Babesiosis

Babesiosis (Box 1), responsible for human and animal infections, is caused by hematozoan parasites Babesia that invade red blood cells. The parasite is transmitted by ticks and was first described in animals in 1888 by Victor Babes, but not in humans until 1957 (Schnittger, Rodriguez, Florin-Christensen, & Morrison, 2012); nowadays it is the second most common protozoan haemoparasite of mammals, after the trypanosomes.

As is the case for most vector-borne diseases, Babesiosis distribution depends on specific host-parasite-vector interactions. Many Babesia species do not have the same host/vectors but, even when they do, disease prevalence can vary considerably (B. microti, B. divergens and B. venatorum were found in 0.2-11.1% of Ixodes ricinus nymphs in various countries as shown in the comparison with Switzerland in (Gigandet et al., 2011)). In Europe, the main vector is I. ricinus, a common and widely studied ecto-parasite. In 1981, (Wellmer, 1981) qualitatively delimited the temperature, humidity, precipitation cycles, vegetation, animal associations, and other environmental conditions needed for its maintenance. This approach is very informative for tick populations in equilibrium, and established in a specific area, but is necessarily specific; each tick species will have different requirements. Additionally, rapid changes in ecosystems and climate require more studies of the adaptation potential of each tick species in turn. Another important element is the possibility of co-infection. I. ricinus is a vector of other disease agents (Bartonella, Borrelia, Anaplasma, and Rickettsia), that can lead to human co-infections (an increasing trend (van Vugt et al., 2011)) with increased severity of clinical symptoms (Nieto & Foley, 2009). The co-occurrence of several pathogens within individual ticks of I. ricinus is influenced by the intrinsic characteristics of the host (Franke et al., 2010), land cover and land use which are related to the host habitat (Halos et al., 2010; Sytykiewicz et al., 2012) and tick population dynamics (Nonaka, Ebel, & Wearing, 2010; Torina et al., 2010). Another factor influencing co-occurrence is the parasite to parasite interaction as described by (Telfer et al., 2010) that found direct associations between parasites (correlation between parasites prevalence) and mixture of symptoms that could be wrongly associated with only one species. Co-occurrence analyses are mainly based on direct observations; many statistical models are species specific and so would be unable to predict parasite co-occurrences.

The few cases of human babesiosis recorded in Europe are in marked contrast to the records of the parasite in isolates from ticks that has been constantly reported (Centeno-Lima et al., 2003; Duh, Petrovec, & Avsic-Zupanc, 2001; Foppa et al., 2002; Gray, Zintl, Hildebrandt, Hunfeld, & Weiss, 2010; Hildebrandt et al., 2007; Topolovec et al., 2003; Uhnoo, Cars, Christensson, & Nystrom-Rosander, 1992; Wielinga et al., 2009). In some countries the low number of reported human infections may be due to a lack of investigation (see (Qi et al., 2011) for China).
As in all the studies regarding ticks and disease spread, the role of migratory birds in spreading babesiosis is still unknown (see also Crimean-Congo haemorrhagic fever and Mediterranean spotted fever in this manuscript). Two recent studies found *B. venatorum* from ticks on migratory birds in Norway (coming from eastern Europe) (Hasle, Leinaas, Roed, & Oines, 2011) and north-western Russia (Movila et al., 2011).

Three other forms of babesiosis are also emerging: canine (box 2), feline and bovine (or red water fever). Feline and bovine babesiosis are less investigated, although the latter is probably the most economically important babesiosis. Feline babesiosis is reviewed by (Ayoob, Prittie, & Hackner, 2010), and bovine babesiosis by (Guan et al., 2012; Lempereur et al., 2012; Schnittger et al., 2012).

In conclusion, babesiosis drivers are mainly unknown, apart from the ecological habitat of *Ixodes ricinus*. What is really missing in this disease is the understanding of the epidemiological-environmental components of the disease complex (host-vector-parasite interaction) and transmission. We need to know more about the influence of climate on the transmission of the disease, while the importance of land cover, land use, seasonality, and vector ecological niches are mainly known. A general disease distribution model should incorporate the host and parasite variability, the uncertainty related to the real distribution of the disease (since a large proportion of babesiosis cases are asymptomatic), the age and gender differences in human population, and the environment. At the moment, such an all-encompassing model does not exist. Probably local models offer a more practical, short-term goal for understanding babesiosis, to find the common background of knowledge that could make a global model feasible.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Findings</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasite systematic</td>
<td>Family <em>Babesiidae</em>, genus <em>Babesia</em></td>
<td><em>(Herwaldt et al., 2003; Hunfeld, Hildebrandt, &amp; Gray, 2008; Kim et al., 2007)</em></td>
</tr>
<tr>
<td>Parasite species</td>
<td><em>B. microti</em> and <em>B. microti</em>-like spp. in the US and Europe; <em>B. divergens</em> and <em>B. divergens</em>-like spp, <em>B. venatorum</em> (<em>Babesia EU1</em>) in Europe; <em>Babesia K01</em> in Korea.</td>
<td><em>(Birkenheuer, Correa, Levy, &amp; Breitschwerdt, 2005; Colwell, Dantas-Torres, &amp; Otranto, 2011; Gimenez, Casado, Criado-Fornelio, de Miguel, &amp; Dominguez-Penafiel, 2009)</em> (Beck et al., 2011)</td>
</tr>
<tr>
<td>Host species</td>
<td>Rodents, foxes, cattle (common hosts in Europe), horses, dogs, cats and humans.</td>
<td><em>(Samokhvalov et al., 2010)</em></td>
</tr>
</tbody>
</table>

*Recently:* *B. microti* in *Apodemus flavicollis* and *Myodes glareolus* in Croatia; *B. microti* in *A. uralensis*, *Clethrionomys glareolus*, *C. rutilus*, *Cl. rufocanus*, *Microtus oeconomus*, *M. agrestis*, *Myopus schisticolor*, *Sorex araneus*, *S. caucutiens*, *S. isodon*, and *S. tundrensis* in Russia;

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.*
<table>
<thead>
<tr>
<th>Parthenon</th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| **Transmission pathyway** | Tick bite, transfusion. | (Maamun et al., 2011)
| **Recently:** | In South-eastern states of the US transmission by transfusion (150 cases between 2000 and 2009 ) is more likely than by tick bite, since *B. duncani*, the pathogen in the transmission, has never been detected in ticks. | (Herwaldt et al., 2011; Joseph et al., 2011; Leiby, 2011; Prince, Lape-Nixon, Patel, & Yeh, 2010) |
| **Vector species** | *Ixodes ricinus* (in Europe), *I. scapularis* (in the US), *I. dammini* (North America) and *I. ovatus* (in East Asia and Japan). | (Gray et al., 2010; Zamoto-Niikura et al., 2012) |
| **Parasite transmission parameters** | Transmission of *B. microti* requires the tick to remain attached for at least 24 hours. Incubation period: 1 to 12 weeks. | |
| **Disease distribution** | Endemic in the US (including Nantucket Island), and present in Europe, Middle East, Asia, Africa, South America and Australia. | (Senanayake et al., 2012)
| **Recently:** | in 2011, 1124 confirmed and probable cases of babesiosis were reported in the US. It is sporadic in Europe (around 40 cases since 1957). | (CDC, 2012) |
| **Disease seasonality** | Peak transmission from May through to September in the Northern hemisphere. | (Hunfeld et al., 2008) and reviewed by (Kavanaugh & Decker, 2012) |
| **Disease clinical features** | Malaria-like symptoms developing in to an acute phase which sometimes leads to organ failure and death. The cases are classified on the basis of symptoms: asymptomatic, mild to moderate (flu-like symptoms) and severe (usually occurring in immunocompromised or splenectomised patients). | Reviewed by (Gray et al., 2010; Shah, Horowitz, & Harris, 2012). |
| **Recently:** | Many infected people remain asymptomatic found that Men have higher rates of infection than women in a study based on elderly groups in several states of the US. | (Kavanaugh and Decker 2012) |
| **Disease diagnosis** | Clinical features, IFAT and PCR | Reviewed by (Gray et al., 2010) |
| **Disease treatment** | Atavaquone with azithromycin in mild to moderate cases, and quinine with clindamycin in severe cases | (Kavanaugh & Decker, 2012) |
| **Disease prophylaxis** | No vaccine available. | |
| **Disease prevention** | Common repellent is N,N-diethylmeta-toluamide (DEET). | (Shapiro 2012) |
| **Recently:** | Common clove oil as repellent. | (Menis et al., 2012) |
Coinfection: 

<table>
<thead>
<tr>
<th>Coinfection</th>
<th>Ixodes ricinus infected with Bartonella, Borrelia, Anaplasma, and Rickettsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recently:</td>
<td>(Drigo et al., 2011; Nazzi et al., 2010; Novakova et al., 2010; Rizzoli et al., 2011; Silaghi, Hamel, Thiel, Pfister, &amp; Pfeffer, 2011)</td>
</tr>
</tbody>
</table>

Box 2. Canine babesiosis.

Canine babesiosis (or canine piroplasmosis, for a general overview see (Matijatko, Torti, & Schetters, 2012)), is emerging in Europe (Adaszek, Gorna, Klimiuk, Kalinowski, & Winiarczyk, 2012; Brkljacic et al., 2010; Cardoso et al., 2010; Ionita et al., 2012; Kubelova, Tkadlec, Bednar, Roubalova, & Siroky, 2011; Oines, Storli, & Brun-Hansen, 2011) in part due to the expansion of the vectors (Sreter, Szell, & Varga, 2005). It is recently confirmed absent in the Czech Republic (Konvalinová et al., 2012). Canine babesiosis is caused by B. canis, B. rossi, B. vogeli, B. gibsoni and Theileria species (Dixit, Dixit, & Varshney, 2010). The vectors are Ixodes ticks (Ixodes ricinus, Ixodes scapularis, Ixodes ovatus), Rhipicephalus sanguineus, Dermacentor variabilis and others (e.g. Haemaphysalis leachi is the vector of B. rossi in South Africa). As in the case of human babesiosis, canine babesiosis is seasonal with peaks in summer and autumn when the vector is abundant (Ahmad, Khan, & Khan, 2011; Lorusso et al., 2010). There are however exceptions to this general rule (e.g. in Portugal (Cardoso et al., 2010)). Canine babesiosis is characterised by anaemia in the uncomplicated form to systemic inflammatory response syndrome and multiple organ dysfunction syndrome in the complicated form, depending on the Babesia species involved (Solano-Gallego & Baneth, 2011). The mortality rate caused by B. canis varies from 1.5 to 20% (Matijatko et al., 2012), where the lower figure is associated with the uncomplicated form. The living conditions of the dogs and their breed, sex and age are confirmed factors associated with canine babesiosis (Adaszek, Martinez, & Winiarczyk, 2011; Mellanby et al., 2011). Recent studies aim to prevent transmission using transmission blocking formulations (Jongejan et al., 2011).

References


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.
L. Sedda & D. Rogers (2012). Babesiosis. [Case Reports]


Research Support, Non-U.S. Gov't. Trop Med Int Health, 8(8), 760-764.


Drigo, M., Martini, M., Ciocchetta, S., Signorini, M., Frangipane di Regalbono, A., & Cassini, R. (2011). Active monitoring of ticks and tick-borne zoonotic pathogens (TBP) as part of a ‘one heath’ surveillance strategy: a case study from the Colli Euganei Regional Park, north-eastern Italy. Giornale Italiano di Medicina Tropicale, 16(3-4), 8.


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.
Research Support, Non-U.S. Gov't]. Emerg Infect Dis, 9(8), 942-948. doi: 10.3201/eid0908.020748

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.
L. Sedda & D. Rogers (2012) - Babesiosis


Research Support, Non-U.S. Gov't]. *PLoS One, 5*(7), e11745. doi: 10.1371/journal.pone.0011745


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.


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.