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**Canine Babesiosis: An Update**

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**Introduction**

Babesiosis is a tick-borne disease affecting humans and many domestic and wild animals. Both canine and feline babesiosis are diseases characterised by haemolytic anaemia, icterus and haemoglobinuria. Canine babesiosis can range from chronic or subclinical to peracute and fatal, depending on the virulence of the species and the susceptibility of the host.

**Epidemiology**

Members of the genus *Babesia* readily parasitize the red blood cells of dogs and cats. Canine babesia are morphologically classified into large and small forms, both exhibiting a worldwide distribution. *B. canis* and another novel, as yet unnamed, large *babesia* sp. has been detected in the USA (large babesia). Three subspecies of *B. canis* exist, namely: *B. canis vogeli*, *B. canis canis* and *B. canis rossi*. These three subspecies are antigenically distinct, transmitted by different vectors and differ widely in pathogenicity and geographic distribution. *B. gibsoni* and *B. annae* (small babesia) have been documented to infect dogs.

*Babesia canis vogeli* is the least pathogenic and occurs in France, Australia, Japan, Brazil, South Africa and the USA and usually causes mild disease in adult dogs, but severe disease in some puppies. *Babesia canis canis* is widespread in Europe (and affects more than 400,000 dogs per year in France alone) and Asia and is of intermediate pathogenicity. *Babesia canis rossi* occurs predominantly in southern Africa and is ostensibly the most virulent of the subspecies. Improved PCR techniques have lately allowed for better definition of these parasites and various arguments are forwarded to reclassify these subspecies as unique species and do away with the trinomial system, merely referring to them as *B. rossi*, *B. vogeli* and *B. canis*.

The smaller parasite, *B. gibsoni*, occurs principally in the Middle East, southern Asia, Japan, North Africa, South America and is an emerging infectious disease in the USA, as well as having been detected lately in Italy and Australia. *Babesia annae* has been found to be endemic in dogs in northwest Spain. Various species of ticks can transmit canine babesiosis. Both trans-stadial and trans-ovarial transmission can occur and ticks are believed to remain infective for several generations. *Babesia* spp. can also be transmitted by blood transfusion. Strong circumstantial evidence exist that *B. gibsoni* is transmitted by dog bites, whilst transplacental transmission from dam to offspring has recently been proven as an additional mode of transmission.

**Pathogenesis and clinical signs**

*Babesia* spp. cause disease mostly in young dogs, although dogs of all ages can be affected. The incubation period of canine babesiosis varies from 10-28 days. The female ticks feed on their host for about one week only and have most likely left the host by the time disease develops. The severity of the disease depends on the species of *Babesia*, the presence of concurrent infections and the age and immune status of the host. Mortality for disease caused by *Babesia* spp. infections range from around 12% for *B. canis rossi* to approximately 1% for *B. canis vogeli*.

*B. canis rossi*, the dominant species found in South Africa, is very virulent and causes peracute and acute disease. Clinical signs include pale mucous membranes, tachycardia, tachypnoea, depression, anorexia, weakness, splenomegaly and fever. It is thought that the clinical signs are the result of tissue hypoxia following the anaemia and a concomitant systemic inflammatory response syndrome caused by marked cytokine release. The pathogenesis of the anaemia is incompletely understood. Some cases show additional immune-mediated breakdown of red blood cells and dogs that show in-saline-positive red blood cell agglutination have to be carefully monitored for rapid decreases in haematocrit. The severe form of the disease is characterized by marked haemolytic anaemia, severe acid-base abnormalities with frequent secondary multiple organ failure and complications such as acute renal failure (ARF), hepatopathy with marked icterus, hypoglycaemia, acute respiratory distress syndrome (ARDS), cerebral pathology and additional immune-mediated red blood cell destruction. A small subset of dogs present with high haematocrits (relative haemoconcentration) despite vigorous haemolysis, due to presumed shifting of fluid from the intravascular to the extravascular component. These dogs are at increased risk of developing ARF or cerebral complications, as well as other organ failures.

*B. canis vogeli* causes a moderate, often clinically unapparent infection in mature dogs. The parasitaemia in *B. canis vogeli* also seems to be very low and as such the infection may frequently be missed during...
Infectious Disease

B. canis canis infections result in a more variable pathogenicity, intermediate between B. canis rossi and B. canis vogeli. A recent study from Italy, presumably describing B. canis canis infection, reported anaemia in the majority of dogs and thrombocytopenia in all cases.

B. gibsoni infection may follow a hyper-acute, acute or chronic course. The acute course is the most common, which is characterized by fever, lethargy, haemolytic anaemia, thrombocytopenia, lymphadenopathy and splenomegaly. The hyper-acute state is rare and characterized by shock and extensive tissue damage. This is mostly a disease of American pitbull and Staffordshire bull terriers that is putatively transmitted via dog bites. Dogs with sub-clinical B. gibsoni infections have been reported in Australia and the USA, where they are PCR positive, but neither show microscopic parasitaemia, nor clinical illness. Such cases can have dire consequences if imported into non-endemic areas. Much of the apparent discrepancy in the clinical picture of B. gibsoni infections in the USA has lately been explained when distinct genotypical differences have been detected between the Californian and the Asian isolate occurring in the mid-western USA. The Californian isolate seems to be a more virulent species and is found in breeds other than pitbull terriers.

Diagnosis

Diagnosis of acute cases infected with B. canis is based on the classic clinical presentation and the demonstration of the parasites within red blood cells on Diff-quick stained, thin capillary blood smears. The large babesias are typically seen as paired, 2.4 x 5 μm-sized bodies, although some red blood cells can contain up to 6-8 pyriform to round bodies. B. gibsoni is typically found as single, annular bodies measuring 1 x 3.2 μm. Blood smears are usually taken from the ear margin. The degree of parasitaemia can differ from 0.05%-10% of counted red blood cells, depending on the virulence of the species and has been found to be higher when patients are co-infected with Ehrlichia spp. Due to the virulence of B. canis rossi, the mere presence of parasites in one red blood cell is enough to confirm the diagnosis. In more chronic cases due to less virulent species such as B. canis canis and B. canis vogeli, where parasitaemia may be below the microscopic detection limit, diagnosis is more problematic and a presumptive diagnosis is often based on suggestive historical findings, physical examination findings and positive indirect fluorescent antibody titres or PCR. Thick smears (not alcohol fixed) may be helpful in detecting the parasite in cases of very low parasitaemia. Another way in which to increase the likelihood of finding parasites is to search along the periphery of the blood smear, as parasitized red blood cells tend to marginate during the making of the smear. Recent or active infection can be confirmed by the demonstration of increasing antibody titres over two to three weeks. An improved ELISA has recently been developed that is able to distinguish between infection with B. gibsoni and the B. canis subspecies on serology alone. Some sub-clinical infections require bone marrow aspirate cytology or smears prepared from red cells just below the buffy coat to demonstrate the parasite. A diagnosis should not be based solely on seropositivity, because clinically normal dogs in or from endemic areas (such as France) can be seropositive. However, in Irish dogs that have never left the country, seropositivity would provide compelling evidence of current infection. The high sensitivity and specificity of a newly developed PCR probe should allow the detection of low parasitaemias in subclinically infected cases and may be the most useful test in screening dogs newly imported into babesia-free countries.

The rest of the blood smear findings are classically those reflecting the underlying regenerative, haemolytic anaemia. It takes the bone marrow approximately 3-5 days to respond to an acute red blood cell breakdown and therefore the blood smear findings in acute cases may appear to reflect those of a non-regenerative anaemia. Thrombocytopenia is a hallmark of the disease, regardless of the Babesia spp. involved and is often marked, but yet petechiation or epistaxis is very rarely seen, except in cases with concomitant Ehrlichia infections. Other haematological findings may include spherocytosis, in cases with secondary immune-mediated haemolytic anaemia and a left shift neutrophilia due to the marked systemic inflammatory response.

Further laboratory findings include elevation of liver enzymes such as ALP, ALT and AST - more so in the patients with marked icterus, reflecting the concomitant hepatopathy in these cases. Serum potassium is often low, especially in icteric cases. Serum bilirubin concentrations are elevated, commensurate with the degree and rapidity of onset of the anaemia and the severity of the accompanying hepatopathy. Azotaemia is present in many dehydrated cases and in those with acute renal failure - this phenomenon is particularly apparent in B. annae infections in Spain. Urea is frequently disproportionately raised to creatinine and is elevated for reasons other than renal disease. Urinalysis may show bilirubinuria, haemoglobinuria, proteinuria,
renal tubular epithelial cells and granular casts. Acid base abnormalities are common with metabolic acidosis (due to raised lactate and raised chloride ion concentration) and respiratory alkalosis being most common.

Prognosis
Recently, research into the most virulent form, *B. canis rossi*, has identified various risk factors for adverse outcome. Dogs with the highest parasitaemias and those with high serum cortisol and low serum thyroxine have the worst prognosis. Dogs with multiple organ involvement, especially those with ARDS, acute renal failure and cerebral forms also have a very poor prognosis.

Treatment
The primary goals are to eliminate the parasite and reverse the life-threatening anaemia.

Prevention
Regular control of the tick vectors by routinely dipping or spraying pets or using tick collars or spot-on preparations is the only effective way of preventing this disease in most parts of the world. Ticks must feed on the host for at least three days in order to transmit *B. canis* and owners should therefore be encouraged to examine their dogs daily for the presence of ticks. A vaccine against *B. canis* has recently become commercially available in France (Nobivac Piro®). Research into developing vaccines for all species of canine babesiosis is ongoing. It would seem reasonable to suggest vaccinations for dogs prior to visiting endemic areas in Europe, since the vaccine has been shown to offer protection against heterologous *B. canis* infection and although not preventing infection, lessens severity of disease in vaccinates.

Summary
The presence of *B. canis canis* and *B. canis vogeli* as well as *B. gibsoni* (Asian isolate) and *B. annae* in Europe is in agreement with the distribution of the tick vectors of these species. The presence of competent tick vectors such as *Dermacentor reticularis* in southwest England, Belgium and Germany and the increasing international mobility of pets can cause babesiosis to spread into previously non-endemic areas, as has recently been demonstrated to occur in the Netherlands in the spring of 2004.

**Further reading**

<table>
<thead>
<tr>
<th>BABESIA spp.</th>
<th>DRUG</th>
<th>DOSE</th>
<th>ROUTE OF ADMINISTRATION</th>
<th>DURATION OF THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. canis</em></td>
<td>Diminazene aceturate (Berenil®)</td>
<td>3.5 mg/kg</td>
<td>IM/SC</td>
<td>Single dose</td>
</tr>
<tr>
<td></td>
<td>Trypan blue (Trypan blue®)</td>
<td>10 mg/kg</td>
<td>Strictly IV</td>
<td>Single dose</td>
</tr>
<tr>
<td></td>
<td>Imidocarb dipropionate (Imizol®)</td>
<td>7 mg/kg</td>
<td>IM</td>
<td>Two doses, 14 days apart</td>
</tr>
<tr>
<td><em>B. gibsoni</em></td>
<td>Atovaquone and Azithromycin</td>
<td>13.3 mg/kg q 8h, 10 mg/kg q 24h</td>
<td>PO/PO</td>
<td>10 consecutive days</td>
</tr>
</tbody>
</table>

Table: Treatment of Babesiosis