Abstracts

This section is published in collaboration with Abstracts of World Medicine and Ophthalmic Literature, published by the British Medical Association, and also includes a great many which are specially commissioned for this Journal. They are divided into the following sections:

- Acute Rheumatism
- Rheumatoid Arthritis
- Still's Disease
- Osteoarthritis
- Spondylitis
- Gout

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

Susceptibility to Rheumatic Fever Markowitz, M. (1968) Circulation, 38, 3

The author, writing from the Mt Sinai Hospital, New York, and the Johns Hopkins School of Medicine, Baltimore, in the Editorial of this issue of Circulation draws attention to the well known, but as yet unexplained, fact that only a minority of individuals who develop group A streptococcal infections are susceptible to rheumatic fever. As there is no evidence that this is due to serological or biochemical characteristics of the infecting organism, the point is made that host factors may be the cause. The high familial incidence suggests a constitutional predisposition, and similarity of clinical manifestations in the same family indicates the importance of genetic factors. However, epidemiological studies seeking genetic markers have revealed contradictory findings, and there appears to be no increased incidence of susceptibility to streptococcal infections amongst siblings of individuals who develop rheumatic fever. Markowitz notes the importance of humoral immune mechanisms, as indicated on the one hand by an apparent hyperreactivity in producing high levels of antistreptococcal antibody in affected individuals, and on the other hand by the absence of any reported case of rheumatic fever in children with hereditary agammaglobulinaemia. Kaplan and Suchy (1964) demonstrated that antibodies to a cell membrane antigen of group A streptococci cross-reacted with human heart muscle. More recently cross-reactivity between streptococcal antigen and glycoproteins of human heart valves was demonstrated by Goldstein, Halpern, and Robert (1967) and the antibodies against the glycoprotein were detected in some children with rheumatic fever. These findings indicate possible immunopathological mechanisms in affected individuals, but the question of susceptibility remains unanswered.

R. N. MAINI

References


Rheumatic fever is a disease with a still significant morbidity in Western Australia.

287 cases of rheumatic fever admitted to hospital between 1957 and 1967, are analysed in this paper, which includes the annual and seasonal incidence of the disease, age, presenting symptoms, and clinical and laboratory findings. The incidence of the disease, which was correlated with the estimated population at risk over the period of the survey averaged from 6 to 23 per 100,000 population; a notable but unexplained increase, apparently occurred after 1965.

The numbers of admissions for acute nephritis and for rheumatic fever are compared, and the former are found to be almost double. It also seems that the specificity of the infecting organism varies from year to year. The author hopes that this hospital study can be used to illustrate the trends of rheumatic fever in Western Australia during the decade under observation, as the hospital concerned is the only children's hospital in the State, and the disease is notifiable (although this is seldom done). The records of hospital admission, however, evidently provide a reasonably reliable index of the occurrence of the disease. Cardiac complications were found to occur in over one-third of all cases.

W. S. C. COPEMAN


Treatment of Acute Rheumatism in Childhood Steen (1970) Practitioner, 204, 109

Problems of Rheumatic Fever and Rheumatic Heart Disease in India. Padmavati, S. (1969) Mediscope, 12, 343 15 refs


Rheumatoid arthritis

Involvement of Muscles in Rheumatoid Arthritis in Young Subjects (L'atteinte des muscles au cours de la polyarthrite chronique évolutive chez le sujet jeune) Havelka, S., and Susta, M. (1969) Rev. Pédiat., 5, 233 8 figs, 12 refs

This report from the Institute for Research in Rheumatic Diseases and the Charles University, Prague, describes the results of muscle biopsy carried out on eleven children with rheumatoid arthritis. Their ages ranged from 7 to 15 years and the duration of the disease from 14 to 8 years. The specimen was usually taken from the vastus lateralis muscle.

On microscopical examination eight of the eleven specimens showed perivascular collections of lymphocytes and plasma cells with occasional eosinophils, which for the most part were scanty and widely scattered. Ten of the eleven also showed some form of abnormality in the muscle cells, such as sarcocellular and endomyosial proliferation, loss of striation, or atrophy.

These findings resemble the changes found in muscle in adults with rheumatoid arthritis: they are apparently nonspecific for rheumatoid disease and are not related to the duration of the disease, while the distribution of the muscle lesions is not related to the pattern of joint involvement. Dystrophy of the muscle cell appears to be more common in the child than in the adult.

J. A. Cosh


At the University Central Hospital, Helsinki, and the Rheumatism Foundation Hospital, Heinola, Finland, standard radiographs were taken of the arms, hands, legs, and feet of 370 patients with rheumatoid arthritis (RA) and of 438 controls (patients in an orthopaedic hospital who had not been immobilized for long periods and who did not suffer any severe systemic or disabling disease). The radiographs were examined for the presence of vascular changes by a single observer; only obvious vascular shadows were noted.

Affected arteries were seen in 57 (15.4 per cent.) of the 370 RA patients and in fifteen (3.4 per cent.) of the 438 controls. The two groups were not matched for age, but the changes were observed at a much younger age in the RA group. [The age and sex of patients in the two groups are not given.] Calcium deposits were seen mainly in the arteries of the leg. Of the 57 RA patients showing radiological changes, 21 had systemic manifestations of the disease. Eighteen patients had had the disease less than 5 years and high Waaler-Rose titles were noted in this group. No correlation was found between immobilization and vascular changes.

The authors consider that the sclerosis and calcification of medium-sized arteries seen in these patients had resulted from the connective tissue disturbance caused by the rheumatoid disease.

B. E. W. Mace


[At University Hospital, Leiden, Netherlands] the use of a germfree inoculation technique and washing the specimen greatly reduced the frequency with which diphtheroids were isolated from the synovial membranes of patients with rheumatoid arthritis. Staphylococci were isolated almost as often as diphtheroids. Until better evidence is available, diphtheroids isolated from pathological material should be considered as airborne contaminants.

Authors' Summary.


An episcleral nodule in a patient with rheumatoid arthritis was shown to have similar histological features to those of subcutaneous nodules.

J. H. Kelsey


Spondylitis

Vertebral Destruction at Unfused Segments in Late Ankylosing Spondylitis RIVELIS and FRIEBERGER (1969) Radiology, 93, 251

Gout


Gout is traditionally said to be found among the rich and overindulgent and in recent years a certain amount of evidence has suggested a tendency for those in higher social classes to have higher serum uric acid values. The present study examines the relationship between serum uric acid levels and social class among 910 persons in Wensleydale, 321 persons in Watford, and 1,213 persons in New Haven, Connecticut, U.S.A. In the men of Wensleydale there was a tendency (of marginal statistical significance) for uric acid to be higher in the lowest social class, with no apparent trend at all in men at the other two places. In women, there was a tendency for uric acid to increase as social class fell in all three places, the trend being significant at New Haven.

It is considered that the discrepancy between this and previous studies is consistent with a multifactorial concept of uric acid control, a certain determinant of uric acid being important in some populations and not in others.

J. T. SCOTT

Carbohydrate Intolerance in Gout DENIS, G., and LAUNAY, M. P. (1969) Metabolism, 18, 770 15 refs

To investigate further the relationship between gout and diabetes mellitus, the authors of this paper from the Department of Physiology, University of Montreal, have studied carbohydrate tolerance in thirty gouty subjects. All thirty were male, their ages ranged from 27 to 52 years, and they had been referred from the Canadian Armed Forces during a 2-year period for management of their gout. None had a history suggestive of diabetes; six were more than 20 per cent. overweight. After determination of the serum uric acid level (modified...
Caraway technique) the fasting patients were given 100 g.
glucose by mouth and blood sugar levels were measured
(modified Folin–Wu method) ½, 1, 2, and 3 hrs later.

The majority of gouty patients did not tolerate the
glucose load as well as normal subjects. According to
the criteria used (Wildberger–Ricketts and Joslin Clinic),
the glucose tolerance test showed borderline abnormality
in 76 and 60 per cent. of cases respectively, and in one-
third of the patients it was sufficiently abnormal to sug-
gest the presence of diabetes. There was no correlation
between the serum uric acid concentration and the blood
sugar level either in the fasting state or 2 hrs after the
administration of glucose.

The authors state that more studies are in progress in
an effort to elucidate the biochemical links between
gout and diabetes.

B. M. ANSELL

Gouty Arthritis as a Complication of Acetazolamide
(Diamox) Therapy for Glaucoma FERRY, A. P., and

A patient developed an acute attack of gout shortly
after concluding a course of acetazolamide therapy for
glaucoma. It is postulated that the hyperuricaemic effect
of acetazolamide may have contributed to the provoca-
tion of this episode.

HOWARD REED

Non-Urate Chromogens in Body Fluids CARAWAY,

The author refers to substances other than urate which
may cause reduction of phosphotungstate in the car-
bonate-phosphotungstate method as 'non-urate chromo-
gens'. These may cause a significant increase in apparent
serum uric acid level. Certain of these substances can be
avoided by using unhaemolysed serum or plasma, and
most of the others eliminated by preliminary oxidation
in alkaline solution. Since some part of the 'non-urate
chromogen' can be destroyed by heating at 56°C, or
by storing, and ascorbic acid is known to cause reduction
of phosphotungstate and is present in plasma, it was
decided to compare ascorbic acid and labile non-urate
chromogen concentrations in plasma.

The alkali-labile non-urate chromogens were shown to
be mainly ascorbic acid. Chromogens resistant to alkali
and uricase in 21 hospital patients had a mean value of
0·17 mg./100 ml. (range 0·08 to 0·29). The very high
serum levels of uricase resistant chromogens that can
occur in renal failure of eclampsia and salicylate therapy
is emphasized. Ascorbic acid may also interfere with the
enzymatic (uricase) spectrophotometric methods of
measuring uric acid since its absorption spectrum overlaps
that of uric acid. Further oxidation of ascorbic acid can
occur under the experimental conditions employed,
which may lead to variation in the blank values.

The author concludes that, provided alkali is used to
destroy ascorbic acid, colorimetric methods are suffi-
ciently accurate for estimation of serum urate. But since
up to 15 per cent. of urinary chromogen may be alkali
and uricase resistant, an enzymatic method is indicated
for measuring urinary urate.

P. J. L. HOLT

Elevation of Plasma Glutamate in Gout. Its Possible Role
in the Pathogenesis of Hyperuricemia PAGLIARA, A. S.,

Articular Chondrocalcinosis (La chondrocalcinose articu-

Editorial: Chondrocalcinosis and Pseudogout (1969)
Canad. med. Ass. J., 101, 824

Polyarthritic Forms of Articular Chondrocalcinosis
(À propos des formes polyarthritiques de la chondro-
calcinose articulaire diffuse. Discussion nosologique.
Rev. Rhum., 36, 724

Diffuse Familial Articular Chondrocalcinosis (Chondro-
calcinose articulaire diffuse familiale) HADDAD, N.,
REBAI-COLIN, M. T., POTANCOK, R., and LOUERTANI, A.
(1969) Tunis. méd., 47, 339–47 figs, 24 refs

Microscopic Studies on Crystals in Skeletal Muscle from
Two Cases of Xanthinuria CHALMERS et al. (1969)
J. Path., 99, 45

Physiologic and Biochemical Basis for the Treatment of
Gout and Hyperuricemia MIKKELSEN and ROBINSON

Effects of Allopurinol on Hyperuricemia Secondary to
Fasting SCHATANOFF, J., DUNCAN, T. G., and DUNCAN,
G. G. (1970) Metabolism, 19, 84 12 refs

Influence of Allopurinol on Uric Acid, Creatinine, Fasting
Blood Sugar, and Plasma Lipids in Gouty Patients (Der
Einfuss von Allopurinol (Zyloric R) auf Harnsäure,
Kreatinin, Nüchternblutzucker und Plasmalipide bei
Wien. klin. Wschr., 82, 78  3 figs, 40 refs

Suppression of Uric Acid Formation from Dietary Nucleic
Acid with Allopurinol BOWERING, J., MARGEN, S.,
Nutr., 22, 1426 1 fig, 4 refs

Gout and Uveitis. Report of a Case KILLEN, B. U.
(1968) Brit. J. Ophthal., 52, 719  8 refs

The Carterton Study: 5. Serum Uric Acid Levels of a
Sample of New Zealand European Adults EVANS et al.

Epidemiology of Serum Uric Acid and Gout: An Example
of the Complexities of Multifactorial Causation

Bone disease

Tenosteochondrosis of the Pubis ROSENKLINT, A., and
figs, 9 refs

Decalcifying Osteoses in Malabsorption in Adults (Les ostéoses décalcifiantes par malabsorption de l'adulte) VIGNON, G., PANUS, D., and CHAPUY, P. (1969) *Rev. Rhum.*, 36, 663 8 figs, 21 refs

Primary Osteonecrosis of the Knee in the Aged. With Reference to 11 Cases (L'ostéonécrose primitive du genou des sujets âgés (A propos de onze observations)) MEGARD, M., MAITREPierre, J., and DURANT, J. (1969) *Rev. Rhum.*, 36, 697 6 figs, 10 refs

Bone Dysplasias, including Morquio's Syndrome, studied in Skin Fibroblast Cultures DANES and GROSSMAN (1969) *Amer. J. Med.*, 47, 708

Bone Formation in Hypercortisonism JOWSEY and RIGGS (1970) *Acta endocr.* (Kbh.), 63, 21


Other forms of arthritis


Diagnosis of Infectious Spondyloïdritis. Thirty Cases of Pott's Disease compared with Thirty Cases of Non-Tuberculous Spondyloïdïtis (Les spondyloïdites infectieuses. Problème du diagnostic. Comparaison de 30 cas de mal de Pott et de 30 cas de spondyloïdite non tuberculeuse) BONTTOUX et al. (1969) *Rev. Rhum.*, 36, 541


Acute Guinea-Worm Synovitis of the Knee Joint SIVARAMAPPA et al. (1969) *J. Bone Jt Surg.*, 51A, 1324


Non-articular rheumatism


A prospective study of eleven cases of polymyalgia rheumatica is presented [from Balmain Hospital, Perth, Australia]. The average age of the eight women and three men in the study was 75 years. Polymyalgia rheumatica as a primary diagnosis was often overlooked, but in fact the history is a most significant feature of the illness. Clinically it is often not possible to distinguish between polymyalgia rheumatica, temporal arthritis and giant cell arthritis, and there is evidence that these three disorders represent a spectrum of a single disease process.

Ancillary diagnostic aids are a high ESR and disturbances of the globulin serum protein fraction on electrophoresis, with a normochromic normocytic anaemia, and occasionally a positive temporal artery biopsy. Steroid therapy has become the treatment of choice. An alternate single-dose regimen has proved satisfactory.

Of the eleven patients, one developed evidence of polyarthritis nodosa, and later Sjögren's syndrome, and finally lymphosarcoma. A second patient, after a complete remission of 9 months, relapsed and, despite increasing steroid dosage, died of cerebral causes. A third patient developed severe congestive cardiac failure and atrial fibrillation, but these complications have since completely remitted.

Polymyalgia rheumatica in this series has been a disorder whose benign nature may be called in question.

**AUTHORS' SUMMARY**

Low Back Pain: Diagnosis by History and Examination CAILLIET, R. (1969) Sith. med. J. (Bgham, Ala.), 62, 1459 8 figs

Hereditary Amyloidosis, the Flexor Retinaculum and the Carpal Tunnel Syndrome LAMBIRD and HARTMANN (1969) Amer. J. clin. Path., 52, 714


Connective tissue studies


Pararheumatic (collagen) disease


A number of tests are available for demonstrating antibodies to DNA in the serum of patients with systemic lupus erythematosus (SLE) but most of them have technical disadvantages.

The easily performed test which is described by the authors of this paper from the National Institutes of Health and the Breck Brigham Hospital, Boston, depends on the differential solubility of DNA and DNA immunoglobulin complexes in ammonium sulphate. While DNA is soluble in 50 per cent. saturated ammonium sulphate, immunoglobulins, whether bound to DNA or not, are insoluble. 14C-labelled DNA and serum are mixed with ammonium sulphate and on binding the radioactive label appears in the precipitate. Estimation of the percentage of radioactive label in the precipitate gives a measure of antibody activity.

The test was made on serum collected from controls (normal volunteers and patients with Sjögren's syndrome, rheumatoid arthritis, multiple myeloma, and serum sickness, or myelomatosis and 33 of 44 sera was shown to be mainly to immunoglobulin G. High binding levels were found in two of 84 normal sera, three of 57 sera from the patients with rheumatic disease, serum disease, or myelomatosis, and 33 of 44 sera from the patients with SLE. In SLE high DNA binding was associated with active disease, nephropathy, and positive LE cell tests and the binding level fell to normal as the disease was suppressed by steroid therapy.

Anti-DNA antibodies were more consistently demonstrated by this method than by complement fixation or precipitin techniques and it is noted that the test can be applied to anticomplementary sera whereas complement fixation cannot.

M. WILKINSON


[In the Department of Medicine of the University of Tennessee College of Medicine, Memphis] a prospective study of seven patients with systemic lupus erythematosus (SLE) was carried out in order to determine the nature of the microvascular injury which characterizes this disease. A detailed evaluation of the clinical features and course and their ultrastructural correlates was made. Of 23 biopsies performed on SLE patients, twelve biopsies from five patients contained characteristic inclusions within endothelial cells. They persisted in the same patients for up to 9 months. They were found in muscle, skin, glomerular and peritubular capillaries. They were present in all tissues actively involved by the disease process and not found in uninvolved tissues of the same patients, non-rheumatic disease patients, or normal individuals. Similar inclusions were also noted in five patients with Sjögren's syndrome and one patient with Goodpasture's syndrome. Immunologic studies failed to demonstrate specific myxovirus antigens in actively involved tissues, antibodies in patients' sera which were reactive with the endothelial inclusions, or unusually frequent or elevated levels of antimyxoxy antibodies in patients' sera. The significance of the inclusions is not yet known, but the data suggest at least two major possibilities:

1. The inclusions are viral in nature and, if so, are likely to be etiologically related to SLE.

2. The inclusions are a reactive phenomenon on the part of the cells at the site of active disease—a reaction which occurs with a high frequency in several rheumatic diseases.

In either event, the findings support the fundamental importance of microvascular injury in several rheumatic diseases.

AUTHORS' SUMMARY


A description of the presenting symptoms and pathology of Wegener's granulomatosis with reference to six cases.
Initial symptoms are usually related to the upper respiratory tract and the lungs and kidney become involved later. Different appearances of the nasal mucosa appear in the early stages of the disease. The established condition has no specific treatment but corticosteroids may be beneficial early.

T. J. FFYTCH


A case of a fully established Sjögren syndrome is presented. A detailed survey of the up-to-date literature is given with comments. The authors think that in their case Sjögren's syndrome was part of a generalised rheumatoid disease.

I. STANKOVIĆ


Impaired Renal Acidification in Sjögren's Syndrome and Related Disorders KALTREIDER and TALAL (1969) Arthr. and Rheum., 12, 538


Polyarteritis Nodosa as a Cause of Perirenal and Retroperitoneal Hemorrhage CAPPS, J. H., and KLEIN, R. M. (1970) Radiology, 94, 143 5 figs, 10 refs


Polyarteritis presenting with Leg Pains GOLING, D. N. (1970) Brit. med. J., 1, 277


Immunology and serology


[At Duke University Medical Centre, Durham, North Carolina] twenty patients with unexplained pulmonary fibrosis and circulating antinuclear factor were identified. Diseases commonly associated with antinuclear factor, such as systemic lupus erythematosus or scleroderma, were excluded. Half of the patients showed typical restrictive ventilatory defects and x-ray evidence of severe fibrotic changes. The remaining patients predominantly had evidence of obstructive airway diseases.

Four lung biopsies were available. Three showed histological evidence of interstitial pulmonary fibrosis. Immunofluorescent study of one of the biopsy sections with pulmonary fibrosis from a patient with only IgM serum antinuclear showed IgM in the alveolar septa. Relatively little fibrosis was present in immunoglobulin-laden areas whereas no immunoglobulin could be demonstrated in the adjacent alveolar septa showing marked fibrosis. Seven out of ten patients with x-ray evidence of severe interstitial pulmonary fibrosis and typical restrictive ventilatory defects had only IgM antinuclear factor in their sera. Altered immunologic reactions associated with the generation of autoantibody may play a role in the pathogenesis of interstitial pulmonary fibrosis.

Authors' summary

The leucocyte-binding factor (LBG) was demonstrated in the globulin fraction of patients' sera by labelling it with fluorescent isothiocyanate. The antigenic factor was demonstrated in the serum of a patient with rheumatoid arthritis, whereas an anti-cytolysis factor was demonstrated in patients with Behcet's syndrome (9 out of 18) Vogt-Koyanagi-Harada syndrome (3 out of 10), ocular sarcoidosis (3 out of 7), Sjögren's syndrome (1), and unclassified endogenous uveitis (1 out of 10). Sixteen out of seventeen patients with positive LBG were found to have active inflammation. No correlation was found between LBG and leucocyte-count, blood groups, CRP, BSR, and ASLO. Administration of corticosteroid had no influence on the incidence of LBG.

S. MISHIMA


The rabbit cornea was injected with bovine serum albumin. A challenge injection with the same antigen was made into the fellow cornea at intervals after sensitization. 48 hours after the challenge, the challenged eye and its regional lymph nodes were studied. The fluorescent antibody technique was used for the detection of IgM- or IgG-containing cells. The degree of the corneal limbal reaction and the corneal oedema paralleled an increase or decrease of IgM- and IgG-containing cells at the corneal limbus but not the titre of serum precipitin.

S. MISHIMA


Inhibition of Complement-mediated Hemolysis by Rheumatoid Arthritis Sera studied in Agarose Gel KASUKAWA, R., YOSHIDA, T., and MILGROM, F. (1970) Int. Arch. Allergy., 38, 168 4 figs, 7 refs

Streptococcal Anti-Group A Precipitins in Sera from Patients with Rheumatic Arthritis and Acute Glomerulonephritis BRAUN, D. G., and HOLM, S. E. (1970) Int. Arch. Allergy, 37, 216 1 fig, 36 refs

Experimental studies with animals


This is a 50-page review of the work on NZB (New Zealand Black) mice since their original discovery by Marianne Bielschowsky at the Otago Medical School, New Zealand, up to 1968. There are 89 references. The natural history, morbidity anatomy, histology, and immunology of the NZB strain and (NZB x NZW) F1 hybrids constitute the bulk of the review. Technical details of the husbandry of the animals are not mentioned. Experimental studies of the genetics and of the cellular transfer of the autoimmune phenomena which characterize NZB mice, and the effects of thymectomy, steroids, and immunosuppressive agents are presented. Recent work indicating a viral aetiology is briefly discussed.

The authors, who are members of the Department of Pathology at Otago University, have produced an interesting and critical appraisal of the present position in this area of experimental pathology.

J. BALL


This paper describes the occurrence of antinucleoside antibodies in a 'lupus-like' membranous type of glomerulonephritis which spontaneously occurs at the age of 4 to 6 months in a very large proportion of the hybrid strain F1 derived from crossing NZB (black) with NZW (white) inbred mice. In this study from the Departments of Microbiology and Medicine, College of Physicians and Surgeons, Columbia University, New York, and from the second Clinica Medica della Università di Roma, fluorescein-labelled antibodies were used which were specific for the bovine serum albumin conjugates of nucleosides containing pyrimidine bases of DNA, i.e. thymine ('anti-T') and cytosine ('anti-C'). These antisera react with 'denatured' DNA without cross-reaction with 'native' DNA. Positive immunofluorescence staining with anti-T and anti-C therefore apparently reflects the presence of denatured DNA. About 80 per cent. of the hybrid strain of mice over 6 months old showed binding of anti-T and/or anti-C in the glomerular capillary walls of the kidneys. Control tests on the specificity of the anti-T and anti-C sera were performed by 'blocking' tests using unlabelled antisera and absorption of the fluorescein-labelled antisera with homologous antigen. Results were only read as positive when fluorescence was markedly better than that obtained using antibovine serum albumin serum alone. In contrast to the results in hybrid mice, none of the kidneys from NZW mice and only two out of nineteen of the NZB mice, showed immunofluorescent anti-T or anti-C antibodies in the glomerular capillaries. The kidney sections were also examined for mouse globulin using fluorescein-labelled antibodies, and these were found in thirteen out of nineteen NZB mice, in twenty out of 27 NZW mice, and in all 51 hybrids more
than 5 months old. In forty of the hybrids the antigen-antibody reaction was in the same area which had bound the antinucleoside antibodies. The association of denatured DNA and globulin is thought to support the hypothesis involving this antigen-antibody complex in the pathogenesis of the disease. The authors note the ease with which the anti-T and anti-C antibodies are demonstrated, indicating that DNA localized in the glomeruli is partially or largely denatured, and they suggest that denaturation of DNA could play a role in the initiation of autoimmunity in the renal disease of NZB/NZW F1 mice.

R. N. MAINI

Passive Transfer of Adjuvant-induced Arthritis and Allergic Encephalomyelitis in Rats using Thoracic Duct Lymphocytes


Trial of Cyclophosphamide on Arthritis induced in the Rabbit by a Homologous Inflammatory Exudate. Historical Study of the Femoro-tibial Synovium 15 Days after the Inducing Injection (Essai du cyclophosphamide sur l'arthrite du lapin provoquée par un exsudat inflammatoire homologue. Étude histologique de la synoviale fémoro-tibiale quinze jours après l'intervention déclenchante)


Abnormal Sulfhydryl-Disulfide Interchange in Serum of Rats with Adjuvant Arthritis: Correction by Anti-Inflammatory Agents


Differences in the Severity of Adjuvant Arthritis in Four Strains of Rats


Experimental Corticosteroid Myopathy

Sheahan and Vignos (1969) Arthr. and Rheum., 12, 491

Early Lesion of Experimental Allergic Orchitis in Guinea-Pigs: An Immunological Correlation


Biochemical studies

Tests of Hypothalamic-Pituitary-Adrenal Function in Man


This investigation was undertaken at the Middlesex Hospital Medical School, London, to assess the value of a number of tests of hypothalamic-pituitary-adrenal function. 102 patients were studied and 126 intravenous insulin tests were carried out, 37 infusions of lysine vasopressin (LVP), fourteen artificial-fever tests with 'E' pyrogen, and 37 tests with metyrapone. The response to intravenous (IV) insulin was assessed on increase of plasma 11-hydroxycorticosteroids (minimum 7 μg./100 ml.) and the maximum growth-hormone level found during the test (normally > 7·0 ng./ml.). Responses to LVP infusion and 'E' pyrogen were detected by increases of plasma 11-hydroxycorticosteroids (11-OHCS): minimum normal increases were 6 μg./100 ml. and 8·5 μg./100 ml. respectively. No consistent change of growth hormone was found after LVP or 'E' pyrogen. Metyrapone was given as 750 mg. 4-hrly for 48 hrs, and response was assessed on the increase of urinary 17-oxogenic steroids (17-OGS) on the second day of administration compared to the control level. The minimum normal increment was 10 mg.

Using these criteria, 53 IV insulin tests on 43 patients gave normal results; twelve of these patients were tested with LVP and four with 'E' pyrogen, and all gave normal increments of plasma 11-OHCS. One out of nine gave a reduced response to metyrapone. In seventeen tests on fifteen patients, there was a reduced GH but normal plasma 11-OHCS response to IV insulin. Six of these patients were thought to have an isolated GH defect. Of the fifteen, six had LVP tests and one received 'E' pyrogen with normal responses. Twelve were tested with metyrapone and two failed to respond.

In twenty IV insulin tests (on nineteen patients) there was no response of plasma 11-OHCS or GH. Eight of these patients were tested with LVP and gave a normal response; seven were given 'E' pyrogen but none of them responded normally. Thirteen tests were performed on patients with acromegaly before treatment and eleven after surgical or deep x-ray therapy. Eight IV insulin tests were performed on patients with Cushing's syndrome.

The following conclusions were reached: an IV insulin test with measurement of plasma 11-OHCS and GH responses is the most sensitive method of detecting minor deficiencies of the hypothalamic-pituitary axis. In two patients in whom other tests gave normal results the response to metyrapone was reduced. Patients who fail to respond to IV insulin may respond to LVP infusions; they appear nevertheless to benefit from replacement therapy. For the detection of residual pituitary function following hypophysectomy it is suggested that an IV insulin test, while the patient is still on replacement therapy with small doses of prednisone, may be of value.

Authors' Summary

Collagenase in the Cornea


A collagenase capable of digesting collagen fibres in the stroma and the native collagen molecule was found in rabbit corneal epithelium. Two substrates were used: reconstituted collagen from guinea-pig skin and 3 μ thick cryostat sections of hexane frozen (~ 60°C) rabbit and calf corneal stroma.

 Cultures of rabbit corneal epithelium, stroma, and endothelium plus Descemet's membrane were placed upon the substrates and incubated in medium 199 in Rose chambers at 35°C.

All the epithelial cultures caused lysis of both substrates but none occurred with the stromal and endothelial cultures.

The epithelial enzyme was inhibited by calf, foetal calf, and chicken serum added to the culture medium, but not...
by human and rabbit serum. EDTA-Na and EDTA-Ca inhibited lysis in concentrations down to 10^{-4} M. The substrates were completely digested by 0.1 per cent. C. histolyticum collagenase but not by 0.1 per cent. solutions of trypsin, α-chymotrypsin, or hyaluronidase.

EDTA-Ca as a therapeutic agent in the treatment of corneal ulcers is suggested owing to its strong inhibition of collagenase activity and low toxicity to cells.

E. S. Sherrard


Homogenates of calf corneal epithelium, stroma, and endothelium and conjunctival epithelium were separated into three fractions by centrifugation giving sediment I at 500 × g., sediment II at 98,000 × g. of the supernatant from I, and the resulting high speed supernatant. A synthetic substrate (a 4-phenylazohexyloxycarbonyl-L-prolyl-L-lysylglycyl-L-prolyl-D-arginine) was used in the assay.

The choice of substrate was based upon its resistance to cleavage by proteolytic enzymes other than bacterial collagenase and, hence, its relative specificity. Nevertheless, the authors question a comparison between animal peptidase detected with a synthetic substrate specific for bacterial collagenase and collagenases demonstrated by lysis and degradation of reconstituted collagen gels.

E. S. Sherrard

Anti-inflammatory Activity of Inflammatory Substances


Indomethacin and Acetylsalicylic Acid in the Treatment of Osteoarthritis of the Hips and Knees


From Westminster Hospital, London, Ontario, a detailed account is given of a double-blind crossover trial with sequential analysis in which indomethacin was compared with acetylsalicylic acid in the treatment of eighteen patients with primary osteoarthritis of the hips and/or knees. The patients were all male and ranged in age between 56 and 85 years. The drugs were given in random order for consecutive periods of 10 days; the dose of acetylsalicylic acid was 1.3 g. and that of indomethacin 50 mg., three doses daily being taken in each case before meals. All patients also received physiotherapy, and ‘pain relievers’ (30 mg. codeine) and night sedatives (100 mg. quinalbarbitone) were available on request. Measurements of muscle strength and of the time taken to walk a standard distance and to climb a standard flight of stairs were made before the trial and after each treatment period, and the numbers of codeine and quinalbarbitone tablets taken in the two periods were noted.

D. Preiskel
All measurements improved during both treatment periods; there was no significant difference in the extent of the improvement as between the two drugs, and the order in which they were taken did not affect the results. There were some minor toxic effects with both drugs. The authors conclude that acetylsalicylic acid, which is cheaper and in general has fewer side-effects, is to be preferred for the treatment of osteoarthritis.

K. C. ROBINSON


In this study from the University of Minnesota Medical School, Minneapolis, the authors investigated the mechanism of aspirin sensitivity.

A clinical study was made of 23 asthmatic patients with aspirin sensitivity, who represented about 4 per cent. of the total number of asthmatics seen by the authors during the period of their study. Half had nasal polyps, and a similar proportion had skin reactions to one or more allergens. Many required corticosteroid maintenance therapy.

A number of immunological experiments were performed. [For details of the methods and results the original should be consulted.] In animals (guinea-pigs, rabbits, and monkeys) aspirin, salicylic acid, and aspiryl chloride bound to bovine γ-globulin or egg albumin were tested as antigens. Protein-bound aspiryl chloride produced acute systemic anaphylaxis in eleven out of twelve guinea-pigs and positive cutaneous anaphylaxis in most rabbits. High passive haemaglutination titres were achieved in the rabbits, and both aspirin and salicylic acid increased the in vitro lymphocyte transformation rate of rabbit cells.

However, sera from nineteen aspirin-sensitive patients did not cause passive cutaneous anaphylaxis in guinea-pigs and did not elicit Prausnitz–Küstner reactions in monkeys. Attempts to produce passive systemic anaphylaxis in guinea-pigs also failed, and sera from the asthmatic patients gave negative results in Ouchterlony double diffusion and microprecipitation tests. Lymphocyte transformation in the presence of aspirin was slightly increased in seven out of eleven patients, but incorporation of tritiated thymidine was not increased.

There is, therefore, no experimental basis so far for an aspirin allergy in man, but the authors think that it is possible than an undefined allergen is formed as a result of contact with aspirin, or that it acts through non-immunological mechanisms.

H. HERXHEIMER


The experiments were done in rabbits. The velocity of epithelialization of a denuded area (diameter 8 mm.) was followed. ACTH given intramuscularly had no effect. The velocity was lowered with sodium salicylate given subconjunctivally but the difference could not be proved statistically. When both substances were given simultaneously cell regeneration was impaired in the first stage by the inhibition of mitoses, by inhibition of migration of the basal cells, and by degenerative changes, but the total time necessary for epithelialization was not prolonged.

M. KLIMA


There is no evidence that indomethacin in therapeutic dosage causes any increase of intra-ocular pressure and there is no evidence that indomethacin exerts toxic effects upon the eye.

A. G. CROSS


An experimental study on rabbits proving that systemic and topical use of prednisolone does not produce any appreciable rise of intraocular pressure in healthy eyes.

S. N. COOPER


A clinical study of 85 patients showed that systemic and topical use of corticosteroids was capable of increasing the intraocular pressure and a fall in outflow facility only in eyes with a glaucomatous diathesis.

S. N. COOPER


The authors’ experience with iatrogenic posterior subcapsular cataract is described and the literature is reviewed.

D. F. COLE


The use of a single dose of systemic steroids given on alternate days in the treatment of steroid-responsive inflammatory disease resulted in reduction of adenra suppression and of side-effects. Clearance of the infection occurred as quickly as with other methods of therapy.

A. G. CROSS


Ibuprofen, Aspirin, and Placebo in the Treatment of Rheumatoid Arthritis—a Double-blind Clinical Trial

(see Abstr. Wild Med., 1970, 44, No. 4, p. 299)

Adrenal Function during Topical Oral Corticosteroid Treatment


Clinical Study of the Antipyretic Action of Indomethacin in Childhood (Studio clinico sull’azione antipiretica dell’indometacina nell’infanzia) Giardini, O., and Cardi, E. (1969) Policlinico, Sez. med., 76, 322 1 fig., 12 refs

Indomethacin in Extra-articular Lesions


Case Histories of Rheumatoid Arthritis treated with Sodium or Magnesium EDTA


Osteonecrosis of the Medial Femoral Condyles after Corticotherapy (Une observation d’ostéonécrose des condyles fémoraux internes après corticothérapie) Duparc et al. (1969) Rev. Rhum., 36, 563

Gastroscopic Findings and Fecal Blood Loss following Aspirin Administration

Kupfer et al. (1969) Amer. J. dig. Dis., 14, 761

Iatrogenic Retinal Lesions caused by Aspirin (Accidentes retinianos yatrogénos motivados por la aspirina) Sedan, J. (1968) Rev. esp. Oto-neuro-oftal., 27, 272 19 refs

Aggressive Management of Rheumatoid Arthritis in the Elderly


Can Flexion Deformities of the Knee in Rheumatoid Arthritis be Prevented and Corrected by Conservative Methods? (Peut-on prévenir et corriger par des techniques conservatrices les attitudes vicieuses en flexion du genou dans la polyarthrite rhumatoïde?) Lenoch, F., Kadlecova, L., and Popek, S. (1969) Rhumatologie, 21, 313 5 figs


Rheumatoid Arthritis: Comparison of Treatment with Monophenylbutazone and Phenylbutazone


Comparison of Codeine Compound and ‘Saridone’ in the Pain of Rheumatoid Arthritis


ACTH or Corticosteroids? A Critical Review


Adrenal Glucocorticoids after Twenty Years: A Review of their clinically Relevant Consequences

David et al. (1970) J. chron. Dis., 22, 637

Cyclophosphamide Treatment of Rheumatoid Arthritis

Fosdick (1969) Arthr. and Rheum., 12, 538

Comparison between Local Injections of Silicone Oil and Hydrocortisone Acetate in Chronic Arthritis


Granulocytopenia, Lupus-Like Syndrome, and Other Complications of Propylthiouracil Therapy

Amrhein et al. (1970) J. Pediat., 76, 54


Clinical Use of Immunosuppression


Review of the Actions and Effects of Immunosuppressive Drugs


Immunosuppressive Therapy in Rheumatology (La terapia immunosupresiva con citostaticos en reumatologia) Del Campo, J. B. (1969) Rev. esp. Reum., 13, 204 10 refs

Surgery

Silicone Rubber Implants for Replacement of Arthritic or Destroyed Joints in the Hand


This is a review of the use of silicone rubber implants for replacement of hand and elbow joints. It describes the development of these joints and their characteristics. The surgical techniques are well described, but the clinical indications are not so well covered. Description
of postoperative care is limited to spring splints. The long-term effectiveness of these joints could not be assessed at this stage.

P. J. L. HOLT


Other general subjects


This report, from Cornell University Medical College, New York, describes a new genetically based disorder of polysaccharide metabolism.

Two female siblings, aged 12 and 3 years, children of a consanguineous marriage, showed progressive grotesque deformities of the trunk and limbs, coarsened facial features, and peripheral corneal opacities. Both children were normal at birth, signs of disease appearing in the older child at age 1½ months and the younger at age 12 months. The x-ray findings, which are described in considerable detail, revealed progressive destructive joint disease and osteoporosis. Although these x-ray changes resembled those of severe rheumatoid arthritis, there were only minimal signs of inflammation and there was no fever or raised erythrocyte sedimentation rate.

Some features of the disease resembled mucopolysaccharide storage disease and, although there was no increased mucopolysaccharide excretion in the urine, high uronic acid content of skin fibroblast culture was found histochemically. This abnormality was present in both parents, as well as in the children, suggesting an autosomal recessive mode of inheritance.

The authors discuss the distinction from rheumatoid arthritis and the relationship with other known mucopolysaccharide storage diseases in detail. J. R. DALY


It is only comparatively recently that the importance of arteritis as a serious complication of rheumatoid disease has been widely recognized. It commonly involves the vessels of the skin, skeletal muscles, and nerves. In a 4-year study of a consecutive series of 102 patients admitted to the Goldwater Memorial Hospital, New York, with rheumatoid arthritis, six developed diffuse vasculitis. Two of these six sustained myocardial infarction as well, and coronary arteritis was discovered post mortem in one. The findings in these two patients are outlined in this paper. The necropsy reports of a further 95 rheumatoid patients were also studied and seven were found to have suffered myocardial infarcts, but no histological evidence of coronary arteritis was reported.

The author concludes therefore that, contrary to current thinking, coronary arteritis is probably not a common cause of myocardial infarction in rheumatoid arthritis, although in the presence of widespread vasculitis a spread to the coronary arteries may culminate in classic myocardial infarction. As in non-rheumatoid patients, however, the major cause of infarction is still atherosclerosis. W. S. C. COPEMAN

