CANINE BABESIOSIS IN THE DEVELOPING WORLD

START

VECTOR BORNE DISEASE

MSD Animal Health

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Andrew Leisewitz graduated from the Veterinary Faculty of the University of Pretoria at Onderstepoort (and the only veterinary school in South Africa) in 1987. He gained an Honors degree soon after this and then completed a residency and Masters degree in small animal medicine in 1995. He went on to become a Diplomat of the European College of Internal Medicine in 2003. He started as a junior academic in the Veterinary Faculty in 1990 and his research focus has been canine babesiosis since then. He has published widely on this disease (over 50 publications) and as an active clinician has spent over 30 years managing this common cause of morbidity and mortality in the Veterinary Academic Hospital. He is currently a full professor of small animal medicine and runs an active research program in canine babesiosis.

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WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Geography

Canine babesiosis in **sub-Saharan Africa** is responsible for significant morbidity and mortality.

Veterinary care in most of this region of the world is very limited and basic care such as vaccination, ecto- and endoparasite control and treatment for common infectious disease is out of reach for the average dog owner.

Surveys of blood parasites infecting domestic dogs in the developing world are comparatively few; therefore, the geographic occurrence of canid babesia in these regions is less well defined than for the developed world.

Climate change (and with it altered vector biology and distribution) and pet owner mobility mean that there is an ever-increasing need for awareness of **infections circulating in domestic dogs** in these relatively neglected areas.

Local environment

Most reports of canine babesiosis emanate from **South Africa** where around 10% of dogs seeking veterinary care in the summer are diagnosed with this disease.

Because most dogs in Africa have no or minimal access to veterinary care, there is almost no data on the incidence of babesiosis on the continent.

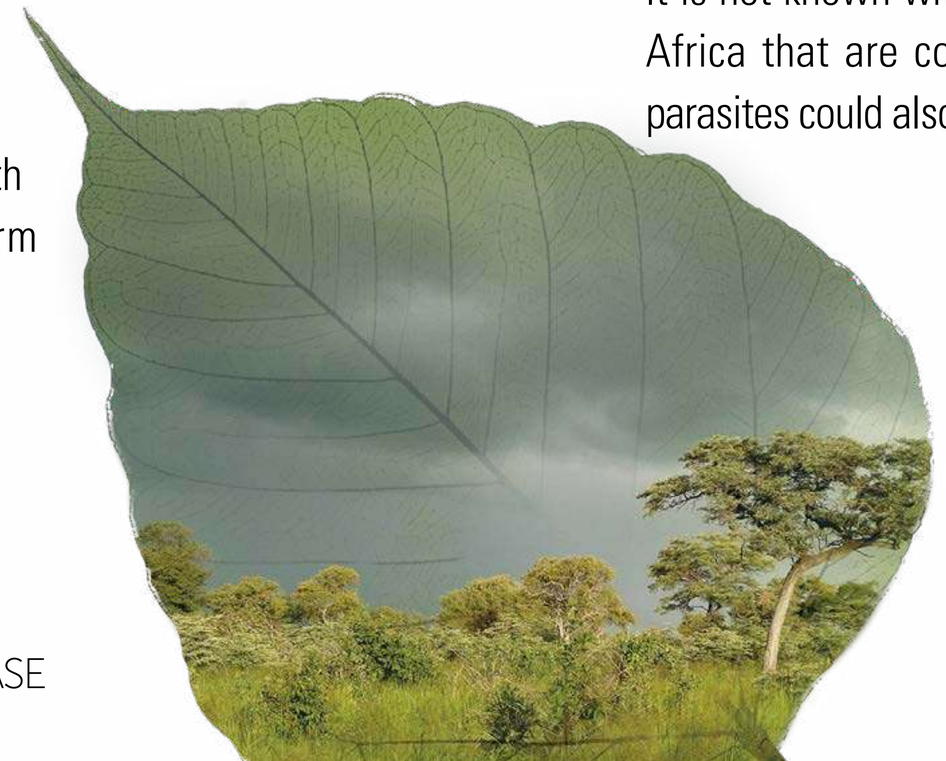
Therefore, the risk of this disease generally remains high because **most dogs live in underprivileged areas** and are not treated for ectoparasites.

WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Favorable climatic conditions

In South Africa most of the country is a summer rainfall area and *B. rossi* is more common in the summer months. In the small area of the country that has a winter rainfall, the disease peaks in winter.

Climatic change could be a factor leading to increased occurrence with longer periods of warm temperatures.



Evidence of disease spread

There is **no evidence** that *B. rossi* is spreading. The parasite is vector specific and the disease distribution mirrors the distribution of the single known tick vector.

It is not known whether ticks non-endemic to sub-Saharan Africa that are competent vectors of other dog babesia parasites could also transmit *B. rossi.*

HOW DOES A DOG **BECOME INFECTED?**

Vector

B. rossi is only transmitted by the ixodid tick *Haemaphysalis elliptica* which has a distribution restricted to the warm moist regions of sub-saharan Africa.

Proportion of vectors infected

Experimental work suggests that <20% of *H. elliptica* are infected. It has been shown that almost all dogs diagnosed with *B. rossi* carried *H. elliptica*.

Reservoir(s)

The hosts of adult *H. elliptica* are various carnivore species, among which are the domestic dog, domestic cat, lion *(Panthera leo)*, and leopard *(Panthera pardus).*

The hosts of the immature stages are diverse rodent species, and they may very occasionally be present on the same hosts as the adults.

The **Black-Backed Jackal** (*Canis mesomelas)* is the natural wildlife reservoir host, carrying the parasite but without clinical signs.

The **domestic dog** appears to be a much more recent spill-over host and hence the severe disease caused by infection.

Probability of transmission

A study that used *H. elliptica* ticks fed on *B. rossi* infected dogs to transmit the infection to naïve dogs found that 10 of 13 dogs developed clinical disease and a patent parasitemia.

Transmission was slow and took longer than 24 hours following tick attachment.

Transmission mechanics

The tick vector is by far the most common means of parasite transmission.

Only adult ticks (not immature stages) apparently transmit the infection although the parasite is transferred transovarially within the tick population.

Other routes of transmission

Transmission by blood transfusion is plausible, but there is no evidence that this has occurred. There are anecdotal reports of transmission *in utero* in dogs. There is no evidence of transmission by dog bite.

WHAT BEHAVIORS
PUT A DOG AT RISK FOR THE DISEASE?

Activities

Behavior that increases tick exposure risks logically increases infection risks.

- Animals from environments where there is minimal veterinary care would also be at increased risk as ectoparasite control is poor in these areas.

- The increased adoption of isoxazoline compounds for ectoparasite control in urban areas has apparently reduced the disease burden within these communities.

CAN A DOG BE INFECTED AND **NOT SHOW SIGNS?**

Risk to the population from subclinically diseased dogs

Subclinically infected dogs could be a source of ongoing infection for the tick vector.

WHAT CLINICAL SIGNS
DOES A SICK DOG SHOW AND WHY?

EARLY SIGNS

- Loss of appetite with signs of nausea and depression is the **first sign** owners usually notice.
- Some owners describe dark or red urine (a result of bilirubinuria or hemoglobinuria).
- Hepatomegaly and splenomegaly are almost always detected on abdominal palpation.
- In rare cases the disease is hyperacute and dogs seizure (characteristic of cerebral disease or hypoglycemia) or are collapsed in shock (characteristic of the hemo-concentrating form of the disease).

The very enlarged spleen and liver of a dog that succumbed to *Babesia rossi* infection. Splenomegaly is almost always easily detected on abdominal palpation.

Progression

- As disease progresses, dogs become weaker and their mucous membranes become more pale (consistent with worsening anemia).
- Icterus is a common finding in more established infections.

Icterus is common in more established disease and is largely prehepatic (as a result of hemolysis). Dramatic yellowing of the gums is easily seen in this image.

Prognostic factors

Compared to other babesial organisms that infect dogs, *B. rossi* is the most virulent.

Clinically the disease is classified as complicated or **uncomplicated** with the complicated forms having a significantly poorer prognosis.

Complicated disease

Defined as evidence of single or multiple organ dysfunction or failure requiring hospital admission.

Mortality is between 10 and 15% of hospital admitted cases. Factors that had a significant odds ratio for death **were:**

Collapse is a common finding in severe disease as a result of *Babesia rossi* infection and is associated with a poorer prognosis.

Prognostic factors

Complications that carry a very poor prognosis include **cerebral disease and hemoconcentration** (which occurs together with **severe hemolysis** and is usually associated with acute respiratory distress syndrome and/or **acute oliguric renal failure**).

Anemia is a very common presentation (>60% of 320 cases had a hematocrit below 0.25 L/L, 35% were below 15 L/L) but the odds ratio for death was not significant for anemia.

A *post mortem* image of the surface of the cerebral hemispheres of a dog that died per-acutely as a result of cerebral babesiosis. There are dark red areas of hemorrhagic encephalomalacia visible on the brain surface.

Prognostic factors

Agonal bloody foam expectoration is sometimes seen as a result of acute respiratory distress syndrome (A and B). The tissue changes associated with acute lung injury (C) and acute respiratory distress syndrome (D) are common in severe *Babesia rossi* infections.

Prognostic factors

Anemia (causing the pale mucous membranes seen in this dog) is a very common clinical finding (A). Hematocrit is a simple and cheap means of determining the degree of anemia – which can at times be profound, as in this case (B).

Prognostic factors

Macroscopic or clinical bleeding is a rare finding in the living dog, however, *Babesia rossi* causes obvious hemorrhage in a wide range of organs that can be seen on post mortem. (A) epicardial hemorrhage; (B) ecchymoses in the diaphragm; (C) hemorrhage into the small intestine; and (D) gastrorrhagia.

Prognostic factors

- **Thrombocytopenia** is present in close to 100% of cases but clinical hemorrhage is very rare although on post mortem examination nearly all cases have obvious bleeding in various organs.
- DIC is a described but rare complication with a poor prognosis.
- Severe mixed acid base abnormalities are usually seen in cases with a poor prognosis (concurrent metabolic acidosis and respiratory alkalosis). These changes are typically seen with **deep and labored breathing** (Kussmaul breathing).
- Warm in-saline-agglutination (ISA) is present in around 30% of cases but does not appear to impact on mortality.
- Prognosis has also been associated with the increased concentrations of various cytokines (TNF, MCP-1 and IL-6 in particular).

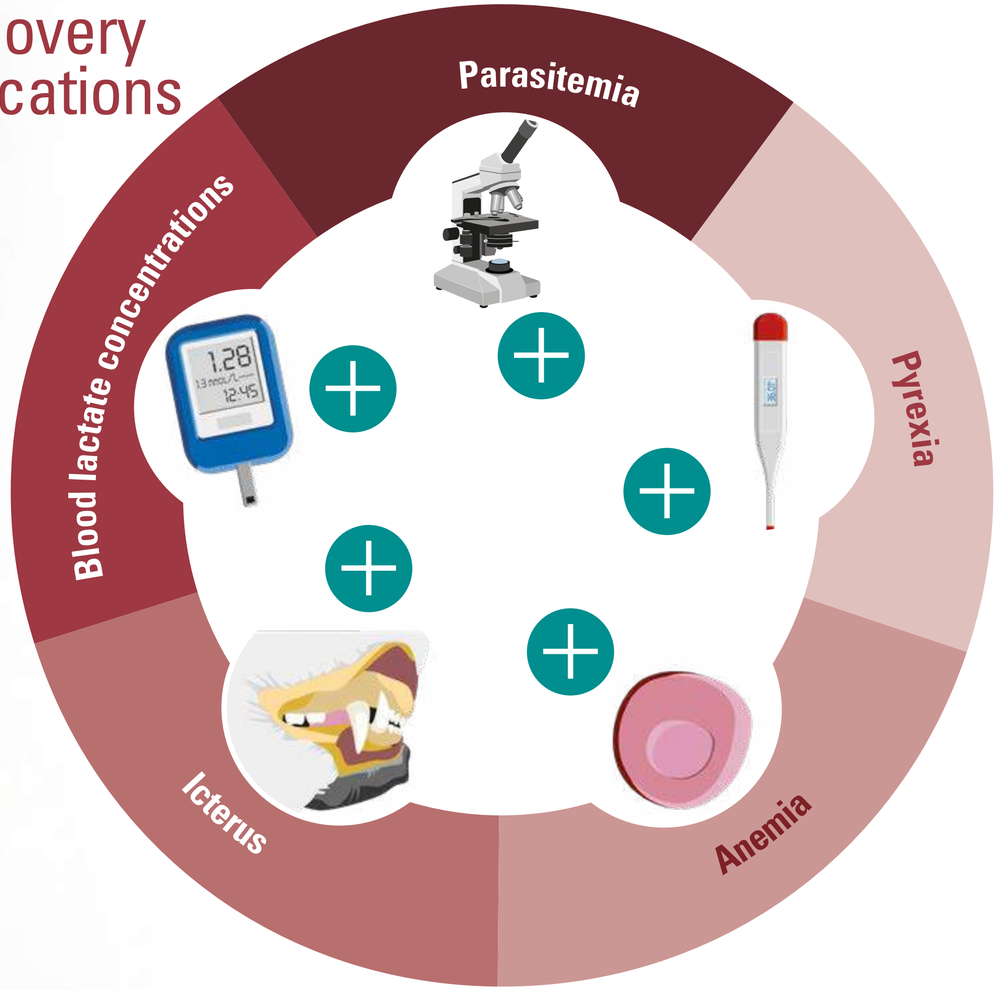
Recovery indications

Uncomplicated cases (treated as outpatients) recover their habitus and appetite within 24 hours of treatment.

Complicated cases admitted for care typically spend 3-5 days in hospital with at least 2 of these in a high care or intensive care facility. Most deaths occur within 24 hours of hospitalization.

WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

Recovery indications



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WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Rapid, table-side

First, record a history and complete a **physical examination:**

- Rectal temperature (usually elevated),
- Femoral pulse (usually increased and described as 'bounding' if the dog is anemic) and respiratory rate
- Auscultate the chest for evidence of lung edema.
- Abdominal palpation. The abdomen may be tense on palpation due to splenomegaly (present in almost 100% of cases). The finding of a palpable urinary bladder is helpful as it reduces the concern of acute renal failure and means urine collection is possible.
- If urine can be expressed, a macroscopic appreciation of bilirubinuria or hemoglobinuria is possible.

Severe hemoglobinuria (seen in a urine collection bag) is not uncommon and occurs as the renal threshold for cell free hemoglobin in circulation is exceeded.

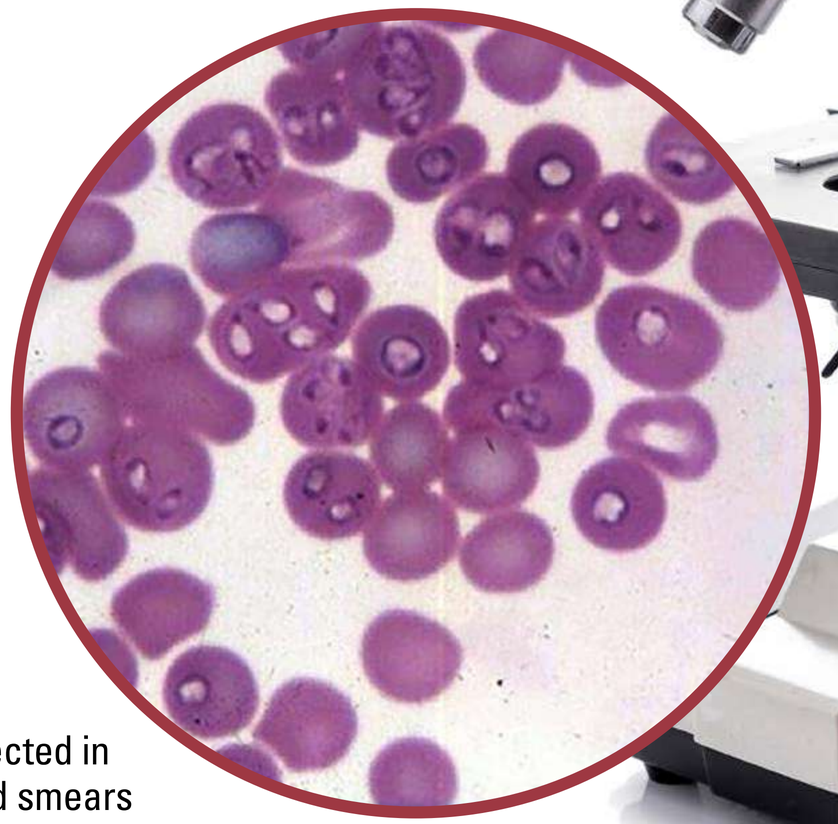
WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

In hospital using microscope or similar equipment

It is routine to prepare a peripheral (capillary) blood **smear** from the ear margin in all dogs suspected of having babesiosis.

Packed cell volume, warm ISA test and blood glucose are routinely run as part of a minimum data base in all dogs that are blood smear positive.

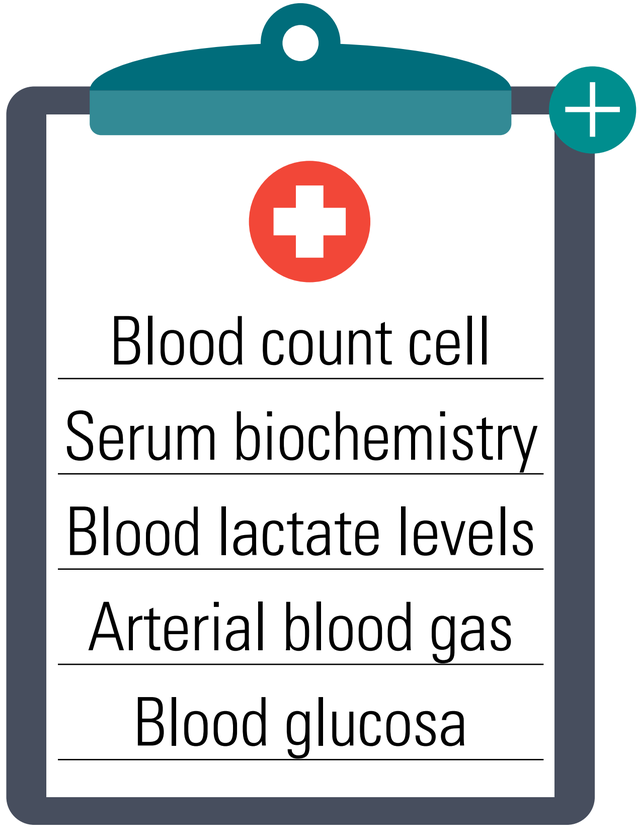
If urine is available (free-flow or cystocentesis) it is helpful to determine if there is hemoglobinuria present.



Babesia rossi parasites are easily detected in clinically ill dogs on thin capillary blood smears (400x, oil immersion, Diff Quick stain).

WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Laboratory



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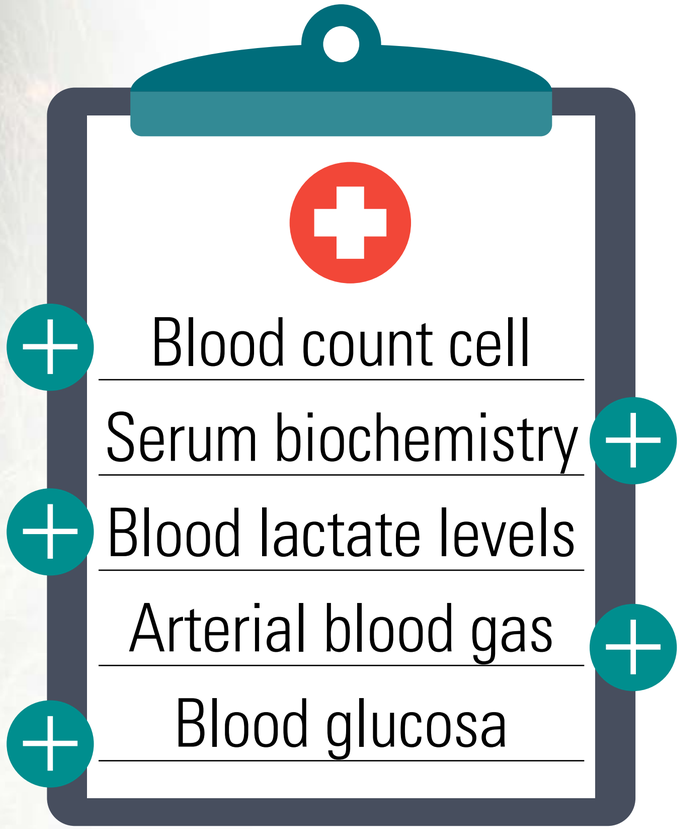
WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Test interpretation



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WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Acute *vs* convalescent

Dogs admitted for hospital care should have at least a daily hematocrit and serum electrolytes determined.

Convalescence is usually quick (within 24-48 hours) and there is generally little need for intensive monitoring in this period.

Death usually occurs within 24 hours of admission and in dogs that have indicators of a poor outcome in this period, even with intensive monitoring and treatment, there is usually little that can be done to alter this outcome.

Measures that have not been assessed but that may alter outcome and that should be investigated include:

- Early use of a mechanical ventilator in Acute Respiratory Distress Syndrome (ARDS)
- Use of dialysis in cases of acute oliguric renal failure.

Although almost all cases with cerebral disease die, survivors have been described but they were all left with devastating neurological deficits.

WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Classes of drugs to use

Diminazene aceturate (an aromatic diamidine) and imidocarb (a urea derivative) are the **drugs** most commonly used to treat *B. rossi.*

Diminazene and imidocarb both have a narrow therapeutic index and their dose must be strictly calculated for dogs whose body weights are carefully established.

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Mono or combination therapy

Some practitioners will follow a dose of diminazene up with a dose of imidocarb several days later and some will repeat the dose of imidocarb if they use imidocarb alone. There is no evidence that combining diminazene with imidocarb or repeating imidocarb is necessary.

Dogs that are In Saline Agglutination (ISA) positive should be immunosuppressed with a short acting **oral glucocorticoid.**

Dogs with complicated disease that require in-hospital treatment typically require a **blood transfusion** (sometimes several) to raise the hematocrit above 0.2 L/L.

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Mono or combination therapy

Additional treatments are typically aimed at supporting whichever organ or organs are dysfunctional or failing:

- Intravenous **fluid therapy** is almost always required following blood transfusion.
- Nasal oxygen may be helpful in cases that have low arterial oxygen tension.
- A prokinetic drug is very often useful and maropitant or metoclopramide is frequently used.
- Although choleretics and various vitamin and mineral supplements are sometimes used, there is no evidence that these offer any benefit.
- Seizure management by means of general anesthesia will be necessary in dogs with cerebral babesiosis (non-neuroglycopenic central nervous system signs).
- Mechanical ventilation will be required in cases with ARDS.
- In dogs that have fragile lung function (usually determined by arterial blood gas), **conservative fluid treatment** is important.
- Dogs in acute renal failure may benefit from dialysis.
- Although severe tachyarrhythmias are frequently observed on ECG monitoring, treating these appears to make no difference to outcome.

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Monitoring for response to treatment

Uncomplicated cases

- Uncomplicated cases that receive a single diminazene or imidocarb injection seldom need further follow up monitoring or treatment.
- Dogs with a moderate anemia or ISA positive test will normally be followed up at least once **24 hours after initial diagnosis and treatment.**

Complicated cases

- Dogs with complicated disease should have frequent (twice daily) hematocrit determination.
- Renal function should be followed biochemically. **Urine production...**
- Serum electrolyte and glucose should be measured as needed to follow response to supplementation.

ARE OTHER PETS OR PEOPLE IN THE HOUSE AT RISK?

Advice to give owners of a sick dog

The disease is not a zoonosis and is not contagious. Tick exposure is the risk factor and effective ectoparasite control is crucial for disease control. This is the only means of prophylaxis. There is no point to treating other healthy dogs in the home for babesiosis.

Can cats get this infection/disease?

Cats are not at risk for *B. rossi* but can get a babesia infection (seen quite commonly in a small geographic area in South Africa) caused by *Babesia felis.* This is a very different disease to the canine disease.

WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

- How to avoid the vector
- Is there a vaccine?
- Is routine testing recommended?

WHAT DOES THE FUTURE LOOK LIKE?

What are the changes being seen with the disease?

Because of the use of oral isoxazoline compounds the incidence of disease among dogs has dropped significantly amongst affluent populations. Disease incidence has not changed in rural settings and among people unable to afford tick prevention products.

FURTHER READING

References

- Allison RW *et al.* 2011. *Babesia canis rossi* infection in a Texas dog. Veterinary clinical pathology / American Society for Veterinary Clinical Pathology 40:345-350.
- Basson PA and Pienaar JG. 1965. Canine babesiosis: A report on the pathology of three cases with special reference to the 'cerebral' form. Journal of the South African Veterinary Medical Association 36:333-341.
- Bohm M *et al.* 2006. Capillary and venous *Babesia canis rossi* parasitaemias and their association with outcome of infection and circulatory compromise. Veterinary parasitology 141:18-29.
- Botha H. 1964. The cerebral form of babesiosis in dogs. Journal of the South African Veterinary Medical Association 35:27-28.
- Bryson NR *et al.* 2000.Ectoparasites of dogs belonging to people in resource-poor communities in North West Province, South Africa. Journal of the South African Veterinary Association 71:175-179.
- Collett MG. 2000. Survey of canine babesiosis in South Africa. Journal of the South African Veterinary Association 71:180-186.
- Foil LD *et al.* 2004. Factors that influence the prevalence of acaricide resistance and tick-borne diseases. Veterinary Parasitology 125:163-181.
- Goddard A *et al.* 2013. Mortality in virulent canine babesiosis is associated with a consumptive coagulopathy. Veterinary Journal 196:213-217.
- Hamel D *et al.* 2011. Canine vector-borne disease in travelled dogs in Germany, a retrospective evaluation of laboratory data from the years 2004-2008. Veterinary Parasitology 181: 31-36.
- Horak IG. 1995. Ixodid ticks collected at the Faculty of Veterinary Science, Onderstepoort, from dogs diagnosed with *Babesia canis* infection. Journal of the South African Veterinary Association 66: 170-171.
- Horak IG *et al.* 2009. Species composition and geographic distribution of ticks infesting cattle, goats and dogs in a temperate and in a subtropical region of south-east Africa. The Onderstepoort Journal of Veterinary Research 76:263-276.

FURTHER READING

Bibliography

- Jacobson LS. 2006.The South African form of severe and complicated canine babesiosis: clinical advances 1994-2004. Veterinary Parasitology 138:126-139.
- Kamani J *et al.* 2019. An annotated checklist of tick-borne pathogens of dogs in Nigeria. Veterinary Parasitology Regional Study Reports 15: 100255.
- Keller N *et al.* 2004. Prevalence and risk factors of hypoglycemia in virulent canine babesiosis. Journal of Veterinary Internal Medicine 18:265-270.
- Kettner F *et al.* 2003. Thrombocytopaenia in canine babesiosis and its clinical usefulness. Journal of the South African Veterinary Association 74:63-68.
- Leisewitz A *et al.* 2019. Disease severity and blood cytokine concentrations in dogs with natural Babesia rossi infection. Parasite Immunology e12630.
- Leisewitz AL *et al.* 2019. A clinical and pathological description of 320 cases of naturally acquired Babesia rossi infection in dogs. Veterinary Parasitology 271:22-30.
- Leisewitz AL *et al.* 1996. Evaluation of the effect of whole-blood transfusion on the oxygen status and acid-base balance of Babesia canis infected dogs using the oxygen status algorithm. Journal of the South African Veterinary Association 67:20-26.
- Leisewitz AL *et al.* 2001. The mixed acid-base disturbances of severe canine babesiosis. Journal of Veterinary Internal Medicine 15:445-452.
- Lewis BD *et al.* 1996. Isolation of a South African vector-specific strain of Babesia canis. Veterinary Parasitology 63:9-16.
- Matjila PT *et al.* 2008. Molecular detection of tick-borne protozoal and ehrlichial infections in domestic dogs in South Africa. Veterinary Parasitology 155:152-157.
- Mellanby RJ *et al.* 2011. Breed and sex risk factors for canine babesiosis in South Africa. Journal of Veterinary Internal Medicine 25:1186-1189.
- Mitchell P. 2015. Did disease constrain the spread of domestic dogs (Canis familiaris) into Sub-Saharan Africa? Azania: Archaeological Research in Africa 50:92-135.

FURTHER READING

Bibliography

- Nel M *et al.* 2004. Prognostic value of blood lactate, blood glucose, and hematocrit in canine babesiosis. Journal of Veterinary Internal Medicine 18:471-476.
- Penzhorn BL. 2011. Why is Southern African canine babesiosis so virulent? An evolutionary perspective. Parasites & Vectors 4: 51.
- Penzhorn BL *et al.* 2017.Black-backed jackals (Canis mesomelas) are natural hosts of Babesia rossi, the virulent causative agent of canine babesiosis in sub-Saharan Africa. Parasites & Vectors 10:124.
- Rautenbach Y *et al.* 2018. Prevalence of canine Babesia and Ehrlichia co-infection and the predictive value of haematology. The Onderstepoort Journal of Veterinary Research 85:e1-e5.
- Reyers F *et al.* 1998. Canine babesiosis in South Africa: more than one disease. Does this serve as a model for falciparum malaria? Annals of Tropical Medicine and Parasitology 92:503-511.
- Scheepers E *et al.* 2011. Serial haematology results in transfused and non-transfused dogs naturally infected with Babesia rossi. Journal of the South African Veterinary Association 82:136-143.
- Schetters TP *et al.* 2009. Comparison of Babesia rossi and Babesia canis isolates with emphasis on effects of vaccination with soluble parasite antigens: a review. Journal of the South African Veterinary Association 80:75-78.
- de Scally MP *et al.* 2006. The elevated serum urea: creatinine ratio in canine babesiosis in South Africa is not of renal origin. Journal of the South African Veterinary Association 77:175-178
- Short EE *et al.* 2017. Climate Change Contribution to the Emergence or Re-Emergence of Parasitic Diseases. Infection and Disease (Auckl) 10 p 1178633617732296.
- Taenzler *et al.* 2016. Prevention of transmission of Babesia canis by Dermacentor reticulatus ticks to dogs after topical administration of fluralaner spot-on solution. Parasites & Vectors 9:234.
- Woolley AE *et al.* 2017. Post-Babesiosis warm autoimmune hemolytic anemia. The New England Journal of Medicine 376:939-946

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