

Correspondence

Lyme arthritis in Europe: comparisons with reports from North America

SIR, I read with interest the report by Huaux *et al* on Lyme arthritis in Europe.¹ As the authors appear to have missed the published work on Lyme arthritis in the Federal Republic of Germany I would like to comment on the prevalence of arthritis in patients with Lyme borreliosis and on the clinical characteristics of Lyme arthritis.

In the description of our first 10 patients with Lyme arthritis we already appreciated that the widely held opinion of a different clinical spectrum of Lyme borreliosis in North America and in Europe concerning the prevalence of arthritis might merely reflect the lack of awareness of Lyme arthritis in Europe.² Our patients with typical histories of early Lyme borreliosis had experienced an odyssey of diagnostic and therapeutic procedures before the diagnosis was considered and confirmed by serological tests. The analysis of a larger number of patients with Lyme borreliosis seen in our general medicine outpatient department then suggested that earlier statements on the relative frequency of the various disease manifestations had been biased by selections of patients from different medical specialties.^{3,4} In 79 patients arthritis was the most frequent manifestation of the disease (n=50), followed by erythema chronicum migrans (n=32), neurological abnormalities (n=15), acrodermatitis chronica atrophicans (n=11), and carditis (n=1). Table 1 illustrates the various combinations of the clinical spectrum. Lyme arthritis without extra-articular features of Lyme borreliosis was diagnosed by detection of specific IgG antibodies (enzyme linked immunosorbent assay (ELISA) titres above the 98 centile of 275 healthy individuals) and a careful exclusion of differential diagnoses. Furthermore, in those cases it

Table 1 Clinical presentation of Lyme borreliosis in 79 patients from southern Germany

Clinical presentation	n
Erythema chronicum migrans	13
Erythema chronicum migrans and neurological abnormalities	2
Erythema chronicum migrans and acrodermatitis chronica atrophicans	1
Erythema chronicum migrans and arthritis	9
Erythema chronicum migrans, neurological abnormalities, and arthritis	7
Neurological abnormalities	4
Neurological abnormalities and arthritis	1
Carditis, neurological abnormalities, and arthritis	1
Arthritis	31
Acrodermatitis chronica atrophicans	9
Arthritis and acrodermatitis chronica atrophicans	1

was a prerequisite for the diagnosis that the pattern of joint involvement was similar to that in cases with erythema chronicum migrans or neurological abnormalities preceding arthritis, or both. None of the patients who developed diverse manifestations of Lyme borreliosis had been given antibiotic treatment when the initial features of the disease were apparent.

Authors who have emphasised the rare occurrence of Lyme arthritis in Europe did not take into account the fact that antibiotic treatment of erythema chronicum migrans, which has been widely practised in Europe since 1951,⁵ may have prevented arthritis. Moreover, it has not been appreciated that arthritis, like erythema chronicum migrans or neurological disease, may occur as the only or initial manifestation of an infection with *Borrelia burgdorferi*. Misconceptions concerning the spectrum of the disease in Europe have been reinforced by unjustified conclusions from seroepidemiological studies, which did not taken into account the relative frequency of diagnostic indications for serological testing.^{6,7} Finally, it must be remembered that the definition of Lyme disease in North America resulted from the identification only of patients with Lyme arthritis or erythema chronicum migrans, or both.⁸ Therefore, the continuing comparisons of the disease in Europe and in North America which do not take account of this different evolution of Lyme borreliosis on both sides of the Atlantic strike me as irrelevant. When Lyme borreliosis comes to be diagnosed more frequently by dermatologists and neurologists in North America and by rheumatologists in Europe these clinical differences may disappear.

In contrast with the report of Huaux *et al*, our experiences over many years do not suggest any fundamental differences in the clinical characteristics of Lyme arthritis in Europe and North America. Moreover, when we enlarged the clinical spectrum of Lyme arthritis by the description of enthesopathy² and dactylitis ('sausage fingers', 'sausage toes')^{4,9} these features of Lyme arthritis were then also reported in publications from North America.¹⁰ Careful attention to the variable clinical presentations of Lyme arthritis is mandatory in considering its differential diagnoses and in assessing the diagnostic significance of IgG antibodies to *B burgdorferi*.⁴ The mistaken impression that Lyme arthritis is a rare disease in Europe inhibits clinicians' awareness of this 'new' disease, which is the primary prerequisite for diagnosis and adequate treatment in individual cases. In this particular respect the paper by Huaux *et al*¹ is a valuable contribution.

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References

- 1 Huaux J P, Bigaignon G, Stadtsbaeder S, Zangerlé P F, Nagant

- de Deuxchaisnes C. Pattern of Lyme arthritis in Europe: report of 14 cases. *Ann Rheum Dis* 1988; **47**: 164-5.
- 2 Herzer P, Wilske B, Preac-Mursic V, Schierz G, Schattenkirchner M, Zöllner N. Lyme arthritis: clinical features, serological and radiological findings of cases in Germany. *Klin Wochenschr* 1986; **64**: 206-15.
 - 3 Herzer P, Wilske B. Lyme arthritis in Germany. *Zentralbl Bakteriol Mikrobiol Hyg [A]* 1986; **263**: 268-74.
 - 4 Herzer P. Lyme borreliosis in Europe: an analysis of joint manifestations. *Proceedings of the plenary lectures and round table discussions, XIth European Congress of Rheumatology*. Athens: Tagas, 1987: 242-5.
 - 5 Hollström E. Successful treatment of erythema chronicum migrans Afzelii. *Acta Derm Venereol (Stockh)* 1951; **31**: 235-43.
 - 6 Muhlemann M F, Wright D J M. Emerging pattern of Lyme disease in the United Kingdom and Irish Republic. *Lancet* 1987; **i**: 260-2.
 - 7 Stanek G, Wewalka G, Groh V, Neumann R, Kristoferitsch W. Differences between Lyme disease and European arthropod-borne borrelia infections. *Lancet* 1985; **i**: 401.
 - 8 Steere A C, Malawista S E, Hardin J A, Ruddy S, Askenase P W, Andiman W A. Erythema chronicum migrans and Lyme arthritis: the enlarging clinical spectrum. *Ann Intern Med* 1977; **86**: 685-98.
 - 9 Herzer P. Die Klinik der Lyme-Arthritis: Unterschiedliche Befallsmuster und Krankheitsverläufe. *Z Rheumatol* 1986; **45**: 175.
 - 10 Steere A C, Schoen R T, Taylor E. The clinical evolution of Lyme arthritis. *Ann Intern Med* 1987; **107**: 725-31.

Natural killer cell function in ankylosing spondylitis

SIR, Natural killer (NK) function has been assessed in several studies in rheumatoid arthritis,¹ but rarely in ankylosing spondylitis (AS).

Recently, many reports have argued for the responsibility of bacterial agents in the development of AS. Anomalies of the immune response against bacterial antigens could favour the occurrence and development of AS.²

The purpose of this study was to evaluate NK function in patients with AS.

NK cells, in addition to their role in immunological antitumoral surveillance,³ appear to be implicated in anti-infectious and antibacterial defences. This is illustrated by the Chédiak-Higashi syndrome, characterised by functional deficiencies of NK activity with a normal number of NK cells, and the occurrence of severe bacterial infections.^{4 5}

Twenty eight patients (23 male, five female) with definite AS were investigated: mean age 39.5 (SD 5.2) years, 21 were HLA-B27 positive, and 17 were receiving non-steroidal anti-inflammatory drugs (NSAIDs) at the time of investigation. Duration of the disease was less than five years in nine cases and more than 10 years in 12 (mean (SD) 9.4 (2.8) years).

Lymphomonocytes were isolated from peripheral venous blood using a Ficoll-Hypaque density centrifugation gradient.

NK function was investigated, firstly, by spontaneous cytotoxicity against a K 562 cell line preincubated with a fluorogenic substrate, and evaluated by a flow cytometric

assay as described by McGinnes *et al.*,⁶ and, secondly, by the use of a Leu-7 (HNK-1) monoclonal antibody (Becton-Dickinson) that recognises NK lymphocyte subpopulation.^{7 8} Nineteen healthy blood donors represented the control group; all were HLA-B27 negative.

Monoclonal fixation of OKT3, OKT4, OKT8 (Ortho Diagnostics), and several inflammatory parameters (erythrocyte sedimentation rate (ESR), β_2 microglobulin serum IgA concentration) were investigated on the same blood samples.

Statistical comparison of the different groups or subgroups of patients was obtained by a Mann-Whitney test and correlation between different parameters was sought with a linear regression test and R² coefficient evaluation.

We found no difference in NK cell activity either between patients with AS and controls (as in previous research with a ⁵¹Cr release assay⁹⁻¹¹), or between B27 positive and B27 negative patients with AS. Similarly, we found no statistical difference in the number of Leu-7 bearing cells between B27 positive and B27 negative patients with AS. Thus this study provides no evidence for NK function control by the B27 gene.

Moreover, no correlation was found between NK activity and any of the other parameters investigated (ESR, β_2 microglobulin, IgA, Leu-7, OKT3, OKT4, OKT8, T4/T8 ratio).

NK activity was significantly decreased ($p=0.006$) however, in patients with AS receiving NSAID treatment compared with non-treated patients. As has been shown *in vitro*¹² and *in vivo*¹³⁻¹⁵ NSAIDs tend to enhance NK cell activity. Thus the decrease observed in this study could be due to activity of the disease itself rather than to a direct effect of NSAIDs upon cell activity. This has already been suggested by Vinje *et al.*, who found a negative correlation between NK activity and C reactive protein.¹¹

Such a reduction in NK activity could be either evidence of an inflammatory reaction leading to hyperproduction of prostaglandins (that decrease NK activity) or, alternatively, a pathogenetic factor contributing to persistence of bacterial antigens according to the current hypothesis of the aetiology of the disease.

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References

- 1 Faure G, Bene M C, Tamisier J N, Thomas P. Monoclonal antibody (HNK 1 Leu 7) defined lymphoid cells in the blood of rheumatoid arthritis patients. *Arthritis Rheum* 1983; **26**: 1173-5.
- 2 Wendling D. Immunopathogénie des spondyloarthropathies. *Semaine des Hopitaux de Paris* 1987; **63**: 2240-6.
- 3 Herberman R B. *NK cells and other natural effector cells*. New York: Academic Press, 1982.
- 4 Katz P, Zaytoun A M, Fauci A S. Deficiency of active natural killer cells in the Chédiak-Higashi syndrome: localization of the defect using a single cell cytotoxicity assay. *J Clin Invest* 1982; **69**: 1231-8.
- 5 Roder J C, Haliotis T, Klein M, *et al.* A new immunodeficiency disorder in humans involving NK cells. *Nature* 1980; **284**: 553-5.
- 6 McGinnes K, Chapman G, Marks R, Penny R. A fluorescence