Rev. Sci. Tech. Off. Int. Epiz., 2015, **34** (2), 627-639

Babesiosis

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Summary
Babesiosis is the disease caused by infection of the erythrocytes of mammals by *Babesia* species, which are Apicomplexa protozoa belonging to the suborder Piroplasmidea and the family Babesiidae. They are different from the Theileriidae, which can also infect white blood cells and endothelial cells. Babesiosis is one of the most important tick-borne infectious diseases of domestic and wild mammals and still poses significant diagnostic and therapeutic challenges for veterinary practitioners around the world. It is an increasing problem worldwide because of the expansion of tick habitats and the increased mobility of animals, which promote the spread of parasites into new geographical areas. *Babesia* species can, exceptionally, infect humans, especially splenectomised or immunocompromised individuals. The majority of human cases involve *B. microti*, a parasite of rodents, but human infections may also be caused by *B. divergens*, which infects cattle, or by *Babesia* related to *B. odocoilei*, which infect cervids. The majority of new developments, in regard to taxonomy, epidemiology, pathogenesis and control, concern canine babesiosis, whereas piroplasmosis in horses or cattle retains the classical description, therefore the focus of this article will be on infection in dogs.

Keywords
Babesiosis – Control – Dog – Pathogenesis – Taxonomy.

Introduction

Babesiosis is caused by the infection of mammals by *Babesia*, an Apicomplexa protozoan belonging to the suborder Piroplasmidea and family Babesiidae. The name commemorates the first description of the disease in sheep and cattle in 1888 by a Romanian bacteriologist, Victor Babes. The family includes over 100 species of protozoans on the basis of their exclusive invasion of erythrocytes in their mammalian hosts. *Babesia* also multiply by budding rather than by schizogony, and lack the hemozoin produced by the closely related genus *Plasmodium*. The fact that members of the family Babesiidae only invade erythrocytes allows differentiation from the Theileriidae (*Theileria* and *Cytauxzoon*), which can also infect white blood cells and even the endothelial cells of blood vessels. Both the Theileriidae and Babesiidae may be called piroplasms, and cause piroplasmosis. This paper will focus only on *Babesia*. Nevertheless, a few parasites are in a borderline situation and not yet firmly defined as Babesiidae or Theileriidae.

Babesiosis is one of the most important tick-borne infectious diseases of domestic and wild mammals and still poses significant diagnostic and therapeutic challenges for veterinary practitioners around the world (Table I) (1). *Babesia* species are considered very specific and cannot infest a wide range of hosts (Table I). Babesiosis is an increasing problem worldwide owing to the expansion of tick habitats and the increased mobility of animals, which promote the spread of parasites into new geographical areas (2, 3).

Traditionally, *Babesia* were classified on the basis of their morphology, host/vector specificity, and susceptibility to drugs. Pragmatically, they are divided into the small *Babesia* group (trophozoites of 1.0–2.5 µm; including *B. gibsoni*, *B. microti* and *B. rodhaini*), and the large *Babesia* group (2.5–5.0 µm; including *B. bovis*, *B. caballi* and *B. canis*). This classification is generally consistent with the phylogenetic characterisation based on nuclear small-subunit ribosomal RNA gene (18S rDNA) sequences, which shows that the large and small *Babesia* fall into two phylogenetic clusters, with the small *Babesia* being more closely related to *Theileria* spp. (with the exception of *B. divergens*, which appears small on blood smears [0.4–1.5 µm] but is genetically closer to large *Babesia*). Molecular genetic analyses can clarify the somewhat confused phylogenetic situation, but sometimes result in the emergence of new species or new groups. It is

Table I
Main *Babesia* species, tick vectors, and hosts

Babesia species	Main hosts	Tick vectors	Geographical distribution
Babesia canis	Dog	*Dermacentor reticulatus, Dermacentor variabilis*	Europe
Babesia canis presentii	Cat	?	Israel
Babesia vogeli	Dog	*Rhipicephalus sanguineus*	Worldwide
Babesia rossi	Dog	*Haemaphysalis elliptica* (formerly *H. leachi*)	Southern Africa
Babesia 'coco'	Dog	?	Eastern USA
Babesia gibsoni	Dog	*Haemaphysalis longicornis* (direct transmission in the USA)	Asia (and USA)
Babesia conradae	Dog	*Dermacentor variabilis*	Southern and western USA
Rangelia vitalii	Dog	*Amblyomma* spp.	South and Central America
Babesia vulpes (formerly proposed as *Theileria annae*) and *'Babesia microti'*-like	Dog	*Ixodes* spp.	Worldwide
Babesia felis	Cat, lynx, puma	?	Worldwide
Babesia leo	Lion, panther	?	Africa and Middle East
Babesia bigemina	Cattle	*Boophilus* spp., *Rhipicephalus bursa, Rhipicephalus evertsi, Haemaphysalis* spp.	Tropical areas
Babesia major	Cattle	*Haemaphysalis* spp.	Europe
Babesia divergens	Cattle	*Ixodes ricinus*	Europe
Babesia odocoilei	Cervids	*Ixodes* spp.	Northern Hemisphere
Babesia bovis	Cattle	*Boophilus* spp., *Rhipicephalus bursa*	Tropical areas
Babesia ovis	Sheep	*Rhipicephalus bursa*	Worldwide
Babesia motasi	Sheep	*Haemaphysalis punctata*	Africa, Middle East, Central Asia, southern Europe
Babesia caballi	Horse	*Dermacentor reticulatus, Dermacentor marginatus, Dermacentor nitens, Hyalomma* spp.	Worldwide
Babesia microti	Rodents	*Ixodes* spp.	Northern Hemisphere
Babesia rodhaini	Rodents	?	Africa

now suggested that the piroplasms should be divided into five clades:

– the *B. microti* group, containing *B. rodhaini*, *B. felis*, *B. leo*, *B. microti*, and *B. microti*-like isolates

– the western United States (USA) *Theileria*-like group, containing *B. conradae*

– the *Theileria* group, containing all *Theileria* species that affect ruminants

– *Babesia* spp. sensu stricto including *Babesia* that affect carnivores, such as *B. canis* and *B. gibsoni*

– a second *Babesia* spp. sensu stricto group composed mainly of *Babesia* spp. that affect ungulates, such as *B. divergens*, *B. odocoilei*, *B. bigemina*, *B. ovis* and *B. bovis* in ruminants, and *B. caballi* in horses.

Babesia species can, exceptionally, infect humans, especially splenectomised or immunocompromised individuals (1, 4). The majority of human cases involve *B. microti*, a parasite of rodents, but some are caused by *B. divergens*, which infect cattle, or *Babesia* related to *B. odocoilei*, which infect cervids. New phylogenetic information has emerged for recently recognised zoonotic *Babesia* spp. such as *B. venatorum* (EU1-3) in Europe and *B. divergens*-like organisms identified in the USA on the basis of 18S rDNA and internal transcribed spacer 2 (ITS2) sequence analysis. Phylogenetic analysis of *B. venatorum* clearly demonstrates that it clusters with *B. odocoilei*, a parasite of deer from the USA, and these two organisms form a sister group with *B. divergens*. *Babesia divergens*-like parasites isolated from humans in the USA, MO1, first isolated from Missouri, but then also in Washington State and Kentucky, are very close to *B. divergens* in terms of 18S rDNA homology and could be considered variants of *B. divergens*.

The majority of new developments concern canine babesiosis, whereas piroplasmosis in horses or cattle retains its classical description, therefore the focus of this article will be on babesiosis in dogs. The first case of the canine disease, referred to as 'malignant jaundice or bilious fever', was reported from South Africa in 1893, and two years later it was found in Italy (5). *Babesia* infections have been described in a side-striped jackal (*Canis adustus*) in Kenya, African wild dogs (*Lycaon pictus*) in South Africa (5) and red

foxes (*Vulpes vulpes*) in Spain (6) and North America (7). Based on these findings, it is thought that *Babesia* spp. may have adapted to domestic dogs from wild canids. Babesiosis is generally more often diagnosed in animals living in rural areas, where they have a greater exposure to tick vectors.

Aetiology and epidemiology

Several species of *Babesia* and *Theileria* can infect dogs. Traditionally two *Babesia* species were identified as the aetiological agents of canine babesiosis: *B. canis* and *B. gibsoni*. *Babesia canis* has a piriform (teardrop) shape and frequently more than one merozoite is found in a single erythrocyte. *Babesia gibsoni* is more pleomorphic.

Large *Babesia* species

By definition, the length of the large form of piroplasm is greater than the radius of an erythrocyte (2.5–5 µm), whereas small *Babesia* measure 0.5–2.5 µm.

Based on the geographical distribution of *B. canis* transmitted by different tick species, its antigenic properties and pathogenicity, Uilenberg *et al.* (8) suggested a trinomial system for the taxonomy of this *Babesia* species. He proposed that parasites transmissible by *Dermacentor reticulatus* be named *B. canis canis*, parasites transmissible by *Rhipicephalus sanguineus* be named *B. canis vogeli*, and parasites transmissible by *Haemaphysalis leachi* be named *B. canis rossi*. Later, molecular methods confirmed the existence of three distinct genotypes of *B. canis* (9, 10), which have recently been considered to be separate species (2).

Babesia canis, transmitted by *D. reticulatus*, is the most common agent of canine babesiosis in temperate regions of Europe (Figs 1 and 2). The occurrence of the disease is associated with the seasonal activity of the tick vector, and clinical cases are reported mostly in spring and autumn (11, 12, 13, 14). *Babesia canis* is described almost throughout Europe (11, 12): in Albania (15), France (16), Portugal (17), Switzerland, Hungary (13), Germany (10), Serbia, Croatia (18), Slovenia (19), Italy (20), Spain and Poland (12, 21, 22), the Netherlands, and Russia (23). Undoubtedly, France is the country in which *B. canis* is the most prevalent (16). There is genetic variability within the species which can explain variations in pathogenicity but also in susceptibility to treatment or in the protection conferred by vaccination (12, 19, 24). The geographical distribution of *D. reticulatus* continues to expand throughout Europe, probably as a result of climate warming, and landscape and socioeconomic changes (25, 26, 27). Autochthonous cases and new endemic foci caused by this species have been reported from the Netherlands (28), Norway (29) and Slovakia (30).

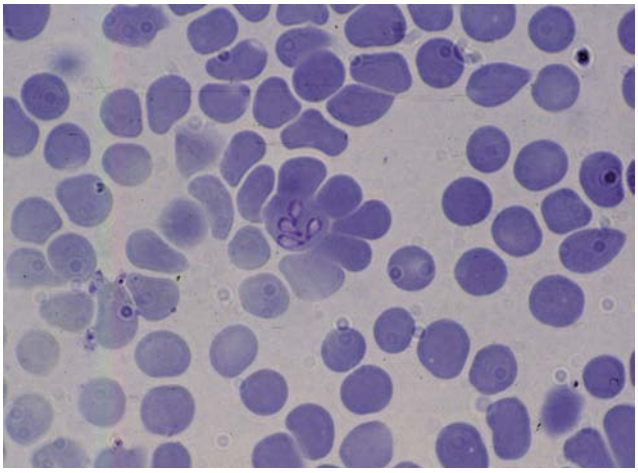

Fig. 1
***Babesia canis* sporozoites in erythrocytes**
May Grünwald Giemsa stain × 1,000

Babesia vogeli, transmitted by *R. sanguineus*, is a less pathogenic species (31). It has been found primarily in tropical or subtropical areas of northern, eastern and southern Africa (9, 32, 33), Asia (34, 35), and northern and central Australia (36). However, clinical cases have recently been described in Europe, in southern France (37), Spain, Portugal (17), Turkey (38), Slovenia (19), Italy (24) and Albania. Canine babesiosis in North and South America is caused by *B. vogeli* (39).

The most pathogenic species, *B. rossi*, is transmitted by *Haemaphysalis elliptica* (syn. *Haemaphysalis leachi*) (5). Originally it was recognised only in South Africa, but it has now been reported in other regions of eastern and southern Africa where its vector tick is enzootic (33).

A new large, unnamed, *Babesia* species has been found in North America (40) and has caused babesiosis in immunocompromised dogs (41). A variant of *B. canis*, *B. canis presentii*, which causes infections in cats, has been identified in Israel (30).

Small *Babesia* species

With regard to small piroplasms, three genetically and clinically distinct species are currently known to cause disease in dogs.

Babesia gibsoni is a virulent parasite in dogs of all ages. It is pleomorphic, manifesting a variety of intra-erythrocytic forms; oval or signet-ring shapes are most commonly described (Fig. 3). It was reported first in Southeast Asia, including India, Japan and parts of China, but also occurs in North and East Africa (34, 35). *Babesia gibsoni* is also a common *Babesia* species infecting dogs in the USA (42, 43, 44, 45); it was imported with Asian dogs many years ago. In

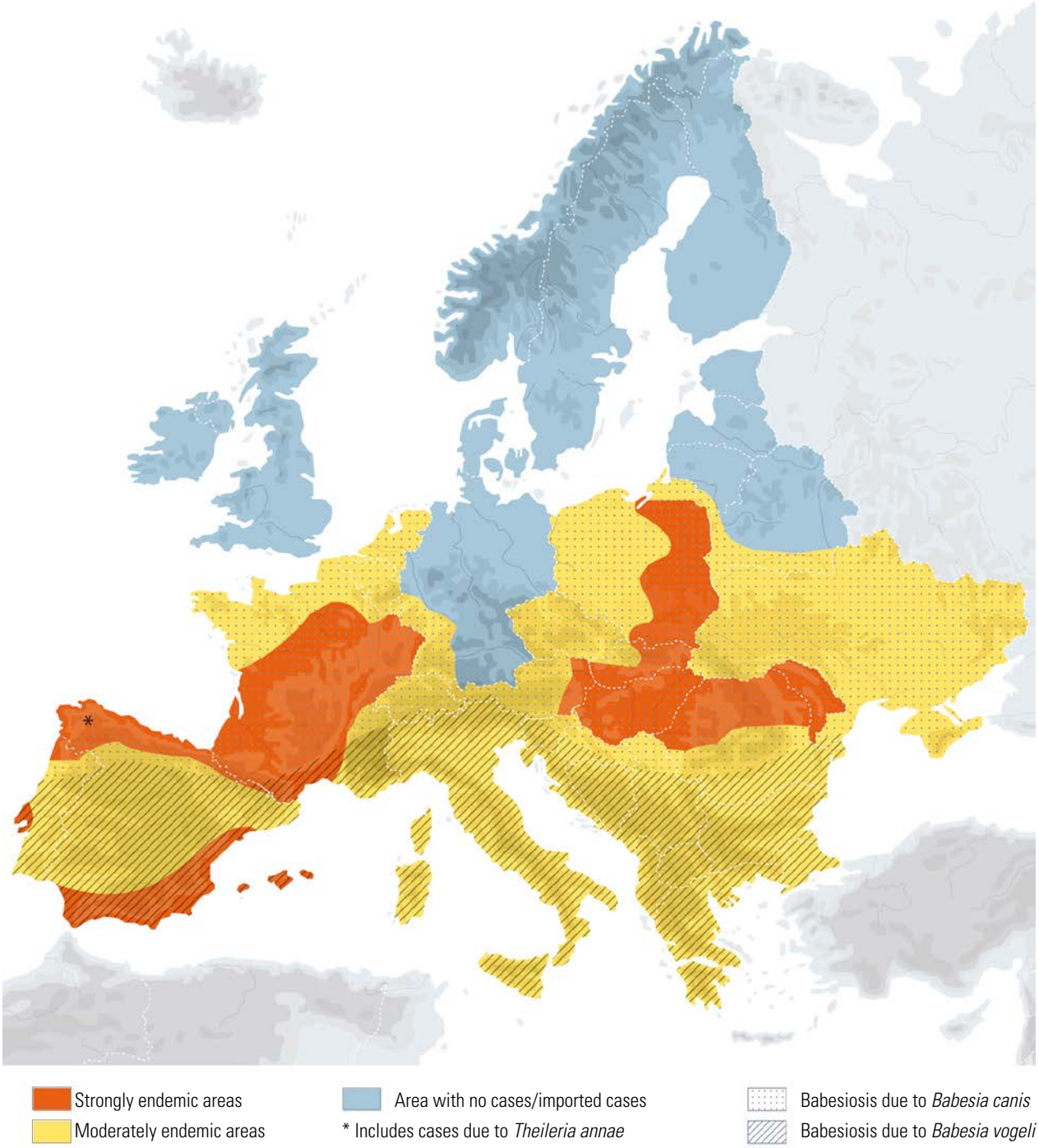

Fig. 2
Canine babesiosis in Europe: species, risk and geographical distribution
Source: Halos *et al.*, 2014 (11)

Europe, cases of canine babesiosis caused by *B. gibsoni* seem to be rare, although they have been reported from Italy, Spain and Germany (46). Known vectors of *B. gibsoni* include the tick species *R. sanguineus*, *Haemaphysalis bispinosa*, *H. longicornis* and *H. leachi*. In the USA, *R. sanguineus* and *D. variabilis* are the most likely vectors (47). Tick bites appear to be the most common mode of transmission of *B. gibsoni* in Asia. In contrast, *B. gibsoni* is more commonly diagnosed in dogs of fighting breeds in the USA and it has been demonstrated that the transmission occurs through bites and blood contact (48).

A small piroplasm species closely related to *B. microti* was detected in dogs in northern Spain. It was named *Theileria annae*, but there is a lack of consensus on whether it should be considered a *Theileria* sp. or a *Babesia* sp. and it

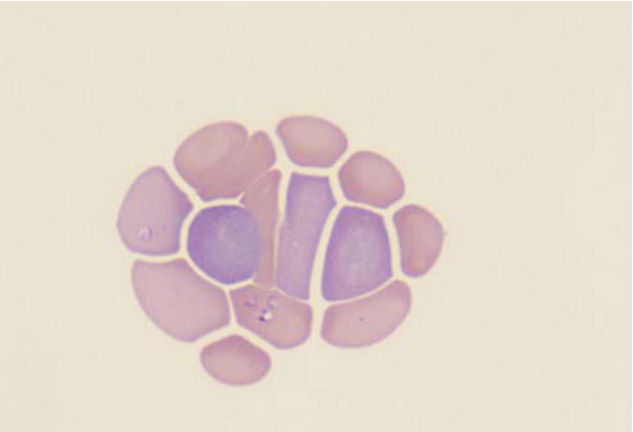

Fig. 3
***Babesia gibsoni* sporozoites in erythrocytes**
May Grünwald Giemsa stain × 1,000

is often referred to as the '*Babesia microti*-like' or 'Spanish isolate' (49, 50, 51). It is thought to be transmitted by *Ixodes hexagonus* in Spain (52). Its DNA has been detected in several tick species, including *I. hexagonus*, *I. ricinus*, *I. canisuga* and also *R. sanguineus*. However, these findings do not provide a clear idea of the capacity of these ticks to act as competent vectors. This small *Babesia* has also been reported in Croatia (19), Italy (31) and Portugal (53). *Babesia microti*-like parasites have been detected in foxes in both Europe and the USA, where infections are subclinical (7). Very recently, genetic analysis has confirmed '*Theileria annae*' to be a *Babesia*, closely related to *B. microti* and, owing to the infection rates observed in wild canids (i.e. foxes) in both Europe and North America, the authors propose that it should be named *Babesia vulpes* (54).

At the beginning of the 1990s, *B. gibsoni* infection in 11 dogs with haemolytic anaemia was reported from southern California (55). Further investigations determined, however, that the small *Babesia* that was responsible for the infection was genetically and antigenically distinct from *B. gibsoni* (56). This Californian species, recently named *B. conradae*, appears to be closely related to *B. vulpes* and to a group of piroplasms found in free-ranging ruminants (deer and sheep) and isolated from humans in the western USA (56, 57). It can be seen in erythrocytes most commonly as a singlet form, and occasionally as a tetrad or Maltese-cross form (55, 56). The vectors of *B. conradae* are currently unknown but *R. sanguineus* and *Ornithodoros* spp. found on infected dogs should be considered possible vectors. According to the results of a serological survey, coyotes may serve as possible reservoirs of this species.

A particular member of the Babesiidae that infects canids, *Rangelia vitalii*, has been described in South America since 1910 (58). The 18S rRNA analysis has demonstrated that it is a small *Babesia* transmitted by *Amblyomma* ticks. It has the capacity to infect not only erythrocytes, but also leukocytes (neutrophils and monocytes) and the endothelial cells of blood capillaries. Clinically, in addition to the classical signs of babesiosis, rangeliosis is known to induce marked jaundice but also haemorrhages, and to cause persistent bleeding from the nares, oral cavity, ears and eyes, and bloody diarrhoea. As for *B. canis*, asymptomatic carriers are described (59).

Sporadic infections involving *T. equi*, *T. annulata* and *B. caballi* have been detected by polymerase chain reaction (PCR) in dogs in Europe (18, 60). Recently, a phylogenetically recognised *Theileria* sp. has been found in 82 dogs in South Africa (61), but its significance is unclear at present and its vector is unknown.

Epidemiological surveys using molecular biology to detect *Babesia* pathogens indicate clearly that several species, not just one, are usually found in one territory (62). The difficulty is that molecular biology, which allows easy sequencing of targeted genes such as 18S rRNA genes, tends to encourage the description of many new species of large or small *Babesia*, and the rationale is not always obvious for the distinction between a new species, a subspecies, and a genetic variant. The recent description by Birkenheuer (40) of a large *Babesia* infecting dogs in North Carolina, with a proposed name of *Babesia* 'coco' (the name of the first infected dog), is an example of this (12, 41).

Transmission

Ticks are infected following ingestion of host erythrocytes parasitised with *Babesia* merozoites. The sexual development of the parasite in the tick gut is followed by sporogony in its tissues. The parasite reaches the tick salivary glands, from which transmission of the infective stage, sporozoites, occurs (63, 64). *Babesia* spp. are transmitted transstadially, from one tick stage to another, and, as shown for some *Babesia* spp., also transovarially through the tick eggs (63).

It has been reported that *B. gibsoni* can also be spread vertically from dam to offspring, by transfusion of infected blood, and via contaminated equipment (42, 65, 66, 67). A high prevalence of *B. gibsoni* infection is observed in fighting dog breeds (e.g. American Staffordshire and pit bull terriers) and transmission by bites has been demonstrated (42, 66). Direct transmission between dogs and transplacental transmission have been suggested as possible modes of infection for *B. conradae* (55, 56, 57).

Pathogenesis and clinical signs

Pathogenesis

After penetration of the cell, *Babesia* multiply via repeated binary fission within the erythrocyte, resulting in up to

16 merozoites. Multiplication of the parasites damages the erythrocyte cell membrane, causing increased osmotic fragility and subsequent intravascular and extravascular haemolysis. Indirect pathways of cell destruction are also important contributors to the pathogenicity of *Babesia*-induced anaemia, which is the predominant clinical syndrome. Immune-mediated haemolytic anaemia is assumed to occur with all *Babesia* spp. following the production of anti-erythrocyte membrane antibodies (1). *Babesia* activate antibody-mediated cytotoxic destruction of erythrocytes, leading to anaemia, haemoglobinaemia, haemoglobinuria, thrombocytopenia and, in cases of massive infection, to death caused by multiple organ dysfunction syndrome (67). Tissue hypoxia is found in severe babesiosis in both dogs and ruminants (68), particularly affecting the central nervous system, kidneys and muscles (12, 69).

Clinical signs

The clinical picture is similar for all *Babesia* infections, whether they involve large or small *Babesia*. The clinical signs depend on the virulence of the parasite species and strain involved, the immunological and physiological status of the dog and concurrent infection or illness (1, 12, 20, 36, 69, 70).

Canine babesiosis may present with a wide variation in the severity of the clinical signs, ranging from a hyperacute, shock-associated, haemolytic crisis to an inapparent, subclinical infection (1, 59, 71, 72, 73, 74, 75). Classical babesiosis has been suggested to be a consequence of anaemia resulting from haemolysis, whereas complicated canine babesiosis may be a consequence of the development of a systemic inflammatory response syndrome and multiple organ dysfunction syndrome, both cytokine-mediated phenomena. Clinical signs of uncomplicated acute babesiosis include fever, pale mucous membranes, jaundice, vomiting, haemoglobinuria, anorexia, depression, splenomegaly and hypotension (36, 72, 75). Clinical manifestations of the complicated form are cerebral babesiosis, shock, rhabdomyolysis, acute renal failure, acute respiratory distress syndrome, acute liver dysfunction and acute pancreatitis (71, 76). The cerebral pathology may be used as a model to better understand the pathogenesis of cerebral malaria in humans (12, 69).

Some dogs remain asymptomatic carriers of parasites, presenting high antibody titres for a period as long as one year (77). This carrier state is known as premunition. The asymptomatic infected animals facilitate the transmission of parasites to tick vectors. Dogs may develop clinical babesiosis several times during their lifetimes because of loss of immunity or as a result of infection with different genetic (and antigenic) strains. Any treatment leading to clearance of the infection may also hamper the development of protective immunity (76, 77, 78).

Diagnosis

The suspicion of babesiosis is initially based on epidemiological data and clinical findings. Changes in the geographical distribution of the vectors have complicated the diagnosis.

Case history and clinical signs

Information on the regional occurrence of canine babesiosis is very important for the diagnosis. Dogs taken to areas where the disease is endemic are particularly at risk (2). A differential clinical diagnosis should be made from other conditions such as anticoagulant poisoning, severe nematode infection or immune-mediated haemolytic anaemia.

Haematological and biochemical findings

The common and typical haematological abnormalities of canine babesiosis are regenerative haemolytic anaemia and thrombocytopenia. Laboratory findings such as a positive Coombs' test, serum protein abnormalities, protein and free haemoglobin in the urine, bilirubinaemia and metabolic acidosis are likely to be associated with *Babesia* (78). The positive Coombs' test may potentially mislead a clinician to give a diagnosis of immune-mediated haemolytic anaemia as the primary disease.

Detection of *Babesia* by microscopic examination

The definitive diagnosis relies on identification of the parasites in stained erythrocytes (Giemsa, Diff-Quick or Romanowsky, Field's, and modified Wright's stains) in blood smears or infected tissues (taken from lymph nodes or spleen) by direct light microscopic examination. The detection of *B. gibsoni* on blood smears may be complicated because many of the erythrocytes in anaemic dogs are vacuolated and pitted (55). The blood smear examination presents a low sensitivity (57) and it is preferable for the sample to be taken from peripheral capillaries such as those in the ear tip or nail bed, rather than using venous blood (36, 37).

Detection of *Babesia* by molecular methods

A large number of molecular diagnostic assays (e.g. nested PCR, real-time quantitative PCR, reverse line blotting technique) and protocols have been reported for the diagnosis of babesiosis (43, 79, 80). These methods are more sensitive than blood smear examination and they allow precise identification at the species, subspecies or genotype levels for individual diagnosis and epidemiological studies of babesiosis (11, 12, 16). Whereas the detection limit of

light microscopy is approximately 0.001% parasitaemia (i.e. around 5,000 infected erythrocytes per ml), PCR is able to detect parasite loads in the region of 50 organisms per ml (43, 81). Nevertheless, blood PCR becomes quickly negative after treatment or in chronically infected animals, which supports the hypothesis that the presence of hypnozoites, most probably located in the spleen or liver, explains the occurrence of relapses in treated animals.

Serology

The indirect fluorescent antibody test (IFAT) is the test most commonly used to detect specific antibody in canine babesiosis (68). Traditional enzyme-linked immunosorbent assay (ELISA) and dot-ELISA tests have a superior sensitivity but significantly lower specificity when compared with IFAT (82). The recent development of recombinant ELISA assays has improved test specificity (83). The IFAT and ELISA are used commonly in epidemiological surveys and experimental studies. Serology does not strongly discriminate among species and subspecies, because antibodies are often cross-reactive between different species and even other protozoans (43, 66, 68, 72). In endemic areas many hosts have antibodies without clinical signs and therefore positive results have to be interpreted carefully.

Treatment

The prognosis is generally good when treatment involves specific anti-*Babesia* drugs and is begun early in the course of disease.

Anti-*Babesia* drugs

Imidocarb dipropionate, at 5.0–6.6 mg/kg given subcutaneously (SC) or intramuscularly (IM) twice at an interval of two to three weeks, is considered to be the reference treatment. During acute babesiosis, the therapeutic response is rapid, with increasing production of new red blood cells within 12–24 h (84, 85, 86). It is effective against *B. canis* and *B. vogeli* but not against *B. gibsoni* infection (44). Treatment of animals infected with the *B. microti*-like piroplasm is less effective and development of renal failure is more frequent.

Diminazene aceturate is also a drug commonly used worldwide. It is given IM at a dosage of 3.5 mg/kg once only. It is effective against *B. canis* and *B. vogeli* and has an effect on *B. gibsoni*. Care should be taken because it has a narrow therapeutic index. Overdosage results in pain and swelling at the injection site, gastrointestinal signs and neurological disturbance (ataxia, opisthotonus, seizures, nystagmus, etc.) (87, 88).

Trypan blue can also be used, at a dose of 10 mg/kg as a 1% solution intravenously (IV) because the drug is an irritant to tissues. It is effective in treating dogs with mild to moderate signs.

The susceptibility of *B. conradae* to anti-*Babesia* therapy has not been well characterised. In the original case series, treatment with diminazene aceturate or imidocarb dipropionate failed to successfully clear the infection (55). Combination therapy with atovaquone (13.3 mg/kg orally [PO] every 8 h) and azithromycin (10 mg/kg PO every 24 h) appears to be an effective treatment for acute and chronic *B. conradae* infection in naturally infected dogs, eliminating or reducing parasitaemia below the limit of detection of the PCR assay (57).

Several other piroplasms, including *B. gibsoni* and *B. microti*, have been shown to respond to combined atovaquone and azithromycin treatment, or to a protocol combining an injection of diminazene (3.5 mg/kg IM, single dose) with one of imidocarb (6 mg/kg SC), followed by daily oral administration of clindamycin (30 mg/kg PO every 12 h) (44, 89).

Other drugs (e.g. phenamidine, pentamidine, parvaquone and chloroquine) have been discontinued or are rarely used. New drugs such as artesunate are being investigated for use against infections with small *Babesia* (90).

Prevention

It was demonstrated more than 30 years ago that the host immune response is able to control *Babesia* infection. Immunity seems to be based on both cellular and humoral responses, with increased phagocytosis of infected erythrocytes, especially in the spleen and liver (12). In enzootic areas, cattle support infection with *B. divergens* or *B. bovis* and only naive imported animals show clinical babesiosis. This kind of immunity has not been observed in dogs. The protection in cattle can also be transferred by colostrum, proving the role of antibodies (91). Attenuation of *B. bovis* by passage in splenectomised calves allowed production of a live vaccine which is still in use in Australia. Unfortunately, reversion to pathogenicity is possible, as has been observed in New Caledonia after the accidental importation of vaccinated cattle from Queensland. To avoid this risk, research on killed vaccines has been intense (92). Many kinds of antigen have been studied, including major surface antigens (MSA) and concealed antigens (i.e. internal antigens). Up to now, only partial protection has been obtained in dogs by using crude extracts of killed *B. canis*. The MSAs seem to act as lures, inducing a strong humoral but non-protective response. There is also great antigenic variability among *Babesia* strains, leading to the

possibility of obtaining a specific immune response against particular strains but not all (93). Only two vaccines against *B. canis* infection in dogs are available on the market, both based on concentration of culture supernatants (94). They contain soluble parasite antigens (SPA) of homologous *Babesia* parasites (91, 93, 94). The nature of the immunity following administration of *B. canis* SPA remains largely unknown, but it is correlated with the antibody response (95). It is thought that opsonisation of free *Babesia* or infected erythrocytes, followed by their phagocytosis, is the basis of the vaccine-induced response (94, 96). The vaccines do not prevent infection but they induce a certain level of protection against the severe clinical signs of canine babesiosis. Vaccination induces protection against the clinical disease in the week after the booster (i.e. the second injection, given three weeks after the initial vaccination), and the duration of immunity is about six months (94, 97).

Prevention of infection can be achieved by control of ticks (98). A protective effect against infected ticks has been demonstrated using experimental challenge in dogs treated with anti-tick products containing fipronil in combination with other agents (Certifect® [Merial]) or afoxolaner (Nexgard® [Merial]).

Conclusion

Despite being identified more than 50 years ago, *Babesia* infections remain common in domestic animals. Vaccine research has not yet discovered an easy solution, but this is also true for the closely related parasite *Plasmodium*, which benefits from large research budgets and programmes, demonstrating the difficulty of the task. Epidemiological changes in babesiosis are noticeable and are mainly due to changes in tick distribution and activity.

La babésiose

F. Beugnet & Y. Moreau

Résumé
La babésiose est une maladie causée par l'infection d'érythrocytes de mammifères par des protozoaires du genre *Babesia*, un membre du phylum Apicomplexa appartenant à la famille des Babesiidae au sein du sous-ordre des Piroplasmidea. Ils se distinguent des Theileriidae, qui peuvent également infecter les globules blancs et les cellules endothéliales. La babésiose est l'une des principales maladies infectieuses transmises par les tiques affectant les mammifères domestiques et sauvages ; elle continue à poser des problèmes aux vétérinaires praticiens du monde entier en termes de diagnostic et de traitement. Elle constitue un problème croissant dans le monde en raison de l'extension des habitats propices aux tiques et de l'intensification des mouvements d'animaux, qui favorisent la propagation des parasites dans de nouvelles zones géographiques. L'infection humaine par des espèces de *Babesia* est possible mais exceptionnelle et survient surtout chez des sujets ayant subi une splénectomie ou immunodéprimés. Dans une majorité de cas, c'est *Babesia microti*, un parasite des rongeurs, qui intervient dans la transmission à l'homme ; toutefois certaines infections humaines sont imputables à *Babesia divergens*, qui parasite les bovins, ou à des espèces proches de *Babesia odocoilei*, parasite des cervidés. La plupart des nouvelles évolutions dans les domaines de la taxonomie, de l'épidémiologie, de la pathogénie et de la lutte concernent la babésiose canine, et c'est donc sur cette maladie que les auteurs mettent l'accent, les connaissances sur la piroplasmose équine ou bovine n'ayant guère évolué depuis les publications déjà anciennes qui leur ont été consacrées.

Mots-clés
Babésiose – Chien – Contrôle – Pathogénie – Taxonomie.

Babesiosis

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Resumen
La babesiosis es la enfermedad resultante de la infección de los eritrocitos de mamíferos por especies del género *Babesia*, que son protozoos del grupo Apicomplexa pertenecientes a la familia Babesiidae, suborden Piroplasmidea. Esto los distingue de los microorganismos de la familia Theileriidae, que también pueden infectar a leucocitos y células endoteliales. La babesiosis, que es una de las enfermedades infecciosas más importantes transmitidas por garrapatas que afectan a los mamíferos domésticos y salvajes, sigue planteando a veterinarios del mundo entero considerables dificultades de diagnóstico y tratamiento. Si supone un problema creciente es porque los hábitats de las garrapatas se están extendiendo y los animales presentan mayor movilidad, lo que favorece la diseminación de los parásitos a nuevas áreas geográficas. Excepcionalmente, las especies de *Babesia* pueden infectar al ser humano, en especial a personas que hayan sufrido una esplenectomía o que presenten inmunodeficiencia. La mayoría de los casos que se dan en el ser humano tienen por agente a *Babesia microti*, un parásito de los roedores, aunque también puede haber infecciones humanas causadas por *Babesia divergens*, que infecta al ganado vacuno, o por babesias emparentadas con *Babesia odocoilei*, que infecta a los cérvidos. La mayoría de los aspectos novedosos en relación con la taxonomía, epidemiología, patogénesis y control de la enfermedad se manifiestan en la babesiosis canina, mientras que la piroplasmosis de caballos y bovinos sigue presentando características que corresponden a la descripción clásica, y por este motivo los autores se centran sobre todo en la infección canina.

Palabras clave
Babesiosis – Control – Patogénesis – Perro – Taxonomía.

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