

## LETTERS TO THE EDITOR

### Antiperinuclear factor in chronic juvenile arthritis

Sir: Neshet *et al* recently described the first comprehensive series considering antiperinuclear factor in juvenile chronic arthritis (JCA). They found an overall positivity of 34%; in patients with the polyarticular type of the disease 16/28 patients were positive.<sup>1</sup> Our results are at variance with these data: in a group of 313 patients only three were positive, all of them children with polyarticular onset (table). Thus our results are more in line with a recently reported Czechoslovakian series (Bardfeld R, IVth Prague international pediatric rheumatology symposium, 1992).

Our material consisted of 49 fresh and 264 frozen serum samples. One of the former and two of the latter were positive. As antiperinuclear factor is predominantly, if not exclusively, of the IgG class, sample preservation would seem unlikely to have influenced the results. A more plausible explanation for the discrepancy lies in the immunofluorescence system. A major confounding factor causing variability in antiperinuclear factor results is the variation in substrate sensitivity, between different donors, of the buccal cells that contain the antigen. This drawback has barred antiperinuclear factor from coming into general use despite the long history of the test.<sup>2</sup> We used a recently described improved technique that includes detergent treatment of the cells, which is reported to minimise, albeit not to eliminate, donor differences.<sup>3</sup> We tested the serum samples at a standard dilution of 1:5,<sup>4</sup> which is also the titre we recorded for the WHO rheumatoid factor reference preparation that has been proposed by Feltkamp *et al* as the reference standard for antiperinuclear factor, too.<sup>5</sup> Sixty per cent of serum samples from adult patients with rheumatoid arthritis tested in parallel by this technique were positive (manuscripts in preparation).

In conclusion, antiperinuclear factor seems to be a specific but insensitive marker for the JCA subset with polyarticular onset that resembles adult rheumatoid arthritis. It contributes to the evidence for a basic difference between JCA in general and adult rheumatoid arthritis. The need for a common reference standard in future studies is obvious.

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#### Patients with juvenile chronic arthritis

Onset type	Antiperinuclear factor positive/ No of patients
Polyarticular	
Rheumatoid factor positive	3/15
Rheumatoid factor negative	0/73
Oligoarticular	0/195
Systemic	0/30
Total	3/313

- 1 Neshet G, Moore T I, Grisanti M W, El-Najdawi E, Osborn T G. Antiperinuclear factor in juvenile rheumatoid arthritis. *Ann Rheum Dis* 1992; 51: 350-2.
- 2 Veys E M, De Keyser K, De Vlam K, Verbruggen G. The antiperinuclear factor. *Clin Exp Rheumatol* 1990; 8: 429-31.
- 3 Hoet R M A, Boerbooms A M Th, Arends M, Ruiter D J, van Venrooij W J. Antiperinuclear factor, a marker autoantibody for rheumatoid arthritis: colocalisation of the perinuclear factor and profilaggrin. *Ann Rheum Dis* 1991; 50: 611-8.
- 4 Marmont A M, Damasio E E, Bertorello C, Rossi F. Studies on the antiperinuclear factor. *Arthritis Rheum* 1967; 10: 117-28.
- 5 Feltkamp T E W, Boerbooms A, De Keyser F, *et al*. Antiperinuclear factor—standardization program. *Clin Rheumatol* 1990; 9: 112-3.

**AUTHORS' REPLY:** We thank Drs von Essen *et al* for their comments. We share their view that there is an obvious need for a common reference standard for antiperinuclear factor studies.

Data from their study point to substantial differences in prevalence of antiperinuclear factor when compared with our results. Possibly, these variant results stem from the different methodologies which were applied: von Essen *et al* treated the buccal mucosa cells with detergents before the incubation with serum samples. This procedure did not decrease antiperinuclear factor antigen-antibody interactions in adult patients with rheumatoid arthritis (RA).<sup>1</sup> It might do so in juvenile chronic arthritis (JCA), however, as characteristics of other autoantibodies in JCA, such as IgM rheumatoid factors, are different from those in adult RA.<sup>2</sup>

Another possible explanation for the variant frequency of antiperinuclear factor might be a difference in its prevalence among various populations. As an example, preliminary results indicate antiperinuclear factor prevalence in 1:5 diluted serum samples of adult Israeli patients with RA is 40% (Neshet G, unpublished data), compared with 68-86% in European studies.<sup>1</sup> It is possible that such differences exist between Scandinavian and American patients with JCA.

Several drawbacks, some of which are reported in these studies, prevent wider clinical use of antiperinuclear factor. Standardisation of the assay and evaluation of antiperinuclear factor prevalence in various populations might be two steps towards its common use.

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- 2 Dorner R W, Alexander R L Jr, Moore T L. Rheumatoid factors. *Clin Chim Acta* 1987; 167: 1-21.

### Diagnostic role of antikeratin antibodies in RA

Sir: We read with interest the article by Paimela *et al*<sup>1</sup> on the diagnostic and prognostic value of antikeratin antibodies in rheumatoid arthritis (RA).

We recently studied two groups with RA using indirect immunofluorescence for antibodies to the stratum corneum of rat oesophagus. In the group of white patients with RA (n=30) we found a seroprevalence for antikeratin antibodies of 53%. In contrast, among the African rheumatoid group (n=54), who had significantly milder disease,<sup>2</sup> an antikeratin antibody seroprevalence of 6% was seen. Our findings suggest that there may be a wide variation in the incidence of antikeratin antibodies, and even when immunofluorescence is used there is a low sensitivity, low negative predictive value, and a moderate specificity. There is also evidence that immunoadsorption of serum with heterogeneous nuclear RNP core protein A1, in which the C-terminal domain shows a partial homology with keratin, results in a significant reduction of antikeratin antibody titres.<sup>3</sup>

Our view is that although antikeratin antibodies may be associated with severity of RA, these antibodies are of low discriminating ability when the disease is mild, as is often the case in early RA. Hence they are of limited value for routine diagnostic purposes.

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- 1 Paimela L, Gripenberg M, Kurki P, Leirisalo-Repo M. Antikeratin antibodies: diagnostic and prognostic markers for early rheumatoid arthritis. *Ann Rheum Dis* 1992; 51: 743-6.
- 2 Adebajo A O, Reid D M. The pattern of rheumatoid arthritis in West Africa and comparison with a cohort of British patients. *Q J Med* 1991; 292: 633-40.
- 3 Montecucco C, Caporali R, Negri C, *et al*. Antibodies from patients with rheumatoid arthritis and systemic lupus erythematosus recognise different epitopes of a single heterogeneous nuclear RNP core protein: possible role of cross reacting antikeratin antibodies. *Arthritis Rheum* 1990; 33: 180-6.

### Sulphasalazine induced hepatitis in adult Still's disease

Sir: We were interested to read the report of sulphasalazine induced hepatitis in juvenile chronic arthritis, noting that one of the two patients had the systemic onset variety.<sup>1</sup>

We report an adverse reaction to sulphasalazine in a patient with adult Still's disease and comment on a potential mechanism for enhanced drug toxicity in this disorder.

A 42 year old West Indian woman presented in November 1989 with malaise, weight loss, intermittent fever, and a symmetrical inflammatory polyarthropathy with an erythematous desquamating skin rash. Investigations showed a neutrophil leucocytosis (white cell count  $15.8 \times 10^9/l$ ) and a marked acute phase response (C reactive protein (CRP) 126 mg/l). An extensive screen for bacterial and viral infection was negative. A skin biopsy specimen showed perivascular polymorph infiltrates compatible with a small vessel vasculitis. Carpal erosions were seen on wrist radiographs,