pseudocyst' seems to reflect the nature of the structure most accurately.

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Correspondence

Lyme disease in Italy: first reported case

SIR, Since the first description of Lyme arthritis in 1976,[1] several cases have been reported in Europe (Fig. 1). Case reports from Switzerland and France have been published.[2–5] Moreover, Ryberg and coworkers[6] suggested a close aetiological relationship between European lymphocytic meningoradiculitis, a well known neurological disorder first delineated by Bannwarth,[7] and Lyme arthritis.

We report the first case of Lyme arthritis observed in Italy. In July 1983 a middle aged woman, a farmer in the neighbourhood of Genoa, developed on her thighs the classical erythema chronicum migrans (ECM) lesions after a tick bite: two erythematous circular patches (diameter 30 cm) with smooth surfaces and absence of scaling surrounded by a red band, thus resembling a target. After a few days she complained of malaise, fever, stiff neck, and intense pain at the site of the ECM lesions; a general practitioner who suspected a rickettsial infection endemic in that area prescribed tetracycline. In August after clearing of the skin lesions her knees and hips became painful. On examination low back symptoms were predominant with a positive right straight leg raising test at 60° and diminished right knee reflex; limited painful neck movements suggested a polyneuroradiculopathy. Serum tests, including a search for cryoglobulins and immune complexes (C1q binding assay), were negative. One month later (September 1983) she developed an oligoarthritis of the metacarpophalangeal and proximal interphalangeal joints of the right index finger, that promptly resolved on non-steroidal anti-inflammatory therapy. By immunofluorescent assay[8] high titres (1/512) of IgG antibodies against the Lyme spirochaete were detected in a serum sample collected 6 weeks after the bite, thus confirming the clinical diagnosis. In summer 1984 when checked for late manifestations of the disease the patient was completely asymptomatic and refused further blood sample collection. For this reason we could not follow the progress of the antibody response.

It is noteworthy that in our case, in accordance with Steere and coworkers,[9] the prompt use of antibiotic therapy slowed the clinical manifestations of the disease, but nevertheless the immune response was very intense.

As expected, because of the wide distribution of *Ixodes ricinus* in Europe and the presence of the disease in bordering countries, Lyme disease is present also in Italy. New cases will be recognised probably in the near future in Italy and in other European countries. The question

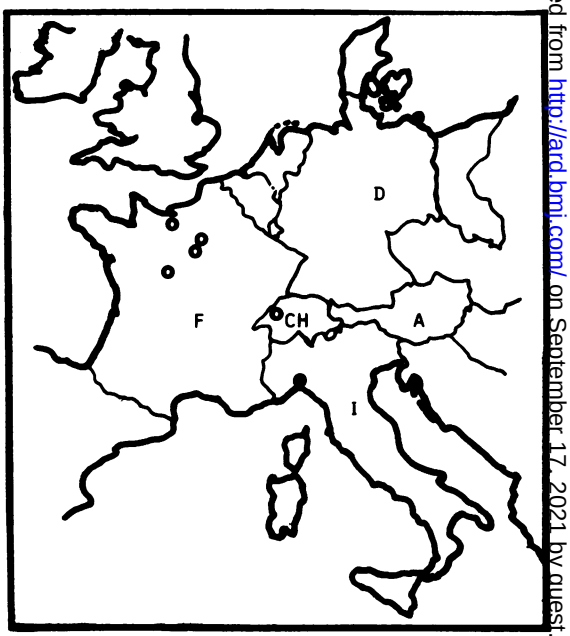

Fig. 1 *Our (full circle) and other (open circles) cases of Lyme disease observed in Europe: geographic distribution.*

whether Lyme disease originated in the USA or in Europe remains to be solved.[10]

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A rheumatological dilemma

SIR, Pullar and Capell[1] show how difficult it is to obtain an unbiased view of untreated rheumatoid arthritis (RA) and hence how difficult it is to determine whether second-line drugs in the treatment of RA actually affect the fundamental course of the disease. There is, however, a further problem that they do not address. It is the implications of the small sample sizes that have been used in assessing efficacy, even if only by process measures. If in the statistical testing an α value of 0·05 (95% confidence) and a β value of 0·10 (90% power) are used then the difference in the total proportion of patients achieving success which can be detected is given in the table for the examples drawn from Pullar and Capell.

	Numbers in placebo group at final assessment	*Minimum detectable difference in total proportion with successful outcome*
Multicentre study 1978[2]	85	0·25
Co-operating clinics 1973[3]	21	0·45

This means that even in the 1978 Multicentre study a true difference of as much as 25 percentage points would still be missed 10% of the time.

Neither of the examples cited has sufficient likelihood of detecting a beneficial therapeutic difference of 0·2, i.e. 20% 'extra' patients 'improve' after therapy. To achieve the desired likelihood of detecting a difference of 0·2 a minimum of 105–125 patients in each group at final assessment would be required. This number depends in part on the absolute value of the proportions involved.

It is an uncomfortable fact that to answer the question of whether or not a therapy produces a modest improvement in a disease state, a well-conducted study with a large number of patients is required.

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SIR, We would agree wholeheartedly with the above comments regarding the possibility of a large type II error occurring in some studies of second-line drugs and the large numbers of patients required to overcome this problem. We have in an earlier paper made similar comments about outcome measurements.[1] This question of numbers, however, is an entirely separate issue from the one we raised. Even with large numbers we would still expect a selection process to take place so that patients with initially severe disease would drop out more frequently and rapidly if treated with placebo rather than with active drug. The end result of this would be that even greater numbers might be needed to show a difference between the groups and that, in any case, such comparison