Heberden Society

Annual Report 1977

The President, Professor V. Wright, announced that Professors E. G. L. Bywaters, J. J. R. Duthie, and J. H. Kellgren had been elected to Honorary Membership of the Society.

Mr. M. Laurence and Dr W. A. Penman had resigned from the Society.

The President recorded with deep regret the deaths of The Rt. Hon. The Lord Cohen and Mr S. L. Higgs, Honorary Members, and Dr R. Michael Mason and Dr G. Loewi.

At the Annual General Meeting held on November 18 and 19, 1977, the following new members were elected.

Ordinary Members:
Dr I. F. MacRae, Dr C. Murray-Leslie, Dr M. F. Grayson, Dr A. K. Clarke, Dr Jacqueline Currey, Dr T. J. Gibson.

Associate Members:
Dr Patricia J. Smith, Dr Layla Kazkaz, Dr H. Bird, Dr Geraldine M. Brough, Dr M. E. T. Roberts, Dr C. J. Moran, Dr J. R. Jenner, Professor E. D. Acheson, Dr R. Travers, Dr R. W. Jubb, Dr P. A. Revell, Dr B. J. Weston. Dr Corina Engler, Professor R. M. Acheson, Dr J. T. Cassidy, Dr B. Bourke, Dr N. Kadir, Dr G. Balint, Dr A. Stockman, Professor J. P. Camus, Dr P. W. Blower, Dr I. W. Tomlinson, Dr N. R. Laurent, Dr C. de Ceuæer, Dr P. J. W. Venables, Dr A. C. S. Keat, Dr R. F. Mangel, Dr D. Y. MacKenzie, Dr C. D. Holland, Dr E. J. Desser, Dr A. Blackham, Dr J. C. W. Edwards, Dr M. B. Richter, Dr Margaret E. Moonsawmy, Mr W. A. Souter, Dr R. A. Williams, Dr C. C. Erhardt, Dr P. L. Kinsella, Dr M. de Silva, Dr M. A. Sattar, Dr P. Hickling, Professor H. J. Glanville, Dr Linda J. Marks, Dr H. N. Misra Dr J. P. Brown, Dr A. L. Thomas, Dr Elisabeth Paice, Dr F. M. Khan, Dr J. T. Dingle, Prof. Dr med. P. W. Hartl, Dr Margaret A. Byron, Dr M. A. Stodell, Dr M. M. Madkour, Dr J. R. Sewell, Dr O. D. Barkley, Dr A. W. Ford-Hutchinson, Dr J. E. Davies, Dr O. J. Hidson, Dr J. E. H. Chapman, Mr S. P. F. Hughes, Dr Myriam Lugon.

Associate Members (Overseas):
Dr Z. S. Alrawi, Dr Pinkwas Fiszman, Dr T. Hadidi, Dr M. J. Willans, Professor H. A. Smythe, Dr A. Stavaras.

Activities
Preceding the Heberden Round in May, a one-day symposium on 'The Aetiopathogenesis of Osteoarthritis' was held at the Welsh National School of Medicine, Cardiff.

The Heberden Round was conducted by Dr K. N. Lloyd at the Welsh National School of Medicine, Cardiff, on May 27, 1977 (Annals, 36, 478-483).

A combined meeting with the Section of Rheumatology and Rehabilitation of the Royal Society of Medicine and the British Association of Rheumatology and Rehabilitation was held in Carlisle on October 13 and 14, 1977 (this issue pp. 290-295).

The Heberden Oration for 1977 was delivered by Dr Barbara Ansell and was entitled 'Chronic arthritis in childhood' (Annals, 37, 107-120).

The Annual Dinner was held on November 18, 1977 at the Royal College of Physicians. Among the guests were Sir Douglas and Lady Black.

Finance
The Society is indebted to the Arthritis and Rheumatism Council for its continued support and records its grateful appreciation.

Library
Report of the Honorary Librarian, E. G. L. Bywaters
The major achievement this year has been the production after two years' work of the New Catalogue, 11 years after the previous one of 1966. In this I was greatly helped by Mr Payne and his successor Mr Cole, by Mr Davenport and by my wife. Full members who pay £1 a year in their subscription for the support of the Library and associate members were each sent a copy, and I hope this has been appreciated. The Heberden Library material has now been grouped, both in the Catalogue and on the shelving in these four divisions: (1) Books published up to and including 1914. (2) Those published in 1915 and after. (3) Serial publications, conference proceedings and symposia. (4) Other miscellaneous presented material—letters, prints, photographs, cartoons, goblets, a gout stool, Dr Heberden's razor, a decanter, and who knows what next!

With the help of Mr Davenport I have also compiled a hand-list of books in the College library dealing with rheumatic diseases and this is available to members on request. We have also received from Dr Kevin Fraser a list of the books in his own historical library.

We acknowledge with thanks the gift of two silver candlesticks from Professor K. W. Walton, past President of the Society.

Accessions this year, mainly gifts from members or authors, have been many and thanks are due to the donors. Most of the books are of quite recent date, a stockpile for future historians. From our Dutch colleagues we received a gift of the first few issues of Acta
Rheumatologia started by van Bremen and others in 1929, but we still lack a number of international and European congress proceedings and would appeal for anyone turning out his bookshelves to bear in mind these still missing items.

Finally, with the assistance of the College librarian, I put out at the Annual General Meeting a display of Rheumatologic Illustrations with comments, which I hope members found of interest. Suggestions for future displays of this historic material would be welcome.

Additions

PART 1

Garrard, Sir Alfred Baring (1819-1907). Die Natur und Behandlung der Gicht und der rheumatischen Gicht. Würzburg. 1861. (From Dr. O. Garrod.


Serny, John Baptist. Spinal curvature, its consequences, and its cure. London. [1840].

PART 2


Cecil, Russell La Fayette (1881-1965) and others. The bacteriology of the blood and joints in chronic infectious arthritis. Repr. from Arch. int. Med., vol. 43, May 1929, pp. 571-605. (From Sir Kenneth Robson.


Collins, Douglas Henry (1907-64). Pathology of bone; prepared for publication by O. G. Dodge. London. 1966. (From MRC Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow, Berks.


Gross, Martin and Greenberg, Leon Arnold (1907- ). The salicylates: a critical bibliographic review. New Haven, Conn. 1948. (From Canadian Red Cross Memorial Hospital.


Rheumatism Reviews, 1935-1941. A reprint of the first eight volumes of the rheumatism and arthritis literature reviews published originally in the Annals of Internal Medicine, vols 8-15. Amsterdam. 1961. (From Canadian Red Cross Memorial Hospital.


Wilde, Percy Robert (1857-1929). The physiology of gout, rheumatism, and arthritis, as a guide to accurate diagnosis and efficient treatment. Bristol. 1921. (From Dr Brian Latham.

PART 3


European Rheumatology Congress. 4th, Istanbul, 1959. Proceedings of the IV European Rheumatological Congress, with meeting of the Ligue Européen contre le rhumatisme. Istanbul. [1959]. (From Dr Paul J. Bilka.)


Ligue Internationale Contre le Rhumatisme, Congres 8e, Genève, Aix-les-Bains, Zurich, 1953. I. Rapports. Genève. (From Canadian Red Cross Memorial Hospital.)


—List of participants. [Kyoto. 1973].

—Scientific programme. [Kyoto. 1973]. (From Dr Paul J. Bilka.)

Ligue Internationale Contre le Rhumatisme. Year book. First ed. [Copenhagen]. 1950. (From Dr Paul J. Bilka.)


Pan-American Congress on Rheumatic Diseases, 3rd, Santiago, Chile, 1963. [Programme and abstracts]. [Santiago. 1963]. (From Dr Paul J. Bilka.)

Pan-American Congress of Rheumatology, 4th, Mexico City, 1967. Proceedings . . . Amsterdam. 1969. (From Canadian Red Cross Memorial Hospital.)

Pan-American Congress of Rheumatology, 4th, Mexico City, 1967. [Programme]. [Mexico City. 1967]. (From Dr Dorothy Gill.)

Pan-American Congress of Rheumatology, 4th, Mexico City, 1967. Resumenes de los trabajos libres. Abstracts of free communications Amsterdam. 1967. (From Dr Paul J. Bilka.)

Pan-American Congress on Rheumatic Diseases, 6th, Toronto, 1974. Program. [Toronto. 1974]. (From Dr Paul J. Bilka.)


Lawrence, John Stewart. Rheumatism in populations. London. 1977. (From Dr J. S. Lawrence.)

Wright, Verna and Moll, John Michael Henderson. Seronegative poliarthritis. Amsterdam. 1976 (From Prof. V. Wright and Dr J. M. H. Moll).

OFFICERS 1978

President: Dr J. Ball, M.D., F.R.C.Path., University of Manchester, Department of Rheumatology, Stofford Building, Manchester, M13 9PT.

Immediate Past President: Professor V. Wright, F.R.C.P., Rheumatism Research Unit, Medical School, Leeds, LS2 9PJ.


Hon. Treasurer: Professor H. L. F. Currey, F.R.C.P., The Bone and Joint Research Unit, A.R.C. Building, The London Hospital Medical College, Turner Street, London E1 2AD.

Senior Hon. Secretary: Dr J. M. H. Moll, D.M., M.R.C.P., Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, Nether Edge Hospital, Sheffield, S11 9EL.


Hon. Librarian: Professor E. G. L. Bywaters, C.B.E., F.R.C.P., 53 Burkes Road, Beaconsfield, Bucks.

General Secretary: M. C. G. Andrews, A.R.C., 8–10 Charing Cross Road, London, WC2H 0HN.

Ordinary Members of Executive Committee:

Dr P. A. Bacon, M.B., M.R.C.P., The Royal National Hospital for Rheumatic Diseases, Upper Borough Walls, Bath BA1 1RL.

Dr A. J. Swanell, M.B., M.R.C.P., Department of Rheumatology & Rehabilitation, City Hospital, Hucknall Road, Nottingham, NG5 1PB.

Dr J. D. Goode, M.R.C.P., Hurn View House, Beverley, Yorkshire, HU17 7DP.

Dr A. M. Denman, F.R.C.P., Division of Immunology, Clinical Research Centre, Northwick Park Hospital, Watford Road, Harrow, HA1 3UJ.
Annals of the Rheumatic Diseases

DR G. R. V. HUGHES, M.D., M.R.C.P., Department of Medicine, Hammersmith Hospital, Ducane Road, London, W12.
DR B. L. HAZLEMAN, M.R.C.P., Addenbrooke's Hospital, Hills Road, Cambridge, CB2 2QQ.

PROGRAMME FOR 1978

March 2-3: Combined Meeting with the British Orthopaedic Research Society, Royal College of Surgeons, London.
June 1-2: The Heberden Round, Aberdeen, by invitation Dr L. Bain.
November 24-25: The Heberden Oration. Annual General Meeting and Dinner, Wembley Conference Centre, London. (Closing date for abstracts: September 15.)

Submission of Abstracts

All abstracts will be considered anonymously, that is without knowledge of the name(s) of the author(s) or the institution of origin, by the Executive Committee.

Members wishing to present original communications to the Society are therefore asked to prepare abstracts which provide sufficient information for assessing the paper on merit—an assessment which amounts to competitive selection between the various abstracts submitted.

In the preparation and submission of abstracts, the following points should be observed:

(1) Abstracts must be typed in duplicate in a 'box' on special reproduction forms, copies of which may be obtained from the Secretariat. Each abstract must be headed by a title, author's names, institution and address. Care should be taken in preparing the abstract as it will be reproduced as submitted. Only one 'box' is permitted per abstract, unless there is insufficient room for a table to be included (see 4 below).

(2) An actual summary of the communication is required. This will usually involve:
   (i) A brief introduction to the work.
   (ii) An outline of the methods used.
   (iii) A summary of the results.
   (iv) A statement of the main conclusions.

(3) Full references to previous work quoted must be given.

(4) Simple tables may be included as long as they are contained within the 'box' on the abstract form. Thus authors wishing to submit abstracts with tables may utilize two 'boxes' if necessary, i.e. one for the abstract and one for the tables.

(5) Accepted abstracts will be published as such with the proceedings of the Society in the Annals of the Rheumatic Diseases, so must be received in a form suitable for publication. In particular, statements such as "The data will be discussed" are unacceptable. Abstracts may be revised for publication after the meeting.

(6) Abstracts should be sent to the Senior Honorary Secretary, The Heberden Society, c/o ARC, 8/10 Charing Cross Road, London WC2 0HN, and must be received not less than ten weeks before the meeting at which it is desired to read the paper.

(7) When submitting abstracts, authors must state whether the communication has been or is about to be read at another meeting; or has been or is about to be published.

(8) The normal length of time for presentation of papers is 10 minutes. However if authors would prefer a longer (15 minutes) or shorter (5 minutes) time, this should be stated when submitting abstracts. The final allocation of time will however rest with the Executive Committee.

(9) Authors will be notified when an abstract is received and when it is either accepted for the following meeting or rejected. Abstracts which are acceptable but which cannot be included in the following meeting will be returned to authors, who may resubmit them for a subsequent meeting if they wish.

(10) It is the author's responsibility to keep the Senior Hon. Secretary informed of the date of publication of any paper submitted to the Society.

Clinical meeting

The following papers were presented at the Annual General Meeting on November 18 and 19, 1977.


Recently considerable change in emphasis has occurred in the clinical description of SLE, largely due to an increasing awareness of the disease, and to the newer serological tests. This study, a prospective analysis begun in 1972, reports on the first 50 successive patients studied. All patients, regardless of apparent disease activity, were admitted to hospital for a 48-hour period on at least one occasion for systematic collection of predefined clinical and laboratory data. The frequency of outpatient attendances was determined according to the clinical status.

(1) 50% of patients had clinical evidence of neuropsychiatric involvement. EEG and brain-scan showed further 16% with subclinical abnormalities. (2) Nephritis was detected in 50% of patients. There was no correlation with other clinical features, including hypocomplementaemia. There was no inverse correlation with neuropsychiatric involvement. (3) 64% had symptoms of pulmonary involvement. Lung function tests showed subclinical involvement in a further 18%. (4) The majority of patients required either no corticosteroids or low doses, and corticosteroid-induced complications were rare. (5) The estimated 5-year survival was 98%. We conclude that mild forms of SLE frequently occur, and favour a more conservative approach to the management of some patients with SLE.
Spontaneous abortion in systemic lupus erythematosus. Association with trophoblast-reactive lymphocytotoxic antibodies. B. Bresnihan, R. Grigor, M. Oliver, R. Lewkonka, R. E. Lovins, W. P. Faulk, and G. Hughes. Department of Medicine, Royal Postgraduate Medical School, London; Department of Basic and Clinical Immunology and Microbiology, Medical University of South Carolina, Charleston.

A high incidence of spontaneous abortion (SA) has been noted in systemic lupus erythematosus (SLE). Comparable studies have failed to show a similar incidence in other connective tissue diseases. In order to investigate the possibility of an antibody-mediated process in SA, sera were obtained during pregnancy from 16 SLE patients. 4 pregnancies ended in SA, and 12 with a normal live birth. The incidence of cold-reactive lymphocytotoxic antibodies (LCA) detected in the SA group was 75% and similar to that detected in a group of 40 nonpregnant women with SLE (63%). In contrast, the incidence of LCA in SLE patients having live births was only 17% and significantly lower than the 2 other SLE groups (P < 0.001). There was no correlation with overall disease activity. Lymphocytotoxic sera were incubated in equal volumes of either purified trophoblast antigens or PBS. The cytotoxicity of sera incubated with trophoblast was significantly reduced when compared to the control sera, suggesting reactivity between LCA and trophoblast. We conclude that the presence of trophoblast-reactive LCA in the sera of pregnant SLE patients may increase the risk of spontaneous abortion.


An increased frequency of α1-antitrypsin phenotype MZ has been reported in both rheumatoid arthritis (Cox et al., 1976) (RA) and obstructive airways disease (Cox and Hubner, 1976) (OAD). Clinically RA is known to be associated with several lung diseases. To study whether this association might be genetically determined, we investigated RA patients both with and without OAD. Subsequently we specifically studied patients with fibrosing alveolitis (FA) with and without RA. α1-Antitrypsin phenotypes were determined in these 4 groups and 200 controls.

**Table Results**

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<thead>
<tr>
<th>pi</th>
<th>Phenotypes (%)</th>
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<tr>
<td></td>
<td>MM</td>
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<tr>
<td>Controls</td>
<td>86-0</td>
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<tr>
<td>(n = 200)</td>
<td></td>
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<tr>
<td>RA (n = 55)</td>
<td>87-3</td>
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<tr>
<td>RA + OAD (n = 33)</td>
<td>78-8</td>
</tr>
<tr>
<td>FA (n = 49)</td>
<td>71-4</td>
</tr>
<tr>
<td>RA + FA (n = 22)</td>
<td>50-0</td>
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<tr>
<td>P &lt; 0.006</td>
<td>P &lt; 0.005</td>
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</table>

There was an increase in the MZ phenotype in patients with RA+FA (P < 0.005) and patients with FA alone (P < 0.006). The MS phenotype was also increased in patients with RA + FA (P < 0.05). Patients with RA alone had a normal distribution of phenotypes. Patients with RA + OAD had a higher percentage of non-M phenotypes than normal.

**References**


Among 173 consecutive outpatients with peripheral arthritis, which persisted for over 6 weeks (c.f. ARA criteria for rheumatoid arthritis (RA)), 40 patients with PRAO differed from RA by 8 clinical and radiological variables (see below), notably by asymmetry and by spontaneous remissions in 74%; from 'incomplete' Reiter's disease (RD) (Arnett et al., 1976) by lack of chronicity, slight female preponderance, and lower B27 association; from ankylosing spondylitis by absence of sacroiliitis, of low back pain or stiffness (Rome criteria); from RD, enteropathic, or psoriatic arthropathies by lack of urethral, mucosal, or skin involvement.

Upon computer analysis (4 distinct approaches) of each patient's 30 variables PRAO emerges not as an 'atypical RA' but as a distinct, homogeneous cluster without significant (P > 0.05) difference between 2 cohorts of B27-positive (22) and B27-negative (18) patients. PRAO might account for a large proportion of epidemiologists' 'possible' and probable RA (none encountered in the present series!) and of mildly symptomatic B27 carriers.

**Table**

<table>
<thead>
<tr>
<th></th>
<th>PRAO</th>
<th>RA</th>
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<tbody>
<tr>
<td>n = 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset (yrs)</td>
<td>31 ± 11</td>
<td>49 ± 13</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>9 ± 1 ± 7-1</td>
<td>42 ± 12</td>
</tr>
<tr>
<td>Remissions (spontaneous)</td>
<td>in 74%</td>
<td>in 5%</td>
</tr>
<tr>
<td>Joints: no. involved</td>
<td>3-2</td>
<td>13-3</td>
</tr>
<tr>
<td>no. of symmetries</td>
<td>0-2</td>
<td>5-1</td>
</tr>
<tr>
<td>Rheumatoid factor in (1 pt)</td>
<td>65-6%</td>
<td>75-8%</td>
</tr>
<tr>
<td>Erosions in</td>
<td>0%</td>
<td>9%</td>
</tr>
<tr>
<td>HLA(B) 27 in</td>
<td>45%</td>
<td>9%</td>
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</table>

**Reference**


Evidence of abnormalities in the calcium metabolic status of patients with rheumatoid arthritis has been accumulating. Some workers have suggested from in vitro studies that bone resorption in rheumatoid arthritis results from prostaglandin E2 activity. We attempted to define more accurately the extent and nature of this problem.
Twenty-three patients with 'definite' or 'classical' rheumatoid arthritis were included in the study. A highly significant number of patients were shown to have hypercalcaemia, hypophosphataemia, hyperphosphatasa, hypercholoraemia, reduced renal reabsorption of phosphate, and increased renal tubular reabsorption of calcium suggesting biochemical evidence of hyperparathyroidism. A hormonal profile showed no increase in parathyroid hormone, but a tendency to raised calcitonin. The sera from these patients were then tested in a bone culture model and the hypercalcaemic sera were found to increase 45Ca resorption.

Rheumatoid arthritis in Jamaica—3 years' experience. W. A. Wilson and G. R. V. Hughes. University Hospital of the West Indies, Kingston, Jamaica; Royal Postgraduate Medical School, Hammersmith Hospital, London.

Much has been learnt from comparative epidemiological studies of the incidence and pattern of rheumatic disease in different countries. Jamaica, with its warm island climate, 2 million population, and multiracial ethnic origin has been of particular interest. Until recently, studies depended on small population surveys, and data obtained by local physicians without special rheumatological training. 3 years ago, with the help of the Wellcome Foundation, a Rheumatology Unit was inaugurated in the University of the West Indies, and the incidence, pattern, and clinical features of patients seen in this unit during the past 3 years was studied.

The incidence of rheumatoid arthritis was similar to that seen in the UK, though there were clinical differences, and vasculitis and systemic complications were rare. The incidence of systemic lupus erythematosus approached that of RA. As expected, ankylosing spondylitis and gout were rare, but osteoarthrosis was seen with similar frequency and pattern to that in the UK.

Notable were the high incidence of infectious polyarthritis (especially gonococcal), sickle cell arthralgia, and sepsis, and rheumatic fever, which is still a major disease on the island.


Caricature in medicine—a subject with a long history—is of social, political, and intellectual interest to the profession. Far from being scurrilous comic scribblings, caricatures at worst might be regarded as academic graffiti, and at best as serious statements in graphic satire.

Caricature surveys of professional societies peaked in popularity in late Victorian times under the influence of 'Spy' (Leslie Ward), 'Ape' (Carlo Pellegrini), and 'Max' (Sir Max Beerbohm). Only lately has the art been revived, and in line with this trend the author has applied his caricature pen to Heberden profiles.

Over the past few years small exhibitions of caricature drawings of Heberden members have been shown at the AGM, and these (some 75 drawings) have now been brought together as a single collection which is housed in the Heberden library.

Recently, the author was invited to draw a further series of caricatures to be entitled 'Heberden Presidents'. The caricatures to be shown represent the first in this new series. Each drawing will be accompanied by a clerihew:

Synovial pathology in Behcet's syndrome. B. Vernon, Roberts, C. G. Barnes, and P. A. Revell. Published in the Annals, 37, 139–145.

Myopathy in morphea. J. S. Percy and A. S. Russell. Rheumatic Disease Unit, University of Alberta, Edmonton, AB. Canada.

Myopathy is not a commonly recognised complication of morphea. 8 patients with morphea have all had either clinical or biochemical evidence of muscle disease. The muscles involved were not necessarily in the same region as the skin plaques. 3 patients had generalised morphea and presented with arthralgia, oedema, and muscle stiffness. All had EMG evidence of myopathy, and muscle biopsy showed an inflammatory infiltrate of the muscloskeletal tissue with fibrosis.

Four patients had a number of skin plaques and had clinical or biochemical evidence of past or present involvement of muscle. One patient had a single skin plaque and raised serum levels of muscle enzymes. 5 had eosinophilia but none had hypergammaglobulinaemia. Considerable disability has resulted from muscle contractures but over the observation period (2–8 years) no other systemic involvement has occurred.

Synovial origin of periartricular structures. W. D. Haas and P. van Heerde. Amsterdam Centre for Rheumatic Diseases and Department of Pathology, Wilhelmina Inagasthuis, University of Amsterdam.

Embryological studies have shown that the synovial lining of the primitive joint space derives from cells lying outside the joint. These cells also form the extra-articular synovial organs: the tendon sheaths and the bursae. We propose that in adult life these periartricular cells do not lose the ability to form joint-like tissue, and that they are responsible for the formation of such juxta-articular structures as ganglia, meniscal cysts, synovial cysts, subcutaneous nodules, and synoviomas.

Evidence of the arthroid nature of these structures is supplied on clinical and histological grounds, in particular the fact that they (may) contain a central cavity, lined by synovial cells. The synovial nature of these cells is confirmed by the presence of hyaluronic acid, a product excreted by synovium which can be selectively stained by a recently described method. Normal as well as abnormal periartricular structures thus appear to belong to the same synovial family, all the members of which (ganglia excepted) may participate in case of affections of a joint, e.g. in rheumatoid arthritis.


As part of a prospective study of the articular and muscular problems associated with bleeding disorders in childhood, all children with these disorders referred to
regional centre are reviewed by a haematologist and rheumatologist. So far 62 haemophiliacs, 9 children with von Willebrand’s disease, and 8 with Christmas disease of longer than 2 years’ known duration have been seen over a 2-year period. 21 of the haemophiliacs had never had locomotor problems. The main joints affected were the knee, ankle, and elbow. However, 8 children had involvement of wrist and fingers. Thigh and calf muscles were frequently involved. In addition tenosynovitis and nodules were found. A similar pattern of joint and muscle involvement was seen in the patients with Christmas disease, only 2 children having no locomotor problems. In von Willebrand’s disease only 4 children had minor joint problems.

The severity of the joint changes bears some relationship to the degree of defect in clotting factor, but marked exceptions were found. 3 children have changes suggestive of coincidental inflammatory arthritis. The progression of joint change and growth disturbance and the effect of treatment have been followed. No children have required surgery.

**Immune responses to salivary and bile antigens in rheumatoid arthritis and Sjögren’s syndrome.** L. Fernandes, S. Sullivan, I. McFarlane, B. Wojcicka, A. Eddleston, D. Doniach, E. Hamilton and R. Williams. *Department of Rheumatology and Liver Unit, King’s College Hospital,* and *Department of Immunology, Middlesex Hospital, London.*

Thirty-two patients with rheumatoid arthritis (RA) were examined for Sjögren’s syndrome (SS). Evidence of this was found in 17. The leucocyte migration inhibition technique was used to test cellular hypersensitivity to partially-purified human salivary antigen (SA) and bile antigen (BA). Sensitisation to SA was found in 16 of 17 patients with SS but only in 5 of 15 patients without SS ($P<0.005$). Also, 15 of 17 patients with SS were sensitised to both SA and BA compared with 5 of 14 patients without SS ($P<0.01$).

Indirect immunofluorescence on sections of normal human liver and submaxillary gland showed staining of the membrane of bile duct epithelium using an antiserum against SA. Conversely, the antiserum against BA stained the salivary duct epithelium. Double immunodiffusion studies confirmed the presence of cross-reacting antigens in salivary and bile ducts.

(1) Cellular hypersensitivity probably plays an important role in the pathogenesis of the secretory abnormalities in SS. (2) The presence of shared antigenic determinants in salivary and bile ducts suggests a possible mechanism for the raised alkaline phosphatase of liver origin commonly found in this condition.

**Changes in the conjunctiva with age and in keratoconjunctivitis sicca.** J. Williamson, *Consultant to Centre for Rheumatic Diseases, Glasgow.*

Very little is known about the conjunctival epithelial changes that occur with increasing age. The fall off in tear quality and quantity of secretion with age to the point of mild keratoconjunctivitis sicca in the over 60-year-old population suggests the need for an examination of conjunctival changes in varying age groups. These are studied in detail by routine light microscopy and electron microscopy. The changes are compared with those in a group of patients suffering from Sjögren’s syndrome and sicca syndrome. The most interesting features are (a) stratification of a mild degree and a fall in goblet cell population in the over 79-year patients; (b) the appearance of hyaline bodies in the over 79-year group of patients; (c) gradation of stratification, mechanical separation of the superficial epithelial cells, and fall in goblet cell population in the patients suffering from keratoconjunctivitis sicca; (d) stunting and depletion of the microvilli on the epithelial surface in patients with keratoconjunctivitis sicca; (e) a possible return towards normality with adequate therapy.


The development of sexually acquired reactive arthritis (SARA) has been studied prospectively in 531 men presenting with nonspecific urethritis (NSU) with regard to the isolation of *Chlamydia trachomatis* from the urethra and the presence of the antigen HLA B27. Arthritis developed in 16 patients and in 36% of these positive isolates were obtained. The lymphocytes of 40% of patients with arthritis bore the HLA B27 antigen. 36.5% of patients with NSU alone also yielded positive cultures of *C. trachomatis,* but in this group HLA B27 was present in only 6.2% (Table).

In this study 20% of the patients with HLA B27 developed peripheral arthritis, showing at least a tenfold increased susceptibility to SARA when compared with patients lacking the antigen. However, there appeared to be no increased prevalence of *C. trachomatis* in the urethral material of HLA B27-positive individuals when compared with patients with other HLA antigens. It appears unlikely that the carriage of this organism is influenced by HLA B27 status.

*C. trachomatis* may be an important pathogen in a proportion of cases of SARA but it is unlikely that it is an exclusive trigger factor for this condition. A number of sexually acquired infectious agents, possibly sharing a common antigenic determinant, may initiate this disease syndrome, as in other forms of reactive arthritis.

Table **HLA B27 and occurrence of sexually acquired reactive arthritis**

<table>
<thead>
<tr>
<th>HLA B27 positive</th>
<th>HLA B27 negative</th>
<th>Total</th>
<th>% with HLA B27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall no. of patients</td>
<td>30</td>
<td>452</td>
<td>482</td>
</tr>
<tr>
<td>No. of patients with arthritis</td>
<td>6</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>% patients with arthritis</td>
<td>20</td>
<td>2</td>
<td></td>
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</tbody>
</table>

**Coxsackie B neutralisation titres in polymyositis.** J. R. Sewell, G. Cambridge, A. Young, R. L. Travers, and G. V. R. Hughes. *Department of Medicine, Royal Postgraduate Medical School, London.*
Coxsackie B viruses are the causal agents in Bornholm disease and have been implicated in other muscle diseases, including polymyositis. Picornavirus-like particles have occasionally been observed in electronmicroscopic studies of affected muscle tissue from patients with polymyositis and dermatomyositis (Chou, 1972). However, no systematic search for evidence of Coxackie B infection in these diseases has been made.

We used a microneutralisation technique to study Coxackie B antibody titres in patients with (i) early polymyositis, (ii) SLE with active muscle disease, and a control group of SLE patients without muscle symptoms. Evidence of recent Coxackie B infection was found in all 5 patients with early polymyositis (Table) and 4 of 5 patients with SLE associated with muscle disease. Only 1 of 11 patients in the control group had similar evidence of recent virus infection. Complement-fixing antibodies to 13 other viruses and to Mycoplasma were also tested, and no high or rising titres were found.

Table **Coxsackie B neutralisation titres: paired sera**

<table>
<thead>
<tr>
<th>Antibody titres</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2 3 4 5</td>
</tr>
<tr>
<td>64</td>
<td>1</td>
</tr>
<tr>
<td>128</td>
<td>1</td>
</tr>
<tr>
<td>256</td>
<td>1 1 2</td>
</tr>
<tr>
<td>512</td>
<td>2 2 2 2 2</td>
</tr>
</tbody>
</table>

1 = first serum; 2 = second serum; >2 weeks after the first.

Single sera from groups of polymyositis patients from New York and Los Angeles were also tested for neutralising antibodies against Coxackie B Group viruses and preliminary results from this study support the possibility of an association between polymyositis and Coxackie B viruses.


**Penicillamine: 750 mg is not the dose.** H. Hill and A. Hill.

Eighty-two patients with definite or classical RA were treated with a maintenance dose of 750 mg penicillamine for a minimum of 18 and a maximum of 42 months. The aim of the study was to determine (1) how many patients remained on treatment at 6, 12, 18, 24, 30, and 42 months after the first prescription was given, and (2) the incidence and time of withdrawals for adverse effects and for reasons unconnected with the prescription of penicillamine.

At the end of one year 40 of the 82 patients had been withdrawn, 10 (12%) were unrelated to treatment, 30 (38%) were for adverse effects. During this first year the unrelated withdrawals occurred randomly, but the withdrawals for individual adverse effects tended to be grouped together, thus thrombocytopenia (4) was commonest during the first 3 months, blistering rashes (5) between the 5th and 12th months, and proteinuria (16) from the 7th to 10 months.

During the second year withdrawals for adverse effects occurred sporadically and amounted to about 6%, whereas withdrawals for unconnected reasons were common and were of the order of 20%. During the third year only occasional withdrawals, either for adverse effects or for unrelated reasons occurred.

The 38% incidence of withdrawals for adverse effects during the first year is unacceptably high even though adverse effects occur rarely thereafter. If, as seems probable, the incidence of adverse effects is dose-related then priority should now be given to searching for a dose which is both effective and associated with decreased toxicity.


Cyclophosphamide (CY) is an important therapeutic agent in the treatment of RA. The precise mechanism of action of CY is unknown, although in animal experiments it is immunosuppressive at high dosage. This trial set out to compare 4 dosage regimens using concurrent thermographic and immunological assessments. 41 patients received CY for from 2 to 6 months in continuous or intermittent oral (A & B), or one of two intermittent IV regimens (C & D). Joint inflammation was measured by quantitative thermography (TI). Delayed hypersensitivity in vitro was assessed using leucocyte migration inhibition (LMT) to a standard antigen, streptokinase.

The oral groups both showed an initial rise in TI. In group A no improvement occurred until 6 months, but in group B improvement was more rapid and was significant at 2, 3, & 6 months. The IV groups showed a steady improvement in TI which in group D was significant at 1, 2, 3, 4, and 8 weeks. LMT showed enhanced immune reactivity at 1–3 weeks in the oral groups, with subsequent return to pre-drug values. The IV group D showed some initial suppression. The difference between groups B and D was significant at 1–3 weeks (see Table). Considering all groups together for the first 3 weeks, the changes in 4TI showed a highly significant correlation with the changes in LMT (r=0.69, P<0.001).

Table **Thermographic (TI) and immunological (MI) data (mean ± SD) of groups B and D over first 3 weeks**

<table>
<thead>
<tr>
<th>Time 0</th>
<th>1–3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TI</td>
</tr>
<tr>
<td>Group B</td>
<td>3.72 ± 0.69</td>
</tr>
<tr>
<td>n = 7</td>
<td>n = 7</td>
</tr>
<tr>
<td>Group D</td>
<td>4.65 ± 0.62</td>
</tr>
<tr>
<td>n = 6</td>
<td>n = 7</td>
</tr>
</tbody>
</table>

MI = migration index from LMT.

*P < 0.01.
This study supports a role for delayed hypersensitivity in chronic inflammation and suggests that CY acts initially by affecting suppressor cell function.


In a drug study of the effect of D-penicillamine and gold treatment on patients with active rheumatoid arthritis, 4 patients out of a total of 45 (30 received penicillamine while 15 received gold) became IgA deficient (i.e. serum IgA <0.8 g/l). In 2 cases the IgA level began to rise after drug treatment was discontinued, but in one case IgA remains undetectable 3½ years after discontinuing penicillamine, although with no apparent ill effects. All 4 patients responded clinically to the drug therapy.

Three of these IgA-deficient patients have been HLA typed and possess the haplotype HLA-A3B40. As the expected incidence of this haplotype is only about 1%, data from the 3 HLA typed IgA-deficient patients represents a substantial increase. Out of 24 rheumatoid arthritis gold/penicillamine study patients, 2 show the presence of the two phenotypes HLA-A3 and B40, but these have not shown any tendency to IgA deficiency.

Subsequent examination of clinical records has revealed 5 other patients (4 had rheumatoid arthritis, one had scleroderma) who have been IgA deficient at some time. Of these, 3 have received gold and one penicillamine. Only one is known to have had a normal IgA level before treatment (with gold). Of 4 who have been HLA typed, 3 possess the phenotypes HLA-A2 and B12, a higher proportion than one would expect.

**Phytohaemagglutinin (PHA) and K-cell cytotoxicity by mononuclear cells from inflammatory synovial fluids (SF).** V. Corrigal and G. S. Panayi. *Department of Medicine and Arthritis Research Unit, Guy's Hospital, London SE1 9RT.*

It is not known whether some of the functional results obtained with lymphocytes from SF of patients with rheumatoid arthritis (RA) are due to the disease or are merely the result of chronic joint inflammation. In order to answer this question, the ability of lymphoid cells, isolated by Triosil-Ficoll sedimentation to kill 51Cr-labelled Chang cells in PHA-induced cytotoxicity and in K-cell cytotoxicity was investigated. Killing was expressed as percent specific release of 51Cr from Chang cells. Synovial fluids and bloods were obtained from 12 patients with RA and 8 patients with other inflammatory joint diseases (IJD-ankylosing spondylitis, psoriatic arthritis, Behçet's, sarcoidosis).

SF lymphocytes from patients with RA or IJD showed similar K-cell cytotoxicity which was significantly depressed compared to blood lymphocytes (Fig. 1). PHA-cytotoxicity was similar in the two groups for both blood and SF. Incubation of SF lymphocytes at 37°C for 1 h or in glycine/HCl buffer or exposure to trypsin or neuraminidase did not lead to the expression of K-cell cytotoxicity (Fig. 2). Hence adsorption of blocking factors (e.g. immune complexes) is probably not the cause of deficient killing.

Thus active K-cells are absent from inflammatory SF and this is not unique to RA. It may be that these cells are sequestered in the synovial membrane where they may be involved in the destruction of antibody-coated target cells.

**Interaction of rheumatoid leucocytes with IgG-IgG complexes and with rabbit IgG fragments.** N. D. Hall. *ARC Research Unit, R.N.H.R.D., Bath and Pharmacology Group, University of Bath.*

In RA there is evidence of an on-going immune response to IgG with the development of delayed hypersensitivity (DH) and with the production of antiglobulins and the formation of IgG-IgG complexes. This study compares the interaction of IgG-IgG complexes and native IgG with rheumatoid and control leucocytes using leucocyte migration inhibition (LMT) as the test system.

Rabbits were immunised with human IgG. Rabbit IgG (antihuman IgG) was prepared, mixed with excess human IgG and fractionated by gel filtration. Large complexes
were shown to inhibit specifically rheumatoid leucocyte migration at a concentration of 5 μg/ml. These complexes were 20-40 times more active in the LMT than native rabbit IgG. The effect was mediated through the Fc region of the IgG since IgG–Fab(α′)3 complexes were inactive, but was independent of complement.

Native rabbit IgG inhibited both rheumatoid and control cells in the LMT. Digestion of this IgG with various enzymes yielded fragments with differing activities (see Table). The plasmin product Fabc inhibited RA cells specifically, whereas the pepsin product F(ab′)2 was inactive.

Table Activity of rabbit IgG and IgG fragments in the leucocyte migration test (mean ± SD)

<table>
<thead>
<tr>
<th>Protein concentration (μg/ml)</th>
<th>Migration index</th>
<th>RA</th>
<th>Control</th>
<th>RA</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facb</td>
<td>F(α′)3</td>
<td>Fab</td>
<td>Fc</td>
<td>Facb</td>
<td>F(α′)3</td>
</tr>
<tr>
<td>250</td>
<td>40</td>
<td>200</td>
<td>200</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>63 ± 17</td>
<td>78 ± 10</td>
<td>93 ± 11</td>
<td>99 ± 4</td>
<td>92 ± 8</td>
<td>65 ± 19</td>
</tr>
<tr>
<td>P &lt; 0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This study supports a role for DH to altered IgG in the pathogenesis of RA. The changes in conformation of the IgG which trigger this response may be induced by immune complex formation or self-association. The latter is known to occur with rheumatoid IgG.


Sixty patients with histologically proven IBD were examined clinically, radiologically, and by 99m technetium labelled stannous pyrophosphate bone scan for objective evidence of sacroiliitis and spondylitis. All patients were tissue typed. Clinical evidence of sacroiliitis or spondylitis was found in 52% of the patients. Sacroiliitis was evident on pelvic x-ray in 15%, one third of whom had classical ankylosing spondylitis. The bone scan was abnormal in 60% of patients with definite evidence of inflammatory disease of the sacroiliac joints. 76% of patients with abnormal scans had abnormal back movements and 85% with abnormal back movements had abnormal scans. A good correlation was seen between radiological sacroiliitis (RSI) and positive bone scans but a number of patients had abnormal scans and normal x-rays. The frequency of the tissue antigen HLA B27 was not significantly higher in our patients with IBD compared with a group of normal controls. HLA B27 correlated poorly with RSI and bone scan evidence of sacroiliitis but correlated well in patients with ankylosing spondylitis. 7 of 9 IBD patients with HLA B27 had abnormal bone scans but a further 17 with abnormal scans were HLA B27 negative. B27 was present to a similar degree in patients with RSI. We conclude that using these criteria, sacroiliitis is more frequent in patients with IBD than previously recognised. HLA B27 may predispose the development of ankylosing spondylitis or an abnormal bone scan but the overall correlation between HLA B27 and clinical evidence of axial arthropathy in IBD is poor.


Despite the prominence of neuropsychiatric features in SLE, no satisfactory method exits for the diagnosis and monitoring of CNS involvement. This study describes the application of a new technique for studying both cerebral metabolism and blood flow in SLE patients using inhaling 15O2 (metabolism), C 15O2 (blood flow). 28 studies were performed in 24 patients. Patients were clinically classified as having definite CNS disease (focal signs or severe psychiatric disturbance) (13); probable (mild to moderate psychiatric disturbance) (7); and no CNS disease (C). Scan abnormalities were seen in 25 of the 28 studies usually affecting several cortical areas. In 6 patients in whom multiple recordings were made, improved oxygen scan appearances correlated with clinical improvement. 15O2 scanning appears to offer a highly sensitive, non-invasive method for studying patients with cerebral lupus.

Clinical meeting, October 1977

A combined meeting of the Heberden Society with the Section of Rheumatology and Rehabilitation of the Royal Society of Medicine and the British Association of Rheumatology and Rehabilitation was held in Carlisle on October 17, 1977.

Guest lecturers were Professor M. Ziff (Dallas, USA) 'The immunological aspects of rheumatoid arthritis and its treatment'; Professor J. J. de Blecourt (Groningen, Holland) 'Total care for rheumatic sufferers'; and Mr. M. A. R. Freeman, 'Joint replacement in arthritis of the lower limb: the role of anatomy'.

The following papers were also presented.

Deaths associated with gold therapy. Reassessment. J. Gumpel. Northwick Park Hospital, Harrow.

'Gold is the most toxic drug in the Pharmacopeia, according to Girdwood' is a Glaswegian statement. But it is not only in Glasgow that such beliefs are held. Girdwood’s impressive survey of deaths associated with medication has long provided a strong foundation for those concerned with the side effect of drugs. Kay’s survey of blood dyscrasias associated with gold therapy confirmed that these do occur, much of the problem being with supervision of gold therapy. For those who never saw these gold disasters, how could one assess Girdwood’s finding that the number of deaths associated with gold therapy assessed per 100 000 EC.10 prescriptions...
England and Wales is greater by a fivefold factor than the next two drugs: warfarin and heparin, also both largely prescribed in hospital rather than in general practice.

Data were collated from the Committee on Safety of Medicines and from May & Baker Limited. Firstly, each EC.10 prescription in 1969 (the midpoint of Girdwood’s study) must have been for a minimum of 15 weeks’ gold therapy, i.e. 15 ampoules. 46 deaths are listed at the Committee on Safety of Medicines in which gold was one of the medications mentioned. 39 of these were due to blood dyscrasia of some form. With Dr W H W Inman of the CSM, an analysis of the other drugs that these patients had also received was made. An independent analysis of the likely causative role of gold in these deaths showed a probability for gold in only 16 of these 39 cases. In many, the gold therapy had long anteceded death. (Finally, the ratio of deaths where gold was listed a million ampoules of Myocrisin supplied fell by 58% in the 5-year period 1971 to 1976 compared with the previous 5-year period.)

Repeat intra-articular injection of yttrium 90 colloid in treatment of persistent synovitis of the knee. J. Winfield and J. M. Gumpel. Rheumatic Diseases Study Group, Northwick Park Hospital, Harrow.

Thirty patients with persistent synovitis of the knee (42 knees) with a poor response to one yttrium 90 colloid injection received a second injection. The predominant disease was rheumatoid arthritis (90%) and each patient was assessed for at least 6 months. The mean time lapse between 1st and 2nd injections was 9.2 months. Methods of selection, injection procedure, and assessment were comparable to those of Gumpel and Roles (1975). Excluded from the study were patients started on gold, penicillamine, or immunosuppressive drugs during the assessment period.

After a second intra-articular injection of yttrium 90 colloid, 20% of patients gained complete resolution of synovitis for a sustained period. 63% gained symptomatic improvement with reduction of synovitis clinically but in 17%, there was no improvement. The latter group all had rheumatoid arthritis, with widespread active synovitis, difficult to control. Increase in instability of the knee after $^{90}$Y was not seen in any of the patients studied.

Reference


Attempts to isolate virus from RA joints have failed. Interference assays are an indirect way of showing the presence of an agent, i.e. virus may fail to grow in cells already infected by the same or closely related virus. Lymphocytes are likely sites of viral persistence as these cells are infected in the pathogenesis of many viral infections. Herpes simplex virus (HSV) fails to grow normally in lymphocytes from the blood of patients with connective tissue diseases (Denman et al., 1976). An abnormality of this nature in RA is most likely to involve cells isolated from affected joints. Interference assays with HSV have been carried out on lymphocytes from the blood and synovial effusions of patients with RA and other forms of arthritis. The most consistent finding (Table) was the failure to grow in lymphocytes isolated from rheumatoid synovial effusions. In contrast blood lymphocytes from nearly all groups except those with early RA and viral arthritis supported HSV replication normally. It was difficult to prepare lymphocytes from other effusions in adequate numbers. The following explanations for abnormal nonpermissiveness were considered: (a) factors such as failure of the necessary lymphocyte proliferative response and blocking of virus receptors by immune complexes were excluded; (b) HSV replication may be blocked by ‘interferon’-like mechanism initiated by persistent infection since small T lymphocytes, isolated from nonpermissive effusion cells by physical methods, supported viral replication but this was reversed by re-mixing; (c) other experiments show that the potentially permissive T lymphocytes in which HSV normally grows may be blocked by defective virus particles.

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of samples</th>
<th>Effusions suitable for study</th>
<th>Lymphocytes Blood</th>
<th>Effusion$^\dagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal controls</td>
<td>42</td>
<td>0</td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td>Early RA$^*$</td>
<td>11</td>
<td>8</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Late RA</td>
<td>23</td>
<td>87</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>'Viral arthritis'†</td>
<td>18</td>
<td>5</td>
<td>3</td>
<td>13 5 0</td>
</tr>
<tr>
<td>Juvenile chronic arthritis</td>
<td>7</td>
<td>9</td>
<td>3</td>
<td>5 2 2</td>
</tr>
<tr>
<td>Inflammatory arthritis</td>
<td>16</td>
<td>7</td>
<td>3</td>
<td>15 1 0 3</td>
</tr>
<tr>
<td>DIP</td>
<td>3</td>
<td>15</td>
<td>0</td>
<td>3 0</td>
</tr>
<tr>
<td>Other effusions</td>
<td></td>
<td>16</td>
<td>4</td>
<td>3 3</td>
</tr>
</tbody>
</table>

*Onset <6 months; $^\dagger$ Presumed 'viral arthritis'; $^\dagger$ = HSV replicated; $^*$ = HSV did not replicate.

Reference

Antinuclear factor as a prognostic indicator for D-penicillamine treatment in rheumatoid arthritis. J. E. Dippy. Rheumatology Department, Princess Margaret Hospital, Swindon.

A clinical impression that those rheumatoid patients with positive antinuclear factor, treated with D-penicillamine, were more subject to serious side effects was tested in a survey of 100 patients under surveillance for at least 6 months unless withdrawn earlier on account of untoward side effects. They were seen at 3- to 6-weekly intervals by the same clinician. 9 had positive antinuclear factor at the start of treatment, and 1 developed neutropenia, 4 nephropathy, and 1 nephropathy and thrombocytopenia. Only 3 patients had no serious side effects. 4 patients developed nephropathy with no antinuclear factor present. Thus, positive antinuclear factor did emerge as a high risk factor for serious side effects.

The results indicate that by excluding patients with antinuclear factor from consideration of penicillamine
therapy, selection of the rheumatoid patient for successful penicillamine treatment will be improved, and lead to better management. The incidence of neuropathy may be halved.

**Distribution of gold in plasma fractions of rheumatoid patients undergoing chrysotherapy.** D. J. Danpure and J. M. Gumpel. Clinical Research Centre, Harrow.

Little is known about the distribution of gold among the plasma fractions in rheumatoid patients undergoing chrysotherapy, although the kinetics of total plasma gold has been well studied. We have measured gold (by neutron activation analysis) in plasma and the globulin, albumin, and 'unbound' fractions (as separated by gel chromatography) from 3 rheumatoid patients at various times after injection of sodium aurothiomalate. A summary of the results is given in the Table.

<table>
<thead>
<tr>
<th>[Gold] (extreme range over 3 or 4 weeks as appropriate)</th>
<th>Patient and dose regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>in:</td>
<td>1: 100 mg/</td>
</tr>
<tr>
<td>4 w</td>
<td>3 w</td>
</tr>
<tr>
<td>Total plasma (µg atom/l)</td>
<td>3.5-35.6</td>
</tr>
<tr>
<td>Globulin fraction (µg atom/l)</td>
<td>1.13-3.43</td>
</tr>
<tr>
<td>Albumin fraction (µg atom/l)</td>
<td>2.51-32.2</td>
</tr>
<tr>
<td>'Unbound' fraction (µg atom/l)</td>
<td>0.35-1.40</td>
</tr>
<tr>
<td>Globulin fraction (% plasma gold)</td>
<td>5.7-25.9</td>
</tr>
<tr>
<td>Albumin fraction (% plasma gold)</td>
<td>60.0-93.0</td>
</tr>
<tr>
<td>'Unbound' fraction (% plasma gold)</td>
<td>1.0-15.0</td>
</tr>
</tbody>
</table>

The differential distribution of gold in the plasma fractions was dependent on the time after injection and, although they were qualitatively similar, quantitative differences occurred between the 3 patients. Whereas the total gold concentration in the plasma increased 5-10 fold to reach a maximum 100 min after injection, the 'unbound' gold only transiently increased 2-5 fold to reach a peak 10-30 min after injection and then returned to preinjection levels. As the majority of the gold was bound to albumin, the gold-albumin profile was similar to that of total plasma. The level of globulin-bound gold also peaked after 100 min but rose only 2-3 fold.

As tissue uptake and excretion of gold might be expected to be strongly influenced by the concentration of the 'unbound' gold in the plasma, this might be a more appropriate parameter to measure than total plasma gold. However, further work is needed to delineate the exact relationship, if any, between the level of 'unbound' gold in the plasma and biological effect.


**Study A:** 30 patients with advancing rheumatoid arthritis were at the stage of consideration for second-line drugs. After full assessment each patient was then randomly allocated to either levamisole or matched placebo for 2 months. All patients were allowed to continue optimal dose of whichever first-line drug they were using.

**Study B:** The principles for selection for treatment with second-line drug prescribed in trial A were applied in this study. Each patient was randomly allocated either to long-term gold or levamisole treatment and monthly regular assessment was done. 40 patients with rheumatoid arthritis participated in this study (20 received gold and 20 received levamisole).

**Results:** Study A showed levamisole was superior to placebo in pain (P<0.05), articular index (P<0.05), digital joint circumference (R.P<0.01, L.P<0.01), erythrocyte sedimentation rate (P<0.01), and joint scanning (P<0.05).

**Trial B—6** patients who completed one year on levamisole showed significant improvement in pain (P<0.05), articular index (P<0.01), titre of rheumatoid factor (P<0.01), and ESR (P<0.05). There was no statistically significant difference between them and the 9 patients receiving gold therapy. There was no change in lymphocyte function or neutrophil granulocyte functions after 2 months' therapy.

**Joint involvement in systemic sclerosis.** C. R. Lovell and M. I. V. Jayson. Department of Medicine, University of Bristol and Department of Rheumatology, University of Manchester.

Joint contracture in systemic sclerosis is attributed generally to thickening of the skin and subcutaneous tissues. It may, however, be due to abnormalities of the joints and tendon sheaths themselves. We have related joint function separately to definite radiological evidence of joint involvement and to the extent of skin involvement. In 124 patients with systemic sclerosis we documented the extent of skin involvement and assessed grip strength and the sum of nail-palm distances for both index and ring fingers when fully flexed. We took plain dorsopalmar radiographs of the hands and analysed them for features of systemic sclerosis and of inflammatory arthritis. Tests for viscosity, rheumatoid factor, and antinuclear factor (ANF) were performed. 11 patients had radiological evidence of inflammatory polyarthritis (group A). Juxta-articular osteoporosis was present in 9 patients. Erosions were seen in 5 patients and loss of joint space in 6, with complete bony fusion in 2. The remaining 15 patients had no evidence of joint involvement (group B). Most patients studied had features characteristic of systemic sclerosis, such as soft tissue calcifications and absorption of digital phalanges. 1 patient only had a positive rheumatoid factor. ANF was positive in 4 patients out of 10 in group A and 5 patients out of 10 in group B. The mean viscosity in patients in group A was 1.72 (SD ± 0.15) and in group B 1.76 (SD ± 0.21). Clinical measurement of joint function was similar overall in both groups. In individual cases, however, impairment of grip strength and finger-palm flexion was associated with flexion deformities of finger joints or with tendon sheath involvement. We conclude that inflammatory changes in joints and tendon sheaths may contribute to joint contracture in patients with systemic sclerosis. These changes cannot be attributed to coincident rheumatoid arthritis.

The association between HLA B27 and ankylosing spondylitis is well known (Brewerton et al., 1973). This led to further enquiry into possible association with other HLA-linked genes at the HLA D locus, but no such association has been discovered (Kip et al., 1977). A diminished mixed lymphocyte response (MLR) has been reported in association with HLA B27 (Nibkin et al., 1976). We have investigated this further to clarify the relationship between HLA B27, diminished MLR, and ankylosing spondylitis. 48 patients with ankylosing spondylitis were studied. There were 39 males; 9 females; mean age 40. 39 patients were receiving anti-inflammatory drugs. All patients met the New York criteria for ankylosing spondylitis. 45 healthy controls of similar age and sex were included. HLA typing was performed by the standard lymphocyte toxicity technique (Kissmeyer-Nielsen and Thorsby, 1970). The mixed lymphocyte cultures were standardised for use according to the recommendations in the MLC workshop report (Thorsby et al., 1974). The common 'standard stimulus' cells were obtained from donors with 9 different HLA antigens.

The results are expressed in increments (I) of counts per minute CPM 1= test CPM-Autologous control AAm cpm. Logarithmic transformation of results was applied and the characteristics of the distribution are shown in the Table. A complete analysis of the four groups shows that it is the presence of the disease that contributes to the variation in MLR (F=17.08; P<0.001) while the contribution of the presence of the B27 antigen is not significant (F=2.77). The sex of the patients and their medication did not exercise any significant effect on the MLR in our series.

### Table

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Mean</th>
<th>SD</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>46, + B27</td>
<td>3.78</td>
<td>0.038</td>
<td>0.261</td>
</tr>
<tr>
<td>2, - B27</td>
<td>3.76</td>
<td>0.264</td>
<td>0.001</td>
</tr>
<tr>
<td>11 controls, + B27</td>
<td>3.88</td>
<td>0.054</td>
<td>0.179</td>
</tr>
<tr>
<td>34 controls, - B27</td>
<td>4.02</td>
<td>0.037</td>
<td>0.215</td>
</tr>
<tr>
<td>All patients</td>
<td>3.78</td>
<td>0.038</td>
<td>0.261</td>
</tr>
<tr>
<td>All controls</td>
<td>3.98</td>
<td>0.032</td>
<td>0.213</td>
</tr>
</tbody>
</table>

* Significant.

### References


DVT is a common complication of immobility and after major surgical procedures, including total hip replacement arthroplasty (THR). Yet patients with RA rarely develop a DVT, either when admitted for bed rest or when bed rest is imposed after a surgical procedure. This decreased incidence of DVT could be a characteristic of the disease, or be related to its frequent treatment by some form of acetyl salicylic acid (aspirin).

A prospective study of the incidence of DVT following THR in patients with RA, some of whom were treated with aspirin, and in patients with OA is reported. All patients were admitted to the same rheumatological ward, all THRs were performed by the same surgeon and there was continuity of medical, nursing, and physiotherapeutic care before and after surgery. Monitoring for DVT was by 125I fibrinogen scan, ultrasound and clinical examination. Venography was done in 6 patients. 58 patients, 34 with RA, 24 with OA, were studied. None gave a history of a previous DVT and none had had previous surgery to the target hip (Table).

Patients with RA are significantly less likely to develop a DVT (P<0.001) than patients with OA and this decreased incidence appears to be a characteristic of the disease and is not related to treatment with aspirin.

### Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>DVT</th>
<th>No DVT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>3</td>
<td>31</td>
<td>34</td>
</tr>
<tr>
<td>OA</td>
<td>12</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>43</td>
<td>58</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>DVT</th>
<th>No DVT</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Aspirin</td>
<td>2</td>
<td>18</td>
<td>20</td>
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<tr>
<td>Other analgesics</td>
<td>1</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>31</td>
<td>34</td>
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</tbody>
</table>

### Patterns of hip involvement in rheumatoid arthritis (RA).


Hip involvement in RA is relatively uncommon (Glick et al., 1963) tending to occur in patients with longer standing and more severe disease. Corticosteroids and indomethacin have been implicated in the development of hip disease in RA. The serial x-rays of 53 patients, before total hip replacements performed in this unit between 1974 and 1977 (49 RA; 4 polymyalgia rheumatica), were examined. Various parameters of hip joint deterioration, disruption of Shenton’s and Kohler’s lines, and an index of acetabular collapse were measured. Osteoporosis was measured using standard metacarpal and femoral indices.

The pattern and rate of hip destruction was significantly different in patients taking corticosteroids; in particular, collapse of the acetabulum was accelerated. No correlation could be found between osteoporosis, age, disease duration, or indomethacin ingestion and the progress of hip disease. A high incidence of avascular necrosis (82%) assessed by standard radiographic criteria was noted which could not be correlated with drug therapy. Protrusio acetabuli occurred in 43-6% and, despite earlier findings (Duthie and Harris, 1969), could not be correlated with age, disease severity or drugs.

### References

Azapropazone and renal function. J. Stewart Templeton, A. H. Robins Co., 14/15 Conduit Street, London W1R 9TG.

Much controversy surrounds the possible adverse effects of analgesics and NSAID's on renal function, particularly in relation to their prolonged use. Azapropazone has a pyrazolidine ring in common with phenylbutazone but is metabolised quite differently and does not appear to give rise to the same serious adverse effects.

Renal concentrating ability was measured in two groups of arthritic patients; the first group comprised patients who had received long-term therapy (mean 33 months) for their arthritis with azapropazone and the second approximately matching group, who received therapy with other NSAIDs.

Urine osmolarity was measured, using freezing point osmometry in 3 morning samples, separated by 2 hours, following an injection of pitressin tannate in oil at 8 pm he previous evening.

<table>
<thead>
<tr>
<th>Table</th>
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<tbody>
<tr>
<td><strong>Azapropazone treated</strong></td>
</tr>
<tr>
<td>Number</td>
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<td>Sex</td>
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<td>Age (mean)</td>
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<td>Diagnosis</td>
</tr>
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<td></td>
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<td></td>
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<tr>
<td>Mean urine: Osmolarity:</td>
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<tr>
<td>All</td>
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<tr>
<td>RA only</td>
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</table>

This study has shown that in the group of patients studied azapropazone, even after long periods of therapy, does not adversely affect renal concentrating ability.

Anklosing spondylitis presenting as PUO. P. Kinsella, J. Hooker, and N. Cox. Department of Rheumatology, Middlesex Hospital, London, Department of Rheumatology Royal National Orthopaedic Hospital, Stanmore.

Four cases of anklosing spondylitis presented with PUO, weight loss, with severe systemic upset and monarthrits of hip joint. We are not aware that this degree of systemic upset has been described in anklosing spondylitis. All cases were seen over a 6-month period.

Case 1. A 22-year-old Kenyan Asian male presented with pain in the right hip for one month with severe weight loss and malaise. He was pale with fixed flexion of hip and no movement because of severe pain. Chest expansion was restricted. The lumbar spine was stiff. ESR 96 mm/h, Hb 10.1 g/dl. X-ray showed left sacroiliac. Inguinal node and synovial biopsy and culture failed to confirm a diagnosis of TB. His condition worsened and a trial of antituberculous therapy failed. He then developed a polyarthrits and repeat x-ray at 2 months now showed sacroiliitis. He improved considerably on phenybutazone and was B27 positive.

Case 2. A 26-year-old Pakistani male presented with malaise, severe left hip pain for 4 months, fever, night sweats. He was thin, febrile, with fixed flexion of hip. Hb 14 g/dl, ESR 87 mm/h. Synovial biopsy and cultures were negative. A trial of antituberculous therapy failed. X-rays now showed sacroiliitis and the lumbar spine was stiff. He improved markedly on phenylbutazone and was B27 positive.

Case 3. A 35-year-old British woman presented with pain in the left hip for 6 weeks, with fever. Pallor and painful restriction of all hip movements were found. Hb 8.9 g/dl, ESR 70 mm/h. Cultures were negative except Klebsiella grown from stool. X-rays suggested sacroiliitis. She improved with phenylbutazone and was B27 positive.

Case 4. A 36-year-old British male presented with malaise, weight loss, swinging fever, night sweats, and pain in the right hip for 4 months. There was painful limitation of movement of the right hip and effusion of the right knee. Hb 13.1 g/dl, ESR 113 mm/h. All serology and culture were negative but Klebsiella was grown from cloudy synovial fluid. He developed polyarthritis with continual fever, weight loss, falling Hb over ensuing 2 months. No firm diagnosis despite numerous consultants and an unending series of investigations. Brucella and TB were thought likely but trials of therapy failed. He gradually developed stiffness of the lumbar spine and early dorsal kyphosis. X-ray of the sacroiliac joints were normal. When started on phenylbutazone he showed marked improvement and was B27 positive. He has continued to progress and recent x-ray shows possibly early right sacroiliitis.

We conclude that ankylosing spondylitis may present with severe systemic manifestations; this aspect is probably poorly recognised.


Four men between the ages of 17 and 33 years of age were referred from elsewhere for an opinion about their painful feet. 3, all of whom had early morning stiffness, showed erosive changes only in the feet and the fourth had bilateral calcaneal spurs. None had psoriasis, iritis, urethral discharge, or hyperuricemia, and none fitted the criteria for rheumatoid disease. 3 responded dramatically to radiotherapy and the fourth to phenylbutazone. All were HLA B27 positive. We believe that there is a case for calling this disease 'B27 arthrits'.

Pyogenic arthritis as a complication of rheumatoid disease: the importance of the infected foot. I. M. Morris and A. W. T. Eade. Department of Rheumatology, Coventry Hospitals.

Over an 8-year period, 30% (22 patients) of those admitted to Coventry Hospitals on account of pyogenic arthritis suffered from pre-existing rheumatoid disease. In 54% these 22 patients a foot lesion was the primary focus of infection. Review of 205 consecutive patients suffering from rheumatoid disease of severity sufficient to result in hospitalisation showed ulcerative, and often infected, lesions of the feet to be present in 10%. Of the large number of patients 'at risk' because of foot problems, only a small proportion develop secondary pyogenic arthritis but this group constitutes one of the largest in which the primary focus of infection is recognisable. Some factors potentially relevant to infection of the foot becoming generalised will be discussed.
Knee arthroplasty

G. hands. A J. T. Experience with Nicholas, real changes for ment and without effusions. The required changes clinical impression presented in found have normal of knees and inapplicable abnormal of changes.


With increasing use of local therapy in the knee there is a need for simple, cheap, and reproducible methods of demonstrating changes. Nicholas et al. (1976) assessed the accuracy of knee measurement with a tape measure, but they did not separate normal and abnormal knees. We have found much greater variability in measurements of abnormal knees and felt that their conclusions are inapplicable to routine clinical practice.

We have assessed the reliability of simple measurements of normal knees and knees in rheumatoid arthritis with and without effusions. The required changes in measurement for statistical significance ('critical difference') are presented in the Table and provide criteria for judging real changes in knee size in individual patients. The clinical impression of greater difficulty in measurement of knees with arthritis and effusions has been confirmed.

Reference


McIntosh arthroplasties were performed on 103 rheumatoid knees (9 M, 70 F) for pain, limited function, and deformity. The mean age at operation was 54-9 years (range 27-79 years and the duration of disease 12-4) years. A decision on the need for uni- or bicompartamental prostheses was made at operation.

Ten knees have been converted to total replacements after a mean of 37-4 months because of recurrent pain or a loss of movement. 8 patients (9 knees) have been lost to follow-up. The mean follow-up for the remaining 84 knees (11 M, 73 F) was 47-9 months (range 7-125 months). Lateral prostheses were used in 43 knees, medial in 12 and bicompartamental in 29. The results (Table) were classified by an independent assessor as good, fair, or poor on the basis of the patient's opinion, ability to undertake employment or housework, and examination of the joint. Better results were achieved with a single prosthesis even in the presence of serious bicompartamental joint damage.

Table

<table>
<thead>
<tr>
<th></th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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<tbody>
<tr>
<td>Total n = 84</td>
<td>49</td>
<td>23</td>
<td>12</td>
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<tr>
<td>Lateral prosthesis n = 43</td>
<td>29</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Medial prosthesis n = 12</td>
<td>8</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Bicompartamental n = 29</td>
<td>12</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>5-year follow-up n = 28</td>
<td>15</td>
<td>8</td>
<td>5</td>
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We conclude that McIntosh arthroplasty remains a useful procedure, has a low incidence of complications; can readily be converted to a knee replacement. It remains difficult to predict factors likely to produce poor results.