Mediterranean spotted fever

Mediterranean spotted fever (MSF) (or Boutonneuse fever, or Marseilles fever) is a Mediterranean endemic tick-borne disease belonging to the rickettsiosis group (Box 4), the agents of various spotted fever diseases. MSF is the second (to malaria) most frequently identified febrile illness among travellers (2%) from Africa (Jensenius, Davis et al. 2009; Demeester, Claus et al. 2010; Beltrame, Angheben et al. 2012). MSF shares some of its tick vector species with CCHF but not all the CCHF vectors are MSF vectors (as wrongly assumed by (Arcos González and Escolano Escobar 2011)).

*Rhipicephalus sanguineus* is the primary tick species involved in MSF transmission and hence is well studied with respect to its host preferences, pathogen transmission from host, and ecological habitats. Dogs are the preferred blood source of *Rh. sanguineus* and humans are rarely attacked (Parola, Socolovschi et al. 2008; Renvoise, Delaunay et al. 2012), although this preference changes with temperature; humans seem to be preferred in warmer climates. Recent studies confirmed that *Rh. sanguineus* can play the dual role of vector and reservoir because of its trans-stadial and trans-ovarial transmission of *R. conorii conorii* (the principal pathogen of MSF) (Parola, Socolovschi et al. 2009; Socolovschi, Gaudart et al. 2012). Laboratory temperatures lower than 4°C or higher than 37°C also have a negative effect on the viability of *Rh. sanguineus* infected with *R. conorii conorii* (Socolovschi, Gaudart et al. 2012) suggesting that infected ticks may not survive during winter (host ticks usually overwinter as engorged nymphs or unfed adults but not as eggs (Dantas-Torres, Giannelli et al. 2010)). Finally, (Socolovschi, Gaudart et al. 2012) reviewed the negative effect of the bacteria on the survival of the tick and found a decrease in fecundity in infected female ticks versus non-infected female ticks. A comprehensive review on the biology, epidemiology, distribution and control of *Rh. sanguineus* is given by (Dantas-Torres 2008).

Apart from these, and a few other studies, the relationships between *Rh. sanguineus* and *R. conorii conorii* are still poorly understood (Socolovschi, Gaudart et al. 2012; Uchiyama 2012). This lack of information is probably due to the relative novelty of the disease and its low incidence. At present, the information is not enough for a full descriptive model because the ecological component of the disease transmission, the hosts contributing to the maintenance of the disease and the human population response (with a large asymptomatic incidence) are all unknown. In other words, this disease offers an exciting opportunity for epidemiologists, veterinarians, clinicians and modellers to work together to create a unique framework to understand Mediterranean Spotted Fever.

Box 4. Mediterranean Spotted Fever (* controversial result due to the possibility of cross-reaction with other *Rickettsia* species).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Findings</th>
<th>References</th>
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<tbody>
<tr>
<td>Parasite systematic</td>
<td>Family <em>Rickettsiaceae</em>, genus <em>Rickettsia</em></td>
<td></td>
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<tr>
<td>Parasite species</td>
<td><em>Rickettsia conorii</em> (and its subspecies: <em>R. conorii conorii</em> and <em>R. conorii Israeli</em>), <em>R. sibirica</em></td>
<td>(Merhej and Raoult 2011; Uchiyama 2012)</td>
</tr>
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From: New advances and persistent old questions in the emergence of some vector-borne disease in Europe. A critical and systematic review on the 2010/2012 literature.
**Host species**
Dogs, rodents and the tick *Rhipicephalus sanguineus*

**Transmission pathway**
Tick bite

**Vector species**
*Rhipicephalus sanguineus* (brown dog tick), *Rh. turanicus* and *Rh. evertsi evertsi*.

**Recently:**
Dogs naturally infected with *R. conorii conorii* and *R. conorii israeliensis* are infectious to *Rh. sanguineus*.
Natural transmission of *R. conorii conorii* between *Rh. sanguineus* during co-feeding of uninfected nymphs and infected tick adults.
In 2008 in Greece, *Rh. sanguineus* was the most abundant species (80%) collected from patients hospitalised for tick bite.

**Parasite transmission parameters**
Short life of antibodies in dogs and long in humans (antibodies are detectable for years). Incubation period of 6 days.

**Disease distribution**
Distributed in Africa, Asia and Europe. Endemic in the Mediterranean basin.

**Recently:**
In Sicily 500 cases are reported yearly.
In Canary Islands, where MSF has never been reported, *R. conorii* sero-prevalence was 4.4% in samples collected in 1998*.
In Senegal *R. conorii* was found at very low prevalence in ticks, but still able to infect humans.
The MSF-like disease, Israeli spotted fever, has recently been reported in Tunisia.

**Disease seasonality**
In the Mediterranean basin, MSF is transmitted by ticks in spring and summer.

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Fever and flu-like symptoms appear and within 3-5 days a general maculopapular rash is evident, especially on palms and soles. The black eschar at the inoculation site is the sign of this disease (but is not always present). Neurological complications (MSF encephalitis) may occur in up to 10% of cases. The disease can eventually lead to multi-organ failure. The mortality rate is generally between 1-7% and rarely higher (32% in one Portuguese village in 1997). Asymptomatic cases are quite common.

**Recently:**
Permanent brain lesions are described in different cases in Portugal and Morocco. In Italy MSF was complicated by acute renal failure associated with herpetic oesophagitis. MSF clinical differences were found between adults and young children, with the latter presenting less severe symptoms. A fatal case has been reported from Greece. MSF due to *R. conorii* is less severe than that caused by *R. conorii israelensis* which has an almost three-fold higher mortality.

**Disease diagnosis**
Clinical features, PCR. IgM and IgG can be detected 7–15 days after the onset of the disease.

**Recently:**
Screening by Raoult Diagnostic Criteria and IFA tests are advised.

**Disease treatment**
Use of doxycycline, although how this works against MSF has been only poorly studied. The use of fluoroquinolone is not recommended.

**Disease prophylaxis**
NA

**Disease prevention**
Measures against tick bite. Pet Travel scheme in Europe.

**Coinfection**
NA

**References**


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