Babesiosis (new or unusual occurrences)

Aetiology Epidemiology Diagnosis Prevention and Control
Potential Impacts of Disease Agent Beyond Clinical Illness References

AETIOLOGY

Classification of the causative agent

Babesiosis is a tick-borne disease of various wildlife (such as lions, deer, primates, rhinos, etc.) caused by protozoan parasites of the genus *Babesia*. Babesiosis affects a wide range of domestic and wild animals, and occasionally humans. Species of *Babesia* vary in their infectivity. Species of *Babesia* relevant to wildlife include: *B. bovis*, *B. leo, B. cati, B. felis*, *B. divergens*, *B. major*, *B. ovata*, *B. occultans*, *B. orientalis*, *B. meri*, and *B. jakimovi.*

Resistance to physical and chemical action

This agent does not survive outside its hosts and can only be transmitted 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"***.

For the purpose of voluntary reporting on diseases in wildlife this card "Babesia (non-bovine)" refers to all Babesia spp, except Bovine babesiosis (B. bovis). Information on B. bovis has to be submitted through the mandatory reports for the OIE-notifiable diseases.

EPIDEMIOLOGY

All *Babesia* species are transmitted by ticks with limited host ranges. The major arthropod vector of *B. divergens* is *Ixodes ricinus*. In some areas, *Rhipicephalus* species are the primary vector for *Babesia*, particularly for species *bigemina* and *bovis*. *B. bigemina* is principally maintained by subclinically infected cattle that have recovered from the disease. The introduction of *Babesia*-infected ticks into previously tick-free areas may lead to outbreaks of disease.

Hosts

- *B. bovis* and *B. bigemina*
  - Water buffalo (*Bubalus bubalis*) and African buffalo (*Syncerus caffer*), American bison (*Bison bison*)
    - Water buffalo are also often infected by *B. orientalis*; infections with *B. bovis* and *bigemina* are typically subclinical
  - White-tailed deer (*Odocoileus virginianus*) in Mexico
  - Zebu (*Bos taurus indicus*)
  - PCR assays detected *B. bovis* and *bigemina* in nilgai antelope (*Boselaphus tragocamelus*), pampas deer (*Ozotoceros bezoarticus*), horses, roe deer (*Capreolus capreolus*), red deer (*Cervus elaphus*), wild boar (*Sus scrofa*), yaks (*Bos grunniens*), impala (*Aepyceros melampus*) and a greater kudu (*Tragelaphus strepsiceros*).
- *B. divergens*
  - Cattle and reindeer *(Rangifer tarandus)*
    - Infections may also be due to *B. capreoli*; infections caused by *B. divergens* have only been definitively identified in asymptomatic free-ranging reindeer
  - Mongolian gerbils (*Meriones unguiculatus*)

        - Other peridomestic rodents are resistant to disease
    - Splenectomised humans and non-human primates are highly susceptible
    - Experimental infections with no clinical signs have been documented in splenectomised ungulates including mouflon (*Ovis musimon*), red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), and fallow deer (*Dama dama*)
- *B. leo*
    - Lions (*Panthera leo*)
- *B. bicornis*
    - Black rhinos (*Diceros bicornis*)
- *B. felis, B. cati*
    - Wild and domestic felids in Africa and India
- Rodents such as mice, rats, voles, and shrews are known *Babesia* reservoirs, but their significance varies by geography and co-existing tick species.

Transmission

- *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*, infection may persist up to 4 years without a vertebrate host
- *Babesia* may also be transmitted by fomites and mechanical vectors contaminated by infected blood such as reused needles or surgical instruments in the field
- Infrequently, calves can become infected *in utero*

Sources of infection

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

Occurrence

Babesia species have been reported in Asia, Africa, the Middle East, Australia, southern Europe, in Central and South America, and in the Caribbean and South Pacific islands. Inconsistencies are present when regarding whether certain species of *Babesia* are persistently pathologic in ungulates; there are often differences in clinical disease status between captive and wild free-ranging infections within individuals of the same species.

DIAGNOSIS

Clinical signs are usually apparent 2–3 weeks after being bitten by an infected tick. Shorter incubation periods have 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 signs may develop rapidly. Infected animals are typically febrile (exception: *B. felis*) and exhibit signs of haemolytic anaemia such as: icterus, decreased appetite, weakness, lethargy, and increased respiratory and/or heart rates. *B. bigemina* often causes hemoglobinuria and haemoglobinemia. *B. bovis*

often causes red blood cell morphology changes that results in the collection of RBCs in capillaries - this is particularly notable in the brain and may cause neurologic signs; other *Babesia* species are not known to cause these morphology changes or neurologic signs. Early stages of *B. divergens* infection may cause severe “pipestream” diarrhoea due to changes in gastrointestinal motility.

In later stages of disease, animals may become severely dehydrated and recumbent. If an animal survives infection, anaemia typically resolves in 7 days, but the individual may remain weak for a longer period of time.

Individuals may recover from acute disease and experience cyclical bouts of parasitaemia separated by asymptomatic periods.

Lesions

- Pale or icteric mucous membranes, subcutaneous tissues, abdominal fat, omenta
- Blood may appear thin and watery
- Swollen liver with a pale, orange-brown colour; enlarged gallbladder 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

- Intravascular haemolytic condition
- Anaplasmosis
- Trypanosomiasis
- Theileriosis
- Bacillary haemoglobinuria
- Leptospirosis
- Haemoparasitic *Mycoplasma* infections
- Rapeseed poisoning
- Chronic copper poisoning

Laboratory diagnosis

Samples

- Several thick and thin blood smears 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
    - Thin blood films should be air-dried, fixed in absolute methanol for 1 minute and stained with 10% Giemsa stain for 20–30 minutes
        - blood films should be stained as soon as possible after preparation to ensure proper stain definition
    - Thick films are made by placing a small drop (approximately 50 µl) of blood onto a clean glass slide and spreading this over a small area using a circular motion with the corner of another slide. The droplet is air-dried, heat-fixed at 80°C for 5 minutes, and stained (without fixing in methanol) in 10% Giemsa for 15 minutes
    - Unstained blood films should not be stored with or near formalin solutions as formalin fumes may affect staining quality; moisture also affects staining quality
- 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)

    - The sample should be kept cool, preferably at 5°C, until delivery to the laboratory.
    - *B. bovis* is sequestered and found in higher numbers in capillary blood
    - *B. bigemina* and *B. divergens* are uniformly distributed through the vasculature and are easily found in venous blood samples
- Samples from dead animals should consist of thin blood films, as well as smears from organs
- Organ smears acquired at necropsy: cerebral cortex, kidney (freshly dead), spleen (when decomposition is evident), heart muscle, lung and liver
    - Organ smears are made by pressing a clean slide on to a freshly cut surface of the organ or by crushing a small sample of tissue (particularly cerebral cortex) between two clean microscope slides drawn lengthwise to leave a film of tissue on each slide
    - Organ smear is then air-dried (assisted by gentle warming in humid climates), fixed for 5 minutes in absolute methanol, and stained for 20–30 minutes in 10% Giemsa
    - Smears of cerebral cortex are especially suitable for the diagnosis of *B. bovis* infections, but unreliable if sample is taken 24 hours or longer after death has occurred, especially in warmer weather
- *Babesia* 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
    - Stained films are examined under oil immersion using (as a minimum) a ×8 eyepiece and a ×60 objective lens
    - Morphology of *Babesia* species are described in various sources, including the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*
    - sensitivity of thick films can detect parasitaemia as low as 1 parasite in 106 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 parasitaemia are very low
    - Parasite identification and differentiation improved by using a fluorescent dye, such as acridine orange instead of Giemsa
- Reverse line blot (RLB) is a hybridisation assay that can be used to detect various blood parasites, specifically *B. felis* and *B. leo.*
- PCR-based techniques are reported to be at least 1000 times more sensitive than thin blood smears and can detect and differentiate species of *Babesia* in carrier infections
    - Most useful for confirmatory and regulatory testing
    - Current assays generally do not lend themselves well to large-scale testing and are therefore unlikely to supplant serological tests as the method of choice for epidemiological studies
- *In-vitro* culture methods
    - Used to demonstrate the presence of carrier infections; *B. bovis* has also been cloned in culture
    - Minimum parasitaemia detectable by this method depends on the facilities available and the skills of the operator but serves as a very sensitive method for the demonstration of infection, with 100% specificity
- Animal inoculation is not suitable for diagnostic purposes

Serological tests

- Serology cannot be used to determine *Babesia* species due to antibody cross-reactivity
- Indirect fluorescent antibody (IFA) test
    - Widely used in the past to detect antibodies to Babesia spp.
    - Low sample throughout and interpretation subjectivity limit utility
- Complement fixation
    - Has been used to detect antibodies
    - Used to qualify animals for importation into some countries
- Dot or slide ELISA
    - Not routinely used diagnostically
- Latex and card agglutination tests
    - Not routinely used diagnostically
- Immunochromatography
    - Not routinely used diagnostically

PREVENTION AND CONTROL

Sanitary prophylaxis

- Eradication of some *Babesia* species, such as *B. bovis,* has been accomplished focally by elimination of tick vectors and/or intensive chemotherapeutic regimes
    - In areas where eradication of tick is not feasible or desirable, ticks are controlled by repellants and acaricides
- Reducing exposure to ticks has been helpful in reducing Babesiosis in managed populations, but this is difficult for wild free-ranging animal populations
    - Frequently utilised methods include repellants, acaricides and regular inspection of animals and premisses
- Endemic environments should be monitored carefully
    - Introduction or translocation of immuno-naïve animals into endemic areas should be considered for conservation and rehabilitation efforts
    - If returning animals to a free-ranging status from captivity, test for carrier status and/or current infection
    - Consider changes in tick/disease exposure due to changes in climate or management practises, host factors, and host management
- Special care in possible mechanical infection of horses with contaminated blood

Medical prophylaxis

Vaccine for *Babesia*:

- Most live vaccines contain specially selected strains of *Babesia* (mainly *B. bovis* and *B. bigemina*)
    - Caution should be used in their employment as they may become virulent in adult animals, may be contaminated with other disease agents, and may lead to hypersensitivity reactions
    - Typically used in younger animals
    - An experimental *B. divergens* vaccine prepared from the blood of infected *Meriones* spp. has also been used successfully
- Killed vaccines are prepared from blood of *B. divergens*-infected calves. There is 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

    - To date, no effective subunit 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
- Vaccines have not been determined to be efficacious in animals other than the cattle for which they are designed
- If animals are contained in a captive facility, utilise tick control methods

Antiparasitics:

- Clinically affected animals (wild and domestic) within known endemic areas, can be 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; reduces clinical signs

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.*

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- Similar to animals, human *Babesia* infections are acquired via bites from infected ticks, commonly via Ixodid ticks
    - Transmission from infected transfusion donors is not uncommon
    - Clinical signs may range from asymptomatic infections to severe disease and/or death
    - Immunocompromised and splenectomised individuals are at highest risk
- Various factors such as increased immunosuppression, landscape and land use changes, animal community structure changes, and changes in vector abundance and distribution have led to an increase in tick-borne diseases - including Babesiosis - in people
- *B. microtti* and *B. divergens* are two of the most common zoonotic causes of Babesiosis in humans in the United States and Europe, respectively. Additional species and geographical locations include:
    - *B. rossi* in South Africa
    - *B. vogeli* in Southern Europe, tropical and semitropical regions worldwide
    - *B. gibsoni* in Africa, Asia, USA, Southern Europe, the Middle East and Australia

Risks to agriculture

- If cattle are living in close proximity to wild free-ranging ungulates, additional precautions should be taken to reduce tick infestations. If a herd is infected, reduced milk yield can be expected.
- Bovine Babesiosis is a listed disease and should be reported accordingly if observed.

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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 2019. Written by Marie Bucko and Samantha Gieger with assistance from the USGS National Wildlife Health Center.