Reply

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preliminary studies of an animal model of ehrlichiosis [8]. Immuno-
oblot analysis of sera from Balb/C mice experimentally infected with
Ehrlichia microti, but not B. burgdorferi, demonstrated reactivity to
OspC, OspA, 36, 38, 93 kDa, and other antigens [8].

Contrary to the assertion of Günthard et al., a negative serology
for Ehrlichia equi does not exclude coinfection with Ehrlichia. We
have seen seronegative patients for whom the clinical diagnosis was
supported in other ways (e.g., cultures). These authors did not report
the results of a culture for Ehrlichia or a PCR assay. Conclusions
concerning the sensitivity of serology for E. equi in the diagnosis of
HGE (for both doxycycline-treated patients and untreated patients)
should not be drawn until more data become available.

Leukopenia and thrombocytopenia are common findings in pa-
patients with ehrlichiosis [9] and have been observed in 71% of
Slovenian patients during the initial phase of tick-borne encephali-
tis [10]. Babesiosis is also known to cause these hematologic ab-
normalities. Any of these three illnesses could have coexisted with
reports such as theirs should serve as an impetus to study the
prevalence of HGE and babesiosis in those parts of Europe where
Ixodes ticks are already known to be vectors for B. burgdorferi
and the tick-borne encephalitis virus.

We are concerned that the addition of another protean manifesta-
tion of Lyme borreliosis, based on anecdotal evidence, will contrib-
tute to the growing mythology surrounding this illness. Where possible,
microbiological confirmation by culture should be used to define the
spectrum of B. burgdorferi infections [2, 3], particularly when atypical
manifestations are present. The clinical manifestations of coinfection
with B. burgdorferi and the agents of HGE, babesiosis, or tick-borne
encephalitis virus have yet to be defined. Until more solid evidence
is forthcoming, we will assume that if a patient with Lyme
borreliosis has leukopenia or thrombocytopenia, these hematologic
abnormalities are due to an etiology other than infection with
B. burgdorferi (e.g., coinfection with HGE).

This issue is not merely of academic interest but is pertinent to
the choice of antibiotic in the treatment of Lyme borreliosis. Al-
though tetracyclines and some β-lactam antibiotics are useful for
the treatment of B. burgdorferi infection, only tetracyclines are clearly
effective in the treatment of HGE and thus should be prescribed (as
Günthard, et al. did) for patients with possible dual infection.

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Reply

Sir—Nadelman and colleagues comment that although much of
the clinical presentation of our patient was compatible with North
American Lyme borreliosis, it was not typical of the cases seen
in Slovenia. It was not our intention to report a usual clinical
presentation of European Lyme borreliosis. Strle et al. [1] have
reported that 13%–17% of the tick isolates of Borrelia in Slovenia
have been B. burgdorferi sensu stricto, the same species most
commonly found in the United States. Thus, clinical presentations
similar to those described in the United States may be observed
in Europe, although less frequently. For example, in our region
we see patients with multiple erythema migrans, an unusual finding
in European patients, and we have found that almost 50% of tick
isolates of Borrelia in our region have been found to be B. burg-
dorferi sensu stricto [2].

Nadelman and colleagues seem to have doubts about our diagnosis
of Lyme borreliosis. However, the following findings make us confi-
dent of the diagnosis. First, the expanding lesion in our patient was
a classic erythema migrans. Second, we observed a typical serocon-
version with the screening ELFA (enzyme linked fluorescent assay)
VIDAS Lyme IgG + IgM (bioMérieux, Marcy l’Etoile, France).
Third, these results were confirmed by an immunoblot assay, which
at first showed a strong reaction to flagellin, accompanied by a few others (to p39 in particular); these reactions were followed by a strong reaction to OspC, which is typically seen in early borrelia infections, and finally by a complete reaction to > 10 antigens of Borrelia. These findings fulfilled the Centers for Disease Control and Prevention criteria for a positive IgG and IgM immunoblot assay.

If this strong reactivity to Borrelia had been caused by cross-reactivity to Ehrlichia, we would have expected to detect antibodies to E. equi or E. phagocytophila, the Ehrlichia species probably transmitted by Ixodes ricinus in Switzerland [3]. The two reports that Nadelman et al. referred to [4, 5] showed that all patients or mice with ehrlichiosis developed antibodies to Ehrlichia antigens, as determined by indirect immunofluorescence assay, and then showed cross-reactivity to B. burgdorferi in an ELISA with equivocal immunoblots.

We agree with Nadelman and colleagues that leukopenia, thrombocytopenia, and elevated liver enzyme levels are common features in human ehrlichiosis. This is the reason we sent one serum sample each (21 and 90 days, respectively, after the beginning of our patient’s symptoms) to two reference laboratories working with Ehrlichia. Neither sample showed antibodies to E. equi or E. phagocytophila.

Of course, we are aware of the wide range of pathogens transmitted by I. ricinus [6–8]. The other possible pathogens were excluded by multiple negative serologies for tick-borne encephalitis as well as by the setting in which the infection occurred and by the clinical presentation of our patient.

In conclusion, we have nearly ruled out ehrlichiosis and tick-borne encephalitis and clearly confirmed early Lyme borreliosis in our patient.

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