BOVINE BABESIOSIS

AETIOLOGY

Classification of the causative agent

Bovine babesiosis (BB) is a tick-borne disease of cattle caused by protozoan parasites of the genus *Babesia*, order Piroplasmida, phylum Apicomplexa. The principal species of *Babesia* that cause BB are: *Babesia bovis*, *Babesia bigemina* and *Babesia divergens*. A recent study suggested that *Babesia* sp. Mymensingh may be an additional species capable of causing clinical babesiosis in cattle. Other *Babesia* that can infect cattle include *B. major, B. ovata, B. occultans* and *B. jakimovi.*

Resistance to physical and chemical action

This agent does not survive outside its hosts and is transmitted mainly through a tick vector. Therefore, parameters associated with resistance to physical and chemical actions (such as temperature, chemical/disinfectants, and environmental survival) are not meaningful. Susceptibility to medicines and vaccines are described under “Prevention and control”.

EPIDEMIOLOGY

Morbidity and mortality vary greatly and are influenced by several factors, such as prevailing treatments employed in an area, previous exposure to a species/strain of parasite, age, cattle breed, and vaccination status.

In endemic areas, cattle become infected at a young age and develop a long-term immunity. However, outbreaks can occur in these endemic areas if exposure to ticks by young animals is interrupted or immuno-naïve cattle are introduced. The introduction of *Babesia* infected ticks into previously tick-free areas may also lead to outbreaks of disease.

Hosts

- *Babesia bovis* and *B. bigemina*
  - cattle
  - water buffalo (*Bubalus bubalis*) and African buffalo (*Syncerus caffer*)
  - reports of disease in white-tailed deer (*Odocoileus virginianus*) in Mexico
- *Babesia divergens*
  - cattle and reindeer *(Rangifer tarandus*)
  - Mongolian gerbils (*Meriones unguiculatus*); other peridomestic rodents are resistant to disease
  - Splenectomised humans and non-human primates are highly susceptible
  - Experimental infection with no clinical signs has been documented in splenectomised ungulates including mouflon (*Ovis musimon*), red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), and fallow deer (*Dama dama*)

Life cycle and transmission

All *Babesia* are transmitted by ticks with a limited host range. Bovine *Babesia* species are principally maintained by subclinically infected cattle that have recovered from disease and by tick vectors via transovarial transmission.

The principal vectors of *B. bovis* and *B. bigemina* are *Rhipicephalus* spp. ticks and these are widespread in tropical and subtropical countries. The major arthropod vector of *B. divergens* is *Ixodes Ricinus.*

- BB is transmitted by ticks
  - Tick vectors of *Babesia bigemina*: *Rhipicephalus microplus* (formerly *Boophilus microplus*) and *Rhipicephalus annulatus* (formerly *Boophilus annulatus*); *Rhipicephalus decoloratus*, *Rhipicephalus geigyi,* and *Rhipicephalus evertsi* are also competent vectors
    - *B. bigemina* transmitted by feeding of adult and nymphal stages of one-host *Rhipicephalus* spp. ticks
  - Tick vectors of *Babesia bovis*: *Rhipicephalus microplus* and *Rhipicephalus annulatus*; *Rhipicephalus geigyi* is also a competent vector
    - *B. bovis* transmitted by feeding of larval stages of one-host *Rhipicephalus* spp. ticks
  - Tick vectors of *Babesia divergens*: principal vector is *Ixodes ricinus*
    - *Ixodes ricinus* is a three-host tick with only adult stages feeding on vertebrates (e.g. cattle)
- *Babesia* sporozoites are inoculated into the vertebrate host by ticks and invade red blood cells (RBCs) where they transform into trophozoites
  - These grow and divide into two round, oval or pear-shaped merozoites which, in turn, are capable of infecting new RBCs; the division process is then repeated
- *Babesia* parasites can be transmitted transovarially between tick generations; in the case of *Ixodes,* surviving up to 4 years without a vertebrate host
- *Babesia* may also be transmitted by fomites and mechanical vectors contaminated by infected blood
- Infrequently, calves can become infected *in utero*

Sources of infection

- Blood infected with *Babesia* parasites and associated vectors of infected blood (especially ticks, but also by mechanical means)

Occurrence

BB is found in areas where its arthropod vector is distributed, especially tropical and subtropical climates. *Babesia bovis* and *B. bigemina* are more widely distributed and of major importance in Africa, Asia, Australia, and Central and South America. *Babesia divergens* is economically important in some parts of Europe and possibly northern Africa.

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) Interface [http://www.oie.int/wahis/public.php?page=home]

DIAGNOSIS

Incubation period is often 2–3 weeks or longer after tick infestation. Shorter incubation periods have however been documented in the field and through experimental inoculation (4–5 days for *B. bigemina* and 10–12 days for *B. bovis*).

Clinical diagnosis

Clinical manifestations of disease associated with BB are typical of a haemolytic anaemia disease process but vary according to agent (i.e. species of parasite) and host factors (i.e. age, immune status). BB is predominantly observed in adult cattle with *B. bovis* generally being more pathogenic than *B. bigemina* or *B. divergens*. Infected animals develop a life-long immunity against re-infection with the same species and some cross-protection is evident in *B. bigemina*-immune animals against subsequent *B. bovis* infections.

Babesia bovis

- High fever
- Ataxia and incoordination
- Anorexia
- Production of dark red or brown-colored urine (less frequent than when infected by *B. bigemina*)
- Signs of general circulatory shock

- Sometimes nervous signs associated with sequestration of infected erythrocytes in cerebral capillaries
- Anaemia and haemoglobinuria may appear later in the course of the disease
- In acute cases: maximum parasitaemia (percentage of infected erythrocytes) in circulating blood is often less than 1%

Babesia bigemina

- High fever and anorexia
- Animals become inappetent, may separate from the herd, and are weak, depressed and reluctant to move
- The mucous membranes become pale, and respiration and heart rate increase
- Anaemia often develops rapidly, and is frequently accompanied by haemoglobinuria and haemoglobinemia
- Jaundice occurs mainly in subacute cases
- Diarrhoea or constipation may also been seen, and a respiratory distress syndrome with dyspnoea can develop in severely affected animals
- Fever may cause abortion in pregnant cows, and bulls sometimes have a temporary decrease in fertility
- Central nervous system signs are uncommon in *B. bigemina* infections
- Some cattle usually die, but in animals that survive, the anaemic crisis generally passes within a week
- Parasitaemia often exceeds 10% and may be as high as 30%

Babesia divergens

- Parasitaemia and clinical appearance are similar to *B. bigemina* infections

Lesions

- Lesions observed are those most often associated with an intravascular haemolytic condition
- Pale or icteric mucous membranes; blood may appear thin and watery
- Subcutaneous tissues, abdominal fat and omentum may appear icteric
- Swollen liver with an orange-brown or paler coloration; enlarged gall bladder containing thick, granular bile
- Enlarged, dark, friable spleen
- Kidneys appear darker than normal with possible petechial haemorrhages
- Bladder may contain dark red or brown-coloured urine
- Possible oedema of lungs
- Petechiae or ecchymoses on surface of heart and brain

Differential diagnosis

- Anaplasmosis
- Trypanosomiasis
- Theileriosis
- Bacillary haemoglobinuria
- Leptospirosis
- Eperythrozoonosis
- Rapeseed poisoning
- Chronic copper poisoning
- Rabies and other encephalitides may also be considered in cattle with CNS signs.

Laboratory diagnosis

Samples

- Several thick and thin smears prepared with blood collected from superficial skin capillaries (e.g. tip of the ear or tip of the tail) of live animals during the acute phase of the disease (appearance of fever); organ smears can be acquired at necropsy (cerebral cortex, kidney [freshly dead], spleen [when decomposition is evident], heart muscle, lung and liver)

- If it is not possible to make fresh films from capillary blood, sterile jugular blood should be collected into an anticoagulant such as lithium heparin or ethylene diamine tetra-acetic acid (EDTA)
- *Babesia* parasites can sometimes be detected in capillary blood taken from the lower limb region one or more days after death
- Serum samples should also be collected

Procedures

Identification of the agent

- Microscopic examination of blood – traditional method of identifying agent in infected animals by microscopic examination of Giemsa-stained thick and thin blood films
  - *Babesia bovis* is more common in capillary blood. *Babesia bigemina* and *B. divergens* parasites are uniformly distributed through the vasculature
  - stained films are examined under oil immersion using (as a minimum) a ×8 eyepiece and a ×60 objective lens
  - morphology of *Babesia* described in various sources, including OIE *Terrestrial Manual*
  - sensitivity of thick films can detect parasitaemias as low as 1 parasite in 10^6 red blood cells
  - *Babesia* species differentiation is good in thin films but poor in the more sensitive thick films
  - adequate for detection of acute infections, but not for detection of carriers where parasitaemias are very low
  - parasite identification and differentiation improved by using a fluorescent dye, such as acridine orange instead of Giemsa
- Nucleic acid-based diagnostic assays – very sensitive particularly in detecting *B. bovis* and *B. bigemina* in carrier cattle
  - PCR-based techniques are reported to be at least 1000 times more sensitive than thin blood smears for detection of *B. bovis*
  - a number of PCR techniques have been described that can detect and differentiate species of *Babesia* in carrier infections
  - current PCR assays generally do not lend themselves well to large-scale testing; unlikely to supplant serological tests as the method of choice for epidemiological studies
  - PCR assays are useful as confirmatory tests and in some cases for regulatory testing
- *In-vitro* culture methods
  - used to demonstrate presence of carrier infections of *Babesia* spp.
  - minimum parasitaemia detectable by this method depends on the facilities available and the skills of the operator but could be as low as 10^{-10}, making it a very sensitive method for the demonstration of infection, with 100% specificity
- Animal inoculation is not suitable for routine diagnostic use

Serological tests

- *Babesia bovis* and *B. bigemina* enzyme-linked immunosorbent assay (ELISA)
  - Indirect ELISAs based on either parasite lysate from infected RBCs or recombinant antigens have been described.
  - Reduction in specificity of the *B. bovis* I-ELISA using recombinant antigens has been noted in some situations
  - Competitive ELISAs have largely replaced the IFA as the diagnostic test of choice for *Babesia* spp. because of the objectivity in interpretation of results and capacity to process high numbers of samples daily.
  - The C-ELISA has been more widely validated in different laboratories, with the antigen recognised by antibody from diverse regions around the world
- Indirect fluorescent antibody test (IFA)
  - Antigen slides are made from jugular blood or RBCs from *in-vitro* cultures, ideally when the parasitaemia is between 2% and 5%.
  - widely used in the past to detect antibodies to *Babesia* spp., but the *B. bigemina* test has poor specificity
  - cross-reactions with antibodies to *B. bovis* in the *B. bigemina* IFA test are a particular problem in areas where the two parasites coexist
  - disadvantages of low sample throughput and subjectivity
- Other tests
  - Immunochromatographic tests for rapid serodiagnosis *B. bovis* and *B. bigemina* were developed.

- dot ELISA, slide ELISA, latex and card agglutination tests
- tests show acceptable levels of sensitivity and specificity for *B. bovis* and, in the case of the dot ELISA, also for *B. bigemina*. however, none of these tests appears to have been adopted for routine diagnostic use in laboratories other than those in which the original development and validation took place. Therefore, adaptability of these tests to routine diagnostic laboratories is unknown

For more detailed information regarding laboratory diagnostic methodologies , please refer to Chapter 3.4.2 Bovine babesiosis in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Diagnostic Techniques" .

PREVENTION AND CONTROL

Sanitary prophylaxis

- Eradication of BB has been accomplished by elimination of tick vector and/or intensive chemotherapeutic regimes
  - in areas where eradication of tick is not feasible or desirable, ticks are controlled by repellents and acaricides
- Reducing exposure of cattle to ticks
  - repellents, acaricides and regular inspection; animals and premises
  - control and eradication of the tick vector
- Cattle develop a durable, long-lasting immunity after a single infection with *B. bovis, B. divergens* or *B. bigemina*, a feature that has been exploited in some countries to immunise cattle against babesiosis
- Endemic environments should be monitored carefully
  - introduction of immuno-naïve animals
  - introduction of new species or strains of disease agent
  - interruptions in exposure to ticks and disease due to changes in climate, host factors and management
- Special care in possible mechanical infection of cattle with contaminated blood
- The development of resistance to acaricides can be a concern.
- Environmental modification can also destroy tick habitats, but in some cases this may be difficult or ecologically undesirable. Natural endemic stability is unreliable as the sole control strategy, as it can be affected by climate, host factors and management.

Medical prophylaxis

Endemic areas

- Clinically affected animals treated with an antiparasitic drug (diminazene diaceturate, imidocarb, amicarbalide); efficacy depends on timely detection early in disease
  - *Babesia* parasites can be cleared from carrier animals
  - Imidocarb has been reported to protect animals from disease but allow development of immunity; caution in regard to residues in milk and meat
- Consideration can be given to blood transfusions and other supportive therapy, if appropriate

Vaccination

- Live vaccine: most live vaccines contain specially selected strains of *Babesia* (mainly *B. bovis* and *B. bigemina*) and are produced in calves or *in vitro* in government-supported production facilities as a service to the livestock industries
  - caution should be used in their employment as they may be virulent in adult animals, may be contaminated with other disease agents and could lead to hypersensitivity reactions; usually used in younger animals
  - an experimental *B. divergens* vaccine prepared from the blood of infected *Meriones* has also been used successfully
- Killed vaccine: prepared from blood of *B. divergens*-infected calves; little information available on level and duration of the conferred immunity
- Other vaccines:
  - Despite the worldwide efforts, the prospects for recombinant vaccines against *Babesia spp*. remain challenging, and to date, no such vaccine is available commercially.

- experimental vaccines containing antigens produced *in vitro* have been developed but the level and duration of protection against heterologous challenge are unclear

For more detailed information regarding vaccines, please refer to Chapter 3.4.2 Bovine babesiosis in the latest edition of the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animal*s under the heading "Requirements for Vaccines".

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE *Terrestrial Animal Health Code*.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated January 2021.