgitation by analysis of left atrial pressure tracings in patients with combined mitral lesions is unsatisfactory. [Authors’ summary]


During the period 1959-62, 171 cases of rheumatic fever were seen at the Children’s Clinic of the Dresden Medical Academy and were investigated with regard to concurrent renal involvement. Microscopic haematuria was often noted during the acute phase (98 cases), but albuminuria and casts in the deposit were found only rarely. In about one-third of the cases pathological findings in the urine persisted beyond the acute phase of the rheumatic fever. There was, however, not a single case of true acute glomerulonephritis with albuminuria, high blood pressure, oedema, and retention of waste products. It is presumed that the cause of the frequent haematuria was “focal nephritis” — or possibly interstitial inflammatory processes were at work. Treatment with amidopyrine increased the haematuria, but did not initiate it, and penicillin in conventional doses had no harmful effect on the urinary findings. In a very few patients indeed was there any residual urinary abnormality on follow up examination.

John Lorber


Three series of experiments were carried out at the Moscow Rheumatic Research Institute to elucidate the role of glucocorticoids in the development of experimental rheumatism. In the first experiment adrenal function was assessed in fourteen guinea-pigs given ten intracutaneous injections of 60 to 120 ml of various strains of β-haemolytic streptococci at intervals of 2 to 6 weeks and in six control animals which were given injections of physiological saline. Of the test animals, twelve developed shifting arthritis of the small joints of the limbs, ten developed antistreptolysin titres of 1:25 to
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1:1,500, and eleven had electrocardiographic changes. In thirteen cases the heart showed changes characteristic of an allergic reaction. The 24-hour excretion of free and combined 17-oxytocorticosteroids in the urine was determined after the 1st, 3rd, 5th, 7th, and 9th injections. In half of the test and control animals the estimations were carried out after administering 2 units of corticotrophin in order to assess the adrenal functioning reserve. It was found that initially there was a doubling of steroid excretion, with normal adrenal functional reserve, but that after the third injection the steroid excretion fell to its initial level and the functional reserve was reduced. The authors consider that in streptococcal infection there is insufficient hormonal reserve to deal with additional stress situations.

The second experiment was designed to determine whether the level of glucocorticoids in the body affected the development of experimental rheumatism in ninety white rats. All the animals underwent unilateral nephrectomy and were maintained on a high-salt diet to favour the development of an allergic reaction. The results were assessed clinically, radiologically, and histologically. It was found that the prolonged administration of cortisone in low dosage (0.5 mg. per 100 g. body weight daily for 6 weeks) caused aseptic arthritis in both adrenalectomized and intact rats, some animals also developing myocarditis and endocarditis. When cortisone treatment was combined with streptococcal infection the results were similar, but the incidence and intensity of the changes were increased. In contrast, high doses of cortisone (2.5 mg. per 100 g. daily for 6 weeks) did not cause joint or heart changes whether the animals were adrenalectomized or not, but the animals did develop a severe septic illness thought to be due to their decreased resistance to saprophytic microflora. Similarly, with doses of 1.5 to 3 mg. of cortisone per 100 g. body weight the effects of added streptococcal infection were less than with the low dosage of cortisone. It is concluded that a low serum glucocorticoid level favours the development of an allergic response to streptococci.

In the third experiment the effects of hydrocortisone and cortisol applied directly to growing connective-tissue cells (monolayer trypsinized cultures of rat fibroblasts) were assessed. It was shown that with suspensions of cortisone acetate (0.035 µg. per ml.) and hydrocortisone acetate (0.035 µg. per ml.) growth was increased by 38 per cent. However, concentrations of 12 µg. per ml. and 0.30 µg. per ml. respectively repressed growth by 40 per cent. Control solutions of progesterone and cholesterol in equivalent concentrations had no significant effect on fibroblast growth. The authors conclude that in stimulating allergic response low levels of glucocorticoid act, at least in part, directly on the connective tissue.

Kathleen M. Jones


This is a fifth paper of a series dealing with the bacteremia associated with dental procedures and its attempted prevention. It is based on a series of 178 cases undergoing single tooth extraction (33 patients), gingivectomy and scaling (47 patients), and filing of root canals (98 patients). Blood samples were taken immediately before, immediately after (0-2 minutes), and after 10 minutes. Local anaesthesia was used.

All pre-operative cultures were negative: single extractions showed positive cultures in 51 per cent., and 24 per cent. were positive at 10 minutes. This compares with 85 and 44 per cent. respectively in a previous similar series in which multiple extractions were done. Similar figures were found for gingivectomy but only 40 per cent. showed positive cultures after scaling and none after root canal filing provided the instrument was not forced beyond the apex. The authors recommend single extractions with minimal trauma for patients with valvular heart disease, with local rather than general anaesthetics. One hour before, intramuscular streptomycin 1 g. and penicillin 600,000 units should be given, and this should be repeated at 12 or 24 hrs afterwards. E. G. L. Bywaters


Epidemiology of Rheumatic Fever. (Epidemiologia de la infección reumática.) Menezes Hoyos, J. (1964). Rev. méd. mex., 44, 145. 2 figs, 5 refs.


Rheumatoid Arthritis


In order to throw further light on the relationship between the chemical changes in the serum of patients with rheumatoid arthritis and the nature and course of the disease the authors studied 154 patients selected from the Arthritis Clinic of Massachusetts General Hospital, Boston, to provide a reasonable sampling of the various syndromes and a wide span of age and duration of disease. Patients were classified clinically as having peripheral rheumatoid arthritis with or without nodules, rheumatoid spondylitis with or without small-joint involvement, rheumatoid arthritis with psoriasis, or rheumatoid arthritis with onset in childhood. A patient was considered to have spondylitis if examination revealed definite limitation of movement of the lumber-dorsal spine. The history of the patient at interview was supplemented by the hospital and clinic records. Radiographs were taken of the hands, wrists, whole spine, and pelvis including hip joints. Laboratory investigations included blood counting and determination of blood group, isohaemagglutinin titre, erythrocyte sedimentation rate (E.S.R.), serum cryoglobulin and hexosamine concentrations, and serum electrophoretic pattern; latex-fixation and cephalin flocculation tests and urine analysis were also performed.

When clinical involvement of the lumbo-dorsal spine was used for the basis for differentiating spondylitis from peripheral rheumatoid arthritis marked differences in sex incidence, age at onset, incidence of nodules and of iritis, and titre of rheumatoid factor were observed between these two groups of patients. The differences were, however, far less distinct when radiological involvement of the sacro-illiac joints was used as the criterion for distinguishing the two groups. When the clinical classification was related to the course of the disease it was observed that the course was most often unremitting in patients with nodules or with spondylitis. An acute onset was associated with a remitting course. The duration of the disease showed a significant relationship with the occurrence of ankylosis in hands and wrists as seen on x-ray examination. Duration of disease was unrelated to other clinical manifestations; for example, there was no greater incidence of nodules in those with longer than in those with shorter duration. Total duration of disease or duration of active disease was unrelated to the laboratory variables studied—for example, the latex-fixation test. A strong relationship was, however, found between the occurrence of the rheumatoid factor and the presence of nodules. The titre of the latex-fixation reaction was higher in patients whose disease ran an unremitting course and in those with advanced x-ray changes in the hands and wrists. Serum γ-globulin level was found to be related to the serum hexosamine concentration, the cephalin flocculation reaction, the E.S.R., the presence of cryoglobulin in the serum, and the titre of the latex-fixation reaction.

C. E. Quin

Sacro-illiac Joint in Rheumatoid Arthritis in Adult Females.


The radiographic changes in the sacro-illiac joints in males with rheumatoid arthritis (RA) have been extensively described by other workers. At the Rheumatism Foundation Hospital, Heinola, Finland, the authors have studied the radiographic appearance of these joints in 278 females (mean age 43.2 years) with definite or classic RA and 147 female controls (mean age 41.9 years) without inflammatory musculo-skeletal diseases. Antero-posterior views of the lower spine and pelvis were obtained, in addition to radiographs of the hands, feet, and other joints, if required, and a system of grading was adopted for evaluation.

It was found that sacro-illiac joint changes tended to be less severe if the RA had begun between the ages of 40 and 49 and more severe if it had started before the age of 20. Moderate and severe changes occurred more frequently when both peripheral and proximal joints were involved. The changes were somewhat milder in those cases which showed a negative serum reaction in the Waaler-Rose test compared with those showing a positive reaction, but not significantly so. Of the 278 cases of RA, four had bilateral fusion of the sacro-illiac joints. Altogether 102 (36.7 per cent.) of the RA patients and 24 (16.3 per cent.) of the controls showed radiographic changes in the sacro-illiac joints. The authors lay stress on the high incidence of radiological changes in the sacro-illiac joints of the control subjects.

D. Preiskel


ABSTRACTS


Still’s Disease


The ocular manifestations of this condition may occur at the time of the articular lesions, but they may also be the first sign. It is important that the eye complications be remembered, and the eyes examined by an ophthalmologist, so that the complications may be treated promptly.

J. H. Kelsey


Osteo-arthritis


The occurrence of cystic change beneath the terminal lamellae of weight-bearing bones in the more advanced stages of osteo-arthritis is reviewed. Such cysts are filled with a connective tissue which may be either fluid or fibrocartilaginous; they have a wall composed of cancellous bone in which the trabeculae have been strengthened by new bone formation. Landells’ theory of their formation (J. Bone Jt Surg., 35B, 643). Through pressure of the synovial fluid during movement following a fracture of the terminal lamella does not explain the frequent occurrence of such cysts in pairs on either side of the joint line nor the existence of a soft plug in such cysts.

It is considered that such cysts are produced by the stresses in the bones when the articular surface is irregular. A study of these stresses is made using a photo-elastic model, viewed by polarized light. The pattern of stresses seen in the models is shown to vary in the same way as does the shape of the cysts seen in osteo-arthritis. The cavity formed is seen as the effect of the gross over-stressing of the bone beneath the lamella, while the strengthening of the cancellous bone in the wall of the cyst is thought to result from a lesser degree of stress. The effect of the articular cartilage on stresses of this type is imitated by an interposed layer of softer material. The stoma is seen as a secondary formation and the plug of soft material satisfactorily explained by the reduced stresses which exist once the stoma has been formed.

A. J. Palfrey


A case is described in which osteo-arthritis of both knees followed bilateral deep vein thromboses of the lower limbs, with obliteration of the veins. It is postulated that the defective venous drainage was responsible
for the osteo-arthritis. A peculiarity of the cases resided in the presence of a bony infarct of the upper end of the tibia, deeply placed towards the marrow-cavity, and radiologically similar to the lesions seen in caiisson-disease. Three further cases are briefly reviewed.

W. T. Menke


Spondylitis


Tests of respiratory function performed on 21 patients with ankylosing spondylitis at the Veterans Administration Hospital, Hines, Illinois, showed a reduced vital capacity (V.C.) together with a raised residual volume (R.V.) and functional residual capacity (F.R.C.) compared with the findings in eight healthy volunteers. These results were in agreement with those reported by other workers. Measurement of total respiratory, lung, and thoracic compliances showed that these were, in aggregate, significantly decreased in the spondylitic patients irrespective of whether they had a low or a normal lung volume. The decreased compliances were found to correlate well with loss of chest expansion, but there was little relation between this and the duration of the disease, the degree of kyphosis, or the severity of x-ray changes, except that when radiological changes were well marked compliances were usually low.

The significance of the decreased V.C. accompanied by raised F.R.C. and R.V. is discussed. It is concluded that loss of elastic recoil of the lungs is unlikely to be the cause as this implies increased thoracic compliance, and the authors consider that the gradual stiffening of the thorax tends to occur around the "mid-point" of relaxation of the isolated bony cage rather than the "physiological" position, when some internal force is exerted by lung elasticity.

B. E. W. Mace

ABSTRACTS


Inflammatory Arthritis


The symptoms and pathology of Reiter's disease are described with particular reference to the oral manifestations, about which there still appears to be some confusion. In different series the incidence of oral lesions varies from 3 to 48 per cent. The lesions on the buccal mucosa, lips, and gingiva are usually red, slightly raised areas, varying from 1 mm. to 1 cm. in diameter sometimes surrounded by a whitish circinate line, and they resemble the changes in circinate balanitis. Small opaque vesicles or areas of glistening erythema, with a granular surface, may also occur. On the palate there may be multiple bright, small, red purpuric spots, which later darken and coalesce. On the tongue superficial erosions similar to geographic tongue may be present. Histologically, the buccal lesions closely resemble pustular psoriasis. H. J. Wallace


Gout is uncommon in women before the menopause and the association of gout and pregnancy is rare. This paper is the case report of a 36-year-old woman who was pregnant ten times and who also had tophaceous gout. The gout was labelled "primary" because there was no evidence of diseases known to cause secondary gout. The chronic pyelonephritis and renal failure present in this case were considered to be the result of gouty involvement of the kidney. A feature of the renal disease was a salt-losing state, with continuing sodium loss in the face of dietary salt restriction.

The authors have reviewed the four other reported cases of gout and pregnancy (apart from this patient who was previously reported in 1959). Of these three, three had renal disease and their pregnancies were complicated by nitrogen retention, which in two developed while the patients were taking a low-salt diet because of pregnancy toxema.

[This is an interesting case but the authors do not discuss the possible role of the renal disease in producing hyperuricemia, nor do they refer to the elevation of serum uric acid which occurs in pregnancy toxema.]

J. T. Scott


It is known that patients with gout usually excrete less urinary urate than do non-gouty subjects whose plasma urate concentration has been raised to the level found in patients with gout by acute loading with urate or its precursors. These findings have led some authors to conclude that impaired renal urate excretion is a cause of hyperuricemia in gout, but this interpretation has been challenged by others. It has been suggested that the difference in renal excretion is due to the acute loading of non-gouty subjects with urate, and data have been reported which show that gouty subjects can excrete large extraneous loads of uric acid as easily as can non-gouty subjects. The present authors, working at the University of Utah College of Medicine, Salt Lake City, have studied the renal excretion of urate in nine gouty and nine non-gouty subjects after loading with 4 g. ribonucleic acid per day for 3 days, and in five non-gouty subjects after loading with 4 to 8 g. ribonucleic acid per day for periods up to 6 weeks. The renal urate excretion of gouty patients
during control conditions has also been compared with that of non-gouty subjects who received ribonucleic acid for 3- to 42-day periods. The urate clearance, urate clearance: inulin clearance ratio, and urinary urate excretion rate were plotted as functions of the plasma urate concentration.

It was shown that these parameters gave higher values for the non-gouty subjects than for gouty patients. Study of the rate of rise of renal urate clearance and excretion with respect to the rise in plasma urate concentration in gouty and non-gouty groups before and after acute urate precursor loading revealed higher values in the non-gouty subjects. When a further comparison of the gouty and non-gouty subjects was made which was identical with the study just described except that the non-gouty subjects had been maintained at hyperuricaemia levels by ribonucleic acid ingestion before being given the 3-day load of ribonucleic acid, the results again showed higher values in the non-gouty subjects. The authors conclude that impaired renal urate excretion can be demonstrated in most hyperuricaemic patients with gout compared with non-gouty subjects with a normal blood uric acid level.

C. E. Quin

Acetyl-zoxazolamine in the Treatment of Gout. (Acétyl-
zoaxazolamine dans le traitement de la goutte.) SERRE,
30, 371. 4 figs.

Sixteen patients with established gout were treated with acetyl-zoxazolamine in doses of up to 400 mg. daily, this maximum being reached after 10 to 14 days. During the first few days of treatment colchicine and phenyl-
butazone were associated.

The effect on blood uric acid was similar to that of zoxazolamine but the action was more gradual in onset, normal blood levels being reached in about 16, as opposed to only 5 days. Equally, there were no cases of renal colic. Three patients in this preliminary series showed transient albuminuria and in one case the blood urea exceeded the normal. No other side-effects were noticed.

W. T. Menke

Chronic Lead Nephropathy: the Diagnostic Use of Calcium
EDTA and the Association with Gout. EMMERSON,

In order to test the possibility that certain renal
disorders may be the result of excessive intake of lead in
childhood, several groups of patients at Brisbane Hospi-
tal, Queensland, were given intravenously a standard dose of sodium calciumedetate (hereafter referred to as calcium EDTA) and its effect on urinary lead excretion determined. This procedure always caused an increase in urinary lead excretion, but in controls this did not exceed 0.06 mg. in 24 hours. Values in excess of this were taken to indicate an abnormal storage of lead in the tissues which might be due to childhood lead poisoning or to industrial poisoning. The five groups of patients examined consisted of:

(a) nineteen controls with no evidence of renal disease;
(b) 22 with chronic lead nephropathy;
(c) 23 with renal disease not due to lead;
(d) nine with a history of industrial lead exposure;
(e) sixteen with chronic renal failure of uncertain
causation.

Of the 22 patients in Group (b), eighteen gave a definite
history of lead poisoning in childhood, and in these the administration of calcium EDTA was followed by a marked increase in EDTA lead excretion which rose from 0.06 mg. on control days to 0.64 to 2.51 mg. In patients with previous industrial exposure to lead the control values were 0.01 to 0.25 mg. before and 0.58 to 11 mg. after the calcium EDTA infusion. Postural hypotension occurred in a few patients after the infusion, but these were receiving hypertensive drugs in the course of treatment for hypertension.

V. J. Woolley

Gout in Women. (La goutte féminine.) RYCKEWAERT,

Corticosteroid-induced Gout. (La goutte cortico-
dépendante.) DAVID-CHAUSSE, J., LENG-LEVY, J., and

Aetiopathogenesis of Gout. (Etiopatogenia de la gouta
med. Esp., 27, 27.

Clinical Studies on Gout in Japan. (Special report at the
7th Annual Meeting of Japan Rheumatism Associa-
Ass., 4, 406.

Bone Disease

Lumbar-sacral Spondylolisthesis. (Sur la spondylolisthésis
lombo-sacrée.) PIZON, P. (1963). Presse méd., 71,
2028. 3 figs, bibl.

The author analyses 700 cases examined radiologically amongst which were 39 samples of spondylolisthesis and 48 of sacrolisthesis and retrolisthesis. The horizontal displacement was measured as a percentage of the antero-
posterior diameter of the vertebal body remaining in
position. Excluding cases in which this figure exceeds
28-5 per cent. and in which abnormalities of the type
classically described may occur, one finds that in a
majority of cases there is no association with spondylolith-
sis, articular abnormalities, or abnormalities of the vertebral shape or angle of the promontary. The detectable abnormality is in the length of the pedicles of the involved vertebra, and it is suggested that there is abnormal perichondral ossification of the centre for the vertebral body and pedicles in a majority of cases. This might lead in turn in some instances to abnormalities of the anterior vertebral vessels, at the involved level. The author further notes the number of cases in which the horizontal displacement is less than 10 per cent., and in which there is usually no clinical evidence of abnormality.

W. T. Menke

Amer. J. Roentgenol., 91, 155. 6 figs, 12 refs.

Metastases in bones peripheral to the elbow and knee
are rare. This paper illustrates four examples of these
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To evaluate the skeletal changes in thyrotoxicosis the authors, at Georgetown University Hospital, Washington, D.C., examined calcium and phosphorus metabolism in fifteen patients with hyperthyroidism but without renal or cardiovascular disease, and in twelve healthy subjects without skeletal abnormalities who served as controls. The response to an intravenous infusion of calcium was the test used to evaluate the physiological status of bone tissue. The infusion, given from 9 a.m. to 12 noon, consisted of 500 ml. of physiological saline containing 10 mg. calcium per kg. body weight in the form of a 10 per cent. solution of calcium gluconate, a minimum of 600 mg. calcium being given. Urinary calcium and creatinine concentrations were estimated. Urinary calcium excretion was measured on the control days and on the day of the infusion and the amount of calcium retained in the body calculated. The thyrotoxic patients included eleven females and one male aged from 19 to 44 years and three older postmenopausal females.

Hypercalcæmia was more frequent than usual in thyrotoxicosis, a raised serum calcium level being found in six of the fifteen cases. In addition hyperphosphataemia was present in nine cases, the highest serum phosphorus level being 6-2 mg. per 100 ml. The serum alkaline phosphatase level was raised in all but one patient, the usual value being 4 to 6 Bodansky units; the authors consider this finding difficult to interpret in terms of osteoblastic activity as liver dysfunction is not uncommon in thyrotoxicosis. Only two patients showed hypercalciuria on the basis of a calcium excretion exceeding 200 mg. in 24 hours. Of particular interest were five patients with a urinary calcium excretion of 50 mg. or less in 24 hours, a lower value than is usually found in healthy subjects. Of the fifteen patients with thyrotoxicosis, twelve retained more infused calcium than the controls; osteoporosis was demonstrated radiologically in six patients, of whom three were postmenopausal.

The authors conclude that the findings are highly suggestive of increased avidity of the skeleton for calcium in thyrotoxicosis and are consistent with the frequent occurrence of osteomalacia in this condition.

I. M. Clean Baird


The patient was a 3-months-old child who died from anaemia. Optic atrophy, except for a small sector, with loss of elements in the ganglion cell layer probably resulted from pressure on the optic nerve from condensation at the base of the skull. Degeneration in limited regions of the motor nerves of the extra-ocular muscles was found.

C. I. Phillips


A 69-year-old man had a short history of miosis and ptosis; there was no response of the pupil to cocaine or adrenaline, indicating a lesion of the second neurone. The cause was hypertrophic osteophytes on the antero-lateral margins of the lower cervical vertebrae.

C. I. Phillips


Non-articular Rheumatism


The incidence of a positive family history of Dupuytren’s contracture has usually been reported as 10 per cent. though a figure of 44 per cent. has been quoted. In this survey fifty unselected patients were studied, a positive family history was obtained in 16 per cent.; a total of 832 relatives were examined and the condition found in the relatives of 68 per cent. of the propositi. The diagnosis was made in those patients in which a nodule was fixed to the palmar fascia or in which knuckle pads were present. The incidence of the contracture amongst the whole series was analysed by age and sex and compared with the incidence amongst the general population, based on published surveys from Lancashire and Victoria, Australia, and on a geriatric survey of 500 patients in Edinburgh. The condition was significantly more common amongst the relatives of the propositi than in the general population. The estimated age of onset has been studied and found to have a mode of 50 in the males and of 60 in the females. A calculation of the expected incidence amongst the relatives of the propositi has been made on the assumption that a single Mendelian dominant was involved; allowance has been made for the high incidence in the general population and for the different ages at onset. This calculation was found to
give a good fit in the males, but expression was less complete than would have been expected in the females. Though the data available were small in number they also showed a poor fit for cousins, and the possible influence of misdiagnosis was discussed. The pedigree of five families is given, and the association with epilepsy and alcoholic cirrhosis considered.  

A. J. Palfrey


This paper reviews the clinical features and laboratory findings and describes the results of arterial biopsy in 23 patients (14 male, 9 female) suffering from the clinical syndrome termed "polymyalgia rheumatica" and seen over a 2-year period at the County Hospital, Växjö, Sweden. The age at onset of the disease in these cases ranged from 55 to 76 years. The onset had been fairly acute, with pain and stiffness in the neck and proximal muscle groups of the limbs; commonly upper and lower limbs were affected simultaneously. Pain was more severe in the muscles than in the joints and was aggravated by movement. The affected muscles tended to atrophy.

All patients had general symptoms of fatigue, anaemia, and loss of weight, while many were febrile. The disease tended to be self-limiting, but could become chronic. In nine cases symptoms or signs suggestive of temporal arteritis were present. The erythrocyte sedimentation rate was raised in all patients and in fifteen was above 100 mm. in the first hour (Westergren). Paper electrophoresis of the serum showed a marked rise in the $\alpha_2$-globulin level in all cases and a slight increase in the $\gamma$-globulin fraction in only seven. The plasma fibrinogen level was above 700 mg. per 100 ml. in ten of the eighteen patients in whom this was estimated. Radiographs of the shoulders and hip joints showed periarticular deposits in the soft tissues in the shoulder region in four and around the greater trochanter in one of the 21 patients examined.

Arterial biopsy was performed on the temporal arteries in 21 patients, on the circumflex scapular artery in six, and on the perforating branch of the femoral artery in five. Histological changes were classified as sclerosis of the blood vessels (present in all cases), giant-cell arteritis (found in twelve of the 21 temporal arteries studied), and non-specific changes (found in four temporal arteries). These findings are considered to support the view that "polymyalgia rheumatica" and temporal arteritis are different manifestations of the same pathological process.

B. M. Ansell


Pararheumatic (Collagen) Diseases


The nephrotic syndrome is frequently associated with hypercholesterolemia, but the author of this paper from the Kaiser Foundation Hospital, Oakland, California, has previously described the occurrence of a normal blood cholesterol level in the nephrotic syndrome in patients with systemic lupus erythematosus (S.L.E.). After reviewing the relevant literature he now reports an additional eighteen cases of the nephrotic syndrome associated with S.L.E. of which five showed a normal serum cholesterol level (below 275 mg. per 100 ml.). In two of these five cases, which are described in detail, ultracentrifugal analyses revealed normal low-density serum lipoprotein values and serum cholesterol levels which were normal at the height of the nephrosis, when the serum albumin level was lowest, and rose slightly during steroid-induced remission.

In the eighteen cases studied there was no correlation between the serum cholesterol and albumin levels. By combining the data of personal and published cases of S.L.E. complicated by the nephrotic syndrome it was possible to compare the findings in 31 normocholesterolaemic and 25 hypercholesterolaemic cases; the only striking difference noted was the shorter survival time of the former (usually a few months). Even in the hypercholesterolaemic cases the serum cholesterol levels reported were not nearly so high as those found in the nephrotic syndrome due to other diseases.

The author concludes that the finding of a normal serum cholesterol level in a case of the nephrotic syndrome should suggest S.L.E. as the probable diagnosis.

M. Wilkinson


A consecutive series of 299 patients with systemic lupus erythematosus [seen at the Cleveland Clinic Foundation] was evaluated, and the statistical correlations with emphasis on mortality are presented. The estimated over-all survival of the group up to 11 years after diagnosis is 53-7 per cent. The life expectancy of a comparable group by age, sex, and race is 96-7 per cent. Males have a poorer prognosis than do females. Adequate corticosteroid therapy appeared to prolong the course of the disease, particularly in the first year after diagnosis. It is postulated that once a patient has survived 2 years after diagnosis, the need for steroids may be less important except in the control of subsequent obvious acute exacerbations of the disease.

[Authors' summary]


This epidemiological study of systemic lupus erythematosus in a defined area of New York City shows the
trend from 1951 to 1960 of:

(1) The annual incidence of newly diagnosed cases,
(2) The mid-year prevalence rate,
(3) The annual mortality rate.

Possible cases were ascertained by searching the records of 37 hospitals, the medical reports of the doctors in the Manhattan Groups of the Health Insurance Plan of Greater New York, and all New York death certificates on which the underlying cause of death was recorded as systemic lupus erythematosus or lupus erythematosus. In all, 71 definite cases were found in the period concerned; the date of diagnosis for each case was arbitrarily set at the time when confirmatory serological or pathological evidence was first detected. The trend rates were calculated by reference to the mid-period population and were standardized for changes in the age, sex, and racial composition of the area over the 10-year period.

The rates for early years, until about 1954, increased rapidly; this increase was judged to be artificial and was attributed to growing awareness of the disease and improving methods of diagnosis. Between 1954 and 1959 the incidence of new cases fluctuated between 10 and 15 per million and the mortality rate, which followed a course parallel to the incidence, varied between 2 and 6 per million. In contrast the prevalence rates continued to increase after 1954, although more slowly, to about 50 per million in 1959. Tables show the average annual age specific incidence of new cases and the prevalence rates, for females only, in 1959-60, subdividing the studied population into three groups—white, Puerto Rican, and non-white. Only eight new cases were diagnosed among men and most of the 58 new cases among women were first diagnosed in the age group 15 to 44 years (26 white, 13 Puerto Rican, and 10 non-white, representing an incidence of 21-5, 52-5, and 70-5 per million respectively). The authors point out that if the rates had been based only on the last 5 years of the period "when the recognition of cases was more complete" the rates would have been 34, 67, and 108 per million respectively. Of the 67 females with the disease in 1959-60, sixty were aged 15 to 44 years; the prevalence rates in this age group for white, Puerto Rican, and non-white respectively were 165, 239, and 470 per million.

During the 10-year period there were 373 deaths in the whole of New York City attributed to systemic lupus erythematosus and the distribution of the average annual mortality by sex, age, and race was similar to that reported for the morbidity rates of the survey area. For example, at ages 15 to 44 the average annual mortality rates among males were 1-6, 1-9, and 4-7 per million among whites, Puerto Ricans, and non-whites respectively; the corresponding rates for females were 9-1, 17-2, and 25-2 per million. The morbidity differences between the races in the survey area were probably real and not attributable to variations in diagnostic facilities.

The authors conclude that there was no evidence of a real increase in morbidity or mortality from systemic lupus erythematosus during the review period, though the prevalence increased steadily, probably because of earlier diagnosis and better medical care. Variations in mortality and morbidity associated with sex, age, and race were characterized (after allowance for age differences) by the highest rates among non-white females, followed decreasingly by Puerto Rican females and white females: the rates were considerably lower in males. It is suggested that further investigation of genetic and environmental influences on systemic lupus erythematosus is required.

E. A. Cheeseman


This paper from the General Hospital, Zadar, Yugoslavia, reports the results of treatment with "resochin" of seventeen patients (8 male and 9 female) with lupus erythematosus. Resochin is a proprietary preparation, tablets of which contain 250 mg. chloroquine phosphate. The series included one female with systemic changes who died after 3 months and three other patients with periodic systemic exacerbations of the disease. Clinical and routine laboratory findings in all cases are tabulated together with details of individual therapy and its results. Treatment was adapted to the severity of the case and consisted in the administration of two tablets of resochin three times daily for one to 3 weeks, followed by one tablet three times daily for 2 to 5 months and thereafter one tablet twice daily.

Results are classified as "very good" in ten cases and "good" in four; only "slight improvement" was noted in one case and there was no effect in two (including the fatal case). Relapse occurred within 18 months in five of the improved cases. Side-effects were few and consisted of diarrhea in one case and generalized rash in one, both of which cleared after cessation of treatment. Three other patients complained of gastric discomfort and headache, and these symptoms ceased when the tablets were taken after meals.


The various types of extracellular haematoxylin bodies found in lupus erythematosus (L.E.) cell preparations and their significance in relation to clinical diagnosis are described in this paper from the Los Angeles County Hospital and the University of Southern California. Haematoxylin bodies are basophilic extracellular aggregations of amorphous or ovoid shape which occur either alone or accompanied by typical L.E.-cells. Approximately 14,000 L.E.-cell preparations from some 3,000 patients were examined, 403 of these patients had haematoxylin bodies on at least one occasion. Only patients who had haematoxylin bodies but did not show L.E.-cells are considered in this report. Three varieties of haematoxylin body are described—a homogeneous round type (resembling the L.E.-cell inclusion body), a "lacy" (lace-like) round type, and an amorphous type. Lacy and
amorphous bodies were found in many conditions and also in preparations from healthy controls.

It was found that extracellular haematoxylin bodies of all three types, in the absence of L.E.-cells, were present on at least one occasion in the preparations from 358 patients, of whom 258 (and one additional “abnormal” control) had homogeneous round haematoxylin bodies. With phase-contrast microscopy L.E.-cells were sometimes observed in preparations from leucocyte suspensions which after they had been fixed and stained showed only haematoxylin bodies.

The authors consider that the finding of homogeneous round haematoxylin bodies is a good indication of the existence of rheumatic disease [contrary to general belief]; they suggest that L.E.-cell formation may occur directly within a single neutrophil without a phagocytic stage, and that haematoxylin bodies may be the end-product of the rupture of L.E.-cells during fixation and are not merely composed of unphagocytosed material, as is generally believed.

M. Wilkinson


Although Hargreaves described the cell phenomenon associated with systemic lupus erythematosus (S.L.E.) in 1948 and a considerable volume of work has appeared in the literature subsequently, there are still some problems which require solution. Perhaps the most important is the question of specificity, because the presence of L.E.-cells has been reported in a number of diseases. At the first Medical Clinic of the University of Szeged, Hungary, the authors have carried out routine searches for L.E.-cells in all cases of so-called collagen disease of indeterminate character since 1954; since 1957 this study has been extended to include cases of rheumatoid arthritis (RA), discoid L.E., and rheumatic fever, and since 1959 to include cases of Sjögren’s disease, epidemic hepatitis, chronic hepatitis, cirrhosis of the liver, haemolytic anaemia, thrombocytopenia, leucopenia, chronic nephritis, and Raynaud’s syndrome. Altogether, they have carried out 3,100 searches for L.E.-cells in 1,500 cases; for routine clinical use the method described by Zinkham and Conley (Bull. Johns Hopk. Hosp., 1956, 98, 102; Abstr. Wild Med., 1956, 20, 172) gave the best results.

In 48 of the 1,500 cases positive L.E.-cell findings were obtained, and in 39 of these the diagnosis of S.L.E. was confirmed by the clinical picture and course, the laboratory data, and the response of the patient to corticosteroid therapy. Consistently negative results were obtained from four patients who had been under observation for many years as suspected cases of S.L.E.; one subsequently developed typical discoid L.E. skin changes and classic rheumatoid involvement of joints. Negative results were obtained in a further ten cases of suspected S.L.E. L.E.-cells were repeatedly found in ten of the 178 cases of RA studied; clinically, these patients could not be differentiated from the others in that group, though one of them developed skin changes typical of RA. The authors state that there seems to be a close connexion between discoid L.E., Sjögren’s syndrome, and S.L.E.

No false positive results were obtained and it is considered that the finding of L.E.-cells has absolute diagnostic value. However, mistakes may arise if a pseudo L.E.-cell, or “tart” cell, is mistaken for a true L.E.-cell. If pseudo cells are found the test should be repeated on at least three occasions. A single examination is of no value and the more frequently the search is carried out, the more likely is a positive result to be obtained. Neither corticosteroids nor chloroquine seem to influence the appearance of L.E.-cells, and the presence of the latter, or their number, bears no relation to prognosis. S.L.E. may present in a number of guises, such as nephritis, carditis, sepsis, or haemolytic anaemia, and a search for L.E.-cells in such cases may therefore lead to the correct diagnosis.

D. Preisig


This is the third pair of identical twins recorded both having systemic lupus erythematosus. In the first-seen Negro girl, a butterfly rash appeared at the age of 15. This was followed by migratory and later persistent polyarthritis, pleurisy, pericarditis, lymphadenopathy, E.S.R. 64 mm./hr, albumin/globulin ratio 2.5/4-1 g. per cent., and proteinuria. L.E.-like cells were seen in the blood and an antinuclear factor test was strongly positive. Treatment with prednisone until age 19 was complicated by pancreatitis and diabetes. A renal biopsy showed wire loops.

Her twin developed polyarthritis at age 19 with periorbital oedema, lymphadenopathy, and pericarditis with fever, E.S.R. 47 mm./hr, proteinuria, albumin/globulin ratio 2.2/4-6 g. per cent., positive L.E.-cell test, and strongly positive antinuclear factor test, positive direct Coombs test, and focal glomerulitis in a renal biopsy consistent with L.E.

The evidence for homozygosity consisted of visual similarity and five matching blood and saliva types. Two male sibs, the mother, and a baby son were also investigated with mainly negative results. One of the sibs showed a positive latex test.

E. G. L. Bywaters


Two patients with generalized scleroderma in whom vascular changes of the retinal arteries could be observed are reported. In the first, who had been suffering from the disease for one year and lost sight in his left eye (the right had had weak functions owing to aphakia after traumatic cataract), 4 weeks before his death from renal complications cotton-wool exudates were found in both eyes with oedema of the macula in the left. The post mortem examination of the eyes showed cytoid bodies in the exudative foci and desquamation of the endothelium of the central retinal artery. Biopsy of the superficial
temporal artery revealed necrosis of the media. All this points to a primary (not nephrogenic) affection of the retinal vessels starting in the intima as a basic process of scleroderma. In the second case, that of a 34-year-old man, a branch thrombosis in one eye was observed with a field defect but intact central vision, and biopsy of the thickened superficial temporal artery demonstrated strongly developed concentric hyperplasia of the intima and plaque formation which was out of keeping with the age of the patient and must be ascribed to the general condition.

L. Wittels


The oral manifestations of circumscribed scleroderma (morphaea) and of systemic sclerosis are described. The former may be complicated by hemi-atherofy of the face and by false ankylosis of the temporomandibular joint. In systemic sclerosis, painful induration of the tongue and gums may occur. The induration of the tongue may cause teeth previously inclined to come into the vertical or even lingual position, resulting in malocclusion. Systemic sclerosis may also cause gross restriction of opening of the mouth with resorption of alveolar bone. There may also be marked thickening of the peri-odontal membrane, especially in the molar region.

H. J. Wallace


Although scleroderma (systemic sclerosis) is known to involve a number of viscera, only four published reports have mentioned hepatic involvement as an associated feature, and then only briefly. For this reason the authors report in detail the eight cases of serious liver disease found among 727 cases of scleroderma seen at the Mayo Clinic, Rochester, Minnesota.

The disease was of long standing in all cases and in two it had been present for 37 and 26 years respectively. All eight patients had Raynaud’s phenomenon and two had oesophageal scleroderma without skin changes. In all cases the erythrocyte sedimentation rate was high. The liver was examined at necropsy in one case and needle biopsy of the liver was performed in four others. Postnecrotic cirrhosis was seen in two cases, chronic cholangiolihepatic hepatitis in one, and hepatitis of doubtful type in two. The authors point out that the pattern of change seen in other affected organs—fibrosis and loss of parenchyma—is similar to that occurring in the liver, but the low incidence of cirrhosis in the present series “hardly suggests a relationship between the diffuse sclerotic process and the chronic hepatic disease”, although this is not ruled out.

E. G. L. Bywaters


The authors describe the history of periarteritis nodosa and its general pathological anatomy. The eye findings—corneal ulcers, necrotizing scleritis, and the fundus findings—are discussed. The authors then discuss the pathogenesis of the eye findings in this disease.

Walter Mayer (Amer. J. Ophthal.)


Description of the course of retinal complications in acute dermatomyositis which developed in a 27-year-old female during the fifth month of pregnancy. The patient was treated from the sixth month with depot ACTH and in the eighth month she was delivered of a healthy child. The skin and particularly the muscle symptoms improved steadily and in parallel the changes in the fundus improved so that after 9 months' treatment the retina was opthalmoscopically healed without sequelae. The report is illustrated by two fundus photographs.

M. Klima

Two patients with undetermined collagen disease are described. In both there were distinct signs of intestinal malabsorption, and a peroral small-intestinal biopsy disclosed changes characteristic of non-tropical sprue. In the patient with generalized muscle disease there was a striking increase in the blood level of various muscle enzymes, in particular of creatine phosphokinase.

[Authors' summary]


This paper describes two patients with fibrocystic disease, having severe pulmonary involvement, who showed clinical and radiographic evidence of pulmonary hypertrophic osteo-arthritis. Although there is only one other such case recorded in the English literature, the authors feel that this complication of cystic fibrosis is not as rare as this might suggest. Radiographic evidence of the disease, in the absence of symptoms, was found in three out of eighteen other children with severe pulmonary manifestation.

A. Garner

Fibrinolysis and the Collagen Diseases. (Fibrinolisi e malattie del collagene.) COCCONI, G., and MISSALE, G. (1964). Ateneo Parmense, 34, 63. 1 fig, 35 refs.


Connective Tissue Studies


Certain established lines of mouse fibroblasts maintained serially in culture for nearly 100 generations are shown to be still capable of producing large quantities of collagen, identifiable by its appearance under the electron microscope and by hydroxyproline assay. The capacity for collagen formation is greatest when the cells are allowed to grow into a multilayer and remain without transfer.

J. A. Chapman


Immunology and Serology


The modification of the Waaler-Rose test described in this paper from the State University of New York, Buffalo, was formulated in order to simplify the performance of that useful test so that it could be used as a bedside slide test. Formalinized sheep erythrocytes [although rather laborious to prepare] have on completion various advantages; thus they retain antigenic sites available to combine with rabbit antiserum, they have a "pattern agglutination" due to non-specific heterophile agglutinins which is easily distinguishable from true agglutination due to a rheumatoid factor in a slide technique, and there is no appreciable loss of activity during preservation at 4°C for at least 2 months.

An evaluation was therefore carried out in order to compare this new slide technique with the standard Waaler-Rose test, the sera tested including 109 selected as already showing positivity by the latex test (Hyland slide technique) and 319 syphilitic sera sent in for serological testing. Assuming a positive Waaler-Rose titre to be 1:40 or more, there were in the first group 75 positive reactions by the standard test and 74 by the authors'
slide test, while in the second group there were 304 negative sera by the standard test compared with 311 by the slide test. A comparison of the formalinized cell slide test with the latex slide test gave closely similar findings, but as in most comparative series the formalinized cell slide test showed a higher specificity, whereas the latex test had the higher sensitivity. No attempt was made to evaluate the clinical value of the new slide test, since the standard Waaler-Rose test has been extensively tested in this respect on many previous occasions.

Harry Coke


At Massachusetts General Hospital, Boston, a series of 66 cases of definite rheumatoid arthritis were studied clinically and serologically for a period of 2 to 2½ years. Clinically, an assessment of disease activity was made on a predetermined protocol based on degree of acute articular involvement, effusion, nodules, morning stiffness, fatigue, fever, weight loss and erythrocyte sedimentation rate. Serologically, the latex-fixation test was used to assess both the titre of agglutination as well as of the thermolabile inhibitor factor occurring as a prozone in a serum containing agglutinating rheumatoid factor.

An initial examination of the reproducibility of the serological results led the authors to conclude that a change in titre of three tube dilutions in the rheumatoid factor agglutination was necessary in order to be considered significant in the titre range of 1:160 to 1:5,120, while a four- or five-tube dilution change was required for the higher titres. The thermolabile inhibition was always reproducible. The correlated data obtained from examination of 450 samples of serum from these patients showed that a direct relationship between disease activity and falling or rising titres in the latex fixation test could not be demonstrated. Temporary remissions occurred in eight patients who had latex test titres below 1:5,120 and varying degrees of thermolabile inhibitor. No remissions occurred in patients with high titres and no inhibitor.

[No mention is made, however, of the methods of treatment employed during the 2½ years of observation.]

Harry Coke


At the New York Hospital-Cornell Medical Center and the New York Veterans Administration Hospital, the authors have investigated the finding previously reported by Boyles (Blood, 1959, 14, 1063) that latex particles of sharply-defined size could substitute for platelets and brain cephalin in thromboplastin generation and thus possessed Platelet-Factor-3 activity. Polystyrene latex particles of diameters ranging from 0.088 to 2.64 µ were suspended in a detergent (composition unknown) in concentrations ranging from 3 to 10 per cent. of solids. Before use the particles were washed once in imidazole-buffered saline (I.B.S.), centrifuged at 10,000 r.p.m., and resuspended in I.B.S. or serially diluted directly in I.B.S. The Platelet-Factor-3 activity of latex particles was assessed by testing with their activity, with or without previous incubation with plasma, in the following systems:

1. Recalified clotting time;
2. Thromboplastin generation test (T.G.T.);
3. Product-I substrate time (Product-I is prepared from the serum and adsorbed plasma of the T.G.T. and is used to accelerate the recalified clotting time of normal platelet-poor substrate to which latex particles have been added as a platelet substitute);

When particles of 0.188 µ at a concentration of 2.6 per cent. were used, the results showed clearly that the particles developed Platelet-Factor-3 activity only when previously incubated with plasma and that without incubation such activity was absent.

The authors postulate that an interaction occurs between the particles and some plasma constituent which is consumed during the process. The nature of the plasma factor is uncertain, but it is heat-labile, not completely adsorbed by aluminium hydroxide, and inhibited by ethylenediamine tetraacetic acid. Untreated latex particles cannot be substituted for platelets in coagulation tests.

J. L. Markson


Serum potassium levels can be accurately determined by flame photometry, but circumstances often delay or preclude such determinations. Selective precipitation of potassium can be obtained with sodium tetraphenylborate (TPB), and this forms the basis of a simple test for the rapid detection of hypokalaemia or hyperkalaemia reported here from Los Angeles County General Hospital and California College of Medicine. A buffered solution of TPB is used, 2 µl of which is mixed with 2 ml serum and centrifuged. The resulting precipitate of potassium TPB is then resuspended in 0.2 ml of the buffered TPB solution and an aliquot of suspension drawn into a uniform-bore microcapillary tube (1.4 mm. inside diameter) to a height of 60 mm. The tube is then flame-sealed and centrifuged for 2 minutes, when the height of the column of sediment is measured to the nearest 0.1 mm. Comparison of the results obtained with this method (in mm.) with those obtained by flame photometry (in mEq. per litre) on the same sera showed a close correlation and enabled an equation to be derived whereby precipitate column measurements could be converted into serum potassium concentrations.

H. Lehmann


The authors at the John Curtin School of Medical Research, Canberra, has studied the part played by auto-antibodies in the normal mechanism of inflammation.
In view of the similarity of the local humoral and cellular effects in the skin after cell injury to the effects of intra-
dermal injection of soluble antigen in an immunized animal, the occurrence of autoantibodies to skin was
studied in experiments on rabbits. Filtered saline extracts of rabbit skin were used as the antigen; sera from
twenty rabbits were tested by means of the tanned ery-
throcyte haemagglutination and complement-fixation
tests for the presence of autoantibodies. All serum
specimens gave a positive result with both techniques;
difficulty was encountered with the tanned erythrocyte
test owing to the occasional spontaneous agglutination of
the tanned cells in the presence of the skin extracts.
From the results of suitable control experiments it was
considered that the findings could be attributed to the
presence of specific autoantibodies. The reaction was
noted to be non-autospecific, since the serum from any
healthy rabbit reacted not only with its known skin com-
ponents but also with the skin from other rabbits.
Further experiments demonstrated the absence of auto-
antibodies against skin in newborn rabbits and in rabbits
1 and 2 weeks of age, while the sera of some 3-week-old
rabbits gave a positive reaction though frequently with
a relatively low titre; at 6 weeks of age the rabbits had
normal adult levels of antibody.

The author suggests that these results could indicate
that in normal rabbits damage to skin cells with release
of cell components might lead to the formation of an
antibody-antigen complex in the vicinity of the injury.

The effect of antigen-antibody interaction in the plasma
could lead to the production of pharmacologically active
substances, including the chemotactic principle respon-
sible for polymorphonuclear leucocyte migration. It is
suggested that the inflammation which occurs after cell
injury is the consequence of an autoimmune reaction and
that a degree of autoimmunity is present in healthy
animals.

R. D. Barnes

Haemochromatosis and Arthritis. Schumacher, H. R.
The author describes two cases of arthritis in associa-
tion with haemochromatosis which he personally ex-
amined. In both cases many of the clinical features of
rheumatoid arthritis were present, but the response to
the latex fixation test was repeatedly negative. A further
analysis of the records of the Wadsworth Veterans
Administration Hospital, Los Angeles, revealed thirty
cases of haemochromatosis. Of these thirty patients,
seven had transfusion haemochromatosis but no arthritic
complaint; among the remaining 23 there were six with
significant osteoporosis, ten with degenerative arthritis
of the spine, and five with peripheral arthritis. The
distribution was significant—that is, involvement of
proximal interphalangeal and metacarpophalangeal joints
—in two cases only. Haemosiderin deposits were re-
ported in the synovia in both cases, and the author
suggests that the direct effect of iron on one of the articu-
late tissues is a likely explanation of the arthritis. In
discussing the findings of others, however, he has to
admit that the degree of synovial haemosiderin deposition
in his series did not differ noticeably between the arthritic
and the non-arthritic cases.

[The abstracter considers that the association could be
due to chance, especially since one of the author’s patients
had a strong family history of haemochromatosis and
since the response to the latex test is not always positive
in long-standing, non-active cases of rheumatoid arthritis.]

R. E. Tunbridge

Serum Haptoglobin in Disease. Owen, J. A., Smith, R.,
20 refs.
The pathological and diagnostic significance of changes in
the plasma or serum concentration of haptoglobin has
been studied at St. Vincent’s Hospital, Melbourne. The
serum haptoglobin levels in 152 healthy subjects (mean
93 mg per 100 ml.; range 10 to 220 mg per 100 ml.) were
measured chemically by the method of Smith and Owen
(Biochim. J., 1961, 78, 723) and compared with those in
patients with various clinical conditions.
An increase in the mean haptoglobin level per 100 ml.
of serum was found in seventeen cases of acute infection
(321 mg per 100 ml.), twelve of chronic infection (255
mg.), seven of rheumatoid arthritis (253 mg.), six of lupus
erythematosus (143 mg.), 54 of carcinoma (216 mg.), 64
of lymphoma, leukaemia, or myelomatosis (147 mg.),
61 of biliary obstruction (190 mg.), three of acute nephritis
(168 ml.), 21 of chronic nephritis (173 mg.), fourteen of
pyelonephritis (217 mg.), three of ulcerative colitis (330
mg.), 22 of arterial disease (161 mg.), five of acute rheu-
matic fever (486 mg.), and forty after myocardial infarc-
tion (213 mg.). Decreased mean haptoglobin levels per
100 ml. of serum were observed in 24 cases of haemolytic
disease (17 mg.), 25 untreated megaloblastic anaemia (26
mg.), and in certain cases of hepatocellular disease. In
most disease categories the range of values was very wide.
The authors conclude that the serum haptoglobin level
is of limited value only as a diagnostic aid in assessing
individual patients, but is more useful for distinguishing
between patients with hepatocellular jaundice and those
with biliary obstruction. Repeated serum haptoglobin
estimations offer a method of following the activity of
such diseases as tuberculosis, rheumatoid arthritis, sys-
temic lupus erythematosus, and ulcerative colitis.

J. E. Page

Serological Abnormalities in Patients with Liver Disease.
Bouchier, I. A. D., Rhodes, K., and Sherlock, S.
The authors at the Royal Free Hospital, London, have
studied the frequency with which antinuclear factors and
other autoantibodies occur in the sera of patients with
various types of liver disease. Tests for the detection of
L.E.-cells and antinuclear factors (ANF), the sheep-cell
agglutination (SCAT) and slide latex tests for rheumatoid
factors, and the tanned-erythrocyte agglutination test for
thyroglobulin antibodies were performed on the sera of
116 patients with liver disease, 104 of them with cirrhosis
(10 alcoholic, 38 "juvenile", 12 primary biliary, and 44
cryptogenic) and twelve with viral hepatitis.

An increased incidence of positive reactions to the
SCAT and latex test for "rheumatoid" factors compared
with the general population was found, most marked in
patients with juvenile cirrhosis (21 and 53 per cent. respectively) and primary biliary cirrhosis (33 and 42 per cent.). These rates were much higher than those in alcoholic cirrhosis (10 and 30 per cent.) or viral hepatitis (8 and 17 per cent.). A high incidence of antinuclear antibodies (42 per cent.) was found in patients with juvenile cirrhosis, though in the majority of sera these occurred in low titre. There was no apparent clinical difference between patients in whom antinuclear factors were found and those in whom they were not. There was also an increased incidence (10 per cent.) of positive titres for ANF in patients with cryptogenic cirrhosis. In only six of the 38 cases of juvenile cirrhosis were L.E.-cells present; no positive results were found in the other groups. The incidence and titre of thyroglobulin antibodies differed little from those found in normal subjects.

The authors discuss the significance of their findings and conclude that they are a reflection of the hypergammaglobulinaemia of liver disease. The positive results in the ANF test they consider to be an indication of abnormal immunological activity which they suggest may be a response to liver damage or an expression of an underlying, possibly genetic abnormality. A. E. Reed


Biochemical Studies


A specific spot observed by one-dimensional ascending paper chromatography has been found in some patients with rheumatoid arthritis, rheumatic fever, lupus erythematosus, scleroderma, and dermatomyositis. It has tentatively been identified as 2,5-dihydroxyphenylpyruvic acid. Urinary output was found to reflect clinical severity. Urinary and plasma tyrosine, already increased in these patients, was further increased by the oral administration of tyrosine, which was thought to aggravate the clinical symptoms; while the converse effect was obtained with low phenylalanine-tyrosine diets. [Biochemical procedures are described in detail but clinical data are deficient.] J. T. Scott


Using Amberlite-treated serum to which measured quantities of ions had been added, it is shown that potassium, magnesium, phosphorus, sulphate, and protein have no effect on calcium emission in the flame photometer. But sodium increases the emission and the effect is linear. Evidence is presented that accurate determinations of serum calcium can be made with the Coleman model 21 flame photometer provided that a standard containing protein is used, and a correction factor of 0.018 mEq/litre of calcium per mEq/litre of sodium differential between the standard and test samples is applied. J. Ball


Although it is not possible to state an absolute age for primary and secondary osteones in a histological section of bone, it is possible to place them in order of age by their particular relationship to one another. The age changes in the concentration of inorganic substances in bone are reviewed: the concentration increases with age and there is a gradient in each osteone so that it is high centrally and falls towards the periphery, but there is a high concentration at the reversal line at the margin of the osteone. The concentration of organic substances is studied by contact microradiography of decalcified frozen sections and of similar sections treated with phosphating acid, and by carbonization of undecalcified sections. These methods show that in young osteones the concentration is low in the reversal line and high in the rest of the unit, with a falling gradient to the periphery; in older osteones the concentration is comparatively

Adrenocortical function was studied in three groups of patients:

1. 68 healthy volunteers;
2. 28 hospital patients convalescent after various illnesses;
3. 33 patients who were severely wasted as a result of different chronic illnesses (but excluding patients with illness of endocrine origin).

To assess adrenocortical function the following were determined:

- Urinary excretion of 17-ketosteroids (17-KS) and of 17-hydroxycorticosteroids (17-OHCS);
- Effect on steroid excretion of administration of ACTH;
- Resting plasma cortisol level;
- Clearance rate of exogenous cortisol; and the response of the plasma cortisol level to insulin-induced hypoglycaemia.

There was no difference between Group 1 and Group 2 (the control groups) in the basal urinary excretion of 17-KS and 17-OHCS, but the urinary response to ACTH was considerably poorer in the hospital convalescent patients than in the healthy volunteers, an observation which, in the authors' view, suggests that care should be exercised in the selection of convalescent patients as controls in an investigation of this kind. The chronically ill, malnourished patients showed abnormalities of adrenocortical function characterized by a low urinary excretion of 17-KS, an impaired response of urinary 17-KS and 17-OHCS levels to ACTH, and a delayed rate of clearance of plasma cortisol. However, the excretion of 17-OHCS was not impaired and the resting plasma cortisol level and the response to hypoglycaemic stress were normal. With improvement in nutrition there was a return towards normal in the responses, indicating that malnutrition was the cause of the changes in steroid metabolism. It is concluded that the effect of malnutrition falls principally upon the enzymes concerned with steroid metabolism in the liver and response to ACTH stimulation in the adrenal cortex. F. W. Chittaway


The blood level of corticosteroids is normally controlled by a feed-back mechanism operating via ACTH production by the pituitary, so that raised levels of corticosteroids suppress the secretion of ACTH and vice versa. The extraordinary speed with which the pituitary responds to a change in blood level of corticosteroids has been demonstrated by this work from St. Mary's Hospital. One mg. dexamethasone was infused continuously over a period of 3 hours into a number of normal controls and the blood level of cortisol determined fluorimetrically. The expected fall began almost immediately and continued to decline exponentially.

Despite virtually complete blocking of cortisone production by dexamethasone infusion, stress in the form of hypoglycaemia resulted in a rapid return of cortisol secretion and hence presumably of ACTH production in the face of continuing dexamethasone infusion. L. E. Glynn


This abstract from the Rheumatism Research Unit at Sheffield describes the results obtained by gas chromatography applied to the study of corticosteroid metabolism. Single peaks were found for cortisol, cortisone, prednisone, and prednisolone, and peaks with identical retention times for the corresponding 17-ketosteroids obtained by bismuthate oxidation. Easily measurable peaks were similarly obtained from the cortisol region of a paper chromatograph of an ethyl acetate extract of a 4-hour specimen of normal urine. When material more polar than cortisol on the paper chromatograph was used, 17-ketosteroids could be identified corresponding to 6β-hydroxy-cortisol, 6β-hydroxy-cortisone, 20α-hydroxycortisol, 20α-hydroxy-cortisone, tetrahydro-cortisol, and tetrahydro-cortisone.

It is apparent even from this very preliminary communication that gas-chromatography will soon enormously expand our knowledge of steroid metabolism, both normal and pathological. L. E. Glynn


The authors describe a long series of animal experiments designed to elucidate some of the actions of corticosteroid hormones with particular reference to the distinction between primary and secondary metabolic effects and the relation of metabolic to anti-inflammatory actions. They conclude that steroids alter rates of metabolism of amino acids, proteins, and fat primarily by exerting inhibitory effects on glucose metabolism. Anti-inflammatory effects also appear to be directly related to inhibition of glucose metabolism. Secondary metabolic effects of exogenously administered adrenocortical steroids (effects on amino acid and fat metabolism) can be prevented by administration of glucose, but primary effects (increased plasma and urinary glucose and glycogen concentrations) are accelerated. The cellular and enzymatic mechanisms of primary steroid action remain unknown. J. T. Scott


Seven subjects, four men and three women, were studied at 1,000 m. above sea level, and again after transportation by helicopter to a height of 4,333 m., where they
remained for 23 days. Adrenocortical function was assessed by the urinary excretion of 17-hydroxy-corticosteroids, 17-oxosteroids, pregnanediol, and pregnanetriol, and by the level of circulating eosinophils. An attempt was made to measure change in emotional activity by means of the palmar sweat index (PSI) which is obtained by counting the number of active sweat glands in a given area of finger pad. The numerous results, clearly expressed in five tables and two figures, show that the increased adrenocortical activity present during the first 24 hours has largely returned to the previous level by the 5th day, that excretion of pregnanediol and pregnanetriol is unchanged, and that the PSI became progressively lower throughout the stay at high altitude. In view of the early return to normal of adrenocortical activity, the latter is probably the result of emotional not hormonal influences.

L. E. Glynn


In a previous paper from the Children's Hospital Medical Center, Boston (Green and others, Amer. J. Dis. Child., 1960, 100, 365; Abstr. Wild Med., 1961, 29, 266) changes in the serum protein pattern in patients with cystic fibrosis were described. In the investigation now reported the authors have studied the distribution of carbohydrate bound to proteins in the serum of 143 patients with cystic fibrosis. Paper electrophoresis was used and staining was carried out by a modification of the periodic-acid-Schiff method (Green and others, J. Lab. clin. Med., 1960, 55, 158). The patients were evaluated clinically and points awarded on the basis of general activity, physical findings, nutritional status, and radiographic appearances in the chest.

It was found that as the patients' condition deteriorated the proportion of the protein-bound carbohydrate present in the $\alpha_1$-globulin fraction showed a marked and progressive increase, although the absolute and relative amounts of $\alpha_1$-globulin in the serum underwent only a slight increase. Both relative and absolute amounts of $\gamma$-globulin in the serum increased with the severity of the disease, but the proportion of bound carbohydrate in this fraction was almost unchanged. A similar increase in the $\gamma$-globulin fraction occurred with age. There was a gradual reduction in the albumin fraction as the clinical rating worsened, and a corresponding reduction in the proportion of albumin-bound carbohydrate. The values for the other serum protein fractions showed no significant change.

The carbohydrates bound to serum proteins are mannose, galactose, fucose, acetylgalcosamine, and neuraminic acid. Elevation of the serum total protein-bound carbohydrate level occurs with age and in pregnancy and in all pathological states in which there is tissue destruction, regeneration, or inflammation. Except in macroglobulinaemia and certain malignant haematological conditions this rise in the total protein-bound carbohydrate level affects all the carbohydrates indiscriminately, but their distribution among the various protein fractions may be altered. Generally speaking an increase in serum protein-bound carbohydrate level is usually associated with an increase in the $\alpha_1$- and $\alpha_2$-globulin fractions, which are normally rich in carbohydrate, but in pulmonary tuberculosis there is an increase in the $\gamma$-globulin fraction with a reduction in its carbohydrate content. The authors' findings show that in cystic fibrosis significant correlations exist between the clinical findings and the distribution of protein-bound carbohydrate, and this is of particular interest in this disease, in which the production of glycoprotein by the mucus glands is abnormal. However, they emphasize that the significance of their observations requires further elucidation.

William H. S. George


Joint disease has been induced in animals by injecting oil and water with adjuvant derived from tubercle bacilli. The joint histology resembled that of Reiter's disease and rheumatoid arthritis, and some animals developed eye, genital, and skin lesions. Prior injection of endotoxins or current injection of protein can inhibit the response.

J. H. Kelsey


In the Department of Metabolic Disease Research of the Upjohn Company, Kalamazoo, Michigan, the authors have studied the ulceration induced in the stomach of rats by administering prednisolone subcutaneously in doses of 0.5 to 10 mg. per day during a 4-day fast. Control animals were given injections of the vehicle only. In order to facilitate the counting of the ulcers each rat was given 30 mg. of ferric chloride in 2 ml. of water by stomach tube once hour before being killed. After death the stomach was dissected out, opened, and immersed in a 2 per cent. acid solution of potassium ferrocyanide, when an intense Prussian blue reaction developed in the necrotic bases of the ulcers, making them easy to distinguish. Sections of the mucosa were also stained by various methods, including the periodic-acid-Schiff method for mucus.

In the control animals no ulcers were found in the glandular portion of the stomach after 4 days' starvation. In contrast, in the prednisolone-treated rats "punched-out" ulcers 0.5 to 5 mm. in diameter were found scattered all over the glandular mucosa except that of the antrum. The incidence of ulceration was related to the dose of prednisolone; thus two out of ten rats given 1 mg. of prednisolone per day developed ulcers, the average incidence for the whole group being 0.8 ulcer per stomach, whereas all of ten given 10 mg. a day developed ulcers, with an average of 17.1 per stomach. Each ulcer was surrounded by a halo of Prussian blue which was shown microscopically to correspond with a zone of actively regenerating mucus glands. Otherwise there was a marked reduction in the amount of intra- and extra-glandular mucus in the corpus of the stomach in the treated animals compared with the controls, though no
such depletion was seen in the antrum. The histological features of the ulcers and the rest of the stomach are detailed and illustrated, and are compared and contrasted with the findings in human stomachs with steroid ulcers.

On the basis of their findings the authors suggest that the gastric mucus normally protects the epithelium from peptic digestion and that the administration of prednisolone reduces the production of mucus (except in the antrum) and renders the mucosa susceptible to ulceration. The zone of regenerating glandular cells around the ulcers is thought to be a healing phenomenon.

In a review of the literature the authors find that the reported incidence of peptic ulcer in patients treated with corticosteroids varies widely, from 0 to 31 per cent., depending largely on whether the individual author has specifically looked for ulceration. It is stressed that steroid ulcers may be symptomless and therefore missed.

M. J. Smith


Inhibition of Protein Denaturation by Antirheumatic or Antiphlogistic Agents. MIZUSHIMA, Y. (1964). Arch. int. Pharmacodynam., 149, 1. 7 refs.


Rate of Escape of Radioactive Substances from the Joint Cavity. (Únik některých radioaktivních látek z kloubní dutiny.) TESÁREK, B., and KOLÁR, M. (1964). Čas. Lék. čes., 103, 545. 2 figs, 8 refs.


Therapy


Postulating that the pregnancy remission of rheumatoid arthritis might be due not to corticosteroid hormones but to the negative calcium balance consequent upon foetal demands for calcium, the authors have given intravenous sodium ethylene diamine-tetra-acetic acid, a chelating agent, to patients with rheumatoid arthritis. They claim, with no further details, that of twelve patients so treated six showed dramatic improvement and five increased physical activity and freedom from pain. A further patient, a girl of ½ with Still’s disease, improved in hospital while receiving the drug subcutaneously and there are before-and-after photographs to prove it.

J. T. Scott


This non-familial case of autosomal recessive Hurler’s syndrome with corneal clouding was treated with steroids from 7 months of age until her death with cardiac failure (confirmed at post mortem) at the age of 38 months. A mediastinal mass presumed to be thymus decreased in size: liver and spleen regressed only on high dosage (100 mg. cortisoline equivalent per day). Corneal clouding showed no change. Psychometric examination showed improvement. Chondroitin sulphate B was the only polysaccharide found in the urine and the amount excreted changed from a mean of 19 mg./24 hrs (range 7 to 27 mg.) on 6 days at a dosage level of 37.5 mg. steroid, to a mean of 26 mg./24 hrs (range 10 to 44 mg.) on 7 days at a level of 100 mg. cortisoline equivalent. Both these levels were considerably lower than two estimations at 7 months of age before the steroid was started (106 and 87 mg./day).

E. G. L. Bywaters


To determine the effect of long-term treatment with corticosteroids in low dosage on the pituitary-adreno-cortical reserve the response to metypaone (methypredapone) was studied at Stoke Mandeville Hospital, Aylesbury, Bucks, in ten patients with rheumatoid arthritis who had been taking 5 mg. prednisone daily at 10 p.m. for 100 to 180 weeks. [If the adrenal glands of patients receiving corticosteroid therapy are still producing cortisol, then by using metypaone to inhibit cortisol synthesis the reduced feedback should stimulate the release of ACTH (corticotrophin) from the pituitary. If then the adrenals are capable of responding to ACTH the excretion of 17-ketogenic steroids in the urine will be increased.]

The 24-hr urinary 17-ketogenic steroid excretion of each patient was measured on four successive days, during which the steroid treatment was continued. On
the third day a total of 5 g. metyrapone was given in five separate doses. On the first two (control) days the urinary 17-ketogenic steroid excretion ranged from 0.9 to 11 mg. per 24 hrs. On the third and fourth days the levels rose in all cases, exceeding the maximum control figures by 4.4 to 33 mg. per 24 hours. In view of this response it was not considered necessary to study the effect of exogenous ACTH in these patients.

Since the control values for 17-ketogenic steroid excretion were lower than normal it would appear likely that the pituitary-adrenocortical axis was partially suppressed, but in view of the response to metyrapone “it may be concluded that the axis does continue to function even when 5 mg. of prednisone is given daily at 10 p.m. for long periods”.  

M. J. Smith


At the K. E. M. Hospital, Bombay, indomethacin was tried in the treatment of twenty patients suffering from rheumatoid arthritis. The patients had not responded satisfactorily to salicylates, phenylbutazone, or steroids, and these drugs were gradually withdrawn as the dose of indomethacin increased. The initial dosage was 50 mg. twice daily after food, but this was gradually increased until there was definite improvement or side-effects occurred; the maximum dose given was 400 mg. four times a day. Laboratory investigations included liver and renal function tests, examination of faeces for occult blood, and x-ray examination after a barium meal. Of thirteen patients in Class III of the American Rheumatism Association Diagnostic Criteria, eight were up-graded to Class II and four out of seven in Class II were up-graded to Class I as a result of treatment. As regards the patients’ own impressions, thirteen thought they had improved. The erythrocyte sedimentation rate was reduced in all cases. In nine cases occult blood was found in the stools during treatment, but in none was there evidence of peptic ulcer radiologically or of impaired liver or renal function. Toxic effects included epigastric pain in ten patients, headache in eight, giddiness in seven, vomiting in seven, diarrhoea in one, drowsiness in five, and a sense of unreality in two.  

C. E. Quin


It has been known for many years that cortisone administered to cholesterol-fed rabbits shows anti-atherogenic properties although it causes a rise in the cholesterol content of the plasma. The fact that a considerable increase in the plasma lipid level occurs at the same time, mainly because of an excess of low-density (Sf 40 to 400) lipoproteins, suggested that cortisone exerts this action by affecting the incorporation of excess cholesterol into a lipoprotein too large to diffuse through the vascular endothelium. This view was widely accepted, with the result that few further investigations into the effect of cortisone on atherogenesis have been carried out.

In a study here reported from Mount Zion Hospital and Medical Center, San Francisco, a thrombogenic magnesium alloy spiral was inserted into the abdominal aorta of 32 young male rabbits which were then divided into three groups:

(1) Twelve were fed on a stock diet with the addition of 2 per cent. cholesterol and 2 per cent. cottonseed oil and received an injection of 5 mg. of cortisone five times weekly;
(2) Fifteen received the same cholesterol-enriched diet without cortisone;
(3) Five received only the simple stock diet.

When the animals were killed and examined at the end of 3 months the aorta in most of the members of Group 1 was either completely free of atherosclerosis throughout its whole length or exhibited very limited atherosclerosis in the ascending portion only. In all the animals in Group 2 the aorta showed some degree of atherosclerosis, which in most of them was extensive and severe. When non-atherosclerotic segments of the aorta of rabbits in Group 1 were analysed chemically they showed as much or more increase in the cholesterol content, compared with those of Group 3, as did the aortas of rabbits of Group 2. Thus cortisone did not prevent the escape of cholesterol from the plasma into the aortic tissue though no gross atherosclerotic involvement was produced by this infiltration. Histological studies of Group 1 aortas confirmed the lipid infiltration of the intima and even of the media, but there was a complete absence of the cellular hyperplasia which was found in Group 2. A similar absence of cellular response was observed in the larger branches of the coronary arteries in Group 1.

The authors thus confirm in detail previous observations that in cholesterol-fed rabbits treated with cortisone the degree of lipid infiltration of the aortic tissue is similar to that usually found in cholesterol-fed rabbits. They ascribe the absence of atherosclerosis in these animals to the elimination of all cellular and fibroblastic response owing to the action of cortisone.  

Z. A. Leitner


Four cases are added to 24 patients traced in the literature (average age 7.5 yrs) who had a raised cerebrospinal fluid pressure, with papilloedema, headache, and vomiting, due to cortisone therapy, especially during the withdrawal phase. The conditions being treated included nephrosis, eczema, asthma, and rheumatic diseases. Blood electrolytes were normal.  

C. I. Phillips

Cataracts in Rheumatoid Arthritis Patients treated with Corticosteroids. IRBY, R., TOONE, E., WITTKAMP, B., and WEISINGER, H. (1964). GP (Kansas), 29, 92. 4 figs.

Posterior subcapsular cataracts were found in fifteen of 76 rheumatoid arthritis patients who had received continuous corticosteroid therapy for a year or more. Ten of the fifteen had visual symptoms. In two control groups totalling 224 patients, there were only nine cases of similar cataracts. No statistically significant relationships could be established between these lesions and the
dosage or duration of steroid treatment.

_James M. Woodward, jun. (Amer. J. Ophthal.)_

**Side-effects of Corticosteroid Therapy.** (Les accidents de la corticothérapie.) _Muller, J.-M. (1963). Presse méd., 71, 2253._

The author discusses the well-known side-effects of corticotherapy in a concise manner under four headings: anti-inflammatory, endocrine, metabolic, and neuropsychiatric. He stresses certain aspects, in particular the risk of gastro-intestinal haemorrhage and perforation, the aggravation of viral, as well as bacterial, infections, and the dangers of 9-α-fluorocortisone, now abandoned for parenteral use. The second part gives a percentile analysis of the major side-effects of corticotherapy and discusses how the newer products, designed to avoid one or the other of these, frequently increase the danger elsewhere, dexamethasone being mentioned in this context. Finally, there is a section on the precautions and contraindications to be observed in prescribing corticosteroids.

_W. T. Menke_


A male patient, aged 32, was treated with ACTH and aspirin for optic neuritis of the right eye. He had never had any gastro-intestinal disturbances but suddenly symptoms of the gastric ulcer and of its perforation appeared. The perforation was sutured and the post-operative course was favourable. Control investigations carried out after a lapse of 6 months showed no abnormalities. The author discusses the pathogenesis of ulceration of the digestive tract developing after ACTH, glyccorticoids, and aspirin, and discusses methods of prevention.

_W. H. Melanowski_


During chloroquine treatment complications in the cornea, retina, and nervous system appeared in 30 per cent. of cases. In early stages the damage is reversible.

_P. Weinstein_


The authors report thirty patients who were given prolonged therapy with 250 mg. Resochin daily. Five developed corneal lesions and one showed early retinal changes. It is emphasized that patients undergoing this form of therapy should be examined regularly by an ophthalmologist.

_M. H. T. Yuille_


The authors discuss their findings in three patients in a series of thirty receiving chloroquine for skin diseases during a period of over 2 months. In two of the patients brownish-yellow deposits appeared in the cornea with the characteristic vortex formation; in the other the retinal vessels narrowed to about one-third of the normal calibre. On cessation of treatment the lesions gradually disappeared. Protective goggles are advocated to avoid these reactions.

_M. H. T. Yuille_


Thirty-nine patients taking chloroquine for varying periods were subjected to visual acuity and colour vision estimation, central and peripheral fields, dark adapto-metry, EOG, and ERG, as well as routine ophthalmological examination. Objective macular changes appear before subjective complaints, the narrowing of the retinal arteries being a late manifestation. Colour vision as tested by the HRR plates appeared normal, so that this cannot be used as a screening test. Periodic testing with the ERG and EOG (either of which may show the earliest sign) is of value.

_M. A. Bedford_


Histopathological findings in chloroquine retinopathy are described in a 38-year-old Negress with disseminated lupus. The principal abnormalities were destruction of the rods and cones and a migration of pigment from the pigment epithelium as far as the inner nuclear layer. It is suggested that chloroquine interferes initially with the metabolism of the retinal pigment epithelium and that secondarily there is rod and cone destruction.

_P. Henkind_


Rats given chloroquine phosphate for 3 months had diminished ERGs when compared with controls. No retinal abnormalities were noted on light or electron microscopy. The ERG changes were not attributed to any effect of chloroquine on the ATPase associated with the visual pigment.

_P. Henkind_

**Screening Test for Chloroquine Retinopathy.** _Copeman, P. W. M., Cowell, T. K., and Dallas, N. L. (1964). Lancet, 1, 1369._ 3 figs, 10 refs.

The authors describe the use of an unmodified electrocardiograph machine to record EOGs.

_P. Henkind_


Other General Subjects


The authors review the clinical, radiological, and biochemical features of eight cases of Morquio’s syndrome. Apart from the main characteristics of craniofacial dysplasia, aural protrusion, and genu valgum, they consider the characteristic changes in the bones of the wrists and hips, and the presence of corneal opacities and hypoacusia. Ligamentary hyperlaxity was noted at the extremities, in contrast with limitation of movement at the shoulders and hips. The rather typical abnormalities of dental enamel they consider to date probably from the third or fourth month of intrauterine life. In the cases considered the familial incidence of the syndrome was 21.8 per cent, and was thus in fair agreement with the 25 per cent. expected in a simple recessive condition.

The authors discuss the excretion of acid mucopolysaccharides. The urinary excretion of hexuronic acids in six of their patients was twice the normal. Furthermore, on extraction by the method of de Ferrante and Rich, the presence of polysaccharides was noted in the 3M NaCl fraction, in contrast with the normal state and with Hurler’s syndrome.

Finally there is a discussion of the differential diagnosis from platyspondyliis and from Hurler’s syndrome. The authors consider their cases to be true examples of the Morquio-Brailsford syndrome, and not so-called ‘late-Hurler’s’.

W. T. Menke


A pedigree (55 members) is given of a family in which hyperuricaemia and gout, ankylosing spondylitis, and anomalies of the lumbosacral junction occurred.

The propositus had all these abnormalities[but there was no clinical or radiological involvement of the lumbar spine, ankylosing spondylitis being diagnosed on the radiograph of the sacro-iliac joints and a complaint of low back pain]. Eleven other members had hyperuricaemia, two gout, four sacro-iliitis, and one typical ankylosing spondylitis. The authors suggest that “ankylosing spondylitis was inherited as an autosomal dominant trait with variable penetrance”.

E. G. L. Bywaters

The report of cases of Behcet’s syndrome in Egypt from which a virus was isolated. Friction appears to be important in the development of cutaneous ulcers. The recurrent virus infection occurs in epithelial cells of the external genitalia, skin, buccal mucous membrane, and in the neuro-epithelial cells of the eye. A. G. Cross


There are certain features of this condition suggesting altered immunity, similar to the other diseases already known to be due to this mechanism, and it is possible that this tendency is genetically determined. It may be that rheumatoid arthritis and Sjögren’s syndrome are expressions of an altered immune mechanism reacting to and damaging a weakly antigenic component of certain glands and connective tissue generally. J. H. Kelsey


Essentials of Rheumatic Affections. (Ser y esencia de al afeción reumática.) KOLAROFF, S. (1964). Folia clin. int. (Barcelona), 14, 242. 3 figs.