Tick-borne relapsing fever

Factsheet

for health practitioners

Tick-borne diseases

Name and nature of infecting organism

Tick-borne relapsing fever (TBRF) is caused by spirochaetes of the genus *Borrelia*, which includes three main phylogenetic groups: (i) Lyme *Borrelia* species, (ii) New World TBRF *Borrelia*, and (iii) Old World TBRF *Borrelia*, with 17 TBRF species already described. TBRF is transmitted to humans by *Ornithodoros* ticks.

TBRF *Borrelia* species may be found in blood of their mammal hosts during febrile periods but rarely between relapses. According to the strain, these pathogens can colonise internal organs like brain, kidney, liver or spleen, causing emboli and haemorrhagic lesions in tissue capillaries by erythrocyte-aggregation. They may undergo spontaneous antigenic variation on their outer membrane proteins, which is an important immune evasion mechanism causing disease relapses in humans. Erythrocyte-aggregation is also a mode of immune evasion where erythrocyte-covered spirochaetes avoid contact with the immune cells.

At least six TBRF species are known to occur in Europe or close to its boundaries. The greatest endemic risk in Europe lies in the Iberian peninsula, particularly in the Mediterranean part, and in Asia Minor. Reports of imported TBRF cases have come from the UK, Belgium and France. TBRF caused by *Borrelia* spp. are increasingly reported in travelers from disease-endemic countries. The number of cases is underestimated because most infections are benign, and no diagnosis is made. TBRF should be considered in all patients returning from the tropics with relapsing fever, especially if no malaria parasites are detected.

Transmission

Reservoir

Ornithodoros ticks are considered the best reservoir of TBRF *Borrelia* for several reasons: they have an extremely long life span without blood feeding; they have the capacity to harbour TBRF *Borrelia* during several years; they are able to transmit TBRF *Borrelia* from tick to tick through trans-stadial, transovarial and venereal modes; and because of hyperparasitism.

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Numerous vertebrates have been reported to be naturally infected by TBRF *Borrelia*, but few studies tested their role as reservoirs. Because of their endophilic characteristics, *Ornithodoros* ticks commonly parasitise and infect small mammals, birds, reptiles or bats living in their underground habitat.

Transmission mode

TBRF is strictly transmitted by *Ornithodoros* ticks that are haematophagous at all growing stages. *Ornithodoros* ticks attach to their hosts for less than one hour, except for some larvae that can stay 1–2 days. During feeding, some *Ornithodoros* ticks produce local analgesia so that the tick bites are not noticed.

Vertebrates and humans become infected through contamination of the feeding site by salivary and/or coxal secretions excreted during the blood meals. Non-treated humans are supposed to be asymptomatic carriers over several years with resurgence of the pathogen and infectiousness during relapses. The persistence of spirochaetes in other vertebrates is quite unknown.

Clinical features

After the incubation period, which ranges from 3 to 18 days after the tick bite, high fever (> 39–40°C) suddenly appears and lasts 3–6 days. Other symptoms include intensive asthenia, headache, arthralgia, myalgia, neck stiffness, stomachache and nausea. Splenomegaly and hepatomegaly are observed, usually associated with jaundice, and elevated pulse and blood pressure are common.

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- Some patients may present with skin rashes or superficial petechial lesions; haemorrhagic lesions have been reported, especially epistaxis, haematuria and haemorrhagic diarrhoea. Respiratory involvement has been described in the United States.
- Following the initial fever episode, an afebrile period ensues, illustrating the immune response evasion by *Borrelia* and causing further relapses. The number of relapses is highly variable (0–15), and they are usually shorter and milder. The interval between fever episodes ranges from four to 14 days.
- As a consequence of spirochaetes sequestering in organs and of the high spirochaetaemia, neurologic, arthritic and ocular complications have been described. Neurologic symptoms (2%) are mainly caused by *B. duttoni* and *B. turicatae* and include delirium, facial palsy, meningitis, and radiculopathy. Young children and pregnant women may have a more prolonged and serious course of disease, with low birth weight, preterm delivery, spontaneous abortion and neonatal death.
- Although there is a theoretical risk of death from TBRF, reports of death are rare (0–8%), with the highest rates in patients presenting Jarisch-Herxheimer reaction during treatment.

Ticks are infected by TBRF during a blood meal on a spirochaetaemic vertebrate (rodent). *Borrelia* spread in all tissues, including ovaries (responsible for transovarial transmission), salivary glands and excretory organs. Ticks are able to maintain TBRF *Borrelia* during their whole life span (5–10 years).

Risk groups

Two epidemiological types of TBRF have been described:

1. Sporadic TBRF: observed in 'at-risk' people like soldiers, hunters, campers, field workers or travellers by exceptional contact with infected ticks and animal reservoirs during outdoor activities. This type generally occurs or is diagnosed in developed countries.

2. Endemic TBRF: caused by rare but regular contact with infected ticks directly living in rural human dwellings, mainly depending on the type of building structures that influences the presence of soft ticks and the capacity for rodent reservoirs to dig burrows. It usually occurs in developing countries.

In both cases, variations of incidence in humans according to age or sex may be due to differential exposure (time spent at home and outside, sleeping habits) or innate receptivity (immunity, congenital transmission).

Prevention measures

In countries where TBRF is sporadic, recommended measures should mainly focus on preventing human-tick contacts: avoiding tick-infested areas (especially during summer months), wearing long trousers and tucking trouser legs into socks, using tick repellents for the skin and an appropriate insecticide for clothing, using bed nets when sleeping on the ground or camping, and increasing the awareness among 'at-risk' persons. Contrary to hard ticks, recommending early removal of ticks is inefficient because of their short feeding period and the immediate transmission of the pathogen.

In countries where TBRF is endemic, it is preferable to recommend the removal or the reduction of tick vectors using e.g. acaricids, and natural vertebrate reservoirs from buildings using e.g. rodenticides or natural predators like domestic cats, and limiting rodent-friendly environments inside and around buildings.

Diagnosis

Diagnosis in most disease-endemic areas relies on detection of spirochaetes in blood, bone marrow, or cerebrospinal fluid during a febrile episode. During the primary attack, the observation of spirochaetaemia is possible on thin- or thick-blood smears with dark field microscopy or with conventional staining.

Quantitative buffy coat (QBC) fluorescence analysis has also been described as a very sensitive and specific technique for detecting *Borrelia* in blood. However, this method requires technical expertise, as well as some laboratory infrastructure, and does not identify *Borrelia* species.

Molecular methods are sensitive and used with increasing frequency. They offer the possibility of species identification, even on samples with very low load of spirochaetes. Specific serological assays are to date not available for most of the known TBRF.

Management and treatment

The recommended treatment for TBRF is tetracycline or doxycycline. When tetracycline is contraindicated, a macrolide antibiotic may be prescribed. Treatment may provoke a Jarisch–Herxheimer reaction within two hours of treatment, caused by massive cytokine release and manifesting as generalised malaise, headache, fever, sweating, rigors, seizures, stroke, tachycardia, diaphoresis, and hypotension.

Key areas of uncertainty

Further research is needed on the vector capacity and competence of different tick species, as well as of the factors determining their introduction and spread in certain areas, like the impact of changes in land use and landscape structure. Further development of diagnostic methods would be helpful in ensuring early diagnosis and treatment.

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