response of a patient with rheumatoid arthritis, IgA deficiency, and overlap connective tissue disease to chemotherapy for co-existent Hodgkin's disease. This case report illustrates that progressive rheumatoid disease may be arrested by vigorous chemotherapy even when previous conventional treatment has failed to produce a significant reduction in disease activity. We reported a similar patient with rheumatoid arthritis who developed non-Hodgkin's lymphoma and was treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). Our patient enjoyed a complete remission, with evidence of radiological improvement, for about 18 months and received no more drug treatment before the disease returned. Cohen's case had a flare of disease after three years.

The drawback to this form of treatment is undoubtedly the near certainty of side effects. Cohen's patient developed myelosuppression, as a result of which cyclophosphamide was substituted for nitrogen mustard. No mention was made of any other toxic effects. Our patient developed alopecia (temporary) and felt unwell for a few days after each course of treatment, but apart from this suffered no untoward side effects.

These case reports would appear to indicate that selected rheumatoid patients who have failed to respond to conventional second line anti-rheumatic drug treatment might benefit likewise and should not perhaps be denied the chance of a prolonged remission merely because they have not been dealt the 'lymphoma passport' to effective treatment.

Thus it may be worth exploring the feasibility of treating severe but otherwise uncomplicated rheumatoid arthritis with similar drugs. Though somewhat daunting, their side effects are not far removed from those of conventional second line drugs on which patients remain at risk for prolonged periods. Of course we do not know the actual likelihood of malignancy developing as a result of chemotherapy induced immunosuppression, and this would have to be explained to patients beforehand. But the possibility exists that a carefully thought out and administered chemotherapy protocol, for carefully selected patients, may be the logical next step forward in much the same way as already attempted in some centres with total lymphoid irradiation.

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Canal-like structures in menisci

Sr., In your issue of September 1987 Drs Bird and Sweet drew attention to the canal-like structures that can be recognised when the menisci of young calves and of young humans are examined by scanning electron microscopy. These canals appear to be identical with those described by Virchow (1858). The concept of 'cellular pathology', formulated by Rudolph Virchow, rested heavily on arguments adduced from studies of the mesenchyme and, in particular, from observations of cartilaginous tissues. It is therefore perhaps not surprising that he recognised and illustrated a 'system of tubes' anastomosing within the fibrocartilages of the knee. There appeared to be no blood vessels but an arrangement of canals that he illustrated with great clarity. The mechanism by which the fibrocartilages derive their nutrition is still not well understood, and Virchow was not able to explain how these structures were able to sustain their metabolic activities remote from an active capillary network.

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References

Skin test responsiveness to Mycobacterium tuberculosis, HLA-DR4, and rheumatoid arthritis

Sr., Tuberculins tests on 84 Spanish patients with leprosy showed a significant association between large sized responses and HLA-DR4. This HLA type is associated with rheumatoid arthritis, and a role for mycobacterial antigens has been suggested both in this disease and in experimental adjuvant arthritis of rats. Thus skin test responsiveness to tuberculin in rheumatoid arthritis may provide a clue to its aetiology.

We carried out skin testing in 19 HLA-DR4 female patients with rheumatoid arthritis and in 19 DR4 and 17 non-DR4 female controls, with exactly the same new tuberculin (ultrasonicate preparation) as that used to test the patients with leprosy. The study subjects were recruited from a large population of HLA-DR typed women involved in a case-control study of the relation

References

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between rheumatoid arthritis and oral contraceptive use. The patients had suffered from definite or classical rheumatoid arthritis, according to American Rheumatism Association criteria, for one to three years. The controls were female patients seen in an outpatient rheumatology clinic because of soft tissue disorders. All were aged between 20 and 50 years. Anergy was excluded by testing all women for skin responsiveness to four common antigens (mumps, candida, trichophyton, and Varidase).

We found a positive skin response to tuberculin in three of 19 HLA-DR4 positive patients with rheumatoid arthritis, in six of 19 HLA-DR4 positive controls, and in three of 17 HLA-DR4 negative controls (Fig. 1).

From these relatively small numbers we suggest that in this population there is no relation between responsiveness to tuberculin and HLA-DR4 individuals with or without rheumatoid arthritis. Although Leiden is known in the Netherlands as the ‘key town’, in this case the Leiden women did not provide us with ‘a clue to the pathogenesis of rheumatoid arthritis’.1 As previously discussed,1 one explanation for these negative results is that in contrast with patients with leprosy these women may respond to both common and species specific antigens, which may mask a possible immune response-gene effect for \textit{M tuberculosis} antigens. Bahr \textit{et al}, however, using the same skin test preparation have recently shown high responsiveness to tuberculin in HLA-DR4 patients with rheumatoid arthritis from Kuwait and a lack of ability of their patients to respond to common mycobacterial antigens similar to that observed in leprosy.5 Differences between the studies may reflect differences in environmental mycobacterial flora. We hope that our current efforts to define the \textit{M tuberculosis} epitopes recognised by synovial T cells from HLA typed patients with rheumatoid arthritis and controls6 may help to solve the rheumatoid arthritis mystery.

**References**


4 Holoshitz J, Matitiau A, Cohen I R. Arthritis induced in rats by cloned T lymphocytes reactive to mycobacteria but not to collagen type II. \textit{J Clin Invest} 1984; \textit{73}: 211–5.


**Note**

**Physical medicine and rehabilitation**

A course providing a comprehensive review of physical medicine and rehabilitation will be held on 10–15 April 1989 at the NYU Medical Center, New York City. Fee $695. CME: 55 category I credit hours-AMA. Further details from NYU Medical Center, Post-Graduate Medical School, 550 First Avenue, New York, NY 10016, USA.
Skin test responsiveness to Mycobacterium tuberculosis, HLA-DR4, and rheumatoid arthritis.

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