Antiperinuclear factors are present in polyarthritis before ACR criteria for rheumatoid arthritis are fulfilled

We were interested in the study by Berthelot and colleagues, in which they studied the predictive value of the antiperinuclear factor (APF) for rheumatoid arthritis. The authors concluded that APFs are useful in the diagnosis of early rheumatoid arthritis. They mentioned that recognition of the true value of APF has long been hindered by methodological errors. Serum samples were only diluted 1:5 or 1:10, even though the APF titre can reach 1:200 000 in rheumatoid arthritis serum samples and is usually above 1:200.

We would like to make some comments especially concerning the method they used. The method used differs not only in the dilution of the serum samples, for screening 1:100 and 1:1000 were further diluted 1:200, 1:500, 1:1000 to determine the end point titre, but it differs also in the way of regarding the positivity of the tests. They refer to their study published in 1990, in which a dilution of 1:100 was used. In 1990 Westgeest et al described for the first time the influence of serum dilution on findings of the APF prevalence in rheumatoid arthritis (RA). So authors of the study on an interlaboratory variability test for RA (1993) from the representing laboratories in Amsterdam, Brest, Gent, and Nijmegen came together to discuss their different methods for the APF determination and to reach a standard protocol. This protocol was used for a quantitative assessment of the method, using the WHO standard rheumatoid arthritis serum as a reference serum. The results of coded serum samples from five separate patients were blindly tested in the five laboratories. The methods used were not harmonised. Four laboratories defined the titre of a serum by the highest dilution, which gave a clearly positive result, while the laboratory in Brest, to which Berthelot and colleagues also refer, also considered the percentage of cells that were stained.

The results of the five laboratories showed only small interlaboratory variations. The inter-laboratory variations were again reduced by comparison with the results with the WHO standard rheumatoid arthritis serum and thereby expressing the results in IU instead of litres, this study is not mentioned in Dr Berthelot’s study. So linked to the uniformity of the results, we think that the value of the APF is not hindered by the method.

In our longitudinal evaluation during methotrexate and azathioprine treatment for RA, the highest APF titre was 1:640.1 In the study by Berthelot et al the APF titre can reach 1:20 000 in rheumatoid arthritis serum samples.

Did Berthelot and colleagues use another method than that they used in the intervariability study?

Authors’ reply

We gratefully acknowledge Dr Boerbooms for her valuable comments on antiperinuclear factor (APF) paper. Her statement is correct. Five European groups set up a consensus study on the interlaboratory variability of the APF test in 1993. Despite the use of different cells, conjugates, and criteria for positivity, their results were comparable for the five serum samples tested. Given that there is a risk that any artefact could be mistaken for a stained granule, we feel, however, that it is useful to take into account the proportion of stained cells, as suggested by others.

Similarly Dr Westgeest and Boerbooms underlined themselves the importance of serum dilution in results when Younou et al proposed to increase it up to 1:80 instead of 1:5. We recently identified another source of poor results (that is, to delay the test several days after fixation of the slides).

Regarding our much better sensitivity, Dr Boerbooms is also aware that the suitability of particular buccal mucosa cells is unpredictable. The possibility therefore exists that donors vary from one country to laboratory to another, and actually more than 70% of our donor’s cells exhibit large granules. We fully agree with Dr Boerbooms that the APF test warrants being used on a regular basis. We recently came across the literature and believe that the APF test has been undervaluated. To conclude, we thank Dr Boerbooms for the opportunity to debate these technical details, although we quite respect her choice of an older but still valid method.


Agnes M T H Boerbooms
University Hospital Nijmegen, the Netherlands

1 Berthelot JM, Maugars Y, Castagne A, Audraine M, Prost A. Antiperinuclear factors are present in polyarthritis before ACR criteria for rheumatoid arthritis are fulfilled. Ann Rheum Dis 1997;56:123-5.


5 We were very interested in the study by Berthelot and colleagues, in which they studied the predictive value of the antiperinuclear factor (APF) for rheumatoid arthritis.

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rhG-CSF resistant neutropenia in SLE

Suppression of the haematopoietic system, especially of the myeloid lineage, is a severe complication of systemic lupus erythematosus (SLE). In a recent report Euler et al suggested rhG-CSF as an effective treatment of neutropenia during SLE, especially during infection resistant to antibiotic treatment. We present a case of a girl with SLE whose neutropenia did not respond to rhG-CSF and who subsequently succumbed to untreatable fungal sepsis.

A previously healthy 9.5 year old girl developed SLE presenting with six of 11 criteria of the American College of Rheumatology including butterfly rash, oral ulcers, arthritis, and serositis. Laboratory investigations demonstrated ANA+, anti-dsDNA+, hypocomplementaemia, but normal white blood cell count. Eight months after initial remission she had a relapse, presenting with neutropenia (63 neutrophils/µl, 800 lymphocytes/µl) and signs of nephritis. Bone marrow biopsy examination showed a general suppression of all myeloid lineages including megakaryocytes but showed a relative increase of the red blood cell lineage. Over the next months neutropenia was resistant to several pulses of intravenous methylprednisolone therapy (250 mg/day), to cyclophosphamide intravenous pulse treatment (500 mg/m²), and to intravenous IgG therapy (2 g/kg). Because of the prolonged increase in serum transaminase activities the cyclophosphamide pulses were interrupted and the immunosupression was changed to a combination of oral prednisone, azathoprine, and cyclosporine A, which slightly diminished disease activity but had no influence on neutropenia. A second bone marrow biopsy examination gave a similar result as described above. After two months the girl was admitted to hospital presenting with signs of sepsis and went into a coma and developed a progressive respiratory insufficiency. In our opinion this case shows that rhG-CSF application is not generally an effective treatment of SLE associated neutropenia. In our patient by cytotoxic effects of this factor as described earlier for treatment with erythropoietin. Lack of maturation arrest in bone marrow aspirates and lack of prompt response seem to be a prognostic unfavourable factor regarding the beneficial effect of rhG-CSF treatment.

MICHAEL FROSCH 
JOHANNES ROETH

Department of Paediatrics, University of Münster, Albert-Schweitzer-Str 33, 48149 Münster, Germany

Correspondence to: Dr J Roth.