ABSTRACTS

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

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

Acute Rheumatism

Rheumatoid Arthritis

Still's Disease

Osteo-Arthritis

Spondylitis

Inflammatory Arthropides

Gout

Bone Diseases

Non-articular Rheumatism, including Disk Syndromes, Sciatica, etc.

Pararheumatic (Collagen) Diseases

Connective Tissue Studies

Immunology and Serology

Biochemical Studies

Therapy

Other General Subjects

At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.

Acute Rheumatism


This preliminary but carefully conducted and controlled study from Emory University, Georgia, found little difference between 21 rheumatic fever subjects on sulfadiazine prophylaxis and a similar number of matched controls in respect of the oral flora (alpha streptococci, coagulase-positive staphylococci, Neisseria, yeast, lactobacilli, fusiform bacilli, and spirilla) after 6 months, except for a significantly increased number of alpha streptococci in the prophylactic group. Antibiotic sensitivity was not studied but is to be investigated.

E. G. L. Bywaters


Rheumatoid Arthritis


Rheumatoid Arthritis


The use of gold salts in the treatment of rheumatoid arthritis is well documented, but the effects of intra-articular injection of such agents (apart from radio-active gold) have not hitherto been described in the literature and the mode of action of these salts remains unknown.

Reporting from the University of Texas Southwestern Medical School, Dallas, the authors describe the outcome of repeated administration of sodium aurothiomalate into the knee joints of twelve patients with rheumatoid arthritis in whom the diagnosis was "classic" in eight, "definite" in three, and "probable" in one according to the ARA criteria. One of these patients had already been receiving intramuscular injections of sodium aurothiomalate for 5 months without much improvement and another had had similar treatment for 2½ years with general improvement but with exacerbation in one knee. Two other patients, one with osteo-arthritis and the other with pigmented villonodular synovitis, were also included in the trial. As a rule sodium aurothiomalate was given weekly in doses of 50 mg. (expressed as elementary gold) for periods of 4–8 weeks in the first instance. In eight of the rheumatoid patients there was a significant fall in both joint swelling and synovial fluid leucocyte count, together with increased mobility and a rise in synovial fluid viscosity; the latter was particularly noticeable in the four patients with bilateral involvement, one knee being injected with the gold salts and the other with saline. The remaining four patients relapsed some 4–9 months following the last injection and required a further course, which reestablished the initial improvement in three. In those patients who did not relapse improvement has been maintained for periods of 2½–7 months. The two patients with nonrheumatoid arthritis showed no response to the treatment. Local reactions in the form of increase in pain and swelling were observed in six, necessitating withdrawal of the drug in one; albuminuria was observed in two cases and a rash in one, again requiring withdrawal of the drug.

The mechanism of the local action of sodium aurothiomalate in suppressing the inflammatory process remains obscure. Two possibilities are discussed—the inhibition of infectious organisms such as mycoplasma or the inactivation of leucocyte lysosomal enzymes.

A. Garner


The authors stress that this is a short review article in contrast to "an exhaustive review which exhausts the reader". It is aimed at the general radiologist rather than the specialist rheumatologist and illustrates from a fair-sized group of patients most of the changes seen in the chest radiograph which are associated with rheumatoid disease.

I. Williams


Still's Disease


Osteo-arthritis


This paper from the Royal National Orthopaedic Hospital, London, provides firm evidence in support of the view that weightbearing joints in limbs affected by poliomyelitis do not develop osteo-arthrosis. 98 patients aged over 35 years who had had poliomyelitis at least 10 years previously were studied; as far as possible they consisted of those patients left with severe paralysis of one leg who walked regularly and who constantly wore one long-leg caliper. In addition to comparing each patient's weaker and stronger leg the authors examined the radiographs of 79 people taken during a field survey conducted by the Arthritis and Rheumatism Council in the Leigh area and reported by Kellgren and Lawrence (Ann. rheum. Dis., 1958, 17, 388; Abstr. Wild Med., 1959, 25, 431).

The incidence of radiographic evidence of osteo-arthrosis in the weaker limbs (31·0 per cent. hips and 5·1 per cent. knees) was considerably less than in the stronger limbs (10·2 per cent. hips and 12·3 per cent. knees) and in the control series (7·6 per cent. hips and 17·1 per cent. knees). There was a striking association between osteo-arthrosis and residual muscle function in the knees: osteo-arthrosis occurred in 15·7 per cent. of 70 knees with full power, in 7·3 per cent. of 82 knees with some paralysis, and in none of 44 flail joints. There was also a (less strong) association in the hips, osteo-arthrosis occurring in 9 per cent. of 67 hips with full muscle power, 5·7 per cent. of 123 with some paralysis, and none in six with flail joints. No correlation was found between the incidence of osteo-arthrosis and the presence of other factors often believed to have an association with it, such as obesity, increased weightbearing activity, the wearing of a caliper, or joint instability. There was also almost no correlation between the incidence of symptoms usually associated with osteo-arthrosis (pain, swelling, and stiffness) and radiological evidence of the condition.

In conclusion, the authors discuss the relevant literature and suggest that the residual paralysis, with its consequent restriction of activity, is responsible for the prevention of the osteo-arthrosis and that this protection may be related to changes in the osseous vascular pattern near the joints of paralysed limbs.

K. C. Robinson


Inflammatory Arthritis


25 cases were examined. Systemic symptoms, such as skin exanthema and genital ulcer, and reactions against some allergic tests were pronounced in females, whereas ocular symptoms which cause blindness were severe in males. In females, marriage, the menopause, and the injection of sex-hormones sometimes caused exacerbation of the disease, and uveitis often recurred around the period of menstruation. An analysis of the urine of the patients showed that there was a reduction in 17-keto-steroid in males but no reduction in oestrogen and pregnandiol in females. Treatment with male hormone, however, showed no effect.

Y. Mitsui


A report of two cases of Behqet's disease with the four principal symptoms fully developed. The first patient had a relatively early finding in the cerebrospinal fluid with symptoms of albumin-cytological dissociation. In the second patient the right eye was already atrophic and encephalography showed a conspicuous theta activity with minimal neurological findings. Within the observation period (four and two years respectively) the visual function in both patients deteriorated to practical blindness.

M. Klima

A report of a case of Behçet’s disease seen in a 28-year-old male.

*R. Asayama*


The report of a typical case of Behçet’s disease which illustrated the typical signs of recurrent uveitis, meningoencephalitis, thrombophlebitis of the leg, erythema nodosum, and aphthous ulcers of the pharynx and oesophagus.

*G. A. Cross*


In a series of 47 patients with Reiter’s disease who in the acute episode had urethritis, arthritis of the peripheral joints and conjunctivitis, or in three cases iritis, pain referable to the spine or sacro-iliac joints was present in forty cases. Of 35 patients with radiographs 2 or more years after onset, twenty had definite bilateral sacro-iliac disease, and twelve of these had ankylosing spondylitis. Of these twenty cases, six had iritis, but among the other fifteen patients only one had this disease.

*G. von Bahr*


Gout


Several published reports have indicated an increase in the number of cases of hyperuricaemia in patients with primary (essential) hypertension. In order to study this finding further serum uric acid levels were determined in 217 patients attending the Hypertension-Nephritis Clinic of the Presbyterian Hospital, New York. The patients consisted of 141 with primary hypertension, 52 with renal or renovascular disease classified as renal hypertension, and 24 with malignant hypertension (in seven of whom a renal cause was present); 119 patients in the series had no previous antihypertensive therapy. A group of 47 healthy subjects were included as controls.

Hyperuricemia, defined as a serum uric acid level exceeding 6·4 mg./100 ml. in males and 5·9 mg./100 ml. in females, was present in 43 per cent of patients with primary hypertension, 44 per cent. of those with renal hypertension, and 75 per cent. of those with malignant hypertension (an incidence of 47 per cent. in the whole series). In the 119 untreated patients the incidence of hyperuricaemia was 38 per cent. There was no correlation between serum uric acid levels and either the height of the blood pressure, the known duration of hypertension, or the serum potassium concentration. However, the incidence of hyperuricaemia in both primary and renal hypertension rose with increasing degrees of azotaemia and also with antihypertensive treatment of any kind, whether with thiazide derivatives or not. Hyperuricaemia was also more frequent in those patients with hypercholesterolaemia.

Since hyperuricaemia occurred with equal frequency in primary and renal hypertension, some factor secondary to the hypertensive process itself was thought to be responsible. A diminished renal tubular excretion of urate was demonstrated in fourteen of seventeen untreated patients, including several in whom the glomerular filtration rate was normal. The mechanism responsible for this altered renal handling of urate was not clear, but could have been related to the elevated serum lactic acid concentration found in seventeen of 21 untreated patients with primary hypertension, all but two of the hyperuricaemic patients in this group having lactic acidemia. The raised serum uric acid levels found in these hypertensive patients were thought to contribute to deterioration in renal function, since in some cases considerable deposits of urate were found in the kidneys at necropsy.

M. Harington


In four cases of gouty arthritis, attacks occurred within 3 days of ocular surgery. It may be inferred that the stress of the surgery precipitated the gouty episodes.

Authors’ Summary


This short and speculative annotation discusses the relation between gout and vascular disease. It is considered by the writer that points of evidence linking uric acid with arterial damage are:

(1) The association of hyperuricaemia with degenerative vascular lesions;

(2) A relationship between purine and lipid metabolism;
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(3) The occurrence of vascular lesions in patients with gout; 
(4) Increased bone-marrow turnover and platelet adhesiveness in patients with gout. J. T. Scott


When blood pressure in dogs was lowered to 30 mm. Hg by bleeding, blood uric acid levels rose to over three times the normal value. Administration of adenosine during the period of shock produced a yet greater rise in blood uric acid concentration. It was postulated that accelerated catabolism of purine nucleotides due to anoxia resulted in an increased production of uric acid. J. T. Scott


Bone Disease


The 21 patients studied by the authors of this report from the Henry Ford Hospital, Detroit, suffered from osteoporosis; eleven had postmenopausal or senile osteoporosis; two had acromegaly (one treated and clinically inactive), three had osteogenesis imperfecta, and five were men in whom the osteoporosis was difficult to classify.

Demethylchlortetracycline was given orally for bone labeling in vivo. Tetracycline is deposited with calcium at the centres of new bone formation and can be visualized by ultraviolet or blue-light fluorescence microscopy of undecalcified bone sections. After such labeling, biopsy was made of the anterior 5 cm. of the eleventh rib and quantitative histological analysis made of mineralized bone sections.

From the data observed, three parameters were calculated and compared with the results of similar studies in normal controls—bone tissue formation rate, mean osteon (Haversian system) formation period, and the number of new osteons introduced into cortical bone per year. With regard to the first of these, both high and low rates of bone formation (but usually low) were found in post-menopausal and senile osteoporosis, while significantly increased rates were found in three cases of osteogenesis imperfecta and in the one case of active acromegaly. Osteon formation time was increased in post-menopausal and senile osteoporosis, while in osteogenesis imperfecta and active acromegaly high normal values were found. The number of new osteons formed each year was variable but preponderantly low in postmenopausal and senile osteoporosis and significantly increased in osteogenesis imperfecta, while a high normal value was found in acromegaly.

T. M. Chalmers


Non-Articular Rheumatism


The author reviews the use of conservative treatment at the Regional Neurological Unit, Brook Hospital, London, in cases of myelopathy due to cervical spondylosis. Of the 38 patients in whom this diagnosis was made between August 1958 and March 1965, seven underwent operations owing to diagnostic difficulty or for other special reasons and seven are excluded from the review because of advanced age, death from other causes, or the development of unrelated diseases. The remaining 24 patients (18 male, 6 female, aged 41-69 years) were all treated with 2-3 weeks' bed rest in hospital followed by immobilization in a plastic or metal frame collar for 2-24 months and have been followed up for 4 months to 6½ years. At each follow-up examination the degree of
motor disability and the sensory symptoms were assessed and compared with the state on presentation.

At the time of review the patients could be divided on the basis of the overall picture of the motor lesion into three groups.

(1) Eight patients were worse, though in five there had been an initial improvement or non-progression lasting for several months to 3 years.

(2) Nine patients remained unchanged so far as their motor disability was concerned, though four had experienced permanent improvement in their sensory symptoms.

(3) Seven patients were improved unequivocally in both motor disability and sensory symptoms, two being virtually free from symptoms.

There were few clinical or radiological features that correlated reliably with the outcome, but all patients in Group 1 gave a history of at least 18 months' symptoms before treatment, whereas in Group 3 the longest history was 1 year. Those who failed to improve within 5 months of starting treatment were unlikely to improve subsequently. Pain and paraesthesiae suggesting root involvement in the arms together with neck pain were more often relieved than motor disability. No improvement was noted in four patients whose diastolic blood pressure was over 115 mm. Hg. The one patient with a single lesion on plain radiography, probably related to disc herniation, improved. Prognosis did not appear to be related to age at onset of symptoms, presence of sphincter disturbance, protein content of cerebrospinal fluid, duration of treatment, or length of follow-up.

The author mentions the increasingly conservative attitude towards treatment of this condition. He suggests that the wide variation in the success rates reported by previous authors (from 77 per cent. of 13 to 46 per cent. of 22) reflects the use of different criteria for selection for treatment and assessment of the results; he stresses that delay in initiating treatment may be a factor determining prognosis. He claims that this study confirms the value of an initial trial of collar immobilization before recourse to surgery, especially in recent cases. It suggests that the condition is relatively benign in the sense that progression to total incapacity is not common, but that in terms of full recovery of function the outlook is poor.

J. S. Cohen


Para-rheumatic (Collagen) Diseases


In this communication from the Rockefeller University, New York, the authors report the results of studies undertaken to determine whether, in patients with systemic lupus erythematosus (SLE), soluble tissue antigens can be detected in the circulation, which might react with the known antibodies to produce renal injury. One such soluble tissue antigen is deoxyribonucleic acid (DNA).

Gel diffusion techniques are described by means of which precipitating antibodies to DNA could be detected in SLE sera. Such antibody containing sera could then be employed to detect the presence of DNA in other sera. Methods are also described for the parallel chemical determination of DNA in serum.

Serial studies revealed that the sera of certain patients with SLE might contain DNA at one time, whereas antibodies to DNA were present at another, and such sera interacted with each other by precipitin and complement fixation reactions. It is suggested that the simultaneous appearance in serum of DNA and antibody might result in the formation of immune complexes of the DNA–anti-DNA type, although attempts to demonstrate such complexes directly in serum have so far failed.

T. M. CHALMERS


The authors of this paper from the Centre Hospitalier Universitaire de Rennes point out that cardiac involvement in scleroderma has been little studied. They have therefore reviewed the records of fourteen of their own cases of scleroderma, and found that clinical, radiological, or electrocardiographic evidence of cardiac disease attributable directly to the scleroderma had been detected in nine. Common symptoms included chest pain (two cases) and shortness of breath (six cases), which is often difficult to distinguish from dyspnoea due to pulmonary effects of the disease. Three patients had clinical signs suggesting cardiac involvement: one had left ventricular failure, one pericarditis, and one pericardial effusion with tamponade (this patient died). Six patients had radiographic evidence of cardiac enlargement. ECG changes appeared early; they were found before the other signs and the authors believe they are the most constant sign of cardiac involvement in this disease. They took the forms of arrhythmias, conduction defects, low-voltage tracings, and evidence of atrial and ventricular hypertrophy.

It is concluded that cardiac involvement in scleroderma is common. The manifestations are diffuse and nonspecific and their prognostic significance bad. Treatment is briefly discussed; steroids have proved not as helpful as were at first hoped, but l-aminocaproic acid has caused some improvement.

A. BRECKENRIDGE

The original, and still current, concept of Takayasu’s disease is that of an arteritis of the supra-aortic vessels, seen mostly in young women. Among nearly 1,000 hypertensive patients treated at the University Hospital of Caracas, Venezuela, the author found ten who had unequal pulses and blood pressures in the different limbs. Nine were females and all but one were aged less than 40 years. Two of the patients were treated surgically and two came to necropsy. Full clinical, pathological, and arteriographic studies showed varying degrees of arteritis involving all parts of the aorta and its branches; the renal vessels were affected in all cases, and the author therefore believes that the hypertension suffered by these patients was renovascular in origin. The symptoms and signs varied according to the number of vessels affected; Takayasu’s ocular signs, not seen in the present series, depend on severe involvement of the carotid arteries.

Syphils and the collagen diseases were eliminated. A raised erythrocyte sedimentation rate was found in all cases, suggesting a chronic inflammatory process. At necropsy, the affected vessels showed thickening of all the arterial coats, and there were pearly-grey intimal plaques quite unlike those seen in arteriosclerosis.

The author claims priority in showing the need for a wider concept of Takayasu’s disease, and would include such cases as those described above and some other forms of arteritis seen in young persons, such as the so-called “atypical aortic coarctation.” He reviews the literature, including earlier work of his own, and suggests as an alternative title for the condition: “diffuse nonspecific aorto-arteritis.”

G. K. Thornton


Four cases of central retinal artery occlusion in association with collagen disease are described. Retrobulbar steroids were given but in all cases systemic steroid therapy was also instituted. The authors recommend the use of retrobulbar steroids in all cases of retinal artery occlusion when the cause is probably a collagen vascular disease.

J. H. Kelsey


The report of a case of systemic lupus erythematosus in which there were symmetrical corneal lesions, the lesions appearing as 1 mm. strands concentric to the limbus in the superficial layers of the stroma. Barrie Jay


Connective Tissue Studies


A direct approach to the study of the metabolism of human collagen has been devised by the authors of this paper from the National Heart Institute, Bethesda, Maryland. They report their examinations of dermal collagen in punch biopsies taken from 34 control subjects and 41 patients with a variety of clinical conditions in which some disorder of collagen could reasonably be expected. The "collagen profile" for each sample of skin was assembled from measurements of the percentage water content, the concentration of total collagen (assayed as $\mu$g. of hydroxyproline/mg. dry weight), the soluble collagen (expressed as a percentage of total collagen), and the ratio of single to double polypeptide chains (the $a:\beta$ ratio). (The details of the techniques used will be published separately.) In the control group the mean values found were: water content, 63.9 per cent.; total collagen, 115 $\mu$g. hydroxyproline/mg. dry weight; soluble collagen, 2.3 per cent.; and $a:\beta$ ratio, 1.04.

A group of patients with dermatological disorders were studied. Those with keloids had an increased water content, soluble collagen content, and $a:\beta$ ratio in the keloids compared with the adjacent normal skin. In these respects keloids resembled recently formed normal scars; in such scars, however, total collagen concentration was reduced, while it was normal in keloids. The lesions of mycosis fungoides had very low total collagen concentrations; in two out of four such cases soluble collagen was increased, and in one the $a:\beta$ ratio was increased.

Patients with heritable diseases of connective tissue (Marfan's syndrome, Ehlers-Danlos syndrome, and cutis laxa) had normal findings except for increased soluble collagen in two cases of Ehlers-Danlos syndrome and a low total collagen concentration in the 1 case of cutis laxa. The findings in homocystinuria were variable, but two patients with classic manifestations had increased soluble collagen and a high $a:\beta$ ratio. Remarkably clinical comparisons have been made between Marfan's syndrome and homocystinuria on the one hand and experimental lamyhrum in animals on the other, the authors point out that no abnormalities were found in the collagen in Marfan's syndrome although defective crosslinkages have been shown to occur in the lathyritic collagen of animals. The findings in the small group of patients with homocystinuria studied were too variable to allow any conclusions to be drawn.

Various endocrine abnormalities were studied. Two patients with primary growth hormone deficiency had decreased soluble collagen, but the collagen profile in a case of acromegaly was normal. A man with untreated thyrotoxicosis was found to have increased soluble collagen.

Certain "collagen diseases" were studied. In untreated and treated rheumatoid arthritis and systemic lupus erythematosus no abnormalities were found even when the skin looked abnormal because of iatrogenic Cushing's syndrome. In scleroderma the soluble collagen was decreased.

An incidental observation was that in certain cases where collagen concentration was normal there were nevertheless significant variations in dermal thickness. Taking the wet weight of the specimens (which were of uniform surface area) as an indirect index of the total amount of collagen beneath a given area of skin, the authors found that patients with Ehlers-Danlos syndrome, osteogenesis imperfecta, and primary growth hormone deficiency had total amounts of collagen which were smaller than those of other subjects.

Discussing their results, the authors point out that their study was not intended to be exhaustive but was preliminary only; however, they feel their work to be a promising introduction to further studies of the metabolism and clinical pharmacology of collagen.

*J. I. Pugh*


In this paper from the Faculté de Médecine et the
Hôpital Cochin, Paris, the authors describe a study they have made of "ragocyes"; that is, phagocytic cells, containing rounded inclusions, which are found in various kinds of joint disorders. The ARA criteria were used for assessing the cases of rheumatoid arthritis. Ragocyes were found in 51 out of 53 cases of "definite" rheumatoid arthritis (96 per cent.), eight out of twenty cases of "possible" rheumatoid arthritis (40 per cent.), three out of 33 cases of non-rheumatoid arthritis (9 per cent.), eight out of fourteen cases of Reiter's syndrome (57 per cent.), both of two cases of psoriatic arthropathy, neither of two cases of ankylosing spondylitis, and two out of a miscellaneous group of 49 patients with various arthroses and other conditions.

In an attempt to reproduce the ragocyte phenomenon in vitro, leucocytes, isolated from human blood by differential centrifugation in dextran solution, were exposed to numerous protein and polysaccharide substances. No success was achieved, but it did prove possible to reproduce ragocyes by exposing leucocytes in vitro to the products of various antigen-antibody reactions (presumably by pinocytosis of the resulting protein aggregates). Other experimental studies of the ragocyes found in the synovial fluid of patients with rheumatoid arthritis suggested that the inclusions contained rheumatoid factor and also either γ-M-globulin or γ-G-globulin. Ragocyes were induced in rat synovial fluid by producing experimental mycoplasma arthritis, "adjuvant" arthritis, and the Arthus phenomenon. It is suggested that these cells are associated nonspecifically with antigen-antibody reactions.

Alan St. J. Dixon


In this communication from the Department of Medicine of the University of Washington, the authors report studies on inclusion bodies seen in the leucocytes present in pathological synovial fluids. They found such bodies to be present in 52 out of 59 effusions from patients with rheumatoid arthritis, and also in eighteen out of 37 effusions from patients with other forms of articular disease. In the latter, the presence of inclusion bodies correlated with the presence of inflammatory synovitis and with the total leucocyte count. Tests for rheumatoid factor were also performed on serum, synovial fluid, and on extracts of the synovial leucocytes. It was found that, in eighteen patients with rheumatoid arthritis, rheumatoid factor was demonstrated in the extract from inclusion-containing cells, and in seventeen of these it was also found in the synovial fluid.

The conclusions to be drawn from this report are that leucocyte inclusion bodies in synovial fluid are not specific for rheumatoid arthritis, and secondly that rheumatoid factor is rarely demonstrated in cell extracts when it is not also present in synovial fluid. T. M. Chalmers


Biochemical Studies


ABSTRACTS


Immunology and Serology


Earlier studies by Hollander and co-workers (Ann. intern. Med., 1965, 62, 271; Abstr. Wild Med., 1965, 38, 122) indicated a possible pathogenetic mechanism for the inflammatory changes observed in rheumatoid arthritis. They found that the introduction of purified autologous 7S γ-globulin (IgG) into unaffected knee joints of patients with sero-positive rheumatoid arthritis evoked a severe inflammatory reaction; IgG from nonrheumatoid individuals was without effect, as also was rheumatoid IgG injected into the joints of osteo-arthritis patients. Thus two criteria appeared necessary for inflammation to develop:

1. Rheumatoid factor must be present in the recipient's serum.
2. Patients must receive their own IgG.

They postulated that complexes of rheumatoid factor are deposited in the joint and are phagocytosed by leucocytes with a consequent release of lysosomal enzymes which cause tissue damage.

In the present study, carried out at the Hospital of the University of Pennsylvania, the reason for the specificity of the inflammatory reaction whereby only the patient's own IgG is active has been investigated. The authors examined the possibility that auto-specificity might be related to the Gm groups attached to the γ-globulin molecule. In a series of experiments two patients with sero-positive rheumatoid arthritis received their own IgG by injection in one knee and an identical dose of rheumatoid IgG with matching Gm factors in the other. In both cases inflammation developed in both joints. Three other patients receiving non-matching rheumatoid IgG showed responses related to the degree of correspondence between the donor and recipient Gm factors.

These results together with those of earlier investigations are taken to mean that to promote rheumatoid inflammation in uninvolved joints there must be:

1. Circulating rheumatoid factor,
2. Donor IgG from a rheumatoid patient,
3. Correlation between recipient's and donor's Gm factors.

A. Garner


**ANNUALS OF THE RHEUMATIC DISEASES**


**Treatment**


A description of the changes in the eye reported in the literature as a consequence of chloroquine with a report of two cases. The importance of ophthalmological control of patients submitted to such treatment, eventually using electroretinography and electro-oculography, is stressed.

*Alfredo Arruga*


In addition to the changes already described in patients submitted to treatment with drugs derived from chloroquine the authors observed a brown dappled coloration of the perilimbal conjunctiva especially intense between 3 and 9 o’clock, surrounding the inferior half of the limbus, and at other times corneal opacities adopting a palm-leaf-shaped aspect, the curves converging at 6 o’clock.

The foveal reflex is often abolished and moderate changes of pigmentation were detected in the fundus, but the obvious fundus generally described was not seen in the authors’ series, probably because all the cases studied had been treated only for a short period and the dosages they were given were low.

In three of the 77 subjects studied electroretinographic changes were detected: an increase of the values of the a-wave and diminishment of the x- and b-waves. None of these patients had clinical signs of retinopathy.

The value of ERG as a method of early diagnosis in chloroquine retinopathy is stressed.

*Alfredo Arruga*


ERG changes are frequent and affect the e-waves and their complexes the b1- and b2-waves.

*J. Rougier*


In 23 patients without chloroquine retinopathy thirteen outlines were found to be abnormal.

*J. Rougier*


Two cases of neuro-myopathy with retinal degeneration and keratopathy are reported.

*J. Rougier*
Anti-malaric treatment toward Kidola but irreversible of Kidola should accentuation of the an city and before the fluorescence The authors seen in which cells drug. of its chloroquine preparations, it is said that un-toward side-effects do not occur with chloroquine diolate (Kidola) but some cases of accommodative asthenopia, keratopathy, or retinopathy after continuous administration of Kidola have been seen.

Some cases of chloroquine retinopathy so far considered irreversible have been found to be reversible when treated adequately after the discontinuance of Kidola. R. Asayama


Three cases of chloroquine retinopathy are reported which have been investigated by intravenous fluorescein angiography. Marked fluorescence of the macula is seen in the arterio-venous phase. This is interpreted as an accentuation of the choroidal fluorescence due to loss of intracellular pigment in the pigment epithelium of the retina.

Fluorescence of the macula in a patient receiving chloroquine should suggest an early stage of retinal toxicity and the method could be used as a screening test. The authors do not claim to have detected normal fluorescence before the onset of visible pigment change. E. W. G. Davies


Chloroquine and its derivatives are mainly deposited in cells which contain melanin (chloroid and pigment epithelium of the retina). (Retinal lesions are secondary and irreversible. The ERG exhibits a decreased b-wave, the pathological EOG precedes the ERG changes. ERG and EOG changes develop before the appearance of the typical retinopathy. Its prevention is guaranteed by periodic ERG controls during treatment with chloroquine or one of its derivatives.

R. Kern


A 32-year-old male was treated for pyrexia of unknown origin with chloramphenicol, streptomycin, and Isomex without improvement. Treatment with steroids brought the fever down but it recurred on discontinuation of the drug.

After 7 g. (average 625 mg. for 10 days) of chloroquine were given he complained of blurred vision. The fundus showed symmetrical, bilateral macular degeneration. No mention is made of the ocular condition after the therapy was discontinued. Since toxic effects on the retina have been reported for much higher doses (785 g.) and for much longer periods (43 months), the case reported is unique (7 g. and 10 days).

Since chloroquine is supposed to adhere to the melanin cells, the author finds it easy to explain that chloroquine could become fixed more easily in pigment-rich Indian subjects.

As regards induced hypersensitivity and aggravating factors, the author only considers the role of tobacco—the patient was a moderate smoker. S. N. Cooper


Rational supervision of the development of new drugs is advocated along the lines suggested by the Dunlop Committee: namely toxicity testing in the laboratory, clinical trials, and the annotation of adverse reactions. In assessing the possible effects of a drug, the action of tissue enzymes to produce a toxic bioproduct should be considered. In some instances the ocular side-effects can be predicted to some extent and a clinical trial can be designed to assess these side-effects.

The assessment of chloroquine retinopathy is given as an illustration. Chloroquine is an aminoquinoline, a drug known to have a high rate of ocular toxicity. The toxic effects of chloroquine on the eye did not become apparent until it began to be used in his dosage.

A screening survey showed that 20 out of 97 patients on chloroquine had retinal changes and it is suggested that routine examination of such patients should include examination of the fundi before the drug is introduced and at 6-monthly intervals thereafter, central field recording, electro-oculography, and detailed colour vision testing.

With the advent of more drugs designed to act on tissues and enzyme systems rather than pathogenic organisms, there is an increasing risk of toxic biochemical effects. The ophthalmologist should learn to detect and assess these adverse effects so that the disadvantages and advantages of therapy can be evaluated for the individual patient. E. W. G. Davies


DeLong and Prien quote an incidence of 20 per cent. of ocular lesions in patients on chlorpromazine therapy. The development of ocular lesions seems to be related to dosage and duration of treatment. In this report 44 patients who had had a low dosage for a long period were studied. The average dose was 160 mg. daily; total dose varied from less than 500 g. to 1,500 g. and the duration of treatment varied from 9 to 12 years. None of the recognized ocular lesions was found in any of the patients.
One explanation of the lack of toxic effect is that on a low dosage the excretion of chlorpromazine keeps pace with ingestion. It is also possible that the out-patients under study were not as punctilious in taking the drug as supervised in-patients reported in other studies.

E. W. G. Davies

Postural Proteinuria: Response to Corticosteroid Therapy.


On the hypothesis that there is some relationship or similarity between postural proteinuria and the idiopathic nephrotic syndrome of childhood, the authors of this paper from the Variety Club Heart Hospital and the University of Minnesota, Minneapolis, investigated the effects of corticosteroids (commonly used to treat this syndrome) on postural proteinuria.

Case records are presented of five children with postural proteinuria, one of whom had previously been known to have idiopathic nephrotic syndrome but none of whom had a history of "significant" renal or urinary tract disease. No proteinuria was noted when the patients were recumbent, no histological changes were present on light microscopy, and no glomerular localization of $\gamma$-globulin and $\beta_2$-globulin was demonstrated by fluorescent microscopy. Creatinine clearance studies gave normal results in all cases, as did intravenous pyelography when it was performed. When prednisone was given in an initial dosage of 60-75 mg. daily, three of the five patients definitely, and one probably, had decreased protein excretion in the upright position to levels below 0.1 mg./ml., the limit of the sensitivity of the qualitative test used for proteinuria. In the remaining patient postural proteinuria was lessened but not abolished by corticosteroid therapy; the postural proteinuria recurred in all patients when prednisone was withdrawn.

The authors conclude therefore that postural proteinuria is the mildest form of the nephrotic syndrome.

A. Pringle


From the Rheumatism Clinic and Institute of Physical Medicine and Balneology, Leukerbad, Switzerland, the authors report a double-blind trial of a new anti-inflammatory agent, HM187 (Promepiazone), on 38 patients suffering from rheumatoid arthritis (RA). The drug is the salicylic acid salt of 1-phenyl-2,3-dimethyl-4-$\beta$-(4-methylpiperidino)propionyl-aminopyrazolone- (5). Previous experiments on animals had revealed satisfactory acute and chronic toxicity, the LD$_{50}$ for rats being 281 mg./kg. body weight. Experimentally, the antipyretic and analgesic effect was slight, but the anti-inflammatory effect was approximately equal to that of Irgapyrin (phenylbutazone + amidopyrine).

The patients, eighteen of whom received HM187 (600 mg. daily) and twenty a placebo, were examined by the same observer before treatment and on the 3rd, 7th, 14th, and 21st days of treatment, when measurements were taken of the swollen proximal interphalangeal joints of the fingers and the ESR was recorded. Physiotherapy was given to both groups during the trial. Of the 38 patients, ten were men (mean age 52), and 28 women (mean age 59). According to the ARA classification, the RA was "probable" in four (11 per cent.), "definite" in 29 (76 per cent.), and "classic" in five (13 per cent.). One patient was in Stage I, five in Stage II, 24 in Stage III/IV, and eight in Stage IV; twenty-two were sero-positive, eight doubly so, and eight were seronegative. (It is not stated whether the two groups were comparable in these respects.)

There was a mean reduction in joint swelling in both groups which was greater in the HM187 group, but the difference between them did not reach statistical significance ($P$<0.05) until the 21st day. By this time the ESR had fallen in the HM187 by a mean of 9.4 mm. in 1 hour, whereas in the placebo group it had risen by 0.63 mm. in 1 hour; however, this difference was not statistically significant. There was no significant difference between the groups as regards analgesic effect. There were no side-effects. It is suggested that a larger dose would probably be well tolerated and produce beneficial results before the 21st day.

D. Preisikel

Contribution to the Study of Ocular Hypertension caused by Dexamethasone in Open-angle Glaucoma. (Contribution l'étude de l'hypertension oculaire provoquée par la dexaméthasone dans le glaucome à angle ouvert.)


From a study of normal eyes, those suspected of having glaucoma, and those with the frank disease, it is suggested that the outflow channels of patients with wide-angle glaucoma contain a substance which increases resistance to aqueous flow under the influence of topical corticosteroids.

S. J. H. Miller

Descemetocele due to Steroid Therapy. (In Turkish.)


A case of descemetocele which developed following steroid therapy in a diabetic male, aged 46, is presented.

C. Örgen

Glucoma caused by Local Corticosteroid Therapy. (Glucoma da applicazione locale di cortico-steroidi.)


Glucoma caused by Corticotheraphy. (À propos du glaucome cortisonique.)


Retinal Vascularization in Subjects treated with Cortisone. (Étude de la vascularisation rétinienne de sujets traités à la cortison.)

ABSTRACTS


Other General Subjects


