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
- Osteoarthritis
- Spondylitis
- Gout
- Inflammatory Arthritides
- Bone Diseases
- Non-articular Rheumatism, including Disk Syndromes, Sciatica, etc.
- Pararheumatic (Collagen) Diseases
- Connective Tissue Studies
- Immunology and Serology
- Biochemical Studies
- Therapy
- Surgery

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


It is known that streptolysin S (SLS) produces a "non-specific" stimulation of lymphocytes from normal donors, 40 to 90 per cent. of the cells undergoing blast transformation, whereas lymphocytes from patients with untreated acute rheumatic fever (ARF) fail to respond in this way. However, lymphocytes from patients with ARF who have received penicillin and from patients with other diseases show the normal 40 to 90 per cent. response to stimulation. The authors of this paper from the Hebrew University-Hadassah Medical School and Bikur Cholim Hospital, Jerusalem, have attempted to use these differences as the basis of a diagnostic test.

Lymphocytes were separated from 5 to 15 ml. heparinized blood and cultured in either calf serum or autologous plasma, and the effects of stimulation with SLS were compared with those of stimulation with phytohaemagglutinin and staphylococcal filtrate. [For details the original should be consulted.]

In calf serum the percentage transformation in response to SLS was less than seven for all of ten children suffering their first attack of ARF. Six out of thirteen patients suffering a second attack of ARF, one out of four suffering a third attack, and all of five with inactive rheumatic fever had percentage transformations above seven, as did seven out of eight normal (adult) controls and eighteen out of twenty children with a variety of non-rheumatic disorders. On the other hand, all the subjects reacted similarly to phytohaemagglutinin and staphylococcal filtrate. The degree of transformation provoked by SLS in a given case often changed (in either direction) if autologous plasma was used instead of calf serum in the culture medium.

The authors discuss their findings and conclude that the value of the procedure as a diagnostic test for ARF "is limited as some patients with acute rheumatic fever react normally while some patients with other diseases show a diminished response".

(ABSTRACTS OF WORLD MEDICINE: Editorial)


At the Perm Medical Institute, USSR, the authors examined the serum for circulating antibodies to cardiac tissue in a series of 192 subjects, of whom 87 were healthy controls, 81 had rheumatic fever (active in 61, inactive in 20), and 24 had "tonsillocardiac syndromes". The technique used was a modification of the indirect Steffens method (microprecipitation in agar).

Anticardiac autoantibodies were demonstrated in only one of the 87 controls, four of the 24 patients with tonsillocardiac syndromes (in two of twenty with "reflex cardiac disorders and myocardial dystrophy" and in two of four with "tonsillogenic myocarditis"), and three of the twenty patients with inactive rheumatic fever. In contrast, in the group with active acute rheumatism, anticardiac antibodies were found in the serum of nine out of nineteen patients with primary rheumatic carditis and of 32 of 42 with recurrent carditis. On the whole, the incidence of anticardiac antibodies reflected the activity of the rheumatic condition and the severity of the carditis and was inversely related to the "indices of streptococcal immunity".

S. W. Waydenfeld

ABSTRACTS


RHEUMATOID ARTHRITIS


Only 191 of the 462 who claimed to have rheumatism had evidence of a classifiable condition. Twenty of these had possible, probable or definite rheumatoid arthritis and the prevalence in the whole group of 3,014 was thus only 0.66 per cent.

Two of the nine patients whose rheumatoid disease antedated the pill improved, as did two of the eleven whose disease postdated the drug. The follow-up period was 6 to 24 months.

A different pattern was found for those with "multiple arthralgia". Three of nineteen women who had this complaint before starting the pill improved, compared with fourteen of the 27 who developed it afterwards.

[The most remarkable thing in this paper is the low prevalence of rheumatoid arthritis in young women]. Mary Corbett

Caeruloplasmin and Green Plasma in Women taking Oral Contraceptives, in Pregnant Women, and in Patients with Rheumatoid Arthritis. Tovey, L. A. D., and Lathe, G. H. (1968). Lancet, 2, 596. 3 figs, 25 refs. Of blood donations reaching the Leeds Regional Blood Transfusion Laboratory about 1 per cent. have green plasma. Most of these come from women taking oral contraceptives, who constitute about 6 per cent. of the blood-donor population. The three conditions in which green plasma is found [the others being pregnancy and rheumatoid arthritis] all have elevated amounts of the blue plasma-protein, caeruloplasmin. A reduction in yellow pigments, previously reported in rheumatoid arthritis, makes the green colour easier to notice. The extractable yellow pigments of normal plasmas are mainly haem and carotenoids. A comparison of the amount of yellow pigments in plasma from women taking contraceptive steroids, with those not on this treatment, showed no systematic difference. The rise in caeruloplasmin in women on oral contraceptives is probably due to the oestrogen components, ethinyl oestradiol or mestranol. Both of these produce the effect.

[Authors' Summary]

Serum Copper in Rheumatoid Arthritis and Ankylosing Spondylitis. [In English] Mäkisara, P., Ruiutsalo, H.-M., Niisslã, M., Ruotsi, A., and Mäkisara, G.-L. (1968). Ann. Med. exp. Biol. Fenn., 46, 177. 8 refs. [At the Rheumatism Foundation Hospital, Heinola, Finland] the serum copper concentration was determined in a series of 176 patients with rheumatoid arthritis and 22 with ankylosing spondylitis. In both diseases the serum copper was increased. In rheumatoid arthritis the increase was correlated with the clinical activity and in both cases with the ESR and some serum protein alterations indicating increasing severity of the disease. The age and sex of patients, the duration and stage of the disease and the positivity or negativity of the Waaler-Rose test were not found to have any effect on the serum copper elevation.

[Authors' Summary]

Among 1,749 specimens of serous fluid from 1,218 patients a special cytological picture was noted in six specimens. Five of the six were from patients with rheumatoid arthritis; and in four of the five rheumatoid nodules were found in pleural tissue specimens. Altogether twelve pleural fluids from ten rheumatoid patients were examined. Specimens were smeared sediments fixed while wet in 95 per cent. ethanol and stained by the Papanicolaou method. The special features of the rheumatoid specimens were (a) a background of orange or red granular material, (b) large elongated cells, and (c) giant round or oval multinucleate cells. *J. Ball*


Marginal furrows, found usually on the inferior part of the cornea, were observed in six patients with rheumatoid arthritis and three with rheumatoid arthritis and Sjögren's disease. Both eyes were affected in four of the nine patients. The lesions were associated with weight vascularization and could remain stationary or progress to perforation. Topical corticosteroids were of no value in treatment.

A. G. Leigh


STILL'S DISEASE


In the present study an attempt is made to define the picture of juvenile rheumatoid arthritis persisting into adulthood; it is in no way a prognosis study as patients were included only if they had had the disease for more than 5 years, with an onset before the age of 15 years, and were now 16 years or over and had joint symptoms at the time of the study.

There were 46 such patients, of whom 36 were female. The mean age at follow-up was 25.7 years (range 16 to 53). The original presentation had been polyarticular in 28 and systemic in only two. Those presenting as monarticular and pauciarticular rarely remained in this state, so that nine of these fourteen patients had developed polyarticular disease by the time of the study. In the other two the type of onset was not determined. The majority of patients had symmetrical polyarticular disease with only small clinical differences from adult rheumatoid arthritis; these included localised growth disturbances, a very high incidence of severe hip disease and low frequency of rheumatoid nodules, these occurring in only four patients. Tests for rheumatoid factor were positive in thirteen and this seemed to be related to the age at onset of the disease. ANF was present in eleven patients, five of whom also had positive rheumatoid factor. Radiological abnormalities of the hands and wrists were seen in thirty patients, in the cervical spine in 24, sacroiliac joints in nineteen, and hips in eighteen. Despite long-continued active disease with radiological change, 35 of the 46 patients had retained relatively good function.

The authors concluded that the course of the disease was unpredictable, as patients with active disease continued to have involvement of new joints during their adult life while eleven patients who had apparently had mild disease during their childhood had developed severe exacerbations in later life. They suggested that patients with juvenile rheumatoid arthritis persisting into adulthood closely resemble patients with an adult onset of the disease.

B. M. Ansell


GOUT


Iron absorption and distribution were studied by the use of oral and intravenous 59Fe in nine hyperuricaemic patients during a control period and while receiving allopurinol. The drug was found to have no measurable effect on iron metabolism. [This finding is in conformity with other studies: there is no clear evidence that the increased hepatic iron produced in animals by allopurinol has any clinical relevance].

J. T. Scott


This is a report of two patients who died of chronic renal insufficiency and in whom tophi were found in the kidneys. These changes were considered to be due to the renal disease rather than "primary hyperuricaemia" because there was no antecedent or family history of gout. [However, in such cases it is very difficult to be sure of the sequence of events unless such patients are seen before the onset of renal failure].

J. T. Scott


This paper is an account of the comparative actions of Allopurinol, Oxypurinol, and Thiopurinol (which is mercapto-pyrazolo-pyrimidine). The action of the last drug on urinary and plasma uric acid is similar to that of the other xanthine oxidase inhibitors; but the compound does not appear to increase the urinary oxypurine level, indicating an additional effect on uric acid metabolism besides inhibition of xanthine oxidase.

J. T. Scott.


Hyperuricaemia has been found in several conditions which cause some degree of acidosis. This prompted the authors of this paper from the Department of Medicine, University of Oulu, Finland, to study the influence of severe respiratory acidosis on serum uric acid levels and urinary urate excretion. Seven patients (4 male, 3 female), aged 18 to 67 (mean 55) years, were studied during intensive therapy for respiratory acidosis. Treatment was by "currently accepted principles". The blood PCO2 and pH, serum uric acid level, and 24-hr excretion of urate were measured daily.

Mean values on the 1st and 5th days of treatment were as follows (ranges are given in parenthesis).

<table>
<thead>
<tr>
<th>Value</th>
<th>Day 1</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid (mg./100 ml.)</td>
<td>11.2 (6.8-14.1)</td>
<td>6.8 (3.5-9.5)</td>
</tr>
<tr>
<td>Urinary urate (mg./24 hrs.)</td>
<td>351</td>
<td>415</td>
</tr>
<tr>
<td>pH</td>
<td>7.223</td>
<td>7.378</td>
</tr>
<tr>
<td>Pco2 (mm. Hg.)</td>
<td>106 (63-150)</td>
<td>57 (45-68)</td>
</tr>
</tbody>
</table>

The urinary excretion of urate reached a peak on the 3rd day of treatment (mean 660 mg./24 hrs). Blood lactate levels were not determined.

The authors conclude that respiratory acidosis is a cause of hyperuricaemia and that these results, in conjunction with findings reported earlier in the literature support the view that "acidosis itself, regardless of its origin, leads to hyperuricaemia". N. Paterson

Answer: The authors conclude that respiratory acidosis is a cause of hyperuricaemia and that these results, in conjunction with findings reported earlier in the literature support the view that "acidosis itself, regardless of its origin, leads to hyperuricaemia". N. Paterson


[From the School of Public Health and the Rackham Arthritis Research Unit, University of Michigan, Ann Arbor.]

Analysis of the uric acid data from the initial examination cycle of the Tecumseh Community Health Study reveals that not only age and sex but also body weight or build should be considered when evaluating serum uric acid levels in disease or relating serum uric acid levels to other physiologic variables. It was found that serum uric acid levels of persons with coronary heart disease were not significantly different from the mean of the population studied and hence cannot be considered an attribute associated with the disease. Furthermore, there appears to be no evident relationship between serum uric acid levels and serum cholesterol or blood sugar, both of which are regarded as risk factors for coronary heart disease. Although there is no consistent pattern of a relationship between uric acid levels and casual blood pressure levels, some trends are suggestive. Of the conditions and disease states studied, only gout and pregnancy differed significantly from the means of the entire population with respect to serum uric acid scores; the levels in gouty subjects, as expected, were higher and in pregnant women lower, confirming reports in the literature.

[Authors' Summary]
ABSTRACTS


Urolithiasis occurred in 21 patients during the use of a carbonic anhydrase inhibitor. In thirteen cases renal colic set in within one month after the beginning of treatment.

The brownish, brittle calculus excreted from one patient was a phosphatic stone. The urinary citrate excretion and calcium citrate ratio of urine obtained from patients given this treatment were compared with normal subjects and patients with urolithiasis.

On the basis of the present data the cause of calculous disease or treatment was considered to be due to alkalisation of the urine. A decrease of urinary citrate was not because of a factor in developing urolithiasis. Most of the patients recovered within the next few days by conservative therapy. R. ASAYAMA


INFLAMMATORY ARTHRITIDES


This is the first case report from the U.S. of a septic arthritis caused by *Serratia marcescens*, a gram-negative rod of the *Klebsiella* group.

A man aged 62 was admitted to hospital with what appeared to be a deep vein thrombosis in the right leg. He was an insulin-dependant diabetic and 3 years previously had been treated for a *Serratia marcescens* urinary infection. 8 weeks before admission, he had suffered a pneumonia-like illness and 4 weeks later became blind in one eye. An ophthalmologist treated his chorio-retinitis with Triamcinolone.

On admission, he was thin and appeared ill. There was no fever but he had a polymorphonuclear leukocytosis and urine culture showed *Serratia marcescens*. He received anticoagulants and the dose of Triamcinolone was reduced. 10 days later, he ran a temperature and developed an obvious arthritis in his right knee.

The effusion was purulent and *Serratia marcescens* was grown from it. Despite orthodox systemic and intra-articular Kana-mycin, his condition deteriorated and led to surgical exploration and drainage of the knee. He failed to improve and joint fluid cultures were still positive. At amputation 28 days after admission, a large abscess was found in the calf communicating with the knee joint. No evidence of a deep vein thrombosis was found. After operation, the urine and wound cultures became negative and the patient is now being fitted for a prosthesis.

This infection occurs when host resistance is low, as for instance in cases of diabetes mellitus and after taking corticosteroid drugs. M. CORBET


This paper, from the department of Medicine, University of British Columbia, is a review in the series "Current Progress". The author outlines important earlier papers on the nature and course of these conditions, and discusses present ideas of aetiology, with particular reference to mycoplasma and bedsonia organisms.

[A useful review for those interested but not involved in this difficult subject]. M. R. JEFFREY


After a review of the clinical signs of the disease, the
author discusses its aetiology: viral or allergic. To those who support an allergic theory, Behcet's disease consists of angioneurotic manifestations of immunological origin. Both theories may be associated to create the disease, the virus having an antigenic power.

S. Vallon.


Post mortem examination of the eyes and lungs has shown important vascular lesions (in the eyes: irido-cyclitis with changes of the choroidal and retinal blood vessels). In the brain the inflammatory lesions are less evocative of the disease. S. Vallon


The reason for the association between genitourinary infection and arthritis is not entirely clear. In this paper from Baylor University College of Medicine, the Ben Taub General Hospital, and Houston Veterans Administration Hospital, the authors review the records of 94 patients in whom gonococcal infection, Reiter's syndrome, or an association of arthritis with a genitourinary infection was suspected. Cultures of joint fluid, urinary tract exudate, skin lesions, and blood had been performed in most cases before treatment was started. Gonococcal and Bedsonia antibodies were measured in sera from some of these patients and also from several groups of control patients not included in the clinical analysis.

Twenty-eight of the patients had arthritis due to organisms of the Neisseria group—N. gonorrhoeae in nineteen cases—as indicated by culture of jointfluid, blood, or metastatic skin lesions. A further seven patients had the full Reiter's syndrome, and one of these also had iritis.

A final diagnosis was not established in the remaining 59 cases. The patients concerned were subdivided into four categories: fourteen with arthritis and skin lesions characteristic of gonococcæmia; fifteen with arthritis and urethritis; four with arthritis and gonococci in the genitourinary tract; and 26 who had acute arthritis but who lacked all of the above additional characteristics. In the last group neither the clinical features nor the results of tests for gonococcal or Bedsonia antibodies were sufficient to establish a diagnosis. Bedsonia antibodies occurred frequently in all groups except controls with rheumatoid arthritis, although only one of the seven patients with Reiter's syndrome possessed these antibodies.

The authors feel that present methods do not allow the certain diagnosis of gonococcal arthritis unless the gonococcus can be cultured from the joint fluid or tissue, the blood, or a metastatic skin lesion. The role of Bedsonia in Reiter's syndrome remains uncertain. J. S. Cohen


The clinical syndrome of transient synovitis of the hip consists of local pain, muscle spasm, restricted movements, normal radiographic appearance, and spontaneous recovery in a few days. Additional features such as mild pyrexia, slight rise in ESR, sterile joint fluid, and nonspecific synovial histology are all compatible with a viral aetiology.

The authors from the Royal Hospital for Sick Children, Glasgow, performed virological studies on seventeen children aged 2 to 12 years with transient synovitis of the hip. There was a history of possible trauma in four and of recent infection in five; eleven were pyrexial and thirteen showed a raised ESR. Paired sera from each patient were tested for complement fixing antibodies to mumps S, mumps V, herpes simplex, adenovirus group, parainfluenza, psittacosis-LGV, Q fever and Mycoplasma pneumoniae, and rubella haemagglutination inhibition. Seven children with other forms of hip disease acted as controls.

Rising antibody titres were obtained in only two patients—one to adenovirus and the other to parainfluenza. One of the six controls also showed serological evidence of current adenovirus infection. Echo 6, Echo 19, adenovirus Type 3, and Coxsackie A4 respectively were isolated on stool culture from four of the seventeen patients; the controls also yielded four different isolations.

These results do not suggest any connection between transient synovitis of the hip and viral infection. It is hypothesized that trauma—minor subluxation during deep sleep—may have caused the syndrome. [It is interesting to note that in seven out of 24 children the initial diagnosis of transient synovitis had to be revised: one developed rheumatoid arthritis, one had tuberculosis, and two had staphylococcal infection.] R. K. Chandra


BONE DISEASE


From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota, and Anatomisches Institut, Basel, Switzerland, the authors report an attempt to treat the symptoms of osteoporosis with fluoride, in the hope of countering the increased level of bone resorption.

Three women, two suffering from senile osteoporosis and one from osteoporosis secondary to tetraparesis, were given sodium fluoride (0.4 to 1.7 mg./kg. body weight daily) for up to 2 years. Tetracycline was given at specific times so that newly formed bone could be identified. To calculate the mean and maximum thicknesses of new bone tissue laid down, the authors made micrographs of 100μ-thick sections of biopsy specimens fixed in alcohol, stained with basic fuchsin, and embedded in methyl methacrylate. The length of surface of bone formed was measured on photographic enlargements of the microradiographs and expressed as a percentage of the total bone surface apparent in the whole section.

In the first patient (a senile osteoporotic aged 75) new bone formation (53 per cent. of bone in the section) was found at rib biopsy after 12 months' fluoride treatment. The bone was poorly mineralized and had a border of osteoid tissue of 50μ wide (normal width 15μ). Fluoride was given at a lower dosage for a further year, together with 600,000 of vitamin D intramuscularly every week during the last 6 months; at a second biopsy 66 per cent. of the bone was new (this value represents the total bone formation over the 2-year period). The new bone found on the second occasion was more normal in appearance and well mineralized, with osteoid borders 15μ wide. The serum alkaline phosphatase level was 30 IU (Bessey) before treatment, 87 IU at the time of first biopsy, and 48 IU at second biopsy.

In the second patient (a senile osteoporotic aged 82), who was given larger doses of fluoride (about 1.7 mg./kg. day), rib biopsy showed 31 per cent. of the bone surface to be covered by bone formed during the period of treatment. This bone was abnormal and lacked mineralization. Vitamin D (600,000 IU intramuscularly every 2 weeks) was given concurrently for 1 month at the beginning of treatment, and during the last 6 months calcium was also given. The serum alkaline phosphatase level was 24 IU before treatment and 29 IU at biopsy 18 months later.

The third patient (aged 58 years) was studied after 7 months' fluoride treatment (at a dosage of less than 1 mg./kg./day), 400 IU of vitamin D being given orally every 2 days during the last 4 months. At biopsy (iliac crest) very abnormal bone, with incomplete calcification, covering approximately 74 per cent. of the bone surface was found. The serum alkaline phosphatase level was 28 IU before treatment and 81 IU at biopsy.

For every case histological sections and microradiographs are shown. The author feels that fluoride is useful therapeutically and concludes that a therapeutic regimen of sodium fluoride (1.1 mg./kg./day) plus a calcium intake of at least 1 g./day and a vitamin D supplement of 400 IU/day should produce favourable results.

I. M. NAIRN


[From King Edward VIII Hospital, Durban, South Africa.] To try to establish whether mechanical stress and muscular activity in earlier life influence the incidence and severity of spinal osteoporosis in old age, lateral x-ray films of the lumbar vertebrae were obtained from three matched groups, each of 100 women 50 to 90 years old. Group A was of rural Bantu accustomed to carrying heavy loads on their heads. Group B was of urban Bantu, mainly in domestic service. Group C was of women of European origin.

Severe osteoporosis occurred in three cases from Group A, two from Group B, and fourteen from Group C. Lesser degrees of osteoporosis could not be assessed precisely enough for inclusion in these figures. Evenly biconcave vertebral bodies, strongly suggestive of osteomalacia, were seen in ten from Group A, five from Group B, and one from Group C. In many Bantu subjects the fifth lumbar vertebra appeared flattened though of good radiodensity and with no marked changes in the other vertebrae; 28 of these were from Group B, and none from Group C.

About a third of each group showed severe degenerative changes in the spine; another third showed milder changes. More cases of spondylolisthesis occurred in the Bantu groups than in the white group. Severe calcification in the abdominal aorta was noted in 24 women in Group C. Mild signs occurred in 35 further women from Group C, in six from Group B, and in only one from Group A. [\textit{Authors' Summary}]


[At St. Vincent's Hospital, Dublin] ten clinical subjects presenting with osteomalacia of intestinal or dietary origin have been studied with respect to renal excr
of hydrogen ion and the appearance of abnormal amino-aciduria.

Five subjects showed defective renal excretion of an acid load and four of these showed spontaneous systematic acidosis. Urinary acidification showed significant improvement in four of these cases following treatment of the osteomalacia. Abnormal generalized amino-aciduria was recorded in two osteomalacic subjects showing advanced bone disease with pseudo-fractures. This pattern reverted to normal following therapy with vitamin D.

It is suggested that these renal tubular abnormalities may have resulted from secondary hypersecretion of parathormone rather than from vitamin D deficiency per se since:

(a) A similar pattern of amino-aciduria was recorded in two cases of primary hyperparathyroidism with cystic bone disease; this pattern reverted to normal following removal of the parathyroid adenoma.

(b) Suppression of secondary hyperparathyroidism by means of calcium infusion in one osteomalacic case resulted in temporary reversal to normal of urinary phosphate excretion, amino-acid pattern, and minimum pH.

(c) Infusion of parathyroid extract in two normal subjects during ammonium chloride loading resulted in elevation of urine pH without significant change in creatinine clearance.

(d) A similar procedure in a subject with combined osteomalacia and hypoparathyroidism resulted in the appearance of abnormal amino-aciduria; repetition of PTE infusion in this subject following vitamin D therapy was associated with elevation of urine pH.

It is suggested that the presence or absence of renal tubular acidosis or abnormal amino-aciduria in osteomalacia may depend upon the degree of bone disease and/or the relative amounts of circulating parathormone and vitamin D. [Authors' Summary.]

Mode of Onset of Osteonecrosis of the Femoral Head.

I. Study of Twenty Cases proved Histologically by Puncture Biopsy (Mode de début de l'ostéonécrose fémoroco-capitale primitive. I. Étude de 20 observations histologiquement prouvées par le forage-biopsie).


A clinical, radiological, and histological study from Toulouse of twenty patients whom the authors claim were suffering from early osteonecrosis of the femoral head.

Fourteen men and six women (mean age 50 years) presented with severe pain and stiffness of the hip without any gross radiological abnormality. In three-quarters of the cases the onset of pain was acute, there was radiation to the thigh or knee and limitation of internal rotation. In five cases the pain was aggravated by coughing without any evidence of a radicular lesion. Straight x rays showed spotty decalcification or small linear increases in bone density only while per trochanteric cine phlebography revealed stasis and reflux into the femoral diaphysis in all cases. The mean intratrochanteric pressure was 27.4 mm.Hg (normal range 12 to 26 mm.Hg) and this rose by 20 mm. after an injection of 5 ml. serum. Histological examination of drill biopsy specimens showed gross and extensive medullary necrosis with areas of bone resorption and fibrous replacement in more than half the cases whilst all showed some evidence of osteoid scars depleted of osteocytes.

The aetiology of osteonecrosis of the femoral head is discussed and the authors suggest that venous stasis may be more important in the pathogenesis than avascular necrosis.

G. Nuki


A case of osteopetrosis is described in which retinal atrophy occurred which could not be accounted for by pressure on the optic nerves. Moreover, the histological changes were similar to those found in vitamin A deficiency and the role of this vitamin in bone metabolism is considered.

P. J. H. Sellors


The case report of a patient with a type of retraction syndrome of the ocular muscles associated with deformity of the cervical spine and fusion of the atlas with the occipital bone.

N. Galloway

Atrophic Skin and Osteoporosis in Patients with Rheumatoid Arthritis and Osteoarthritis [In Danish]. Andersen, R. B. (1968). Ugeskr. Laeg., 130, 2120. 5 figs, 17 refs.


NON-ARTICULAR RHEUMATISM


CONNECTIVE TISSUE STUDIES


It was shown that treatment of synovial fluid collected in heparin with hyaluronidase increased the total cell count mainly by facilitating clearance of the fluid in the stem of the pipette. However the tendency for granular precipitates to occur in some fluids makes the method unsuitable for general use. Preliminary observations indicate that precipitates may be avoided by replacing heparin with E.D.T.A.

J. Ball


Histological examination of the extra-ocular muscles of varying age groups (premature infants to the aged) shows that the elastic tissue is almost absent in early childhood but develops during the period of growth to become constant about the age of 15. In the elderly (over 66) there are accumulations of functionally inferior elastic masses.

Collagen connective tissue content increases during ageing but loses its cellular characteristics and becomes almost homogeneous. T. J. ffytche


This paper, from the Rheumatism Research Laboratories of the Wellcome Medical Research Institute, describes the light-optical appearance of cells obtained from rheumatoid synovial membrane and grown in culture. The cells were released from the synovial membrane by the action of trypsin and were cultured on cover-slips in medium containing 20 per cent. foetal calf serum. Five main cell-types were recognised: small lymphocytes; rounded mononuclear cells resembling macrophages; elongated fibroblastic cells; large cells, probably derived from synoviocytes, with abundant cytoplasm extending into two or more polar processes and with an oval nucleus containing up to three nucleoli; multinucleated giant cells commonly containing up to 100 nuclei. The appearance of these cells on the seventh day of culture is shown in one figure. J. A. Chapman


At the National Institutes of Health, Bethesda, Maryland, the authors have examined the collagenase activity *in vitro* of specimens of synovial tissue obtained at operation from 24 patients with "definite" or "classic" rheumatoid arthritis (ARA criteria) and from eight others with various types of noninflammatory joint disease.

The tissue, which was cut into small pieces, was cultured in Tyrode's solution with added streptomycin and penicillin for 96 hrs at 37°C. The culture was then centrifuged and enzyme activity measured in the supernatant fluid with a substrate of reconstituted salt-soluble rat skin collagen labelled *in vivo* with 14C-glycine. Trypsin controls were used to indicate the extent of non-specific proteolytic breakdown of the collagen gel. In addition, the effect of any enzyme present on dilute collagen solutions was studied by viscometry and acrylamide gel electrophoresis. In the rheumatoid arthritis specimens the severity of the inflammatory process was assessed from the histological appearances without prior knowledge of collagenolytic activity. [For technical details the original paper should be consulted.]

Collagenase activity was found in twenty of the 24 specimens from patients with rheumatoid arthritis and in none of those from patients with noninflammatory joint disorders. The synovial collagenase reduced the specific viscosity of collagen solutions and gave rise, as shown by electrophoresis, to discrete units of lower molecular weight. Viable tissue was necessary for the production of collagenase *in vitro*, which was prevented by freezing and thawing the tissue before incubation. Collagenolytic activity was generally related to the cellularity of the tissue, as indicated by its DNA content, and was also directly related to both local and systemic disease activity.

G. Loewi

From the University Orthopaedic Clinic and Polyclinic, Münster, W. Germany, the author reports electrophoretic studies of substances extracted with 6 per cent. hydrochloric acid from connective tissue of the joint capsules of eight nonarthritic subjects, eight patients with osteoarthritis, and eight with rheumatoid arthritis. [For details of the technique the original should be consulted.]

The electrophoretic curves for normal and osteoarthritic tissues were very similar, showing a peak between 5.8 and 7.1 cm., and this correspond with he similar microscopic and ultramicroscopic appearances. With material from rheumatoid joints, however, the peak lay between 8.2 and 11 cm. This difference may be attributable to the thinner and more immature connective tissue fibrils present in the rheumatoid joint capsule. It is suggested that electrophoresis provides another means of distinguishing degenerative from rheumatoid joint disease.

D. Preiskel


PARARHEUMATIC (COLLAGEN) DISEASES


Forty patients with systemic lupus erythematosus have been followed up for a period of 5 to 72 months after initial evaluation, in a study from the Departments of Medical and Surgical Pathology, Hospital of the University of Pennsylvania. In an attempt to evaluate the prognostic significance of a number of objective para-
meters in lupus nephritis, serial assessments of renal status were performed in all patients irrespective of the presence or absence of evidence of renal involvement at the time of initial evaluation. Features noted were microscopy of urinary sediment, quantitation of proteinuria if present, blood urea nitrogen, serum creatinine and endogenous creatinine clearance. Renal biopsies were performed in all subjects and an arbitrary histological score was allotted depending on the proportion of involved glomeruli. Three clinical groups emerged from the study: those with no evidence of renal involvement either on clinical or biopsy grounds in general maintained stable renal function for the duration of the follow-up, while those with advanced renal involvement initially, usually pursued a rapidly progressive downhill course. However, a third group emerged (fifteen of the forty subjects studied) which showed poor correlation between initial renal assessment and subsequent course, e.g. progressive deterioration in spite of relatively minor histological features, or stable renal function in the presence of advanced histological changes. The response to high dose corticosteroid therapy studied in seven cases was also found to be variable. The authors conclude that the prognosis of lupus nephritis may vary significantly from patient to patient, and may correlate poorly with clinical or histological assessment of renal function.

W. Wilson Downie

Retinopathy due to Progressive Systemic Sclerosis.


This paper from the Institute of Ophthalmology, University of London, the Rheumatology Unit, St. Stephens and St. Mary Abbots Hospital, London, and the Radcliffe Infirmary, Oxford, describes the ocular changes in two cases of progressive systemic sclerosis (PSS) examined at autopsy. Conventional macroscopic and light microscopic appearances are described along with the first published descriptions of retinal digest and electron microscopic preparations of the eye in PSS. The appearances are similar to those seen in hypertensive retinopathy, and are considered to be the end result of focal fibrinoid change in the choroidal-retinal vasculature. Discussion of possible mechanisms suggests that the vascular changes are due to primary scleroderma vascular damage, rather than to secondary hypertension from renal involvement in view of the relatively low levels of recorded blood pressure.

W. Wilson Downie

Systemic Lupus Erythematosus in Childhood: Analysis of 42 Cases, with Comparative Data on 200 Adult Cases followed concurrently.


This interesting study of 18 years’ experience at New York University Medical Centre involves 42 children and 200 adults (aged 16 or more at onset) with systemic lupus erythematosus. “All patients fulfilled the criteria set forth by Dubois, 1966.” Evaluation of results is some-

what handicapped by the number of cases “lost to observation”, which fails to differentiate between those genuinely lost and those not followed longer: this amounts to 95/200 in adults and 12/42 in children followed for 5 years. There is also a high but differing 5-year mortality (16/41 children and 24/200 adults), which adds to the difficulty of interpretation, especially by the end of the full 18 years of the survey.

Combining both series, females showed a peak incidence in the 16 to 25-year age group, not seen in males. The median age at diagnosis was 14 years in children, 2 years later than the presumed age at onset. Both initially and later, in children as well as in adults, joint and skin manifestations were by far the most prominent, accounting for an erroneous initial diagnosis of rheumatic fever in ten cases and of rheumatoid arthritis in four cases. Psychosis was sometimes attributed to steroid therapy and sometimes to the disease itself, in the latter instance often clearing with increase in steroid dosage. Perhaps the most interesting tabulations are those which compare the adults with the children, in regard to clinical manifestations (hepatosplenomegaly or lymphadenopathy being commoner in children) and in regard to laboratory manifestations. Rheumatoid factor was present in about a quarter of both adults and children.

Prognosis is considered in terms of life tables. Eighteen of the juvenile group were known to have died chiefly of infection or renal failure, the median duration of disease from diagnosis to death being 1½ years. In the surviving children the median survival period was 5½ years. Comparison with the adult series showed a poorer survival rate in children both in cases with renal disease and in those without.

(This study includes many data which cannot be briefly summarized and for which the original must be consulted.)

E. G. L. Bywaters


Following the findings of racial differences in the incidence of disseminated lupus erythematosus with a sequence of Negro, Puerto Ricans, and non-Puerto Rican whites, and a similar distribution of serum proteins, the authors have now studied the effect of BCG inoculation in such groups. The population consisted of schoolchildren who were immunized when found to be mantoux-negative. Positive reactors to 5 units PPD following immunization were 37 per cent. for non-Puerto Rican whites, 44.4 per cent. for those of Puerto Rican origin, and 58 per cent. for Negroes. Sizes of reactions followed a similar distribution.

G. Loewi

Clinical Significance of the Study of Autoimmune Processes in Systemic Lupus Erythematosus and Certain Other Collagen Diseases [In Russian].


At the Swerdlowsk Medical Institute, USSR, the
ANCILLARY OF THE RHEUMATIC DISEASES

The authors carried out various immunological tests on sera from 134 patients with systemic lupus erythematosus (SLE), 31 with scleroderma, nine with dermatomyositis, and eleven with polyarteritis nodosa. The investigations included determination of incomplete "warm" antierthrocytic antibodies (Coombs), complete "cold" antierthrocytic agglutinins (Lippelt and Nogalski), complete and incomplete antileucocytic antibodies (in the serum and on leucocytes), and anti-DNA antibodies (passive haemagglutination reaction and antibody neutralization reaction).

The direct Coombs test was positive in about half the cases of SLE, polyarteritis nodosa, and dermatomyositis and about a quarter of those of scleroderma; a correlation was demonstrated between the results of this test and the presence of anaemia. Studies of complete antierthrocytic agglutinins and of antileucocytic antibodies reacting with leucocytic cytoplasm showed no evidence of a rise in titre. Antibodies to DNA were demonstrated in high titres (1: 640-1: 2,560) only in cases of SLE and only in periods of increased activity, and it is suggested that this finding may be of diagnostic significance. The titre of the passive haemagglutination reaction was found to undergo earlier changes than other laboratory indices and may thus be useful in assessing progress and response to treatment. With the antibody neutralization reaction three types of anti-DNA antibodies were demonstrated in cases of SLE, indicating different degrees of interference with DNA metabolism at various stages of the pathological process. In scleroderma interference with DNA metabolism was less evident and in polyarteritis nodosa it appeared to be absent.

- S. W. Waydenfeld


A case of disseminated lupus erythematosus associated with benign intracranial hypertension and papilloedema.

The optic disc changes were studied by fluorescein angiography.

- T. J. ffytte


This paper describes a Caucasian child who developed lesions on the thighs at the age of 10 months and by the time she was investigated at the age of 18 months had depigmentation and extensive linear sclerodermatous lesions from the mid-trunk downwards, together with bluish/brown areas on the dorsum of the hands and the arms. A biopsy from the left thigh was compatible with a diagnosis of scleroderma. The urine showed a strongly positive ferric chloride test and the serum phenylalanine was 30 mg. per cent. Treatment with a low phenylalanine diet led to a fall in the serum phenylalanine levels and over the next 2 years there was definite softening of the sclerodermatous lesions of the lower extremities but new sites became involved in the neck and upper limbs. During her third and fourth years dietary difficulties allowed a rise in serum phenylalanine, again with an increase in size of the new lesions in the upper limbs. Attention is drawn to two similar cases in the literature.

These workers also studied nine patients (5 female and 4 male) aged from 3 to 14 years with scleroderma; none of these showed excessive urinary levels of phenylalanine or hydroxyphenylacetic acid.

- B. M. Ansell


At Monash University and Alfred Hospital, Melbourne, Australia, the authors have examined sera from 33 patients (27 women) who had suffered from scleroderma for 1 to 26 years. Autoantibodies were sought against nuclei, smooth muscle, and thyroid cytoplasm and colloid by immunofluorescent techniques. Monospecific fluorescein-conjugated IgG, IgA, and IgM antiserum were used in typing the anti-nuclear activity. Anti-skin activity in the patients' serum was sought with samples of skin from patients and normal controls. All the sera were also tested for antithyroglobulin (using the tanned erythrocyte technique) and rheumatoid factor (with the latex technique).

One specimen gave a strongly positive, nine a moderate, and two a weakly reaction in tests for antinuclear factor. With one exception all the antibody-containing sera gave the speckled as opposed to the homogenous type of reaction, and the nuclear staining was wholly due to immunoglobulins of IgG type. Anti-nuclear activity was not seen.

Three sera reacted with thyroid cytoplasm and two with gastric parietal cells. Tests for antibody to thyroglobulin and smooth muscle all gave negative results. Rheumatoid factor was detected in fourteen specimens; after heat inactivation only four still gave positive results, whereas in a control study of patients with rheumatoid arthritis heat inactivation failed to reverse the result in 32 out of 46 cases. Immunofluorescence did not reveal antibodies to skin in any case.

The authors cannot relate their findings to the pathogenesis of scleroderma or to the clinical severity of the disease. However, they postulate that the high incidence of rheumatoid and antinuclear factors in scleroderma indicates that patients with this disease process have an abnormally sensitive immunological system that reacts to antigenic stimuli to which normal individuals do not respond. 24 of their patients had a creatinine clearance less than 90 ml./min. and it is possible that the autoantibodies may contribute to the vascular changes, especially the renal ones, found in scleroderma.

- R. Eric Potts

From the laboratories of the Central Military Medical Command, Moscow, the authors describe the histological changes associated with temporal arteritis as seen in 5 male patients aged 22 to 40 years. This group differed from others reported elsewhere in the relatively young age of the patients, the mildness of the clinical picture, and the absence of atherosclerosis. Identical histological changes were demonstrated in two cases of "congenital posttraumatic vascular disease" in men aged 17 and 20 years.

It is stated that three phases can be distinguished in the development of temporal arteritis:

1. The phase of acute inflammation of the arterial wall and perivascular tissues, with eosinophilia, perimesenchyme of the intima with plasma, destruction of the elastic tissue, and formation of thrombi.
2. The phase of organization of the inflammatory infiltrate and of the thrombi, with formation of giant-cell granulomata.
3. The phase of cicatrization and hyalinization, with formation of collaterals based on the vasa vasaorum and followed by thromboarteritis of the compensating channels.

Temporal arteritis seems thus to belong to the group of allergic disorders and bears no relation to atherosclerosis.

S. W. WAYDENFELD


The authors describe their experience in treating seven patients with Raynaud’s disease and reflex neurodystrophy associated with the carpal tunnel syndrome. (The cases are described in detail.)

In four instances the clinical suspicion of carpal tunnel compression was aroused by the presence of acroparaesthesiae. In one typical case, a religious sister aged 32 had had Raynaud’s syndrome since the age of 5; it was associated with acroparaesthesiae of the fingers at night relieved by movement of the fingers or arms. Three injections of dexamethasone into the carpal tunnel at 10-day intervals cured her symptoms, but she subsequently required a further two injections; thereafter there were no more attacks of Raynaud’s syndrome or acroparaesthesiae.

Two other patients with Raynaud’s syndrome had no symptoms of carpal tunnel compression, but electromyography showed delay in conduction in the median nerve. In both instances improvement was found after corticosteroid infiltration of the carpal tunnel.

A single case of severe reflex neurodystrophy of the hand following a fracture of the radius is also reported. There was improvement the day after injection of corticosteroid; the oedema of the hand disappeared, and increased flexion of the fingers and wrist was obtained.

W. E. S. BAIN


This paper from the Mayo Clinic analyses the clinical features of 279 patients in whom a diagnosis of dermatomyositis or polymyositis was made before 1959. 151 patients were known to be living 4 years after diagnosis and 87 patients had died. Women were twice as commonly affected as men and the highest incidence was in the fifth and sixth decades.

Remissions were more common in the early months of the disease. Skin involvement did not affect the prognosis. Contractures developed in 42 patients and calcinosis in 45, of whom 29 were children.

Sixteen patients had a malignancy and eight of these had died. The cause of death was known in 26 other patients, respiratory infections accounting for twelve.

Improvement or remission was seen in 61 out of 122 patients given no steroids, twelve out of 38 given less than 50 mg. cortisone per day (or equivalent), and 75 out of 119 given higher doses.

[Evidence for the equality of the steroid treated and untreated groups of patients, of random allocation of patients to the groups, and of the criteria for using steroids is not given, which vitiates the therapeutic conclusions.]

M. R. JEFFREY


The historical features of Sjögren’s syndrome resemble those of Hashimoto’s thyroiditis and it has been shown that thyroglobulin autoantibodies are increased in patients with Sjögren’s syndrome. This study investigated the incidence of Sjögren’s syndrome in patients with primary hypothyroidism and thyrotoxicosis. No increase in incidence was found when compared with a series of controls.

W. E. S. BAIN


Kerato-conjunctivitis sicca being only one of the triad in Sjögren’s syndrome (the other two being xerostomia and polyarthritis), the authors describe the diagnostic criteria for involvement of the joints, and the lacrimal and salivary glands.

The study is based on fifteen cases, in which serum analysis, Bentonite flocculation test, haemagglutination
test, and biopsies of the lacrimal and salivary glands were carried out. The interrelations are well brought out and the importance of serum studies is emphasised to differentiate true cases of kerato-conjunctivitis sicca from dryness of the cornea due to local conditions.

S. N. Cooper


Sjögren's disease may be due to an autoimmune dacryosial conjunctivitis. Azathioprine may benefit some patients with severe and progressive keratitis sicca. Details are given of one case in which the dryness of the eye was markedly improved. Azathioprine is being given to another patient with lichen planus of the conjunctiva.

Ronald Lowe


After reviewing the literature the author concludes that the sicca syndrome is a sign of a general adenopathy on the basis of general autoimmunity as several antibodies specific to glands or unspecific are often demonstrated.

G. von Bahr


Reported involvement of minor buccal glands in Sjögren's disease prompted the authors of this paper from the University of Glasgow Dental Hospital and School to study these glands not only in Sjögren's disease but in rheumatoid arthritis and various other connective tissue diseases using a labial biopsy technique.

Forty patients were studied: two males and eight females (mean age 65 years) had Sjögren's disease; three males and seven females (mean age 60) had rheumatoid arthritis; two males and four females (mean age 58) had osteoarthritis; six males (mean age 32) had Reiter's disease; one male and three females (mean age 42) had psoriasis; and one male and three females (mean age 38) had scleroderma. Biopsy material was taken from the minor salivary glands of the lower lip by a technique which is described. Specimens of minor gland tissue were also obtained from sixty subjects *post mortem* and were used for control purposes. Histological grading of the specimens depended on the presence of lymphocytic foci and/or diffuse lymphocytic invasion. A "focus" was defined as an aggregate of fifty or more lymphocytes and histiocytes, usually with a few plasma cells peripherally. The patients with Sjögren's disease also had sialographic studies and their salivary flow rate was measured.

Six of the ten patients with Sjögren's disease had more than one focus of lymphocytes per 4 mm², three had one focus per 4 mm², and one (male) had a moderate lymphocytic infiltration. Four of the ten patients with rheumatoid arthritis had one focus per 4 mm², and one had a slight lymphocytic infiltration. Of the twenty patients with other connective tissue disorders, one with Reiter's disease and one with psoriatic arthritis showed slight lymphocytic infiltration; one with scleroderma had one focus per 4 mm². The remaining seventeen had normal biopsies. Of the sixty subjects examined *post mortem*, a moderate lymphocytic infiltrate was noted in sixteen, but no foci were present. The results of the biopsy study compared very favourably with both the sialographic investigation and measurement of the parotid flow rates. It is concluded that labial biopsy is as valuable an investigative procedure as the other two techniques in Sjögren's disease.

P. J. TARIN


A double-blind cross-over trial of the mucolytic agent acetylcysteine was conducted on thirty patients suffering from kerato-conjunctivitis sicca. Results showed a significant improvement over those obtained with the use of carboxy methyl cellulose when judged by degree of conjunctival and corneal staining, mucous shreds, and filaments. Subjective impressions are obscured to some extent by the fact that existing preparations of acetylcysteine cause slightly more discomfort than methyl cellulose.

A 20 per cent solution of acetylcysteine at pH 7.0 was prescribed and used 2-hourly.

E. W. G. Davies


A case report of a man aged 60 who was diagnosed *post mortem* as having had acute disseminated angitis, but not typical polyarteritis nodosa. Previous to death he had an enlarged lacrimal gland and this showed inflammatory changes but no vascular lesions. The role of tetracyclines in causing sensitivity diseases is mentioned.

J. H. Kelsey


Report of two cases of collagenous nodular periarteritis in teenagers. Five haemorrhages were seen on the skin of the hands and on the chest and face, in the conjunctiva and retina, particularly in the region of the macula and optic nerve. These haemorrhages were a vivid red. Both patients died within a few months of their first being seen. The author presents the cases to show that collagenous nodular periarteritis can involve the ocular coats.

Una Dean

ABSTRACTS


Haptoglobins are mucoproteins in human serum which bind haemoglobin. They vary qualitatively as well as quantitatively in a number of diseases, and 3 phenotypes have been recognized by starch gel electrophoresis. In the investigation here reported from King's College, University of London, qualitative and quantitative measurements of serum haptoglobins were performed on 24 patients with the nephrotic syndrome, 52 were proteinuria from other causes, and 45 with rheumatoid arthritis; 53 healthy students and 49 randomly selected hospital patients who were all "reasonably healthy" served as controls.

The nephrotic patients had a mean serum haptoglobin level (mg/100 ml.) of 286±7 (SD = 133±2), while that of the patients with proteinuria was 117±5 (SD = 64±3) and that of the patients with rheumatoid arthritis 21±4 (SD = 9±6); the level of the students was 85±4 (SD = 27±8) and that of the control patients 98±3 (SD = 45±9). In the case of

IMMUNOLOGY AND SEROLOGY


[From the Broegelmann Research Laboratory for Microbiology and the University of Bergen, Norway.]

The mixed agglutination procedure was applied to sections of synovial tissue from patients with rheumatoid arthritis. The tissues were examined with three test systems:

(1) sheep erythrocytes sensitized by rabbit antiserum,
(2) human O Rh-positive (CD) erythrocytes sensitized by anti-Rh serum "Ripley",
(3) rabbit erythrocytes sensitized with mercaptoethanol-treated pooled human serum.

Adsorption of the sensitized cells to the tissue sections was obtained in most of the cases. This mixed agglutination was inhibited by denatured γ-globulin and by antibodies to γM, indicating that the reaction depended on RF [rheumatoid factor] bound in the synovial tissue. Of 31 patients with rheumatoid arthritis, tissue from thirty gave positive reactions. Tissue from many patients also gave a positive reaction with RF applied to the tissue, indicating that the reactant for RF is bound in the tissue.

[Authors' summary.]
rheumatoid arthritis the clinical activity of the disease was related to the haptoglobin level. In neither renal disease nor rheumatoid arthritis was there any correlation between haptoglobin phenotype and increase in haptoglobin level.

The authors conclude that serum haptoglobin levels are useful for following the course of treatment but not for diagnosis in the disorders studied.

William H. S. George


This study from the Institute for Experimental Medical Research, Oslo University, sought to explain why the reactions of some rheumatoid arthritic joints have a relatively low titre of rheumatoid factor compared with the serum when tested by the agglutination of human D cells coated with anti-D serum, but at an approximately equal titre to the serum when tested by precipitation with heat aggregated human \( \gamma \)-globulin. By comparing the results of density gradient ultracentrifugation of these fluids at pH 7.4 and 3.6, it was found that the low agglutination titre for rheumatoid factor was due to the binding of the factor by aggregated \( \gamma \)G present in the fluid. The dissociation of these complexes at the acidic pH enabled the full agglutinating activity of the rheumatoid factor in the IgM fraction to be revealed.

Similar experiments on the whole rheumatoid sera revealed a similar masking of agglutinating activity by the binding of \( \gamma \)G to the rheumatoid \( \gamma \)M globulin. In the serum, however, in contrast to the joint fluid this inhibitory \( \gamma \)G is apparently in its native non-aggregated state. This was shown by the binding of non aggregated \( ^{125} \)I labelled \( \gamma \)G to the rheumatoid \( \gamma \)M and by the ability of native \( \gamma \)G from several sources to inhibit the agglutination of human group OD\( _{a} \) cells coated with anti-D sera irrespective of the Gm or \( \gamma \)G subgroups of these coating sera. The conclusion is therefore drawn that rheumatoid factors may react with some determinants on entirely native autologous \( \gamma \)-globulin.

L. E. Glyn


The authors, working at the Cook County Hospital, Chicago, detected factors reacting in the latex fixation (tube) test in the pleural fluid at a titre >1 in 160 in 41 per cent. of patients with bacterial pneumonia, 20 per cent. with carcinoma, and 4 per cent. with tuberculosis. Titres >1 in 1,280 were found in pleural fluids from 6 to 15 per cent. of this total of 65 non-rheumatoid patients investigated. No data on rheumatoid patients is included for comparison. Titres of rheumatoid factor in pleural fluids did not correlate with serum titres in the same latex test or with the total protein content of the two fluids.

N. R. Ling


This paper from the Instituto Nacional de Cardiologia, Mexico, examines the response to aggregated IgG of rabbits experimentally paralysed with native IgG. Nine rabbits rendered unresponsive to native human IgG were injected intravenously with 40 mg. heat-aggregated human IgG. Six of the rabbits developed an antibody which reacted with human IgG in a latex test, which was unreactive towards native human and rabbit IgG and which was entirely absorbed with heat-aggregated rabbit IgG. This rabbit rheumatoid factor was shown to be of IgM type in three of the antisera. None of the eight rabbits injected with 40 mg. heat-aggregated rabbit IgG produced antibody.

N. R. Ling


A thorough immunological study of anti-\( \gamma \)-globulin factors in 43 patients with bacteriologically proven subacute bacterial endocarditis is reported from the Arthritis Unit, the Department of Medicine, and the Department of Paediatrics of the University of Minnesota College of Medicine.

47 per cent. of the patients had positive latex tests (Singer and Plotz). There was a significant correlation of positive latex tests with duration of disease but none with the age of the patient or the type of organism. Oudin tube quantitation of immunoglobulin classes showed a striking correlation of rheumatoid factors with elevations of IgG but not IgA or IgM. Antibacterial absorption experiments resulted in only about 15 per cent. absorption in both latex positive and negative cases suggesting that anti-\( \gamma \)-globulin factors were not related directly to antibacterial \( \gamma \)G antibodies. Agglutination and complement-fixation titres were higher against bacteria isolated from the blood cultures of latex positive cases but there was no correlation with Gm group type. A study of immunoglobulins, latex tests, antithymoid antibodies, and antinuclear factor in the kindred of seventeen of the patients revealed no striking differences between those with and without rheumatoid factors.

G. Nuki


This work was conducted at the University of California, Los Angeles, to determine the relationship of antinuclear factors to the clinical diagnosis, specificity for different antigens, and the Ig class and importance of pattern in immunofluorescence. 78 sera, some stored since 1957, were used. Tests were DNA spot tests and indirect immunofluorescence on human leukocytes, patterns being recorded as shaggy, solid, or speckled. Another substrate used was rat liver, unfixed. Three-layer tests were used to determine Ig class. Precipitation
of sera with single-stranded DNA was performed. Serum binding was determined using a C14-labelled T4 phage DNA. Complement fixation with DNA and rheumatoid factor tests were also performed.

The bright shaggy type of fluorescence occurred most frequently in systemic lupus sera which were shown to contain antibody to DNA in other tests, but also occurred in non-lupus sera and when no DNA antibody was shown. Ig class was unrelated to the pattern, which was affected by dilution and choice of substrate. The pattern of fluorescence also showed no good correlation with clinical diagnosis.

G. Loewi


The incidence of antinuclear factors reacting specifically with the nuclei of granulocytes (gran. react. ANF) was investigated in 84 patients with rheumatoid arthritis at the Statens Serum Institute, Copenhagen. The immunoglobulin class of these ANF were determined by means of serological reagents specific for IgG, IgA and IgM.

Positive results were obtained in 56 of these patients. The staining was of the homogeneous kind and the globulin class responsible was IgG in 61 per cent., IgA in 62 per cent., and IgM in 68 per cent. of the positive cases. 28 of these same cases also gave positive reactions with nuclei of other tissues. The only significant clinical correlation of these gran. react. ANF was with nodules; all fourteen patients with nodules gave positive reactions.

The earliest of these ANF to appear were of the IgM and IgG classes, and the sequence is suggestive of a true immune reaction to nuclear antigens. This is also supported by the much later appearance of the factor reacting with other nuclei.

L. E. Glynn


This work was prompted by the possibility of an immune role in untoward reactions to aspirin. Experimentally, immune reactions to aspirin have been elusive, but the present authors, on immunizing rabbits with a conjugate, have found antibodies. Aspiryl-chloride was made and conjugated with different proteins. Antibodies were sought by precipitation and tanned-cell haemagglutination. Immunization with aspiryl-bovine y-globulin gave rise to antibodies to hapten, carrier, and a hapten-carrier combination. When aspiryl-rabbit y-globulin was used, no antibody to the carrier was found, but the other reactions were similar. By precipitation-absorption, there was no evidence of antibody to the hapten-ovalbumin combination but otherwise the reactions were similar to those with other carriers.

G. Loewi


In 4- to 5-week-old rats arthritis could be produced invariably and in some animals uveitis as well by a single injection of Freund’s adjuvant (heat dried tubercle bacilli in mineral oil) into the anterior chamber. The arthritis occurred in one or several joints after a latency period of 10 to 16 days. The uveitis could be noted at the earliest on the 13th day and on the 39th day at latest, and varied greatly in its intensity. Histological examination of the uvea showed diffuse, non-granulomatous inflammation of the iris and ciliary body. An allergic reaction of the delayed type is assumed and discussed with reference to an immunological basis of spontaneous endogenous uveitis.

L. Wittels


ANNALS OF THE RHEUMATIC DISEASES


Immune Deposit Diseases; or, of Mink and Mice. Williams (1968). Arthr. and Rheum., 11, 593.

BIOCHEMICAL STUDIES


Previous work has shown that amyloidosis in mice induced by repeated subcutaneous injections of casein can be transferred to syngeneic recipients by passive transfer of spleen cells. An important difference between this transferred form of the disease and that directly induced by casein is the variable involvement of the lungs in the former and its rarity in the latter. The work reported here from the University Institute of Pathological Anatomy, Copenhagen, shows that the lung lesions arise in all probability from the aggregates of transferred cells trapped in the alveolar capillaries.

Donor mice were injected subcutaneously with casein daily for 7 days. At this time no amyloid had as yet developed in the spleen. Cells prepared from these spleens were then injected intravenously in a dose of 50 x 10⁶ cells, and the recipients then injected daily with casein (0.5 ml of a 5 per cent. solution) for 7 days. A daily injection of nitrogen mustard (0.05 mg. in 0.5 ml saline subcutaneously) was then given for 5 days and the mice killed next day and their organs examined for amyloid. Widespread amyloidosis was found with lung involvement in each animal.

A repetition of the experiment in which animals were killed at daily intervals after cell injection showed that amyloid first becomes detectable on the sixth day. That this arises at the site of lodgment of cell aggregates in the alveolar capillaries was confirmed by the higher incidence of these amyloid deposits in animals receiving a higher proportion of the injected cells as aggregates.

L. E. Glynn


The transfer of amyloidosis to syngeneic recipients has previously been accomplished by means of spleen cell suspension and spleen cell homogenates.

The present report describes such a transfer using whole spleens from casein-treated amyloidotic mice. Slices of spleen were grafted to one kidney of the recipients. Nitrogen mustard was given to accelerate amyloid formation.

The results showed that reabsorption of the grafted amyloid in the normal recipients did not occur and that the grafts induced generalised amyloidosis in the host tissues, suggesting that a “trigger substance” is responsible for the initiation of amyloid formation. D. J. Ward


The excretion of 1β-hydroxytetrahydrocortisone (1β-OH-THE) has not been shown to occur in man normally or after administration of ACTH. The present authors from Sheffield and Region Endocrine Investigation Centre and the Department of Chemistry, University of Sheffield, describe in detail the isolation of this material from the unconjugated fraction of the urine of a patient with Cushings syndrome on cortisols. Previously it had been noted that patients suffering from this disease and on cortisol consistently excreted varying amounts of an unknown polar metabolite.

The patient studied here, female and 42 years of age, was given an oral dose of 1, 2-H-cortisol (2.24 x 10⁶ cpm.) in 50 ml 10 per cent. ethanol and the two subsequent 24-hour specimens of urine were collected. Cortisol excretion rate was 185 mg./24 hours. Methods of extraction and identification are described in detail in the paper and it is noted that because of the high water solubility of the isolated material adequate recovery from urine necessitates salting out of the aqueous phase before extraction ethyl acetate or tetrahydrofuran. As washing with alkali to remove interfering chromogens leads to a loss of 1β-OH-THE the authors suggest that an ammonia-based partition system is more satisfactory for the isolation of unconjugated steroids.

The material isolated in the present experiments behaved chromatographically as 1β-OH-THE, its infrared spectrum being identical with that of an authentic sample of 1β-OH-THE indicating a molecular weight of

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Metabolism of Cortisol in Rheumatoid Synovial Tissue. MURPHY and WEST (1968). Arthr. and Rheum., 11, 696(a).

THERAPY


This study from the Hospital de la Santa Cruz y San Pablo, Barcelona, reports the effects of a new phenylbutazone derivative, the trimethylgallate ester, on 67 patients of both sexes and various ages who suffered from a number of rheumatic states but not rheumatoid arthritis; these included knee and hip changes, episcleritis, and spondylitis of the lumbar and cervical spines. The duration of treatment varied from 2 to 30 days, and the capsules, which contained the equivalent of 200 mg. phenylbutazone, were given three or four times daily immediately after meals. In fourteen cases the dosage was modified because of lack of improvement or intolerance.

Irrespective of diagnosis, most patients had a good response as judged by loss of pain and reduction in joint disability; the results were graded as "excellent" or "good" in 81 per cent. of cases and "acceptable" in 11 per cent. The optimal dosage was thought to be three capsules daily (equivalent to 600 mg. phenylbutazone). The main serious side-effect in this short trial was gastric intolerance, which occurred in 4-5 per cent. of cases.

B. M. Ansell


Both hot and cold packs have been applied to chronically inflamed joints, but there is no general agreement as to which method is more effective and controlled observations seem to be lacking.

Fourteen patients (20 knees) with "definite" or "classic" rheumatoid arthritis (ARA criteria) admitted to the Royal National Hospital for Rheumatic Diseases, Bath, Somerset, were treated with either hot packs or ice packs which were wrapped round the knees and kept in position for 20 minutes. The mean duration of the arthritis was 14 years; fourteen patients were seropositive and six were receiving oral corticosteroid therapy. During the second and fourth weeks of the 5-week trial period, each patient (by random selection) received either a 5-day course of ice packs or a 5-day course of hot packs and then after a 9-day period free of treatment the type of treatment was reversed. Assessments of pain, range of movement, and joint temperature were made before, during, and after treatment, and the patients' impression of the value of each treatment was also recorded.

There appeared to be little difference between the two groups of patients when tested objectively, but the majority of patients preferred the ice packs. Pain and stiffness improved in slightly more patients when ice packs were applied, but both forms of treatment were equally effective in improving the range of movement. Eighteen of the twenty knees improved to some extent during the trial period. Possible explanations for the beneficial effects that these apparently opposite types of treatment had on rheumatoid arthritis of the knee are given.

J. B. Millard


In experiments reported from the Medical Clinic and Polyclinic of the University of Münster, W. Germany, the authors studied the effects of phenylbutazone and prednisone, separately and together, on the formation of granulomata in response to the implantation of cotton-wool pellets subcutaneously into rats. The effects were measured not only by weighing the granulomata, but also by determining the amounts of injected 35S-sulphate and 14C-leucine incorporated in the sulphomucopolysaccharide and protein of the granulomatous connective tissue respectively. Four groups of ten rats each were used; one group remained untreated as controls, the second received prednisone by mouth in a daily dose of 10 mg./kg. body weight, the third received phenylbutazone intraperitoneally in a daily dose of 200 mg./kg., and the fourth received both drugs, but in half the above dosage. Medication was given for 5 days before and 7 days after implantation of cottonwool and
the animals were killed at the end of this time, five in each group having received 1 mCi of $^{35}$S-sulphate and five $5 \mu$Ci of $^{4}$C-leucine intraperitonally 24 hrs before death. The granulomata (2 in each animal) were then excised, weighed, and their content of the two isotopes determined. The mean results for the four groups, expressed as percentages of the control values, were as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight of Granuloma</th>
<th>Uptake of $^{35}$S sulphate</th>
<th>Uptake of $^{4}$C-leucine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Prednisone</td>
<td>57</td>
<td>46</td>
<td>60</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>52</td>
<td>46.3</td>
<td>49</td>
</tr>
<tr>
<td>Prednisone + phenylbutazone (half dosage)</td>
<td>28</td>
<td>28</td>
<td>35</td>
</tr>
</tbody>
</table>

It was thus shown that both prednisone and phenylbutazone, acting separately, have a marked inhibitory effect on the production of granulomatous connective tissue and on its sulphomucopoly saccharide and protein metabolism and that the two drugs act synergically when given in combination. This may explain the steroid-saving effect of phenylbutazone in the treatment of such diseases as rheumatoid arthritis.

[Abstracts of World Medicine: Editorial]


At the Institute of Rheumatology, Moscow, the authors have studied the effects of salicylates, glucocorticoids, and pyrazoline derivatives on the level of nicotinamide adenine dinucleotide (NAD) in the blood of 125 patients with rheumatic fever, 177 patients with non-rheumatic diseases, and 28 healthy controls. The blood NAD and NAD phosphate levels were determined by the Levitas method.

Apart from a slight rise with increasing activity of the disease, no differences were found in the initial NAD levels of the three groups. An analysis of 184 courses of treatment with various preparations singly and of 200 courses of combined therapy showed a marked therapeutic response to salicylates and, less markedly, to corticosteroids was associated with a statistically significant reduction in blood NAD level; such a reduction did not occur in the absence of a therapeutic effect. A therapeutic response to pyrazoline derivatives, on the other hand was associated with a significant rise in NAD level. In both instances a therapeutic response was associated with a significant fall in the level of ATP. In spite of their widely differing chemical structures, therefore, all the preparations in question seemed to interfere with the energy metabolism of the inflammatory process. The effects of combined therapy are discussed.

S. W. Waydenfeld


Organ transplantation has led to an increased interest in the use of antimetabolic drugs, whilst increased knowledge of the various immunologically-related diseases and their treatment has recently stimulated such interest still further. Such drugs have been shown to possess both immunosuppressive and antiinflammatory effects, although the method of production of these effects is not fully understood. It is known that 6-mercaptopurine (6-MP) has an inhibitory effect on nucleic acid synthesis and that it can virtually eliminate the appearance of mononuclear cells at a local inflammatory site under certain circumstances.

The present authors, working at Dallas, Texas, have investigated the possibility that 6-MP might suppress inflammation through interference with the proliferation of the precursors of the mononuclear cells. Their results show that its administration decreases predominantly the numbers of monocytes and large proliferating lymphocytes in the blood, concurrently with the decrease in tissue mononuclear cells at sites of inflammation and in the urine, appears to them to be the basis of its antiinflammatory effect. Their findings suggest, therefore, that the antiinflammatory effect of 6-MP results from suppression of a bone marrow response to local inflammation which affects principally the proliferating precursors of blood monocytes and large lymphocytes. The possible therapeutic importance of this action of 6-MP in the treatment of inflammatory and immunologically mediated diseases is discussed at length.

W. S. C. Copeman


This report from Johns Hopkins University School of Medicine and Hospital concerns one patient with chronic asthma who developed severe corticosteroid myopathy after 40 years of treatment with methylprednisolone in a dose of 12 mg daily. Substitution of prednisone resulted in a complete recovery of muscle power over the next 6 months and diminution of the muscle wasting.

The muscle pathology was examined by light and electron microscopy. The most striking feature in the electron micrographs was massive accumulation of glycogen in most muscle fibres. The authors suggest that inhibition of muscle phosphorylase by the steroid could be responsible for this finding.

The literature on steroid myopathy is comprehensively reviewed. It is emphasised that myopathy can occur with all the commonly used corticosteroids but the incidence is higher with steroids having a nine alpha fluorine configuration.

D. A. Pitkeathly


500 consecutive admissions to a Veterans Hospital (488 male, 12 female) were questioned about their analgesic habits; 32 were considered to take excessive quantities, defined as at least five aspirin tablets daily (four
ABSTRACTS


This study, from the Department of Pharmacology, Queen's University, Kingston, Ontario, was prompted by current interest in the possible ill-effects of taking analgesics in fairly large dosage for long periods.

After a review of previous work in animals, the author reports studies upon groups of young male rats which were given a daily dose of aspirin by stomach cannula. Doses ranged from 0-21 to 1-50 g./kg.

Three indices of toxicity were calculated:

(i) The maximum daily dose, which killed no animals in 100 days ("LD₀")

(ii) The dose which killed 50 per cent of animals in 100 days ("LD₅₀")

(iii) The dose which killed all animals at 100 days ("LD₁₀₀")

The mean values observed were LD₀ = 0-098 g./kg., LD₅₀ = 0-243 g./kg., and LD₁₀₀ = 0-409 g./kg.

With the largest doses animals died of convulsions and respiratory failure. At lower dosage levels animals which died showed evidence of renal damage and respiratory failure in hypothermia.

Histologically, visceral capillary congestion, glandular atrophy, and gastric hypertrophy were common. Larger doses produced degenerative changes in liver and kidney, a stress reaction in thymus and adrenal, gastric ulcers, and pneumonitis.

The relevance of the results to human patients is discussed.

M. R. Jeffrey


Peripheral injection of hydrocortisone into rats was found to produce an increased activity of tryptophan pyrrolase in the liver. This was followed by a decrease in the brain content of 5-hydroxytryptamine. Allopurinol, which is an inhibitor of pyrrolase, prevented these changes. The possibility is discussed that the characteristic early morning waking of endogenous depression may be associated with high pyrrolase activity resulting from high morning blood cortisol; and that pyrrolase inhibitors might be of value in treatment.

J. T. Scott.


[From McMaster University, Hamilton, and the University of Toronto, Canada.]

Acetylsalicylic acid (ASA, aspirin) and sodium salicylate inhibit platelet aggregation induced by collagen, antigen-antibody complexes, γ-globulin-coated particles or thrombin. These compounds suppress the release of platelet constituents, such as adenosine diphosphate (ADP) and serotonin, induced by such stimuli. Since ASA and sodium salicylate do not inhibit ADP-induced platelet aggregation, it appears that their effect on the action of the other stimuli is due to a decrease in the amount of ADP released. The administration of ASA to rabbits (in doses which inhibited collagen-induced platelet aggregation) impaired hemostasis, prolonged platelet survival, and diminished the amount of deposit formed in an extra-corporeal shunt.

[Authors' summary.]


[From Mount Sinai Hospital and the City Hospital of Elmhurst, New York.]

Ingestion of 1-5 g. aspirin, but not of sodium salicylate, produced a significant prolongation of the bleeding time in six normal male subjects when compared with the effects of a placebo. Similar differences in the effect of the two drugs on platelets was also observed. Aspirin ingestion resulted in impaired platelet aggregation by connective tissue and was associated with a decreased release of platelet adenosine diphosphate (ADP); sodium salicylate had no effect on these values. In vitro, incubation of platelet-rich plasma with an optimum aspirin concentration of 0-50 mMol/l. (0-045 mg./ml.) inhibited both the adhesion of platelets to connective tissue and the release of ADP as well as the secondary wave of platelet aggregation produced with ADP or epinephrine [adrenaline]; sodium salicylate had no effect on these reactions, which were also normal in patients with von Willebrand's disease. The inhibitory effect produced by ingesting a single 1-8 g. dose of aspirin was detectable for 4 to 7 days at which time salicylate was no longer detectable in the blood, which suggested an irreversible effect on the platelet. Aspirin also inhibited the release of platelet adenosine triphosphate (ATP), but had no effect on the platelet surface charge, available platelet ATP, or ADP, or the destruction of ADP by plasma ADPase. These studies lend further support to the hypothesis that ingestion of aspirin, in contrast to
sodium salicylate, prolongs the bleeding time by inhibiting the release of platelet ADP, reflecting the findings in other cell systems which suggest that aspirin alters membrane permeability.  

**Authors' Summary.**


At the Royal North Shore Hospital, Sydney, New South Wales, the authors have compared the ability of aspirin powders of different particle size—coarse (aspirin-16) and fine (aspirin-120)—to produce gastrointestinal blood loss. Of the nine subjects studied, four (1 woman, 3 men) were under treatment for tuberculosis and had no history of gastrointestinal symptoms or blood loss and were not suffering from haemoptysis. The other five (4 women, 1 man) had iron deficiency anaemia of unknown aetiology but had all had occult blood in the faeces repeatedly during the past 12 months, though no lesion of the gastrointestinal tract was demonstrable radiologically. The two preparations of aspirin were put up in gelatin capsules and each was administered to every subject in a dose of 600 mg. four times daily for a test period of 3 days. The order of administration was varied and an interval of 4 to 10 days separated the two test periods. Gastrointestinal blood loss was measured by estimating the loss of $^{51}$Cr-labelled erythrocytes in the faeces, the mean daily blood loss being determined during a preliminary control period of 3 to 7 days and during each trial period and the 3 subsequent days.

Both types of aspirin produced an increase in mean daily blood loss over the control value in all subjects, but on average the loss was 105-4 per cent. greater with aspirin-16 than with aspirin-120 ($P < 0.05$). This difference was more marked (160-2 per cent.) in the subjects with previous occult bleeding, but was insignificant when those with tuberculosis were considered separately. Moreover, the mean daily blood loss was greater in the former group than in the latter for both aspirin preparations.

The authors discuss the various factors affecting the action of aspirin on the gastric mucosa and point out that particle size is only one of these, other including the area and duration of gastric contact. They conclude that since it appears that aspirin will cause some bleeding in most people if analgesic blood levels are to be attained, the search for the safest possible alternative with equivalent analgesic properties must go on.  

**Corticosteroids and Ocular Tension.** (Corticosteroides y tensión ocular.) González Tomás, J. (1967). *Arch. Soc. oftal. hisp.-amer.*, 27, 1062. 88 refs.

The author warns against cortisone glaucoma and bases his argument on an exhaustive review of the literature on the subject. The importance of tonometric control of patients submitted to corticosteroid treatment is stressed. Pharmaceutical firms that prepare drops and ointments including a steroid should add to the accompanying sheet containing the contraindications and indications of the preparation a note indicating the advantage of ocular tension control if the drug is used for more than 2 weeks.

Alfredo Arruga

**Steroids and Glaucoma** [In Hungarian]. Weinstein, P. (1968). *Szemészeti*, 105, 169.

Recent examinations have shown that the glaucoma developing after general and local application of steroids is of genetic origin. Glaucoma simplex has been found in most of the ascendants of such patients. The pathomechanism is not clear. Very likely the swelling ability of the mucopolysaccharides in the chamber-angle is altered by the steroids and the permeability of the angle decreases. A subacute attack of glaucoma after steroid treatment was observed by the author.

**Authors' Summary**


Systemic prednisolone given to rats enhanced the development of galactose cataract and about one third of animals also had granular opacities when this was associated with the simultaneous administration of phenylbutazone.

No cataract was produced solely by prednisolone.

R. F. Fisher


A further short report showing about a 50 per cent. incidence of this type of cataract in seventeen children.

R. F. Fisher


**Supervision of the Eyes during Prolonged Treatment with Synthetic Anti-malarial Drugs.** (Results in 237 Patients followed up on average for 4 Years) (La surveillance oculaire au cours des traitements prolongés par les antimalarials de synthèse. Résultats chez 237 malades suivis en moyenne pendant 4 ans.) Bertrand, J. J., Debeyre, N., Kahn, M. F., and Ryckevaert, A. (1968). *Presse méd.*, 76, 2139. 4 figs.
Pigmentation and Retinopathy due to Chloroquine. 


Use of Ketophenylbutazone (Ketazon), Oxyphenbutazone, and Proteolytic Enzymes in Rheumatism (Associação de cefotifenibutazona (Ketazon), oxifenibutazona y enzimas proteolíticas en afecciones reumáticas). FRANCE, O. (1968). Rev. méd. Chile, 96, 531. 6 refs.


SURGERY


The author reviews the role of the orthopaedic surgeon in the management of rheumatoid arthritis affecting the hip and knee, his views being based upon experience at the Lahey Clinic.

Synovectomy, he believes, “is probably the most valuable procedure available at the present time in the surgical treatment of rheumatoid arthritis”. This statement, however, is supported by no evidence.

Intra-articular steroid injections and aspirations are discouraged. Advice regarding operative treatment of the hips follows that generally accepted in the United Kingdom before the advent of total replacement arthroplasty.

Synovectomy of the knee is only considered if there is flexion of the joint to 90° and no more than a 20° flexion deformity. The other indications are less clearly defined, but after operation early movements and suction drainage are advised. Arthroplasty receives little attention because the operation has not been performed at the Lahey Clinic.

Arthrodesis of the knee, generally considered one of the best operative procedures in the United Kingdom, is dismissed in four lines.


This is a study of the changes that follow transplantation of the proximal 1 cm. of the proximal phalanx with its articular cartilage to a similar situation in another metacarpophalangeal joint of the same dog. The work was carried out at McGill University, Montreal.

130 such “half-joint transplants” were done in seventy adult dogs with a view to the comparison between one component of the joint deprived of its blood and nerve supply and the other with this supply relatively undisturbed and, of course, without the complications of genetic factors of rejection encountered in homografts.

Within 3 months the articular cartilage of the graft had disappeared, but not until 24 weeks did all joints show radiological evidence of deterioration. At 18 weeks, there was histological evidence of re-vascularization of the bony portion of the graft. By 36 weeks, fibrocartilage had replaced the articular cartilage of the graft. As might be expected with these gross changes, the nongrafted component of the joint also suffered progressive degenerative changes.

The authors do not answer the question they set themselves in planning their experiment, namely, an analysis of the mechanism of the progressive cartilage destruction. They merely confirm that it occurs. However, they do conclude that the synovial fluid changes occur too late to be important, that nutrition of the cartilage from the marrow of the graft was impossible because of the immediate ischaemic necrosis, and that sensory nerve destruction was of no importance. Mechanical factors such as poor alignment of the graft, however, they felt might be important.

Rodney Sweetnam


One of the most characteristic histological features of the rheumatoid hand is atrophy of the intrinsic muscles. In 1949 Kestler said that this characteristic deformity “is the result of simultaneous factors of which the primary and dominating feature is the direct involvement of the intrinsic muscle apparatus proper by the rheumatic process. The wonderful precision balance of the intrinsic apparatus is disturbed through this, establishing the first link in a chain of pathological sequences.” He described histological changes in all these muscles in eleven cases of rheumatoid arthritis. The present authors, at the Canadian Red Cross Memorial Hospital, Taplow, Maidenhead, Berks, tried to evaluate the degree of involvement of the dorsal interossei in 28 cases and to determine whether these changes were related to the severity of the general disease or to any specific hand deformity.

A total of 31 biopsy specimens were obtained during operations on the hand, and were examined by light microscopy after staining with haematoxylin and eosin. In fourteen the appearances were normal; in nine there was evidence of wasting without cellular infiltration; and eight showed chronic inflammatory changes. Patients with wasting had a slightly longer average duration of the disease than the other two groups and were slightly...
more frequently seropositive. The only association between muscle changes and particular hand deformities was a higher incidence of wasting in hands with ulnar deviation, either alone or together with metacarpophalangeal subluxation—that is, the most severely damaged hands. Inflammatory changes showed no correlation with any type of deformity. It seems to the authors, therefore, that the atrophic changes in the intrinsic muscles of the hands in rheumatoid arthritis are more likely to be secondary to gross deformity and limitation of movement than primary aetiological factors.

W. S. C. Copeman


OTHER GENERAL SUBJECTS


The idea that all these diseases might have a common pathogenesis such as a disordered immune tolerance, prompted this study which sets out to compare prevalence with geography.

The available data for these conditions in the U.S.A. show that rheumatic fever, rheumatic heart disease, and multiple sclerosis occur more frequently with increasing latitude. There does not appear to be such a definite trend with rheumatoid arthritis in which the data is limited.

It is pointed out, however, that the prevalence of multiple sclerosis and rheumatoid arthritis amongst immigrants to Israel is similar to that in the country of origin.

[No mention is made of the possibility that diagnostic skill or availability of records increases with latitude.]

Mary Corbett


A hundred patients with the Ehlers-Danlos (E-D) syndrome were fully examined at St. Thomas's Hospital, London.

In 29 patients without affected relatives the disease was apparently sporadic, while 71 were members of 22 families. In all but two of these 22 families inheritance appeared to be of the autosomal dominant type usual in this condition. In the other two families (one of which included six affected males) the pattern of inheritance was that associated with an X-linked recessive character. It is significant that in these two families four affected males had five unaffected sons.

The possibility of autosomal dominant inheritance with incomplete penetrance, the supposed female carriers really being frustes, seems unlikely for the following reasons. No forms frustes were encountered in the other twenty families, and the clinical features of the patients with the apparently recessively-inherited disease differed from those of the others: in these two special families the hyperextensibility of the skin typical of the E-D syndrome was marked in all eight affected members, but the tendency of the skin to split was unusually slight; five patients had typical molluscoid pseudotumours, but the calcified subcutaneous spheroids common in E-D syndrome were present in only two; joint hypermobility with orthopaedic sequelae was marked in five patients, but was limited to the digits. However, a liability to bruising, common in E-D syndrome, was present in most of the affected members of the apparently recessive group. Three patients from among the 29 apparently sporadic cases showed phenotypical similarities to the patients with the apparently recessive type of E-D syndrome.

Sixteen members of the family with six affected males were investigated for Xg grouping. One mother had passed on both the E-D gene and the negative Xg gene to one son, who was thus a non-recombinant, and the negative Xg with her "not E-D" allele to another son, who was thus a recombinant. This finding of a recombinant and a non-recombinant in the family indicates that the loci for Xg and the E-D gene are not close to each other on the X chromosome. Furthermore, the finding that only one of the affected members of this family has deutan colour-blindness suggests that the locus for E-D cannot be very near that for deutan.

Joan R. Gomez
Diffuse Degeneration of the Cornea in a Case of Waldenström’s Macroglobulinaemia. (Diffuse Hornhautdegeneration bei einem Fall von Makroglobulinämie Waldenström.) Gloor, B. (1968). Ophthalmologica (Basel), 155, 449. 5 figs, 37 refs.

The case described concerned a woman of 53 years with visual disturbances dating back 7 years earlier. They were due to bilateral degeneration of the cornea in form of a lattice-like transformation of the deeper aspects. Keratoplasty was performed in one eye which healed after some initial difficulties and apparently induced a regression of the degenerative alterations in the remaining portions of the host cornea. No such improvement occurred in the unoperated eye. At the time of the operation it was found that the patient had Waldenström’s macroglobulinaemia. Since the corneal dystrophy deviates from any known forms, it is assumed that it is associated with the haematological anomaly. The microscopic study of the trephined corneal disc demonstrated hyaline deposits between the lamellae in the deeper half of the stroma. The lamellae themselves show fibrinoid degeneration and are impregnated with the “foreign” substance. Its origin is discussed, but it is regarded as unlikely that it is a paraprotein diffused from the blood into the cornea.

L. Wittels

Annals of the Rheumatic Diseases


With reference to the author’s previous studies on homocystinuria, 23 patients with Marfan’s syndrome were examined. Using a very sensitive method of column chromatography, he found seven cases of homocystinuria among them. This would mean that an incidence of 25-30 per cent. of homocystinuria can be anticipated in such cases. A quantitative evaluation of homocystinuria shows that the levels vary from case to case: therefore, no complete blockade of the enzyme formation should be assumed to exist, as, e.g. in phenylketonuria. The further question is how far the two syndromes can be separated in view of homocystinuria being associated with other symptoms. Quantitative amino acid analysis shows that both in Marfan’s syndrome and in homocystinuria, and in contrast to the normals, there is no increased proline and hydroproline elimination. The additional symptoms occurring in homocystinuria show that though the genes for the two syndromes are closely related, the gene for homocystinuria appears to exert its effect earlier than that of Marfan’s syndrome.

L. Wittels


A patient is presented with Marfan’s syndrome and an associated anterior cleavage syndrome (mesodermal dysgenesis).

J. L. Baum


A case report in two sisters (second and fourth) of the rarer variety of the opposite of Marfan’s syndrome.

Skeletal changes: stumpy growth, short and thick extremities, thick and broad fingers. Hands and feet spade-like.

Ocular changes: Large globular corneas; intercalary ectasia; lenses either cataractous or dislocated. In one eye there were lens-cornea synechiae.

The identical and dissimilar features between the two sisters are compared. No other member of the family (which consisted of five brothers and four sisters) was affected.

The younger sister, married at fourteen, had two abortions and one still birth. The elder one, married at thirteen, had two abortions. Neither had had a single full-term delivery.

S. N. Cooper


The authors describe a case of the Groenblad-Strandberg syndrome which for many reasons of an anatomo-physiological and clinical nature may be associated with Sorsby’s syndrome.

M. G. Bucci


A review of the literature and presentation of two cases of the Groenblad-Strandberg syndrome.

Treatment is at present unsatisfactory, although one author recommends vitamins A and E, while another has found that ACTH and prednisolone improved the condition of the eye and skin.

Una Dean


The authors observed a patient of 37 years with the Groenblad-Strandberg syndrome, angioid streaks, degen-erative macular lesions, and elastic pseudo-xanthoma in the region of the cutaneous folds.

P. Vancea


This is an account of joint function in patients with severe burns and it is of some interest because the situation is one which lies outside the experience of most rheumatologists. Joint function after burns injuries may be affected by para-articular ossification, septic arthritis, dislocation, or soft tissue contracture. The authors discuss management and treatment which may include excision of ectopic bone and suitable positioning, physical therapy and splinting, skeletal traction and by other surgical methods.

J. T. Scott