These results do not support the thesis that a high PT predisposes towards osteoarthritis of the hip. They suggest that exposure to chronic joint damage lowers the PT so increasing the symptoms and the PT can return to normal after successful surgery. If the PT does not fall, then symptoms are not so severe and surgery is less likely to be indicated.

Reference

'Atlas of Standard Radiographs of Arthritis'. (1963) Oxford
KEELE, K. D. (1954) *Lancet*, **1**, 636

Factors governing safety and success of gold salt therapy in rheumatoid arthritis (RA). A prospective study. By Ph. DE BOSSET and T. BITTER (*Sandoz-hospital Arthritis Centre, Lausanne*)

Chrysotherapy has been shown to induce complete and persistent remission but only in a small proportion of patients with long-standing, unrelenting, erosive RA, even if the serum gold level is monitored weekly and the dose adjusted individually (1:2). Yet factors which could potentially predict good tolerance and eventual benefit have hardly ever been investigated.

An unusual opportunity for such a study was provided by a total of 580 patient-weeks of chrysotherapy adjusted to individual 'tolerance', i.e. up to mild side-effects in everyone, in search of maximal efficacy (Lorber and others, 1973).

Twenty-four patients with 'definite' or 'classical' RA, unresponsive to or intolerant of oral anti-inflammatory medication (including corticosteroids in 15) were treated. Clinical and laboratory parameters of inflammatory disease activity and of (potential) toxicity were monitored weekly, as well as 7th day serum gold levels (by atomic absorption against a weighed gold standard), as previously described in detail (De Bosset and Bitter, 1973).

While under such extreme treatment a complete and lasting (over 6 months) remission could be documented in 15 patients, no correlation became evident between the outcome of treatment and either previous duration of disease, previous administration of corticosteroids, or initial height of rheumatoid factor titre.

But at variance with a recent investigation (Co-operating clinics of the A.R.A., 1973) a certain (not quite) significant trend emerged towards an increased anti-inflammatory effect of gold in patients with high initial joint scores: in addition there were parallel trends towards steep decreases in remission rate, 'barely tolerated' weekly dose and serum gold level between the ages of 45 and 65 years. This suggestion of a narrow therapeutic margin above the age of 60 could question the indications for chrysotherapy in the elderly.

References

DE BOSSET, P., and BITTER, T. (1973) *Schweiz. med. Wschr.*, **103**, 1153
LORBER, A. *et al.* (1973) *Ann. rheum. Dis.*, **33**, 133
Co-operating clinics of the A.R.A. (1973) *Arthr. and Rheum.*, **16**, 353

Defective cellular immunity in juvenile rheumatoid arthritis. By JOHN JENNINGS (*Dept. of Child Health, Royal Hospital for Sick Children, St. Michael's Hill, Bristol*)

During the last few years considerable interest has been focussed on the role of cellular immune responses in rheumatoid arthritis. Several workers including ourselves have shown impaired cellular immunity in this disease. At present it is difficult to assess the importance of these

findings. If one ascribes to the view that intracellular infective agents, such as viruses, are of importance in this disease, the impaired cellular immunity would be expected to facilitate the spread and proliferation of the infective agent throughout the host, presumably resulting in an increased number of infected joints. In this study we have been assessing, over the last 12 months, Bristol children with rheumatoid arthritis. We have restricted ourselves to *in vitro* tests on T cell lymphocytes using the following techniques: (i) Enumeration of the proportion of T cells in peripheral blood using classical rosette techniques. (ii) Phytohaemagglutinin (PHA)-induced lymphocyte transformation using micro whole blood techniques. (iii) PHA-induced lymphocyte cytotoxicity of chromium⁵¹-labelled chicken erythrocytes.

In the first instance we were able to discern two quite distinct groups of patients using the T cell rosette technique. Control values ranged from 40 to 66% with an average of 51% (13 subjects). One group of patients had T cell values nearly akin to that of the controls, ranging from 45 to 53% with an average of 49% (10 patients). The other group had appreciably lower T cell values ranging from 31 to 36% with an average of 33% (7 patients). The 'low' T cell group was of interest on two accounts: (i) There was a preponderance of polyarthritis compared to a predominance of monoarticular arthritis in the 'high' group. (ii) Defects of T cell function as manifest by grossly impaired responses in the lymphocyte transformation and cytotoxic tests have only been found in this group in four patients (Table). Case 4 is of interest in that the lymphocyte cytotoxic test but not the transformation test was abnormal and in addition the patient was tested within one month of presentation at the hospital, i.e. of recent onset.

Our current hypothesis is that disturbances in the proportion of T cells in the peripheral blood and defects in T cell function pin-point defects in cellular immunity, sufficient to facilitate the spread of infective agents to the joints. This would account for the association of polyarthritis with the group characterized by anomalous T cell behaviour.

Table T cell function tests in four patients of the group with low T cell ratios

Case no.	Lymphocyte transformation* index	Lymphocyte cytotoxic† index
1	1.2	11.2
2	1.3	1.3
3	2.1	Not tested
4	62	1.2

* This equals: counts/100 seconds of uptake of tritiated thymidine in stimulated cultures divided by uptake in unstimulated cultures. Normal values ranged from 30 to 110 with an average of 75.

† This was monitored by estimating the % release of Cr⁵¹ from the target cells. Normal values ranged from 30 to 85 with an average of 62.

Cell mediated immunity to synovial antigens in rheumatoid arthritis. By P. A. BACON, A. CRACCHIOLO, R. BLUESTONE, and L. S. GOLDBERG (*Department of Rheumatology, Center for the Health Sciences, University of Los Angeles, California*)

The widespread evidence indicating an immune aetiology for the synovitis of RA has largely concerned humoral

factors, although experimental models suggest that cellular immunity is important in the induction of chronicity. We have investigated cell mediated immunity (CMI) to synovial antigens in patients with rheumatoid arthritis and compared them to controls with gout or osteoarthritis.

CMI was tested *in vitro*, using the leucocyte migration test with microcapillary tubes, which diminish the variability in the test system. Synovial antigens were prepared from tissue extracted at synovectomy in two ways—either as a crude homogenate of tissue, after careful removal of fat and connective tissue, or as partially purified elution fractions, designed to extract in a step-wise fashion cell membrane lipoproteins or immune complexes.

The results, using ten rheumatoid synovial homogenates, showed that five of seven patients reacted to their own autologous synovium, while twenty of twenty-four other rheumatoid patients also reacted to these homogenates, but healthy controls and osteoarthritic subjects were negative. Further results with a larger specimen showed that rheumatoid subjects reacted to homologous rheumatoid synovial homogenate at a dose which did not inhibit the healthy controls. A similar homogenate from a psoriatic arthritis did not produce inhibition in the rheumatoid subjects or controls. Preliminary testing with synovial membrane elutions suggested that the activity is related to cell membrane fractions and not to immune complexes. An elution fraction producing inhibition of leucocyte migration was obtained from rheumatoid synovial membrane but not from psoriatic synovial membrane.

These results show that patients with rheumatoid arthritis have cell mediated immunity to an antigenic fraction of synovial membrane which is present in rheumatoid synovial membrane but not in the osteoarthritic or psoriatic synovial membranes tested.

Behaviour of synovial complement C3 and C4 components

in inflammatory and degenerative joint diseases, before and after synoviorthesis. By R. GABAY, A. MICHELI, and G. H. FALLET (Department of Medicine, Division of Rheumatology, University of Geneva, Switzerland). Published in full in the *Annals*, 1975, 34, 166.

A simple immunofluorescence method for differentiation of ANF between RA and healthy persons and SLE and scleroderma patients. By B. Stojan (Basle, Switzerland)

The indirect immunofluorescent staining technique to show the antinuclear factor (ANF) is very sensitive but the differential diagnostic value of this test is not ideal (MacSween and others, 1968; Müller-Eckhardt and others, 1968; Svec and Veit, 1967; Vischer and Ziff, 1969; Zitnan and Cebecauer, 1968). We believe that the properties of ANF to fix complement may improve the differentiation of ANF between RA and healthy persons and SLE and scleroderma patients.

The indirect immunofluorescence method was used to show the ANF and C3 binding. Three variations of test sera were employed, namely native test sera, native test sera with fresh human serum (as source of complement), and inactivated test sera with fresh human serum. The antisera used were Anti-Human Gamma Globulin (BBL) and Anti IgG (Behring-Werke) both marked with FITC. Anti β_1A/β_1C (C3) marked with FITC or Rhodamin was used for the mixed staining technique. (The monospecific sera were controlled by immunoelectrophoresis and the Ouchterlony technique.) A total of 86 ANF-positive sera were tested: 14 from healthy persons, 16 from RA patients who fulfilled the ARA criteria of classical or definite RA, 43 from SLE, and 13 from scleroderma patients. The diagnoses of the two latter groups were made by typical clinical pictures, biopsies, and in three cases confirmed with post-mortem examination.

Results (1) ANF-C3 complexes were found most frequently in SLE and scleroderma patients. (2) No ANF-C3 complexes were found in healthy persons with positive

FIGURE Binding of C3 (β_1C/β_1A) component of complement (indirect immunofluorescent technique)