A survey of feline babesiosis in South Africa

L S Jacobson\textsuperscript{a}, T Schoeman\textsuperscript{a} and R G Lobetti\textsuperscript{b}

\textbf{ABSTRACT}

South Africa appears to be the only country where feline babesiosis is a significant clinical entity in domestic cats. Little is known about its epidemiology or the clinical challenges facing practitioners. A questionnaire posted to 1760 South African veterinarians was returned by 16\%, representing approximately 40\% of practices. Just over half reported seeing feline babesiosis, with most cases occurring in the coastal areas of the Western Cape, Eastern Cape and KwaZulu-Natal Provinces. Overall incidence is highest in summer, but seasonality is less pronounced in non-seasonal and winter rainfall areas. No age, breed or sex predisposition was identified. Weight loss, weakness, anaemia, fever and icterus are common clinical findings. Complications include hepatopathy, renal failure, pulmonary oedema, cerebral signs, immune-mediated haemolytic anaemia and concurrent infections. The antibabesial drug of choice is primaquine phosphate. Response to therapy is generally good, but recurrence and chronic infections were identified as problems. The average mortality rate was 15\%. Approximately 3000 cases are seen annually by the respondents, at an estimated cost of R\(750\ 000\) to the owners. Feline babesiosis is a significant problem in South Africa, and further investigations of taxonomic status, concurrent infections, chemotherapy, complications and management of refractory cases are warranted.

\textbf{Key words:} Babesia felis, babesiosis, feline, South Africa.


\section*{INTRODUCTION}

Babesia felis Davis, 1929, is an intra-erythrocytic haemoprotezoan parasite of domestic and wild felids\textsuperscript{13}. A number of piroplasms of Felidae have been described in greater or lesser detail, leading to a considerable amount of confusion regarding nomenclature. Dennig\textsuperscript{2} proposed that the felid piroplasms be divided into 2 small babesias, B. felis and B. cati Mudalier, 1950, and 2 large babesias, B. herpailuri Dennig, 1967 and B. pantherae Dennig, 1972. Of the 2 small babesias, only B. felis has been reported to occur in domestic cats. The original B. felis parasite was isolated from a Sudanese wildcat and was transmissible to domestic cats but did not cause clinical illness\textsuperscript{6}. By contrast, a morphologically similar parasite in domestic cats in South Africa, first described in 1937\textsuperscript{13,20} and considered to be B. felis\textsuperscript{2}, readily causes a potentially fatal disease in cats\textsuperscript{25}. Babesiosis in domestic cats, probably caused by 2 or more species, has been reported sporadically from other countries\textsuperscript{7,8,12,21}, but as a significant feline disease it appears to be a distinctly South African phenomenon.

The distribution of feline babesiosis in South Africa has not been established. All reported cases to date, apart from a newly identified focus in Mpumalanga\textsuperscript{23}, emanated from the western and south-western Cape coast (Cape Town and environs\textsuperscript{6,22}, Stellenbosch area\textsuperscript{3}, and Knysna\textsuperscript{6,23}). Robinson\textsuperscript{25} also mentioned Port Elizabeth. It is likely that feline babesiosis, in common with other Babesia parasites\textsuperscript{24}, is transmitted by tick, but the vector has not been identified\textsuperscript{23}.

Typical clinical signs are anaemia, anorexia, lethargy and weight loss\textsuperscript{4,13,20,25}, with anaemia being the most consistent\textsuperscript{4,23}. Icterus is occasionally present\textsuperscript{4}. The disease follows a chronic course\textsuperscript{2}, and affected animals may show little sign of illness until an advanced stage\textsuperscript{2}. Futter\textsuperscript{4} reported that most cats with naturally-occurring babesiosis were less than 2 years old, and that older cats with babesiosis often had concurrent illness. Diagnosis is based on identification of intra-erythrocytic parasites on thin blood smears. As the parasites are small, visualisation with 10 \% Giemsa is preferable to the more commonly-used rapid stains, although it is less convenient\textsuperscript{4}. Babesia felis is about 2/3 the size of B. canis\textsuperscript{25}, parasites are usually rounded or irregularly circu-

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\textbf{RESULTS}

Two hundred and eighty-five replies, representing 240 practices, were returned. This constituted a return rate of 16\% of individuals, and approximately 40\% of practices. Twenty-five replies were discarded, leaving 260 for analysis. The percentage of returns per province was reasonably similar to the percentage of practices to which surveys had been sent, although there was some bias towards higher returns from those prov-
Epidemiology

Fifty-five percent (144/260) of all respondents reported that they saw feline babesiosis. The Western Cape, Eastern Cape and KwaZulu-Natal had the highest proportion of positive responses and the highest numbers of cases per annum (Figs 1, 2). These provinces will be referred to as ‘endemic’ provinces throughout this article (the quotation marks indicate that the disease is not endemic in the inland areas). All but 1 of 23 practices that reported seeing >48 cases per annum were on or very near the southern Cape coast, from Cape Town in the west to Port Elizabeth in the east (Fig. 2A,B).

The exception was a practice in Howick (Fig. 2C). All the Gauteng respondents who saw feline babesiosis reported <4 cases per annum, indicating that the disease in this area is sporadic and almost certainly non-endemic. Three Gauteng practitioners said they had diagnosed babesiosis in cats that had never left the Gauteng region. One respondent in Mpumalanga (Nelspruit) and 1 in the Free State (Bloemfontein) reported 4–12 cases per annum.

Although the disease was reported to occur more frequently in the summer months countrywide, the ‘endemic’ provinces varied, with strong seasonality in KwaZulu-Natal, a less pronounced pattern in the Eastern Cape and an almost non-seasonal distribution in the Western Cape (Fig. 3). Predictably, the number of infections contracted when cats were taken on holiday was high in the non-endemic provinces and low in the ‘endemic’ ones. Most respondents considered that there was no breed (91%; 120/132), age (83%; 110/132) or sex (98%; 130/132) predisposition.

Owing to the structure of the questionnaire, only an estimate of total case load was possible, but a figure of approximately 3000 cases per annum was reached. The

Clinical aspects

The most frequently-reported complaints by owners were depression/lethargy (92%; 132/144) and anorexia (85%). Other complaints (in descending order of frequency) were weight loss (36), anaemia (16), weakness (9), vomiting (7), pica (6) and icterus (4). Several respondents commented that feline babesiosis is a chronic, insidious disease, and that cats are often very ill by the time the owner realises there is a problem. In certain areas owner awareness is higher and babesiosis is diagnosed earlier. One comment was that some cats appear ‘unthrifty’ but not ill, and are found to have parasites on a blood smear; in these cases, condition and habitus improve markedly after anti-babesial treatment.

The most common clinical finding was anaemia (95%; 135/142), followed by fever (50%), icterus (45%), splenomegaly (24%), poor condition (20%) and anorexia (19%). Other reported findings were weakness (18), depression/lethargy (9) and respiratory signs (9). The latter included coughing, hyperventilation and dyspnoea. Although fever was frequently mentioned, several respondents commented that it was an inconsistent finding, and/or that cats with babesiosis tended to be afebrile.

Sixty percent of respondents (87/128) saw complicated feline babesiosis. Five percent saw complications often, 34% sometimes and 38% rarely. The frequency of complicated cases varied depending on the number of cases seen annually – for example 0% (145) of practitioners who reported <4 cases per annum said they saw complications often, and 60% never saw them, compared with 19% (4/21) and 10%, respectively, for those who saw >48 cases per annum. Complications did not appear to cluster in any area. One hundred and twenty three complications were listed by 57 respondents. These were: hepatopathy (34); renal failure (31); pulmonary oedema (16); cerebral signs (12); concurrent infections (11); immunemediated haemolytic anaemia (4); thromboembolism (3); bleeding tendency (3); heart failure (2); gastric ulceration (2) and miscellaneous others (5). Two reported iliac thrombosis as a thromboembolic complication, and 1 had seen sloughing of the tail tip. Concurrent infections reported were feline immunodeficiency virus (FIV) and/or feline leukaemia virus (FeLV), haemobartonellosis, feline infectious peritonitis (FIP), bacterial pneumonia, urinary tract infection and viral upper respiratory infection. Congenital babesiosis in a litter of kittens was reported by 1 respondent.

Regarding laboratory findings, relatively few respondents appeared to request external laboratory tests on cats with babesiosis, with most answers relating to in-house testing. Parasitaemias, on average, were reported to be high by 12% (17/143), moderate by 38%, low by 28% and variable by 22%. Regenerative anaemia, monocytosis and neutrophilia were common findings. Elevated bilirubin and/or liver enzymes were considered common by 24/131 respondents, and
Fig. 2A–C: Distribution of feline babesiosis in the whole of South Africa and ‘endemic’ provinces, as reported by veterinary practitioners.

A. South Africa.
B: Western and Eastern Cape Provinces.
C: KwaZulu-Natal Province.
azotaemia by 4. Immune-mediated haemolytic anaemia was frequently found by 3. Four respondents reported that concurrent haemobartonellosis, FIV and/or FeLV were common laboratory findings. Eighty-seven percent of respondents (103/118) thought that the vector was a tick, but little specific information was provided.

Chemotherapy

The vast majority of respondents (95 %; 129/136) used primaquine phosphate as the antibabesial of choice, with the rest listing diminazene (2), doxycycline (2), imidocarb (2) and oxytetracycline (1). A generally-accepted dosage regimen for primaquine (1 mg per cat every 36 hours for 4 treatments, followed by 1 mg weekly for 4 weeks)* was used by 36 % (41/113), with another 41 % using a very similar regimen, which differed in that either the dose was calculated according to body mass and/or the duration of treatment was altered. Some used blood smears to determine the duration of treatment. Twenty-three percent used dissimilar dosage regimens, which varied wildly. Lifelong or repeated treatment with primaquine was considered necessary by several practitioners. One suggested that the recommended dose was too low and that primaquine was safe at higher doses. Another commented that owner compliance, rather than drug efficacy, was the problem. Another observed that primaquine caused pica.

Thirty nine percent (53/136) listed a 2nd and sometimes a 3rd chemotherapeutic drug. It was not always clear whether these were used if primaquine failed, or as a routine adjunct. The most common drug in this list was doxycycline (21/53), followed by diminazene (20), imidocarb (13) and trypan blue (8). The dosage for imidocarb (as Forray-65, Schering-Plough AH) ranged from 0.3–0.5 mg/cat to 0.5 mg/kg, with some repeating the drug after 48 hours and 1 after 8 days. Diminazene was generally used at the canine dose or at half this dose. Only 1 dosage regimen was used for trypan blue, and this was the same as the dog dose. Doxycycline was usually given per os at 5–10 mg/kg daily for 1–2 weeks.

Supportive treatment

A large selection of supportive treatments was used (detailed in Table 1). Vitamin/mineral preparations were used by most respondents, and fluid therapy, corticosteroids, liver support, blood transfusion and antibiotics were also frequently administered. There was an overlap between vitamin/mineral and liver support preparations. When analysing these data, the treatment was classified as vitamin/mineral’ if explicitly stated, or if the preparation listed was nonspecific (such as B vitamins and iron), and as ‘liver support’ if explicitly stated, or if the preparation listed was nonspecifically indicated for liver support (for example, Bykahepar or Essentiale). Corticosteroid use varied, with some using corticosteroids routinely, and others only for specific indications. Nutritional support, often including prescription diets, was provided quite frequently. Blood transfusions were not required for most cases, but when indicated were given by a large number of practitioners.

Response to treatment, cost and outcome

The clinical response to treatment was generally favourable. The respondents felt, on average, that the response was good in 78 % of cases, poor in 17 %, fair in 32 % and uncertain in 29 %. Parasite clearance was considered poor (no effect) by 1 % of respondents (1/133), fair by 37 % and excellent by 29 %, with 34 % being unsure. Several commented that cats that responded poorly to therapy, those that had clinical recurrences or complicated disease, and those that died, often had concurrent infections such as FIV, FeLV, haemobartonellosis and FIP. A number felt that clinical feline babesiosis was a stress-related disease and that the ability to suppress parasites and recover required a normal immune system.

Most saw recurrence of parasitaemia after treatment in at least some cats, with only 21/102 reporting that they did not see this at all and that it occurred in 50–99 % of cases. It was difficult to assess how often asymptomatic parasitaemias occurred after treatment, as many respondents did not make repeat blood smears from cats that had recovered clinically. Practitioners were asked if they ever saw parasi-

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*We have been unable to establish the origin of this regimen and recommend that it be revised (see Discussion).

Table 1: Supportive therapy administered by veterinary practitioners to cats with babesiosis (summary of 135 replies).

<table>
<thead>
<tr>
<th>Type of therapy</th>
<th>Number of mentions</th>
<th>Percentage of respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin/mineral preparations</td>
<td>108</td>
<td>80</td>
</tr>
<tr>
<td>Fluids</td>
<td>73</td>
<td>54</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>63</td>
<td>47</td>
</tr>
<tr>
<td>Liver support</td>
<td>60</td>
<td>44</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>58</td>
<td>43</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>48</td>
<td>36</td>
</tr>
<tr>
<td>Nutritional support/appetite stimulants</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>Cage rest</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatories/antipyretics</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Anabolic steroids</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>6</td>
</tr>
</tbody>
</table>

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Fig. 3: Seasonal incidence of feline babesiosis in the whole of South Africa and ‘endemic’ provinces, as reported by practitioners. The data represent the number of respondents who marked a particular month as a high-incidence month. KZN = KwaZulu-Natal (total number of usable replies (n) = 24); WC = Western Cape (n = 48); EC = Eastern Cape (n = 18); RSA = whole of South Africa (n = 107).
taemias in healthy cats that were presented for other reasons. Again, responses were difficult to analyse, as many never or rarely made blood smears from healthy cats. Most (70/127) said they never saw parasitaemias in healthy cats, 35 rarely, 15 sometimes and 7 often. All those who often saw asymptomatic carriers practised in endemic coastal areas. The average overall mortality rate was 15%, with 78% (89/114) of respondents reporting mortality rates of 0-20%. The average mortality rate of 21% in KwaZulu-Natal was approximately double that for the other "endemic" provinces (11% Eastern Cape and 10% Western Cape).

**DISCUSSION**

This survey provided a reasonably representative picture of feline babesiosis as seen in private veterinary practices in South Africa. Although the return rate for individuals was low, the proportion of practices represented in the replies was relatively high. It was expected that there would be bias, with a greater return rate from practitioners in "endemic" provinces. This did occur, but was somewhat less pronounced than expected (see Fig. 1).

The survey confirmed that feline babesiosis is endemic along much of the South African coast, from KwaZulu-Natal to the Western Cape. There have been no previous reports of the disease from the Eastern Cape and KwaZulu-Natal. Although the distribution is largely coastal, some cases were reported from relatively far inland in "endemic" areas, particularly in KwaZulu-Natal. The seasonal distribution appears to be related to rainfall patterns and supports the likelihood of a tick vector.

The clinical picture reported was, overall, very similar to that previously described. Anaemia is the most consistent sign of feline babesiosis. Fever is far more contentious – although half the respondents said it occurred, several remarked explicitly that it was an inconsistent finding or did not occur. Cats with experimental babesiosis are consistently afebrile, even in the acute phase, and only 5/70 cats with naturally-occurring infection had fever.

It is possible that concurrent infection is needed to trigger pyrexia in feline babesiosis, as suggested by Futter's observation that the 5 pyrexic cats also had other infections. Pica is a newly-reported clinical finding and is probably related to chronic anaemia, which is associated with geophagia in people.

Complicated feline babesiosis has not previously been reported. It would appear from the survey that many complications are similar to those occurring in canine babesiosis. Further investigation is required to assess which complications are associated with the primary disease and which are exacerbations of underlying conditions or manifestations of concurrent infections. Numerous concurrent infections were reported by respondents and should be suspected in cats with babesiosis, particularly in symptomatic adult cats in an endemic area, and in affected cats that have fever, do not respond readily to therapy, or have frequently recurring clinical signs. Haemobartonellosis warrants particular mention, as it can manifest with very similar signs to feline babesiosis, may not be present in peripheral blood, and can be difficult to recognise on blood smears. Giemsa (10%) is more likely than rapid stains to demonstrate both *Haemobartonella* and *Babesia* parasites, and is recommended particularly in areas in which feline babesiosis is endemic.

All small *babesias* and *B. felis* in particular are relatively refractory to chemotherapy and, frequently-treated treatment may need to control infections. The large number of drugs and treatment regimens reported in this survey reflects this problem. Those treating the disease must be aware that sterilisation of the infection is not a realistic goal, and that the aim must be clinical cure and resolution of anaemia, in conjunction with reduction in parasitaemia. Cats with asymptomatic parasitaemias should be clinically and haematologically monitored at regular intervals; treatment in these cases is unnecessary in the absence of clinical signs or anaemia.

The only drug that is reliably and consistently effective against *B. felis* is the antimalarial, primaquine phosphate. A dose of 0.5 mg/kg primaquine per os 1 to 3 times, or single injections of 0.5-1.0 mg/kg, resulted in dramatic reduction in parasitaemia and increased haematocrit within 3 days. Initial degeneration of parasites is rapid, but might be difficult to assess owing to the small size of the organisms. In the initial studies, the oral dose often caused vomiting in clinical cases, with obvious implications for efficacy; however, this problem was not mentioned by respondents in this survey. Recrudescence occurred 2-3 weeks after initial treatment, and a repeat dose of 0.5 mg/kg was well tolerated. Primaquine does not sterilise the infection and a carrier state can persist for years. It is unclear how Potgieter's recommendations evolved into the commonly-used treatment regimen for feline babesiosis. We feel that this regimen should be reassessed, considering the lack of evidence that it is superior, as well as increased cost and inconvenience to owners. At the very least, we would urge veterinarians to revert to using 0.5 mg/kg, rather than 1 mg (2 tablets) per cat, as the latter approach guarantees underdosing in any cat over 2 kg. Many practitioners reported using primaquine over long periods without apparent adverse effects, but this practice should be based on clinical and haematological abnormalities rather than the presence of parasites alone. High doses of primaquine should not be attempted, as single doses above 1 mg/kg were lethal in 4/4 cats. Primaquine is currently available on prescription from Kyron Laboratories, as 0.5 mg tablets and as a powder.

As for drugs that are reportedly ineffective against *B. felis*, the list is impressive, and includes diminazene, imidocarb, trypan blue, oxytetracycline, chloroquine, phenamidene, enfluavine, and a sulphonamide-trimetrimethoprim combination. Some of these drugs result in a degree of clinical improvement or reduction in parasitaemia, but this is temporary or extremely variable. Practitioners use a number of these drugs for feline babesiosis. Since many are not registered for use in cats, some have a low margin of safety and there is very little evidence of efficacy, this does not currently appear to be rational. Doxycycline, however, is a useful adjunct to primaquine in feline babesiosis, since tetracyclines are in some instances effective against the small *babesias*, doxycycline is safe, it is effective against *Haemobartonella* and has a broad antibiotic spectrum to combat other concurrent infections. The recommended dosage for *Haemobartonella* is 5 mg/kg BID for 21 days.

The mortality rates for feline babesiosis vary widely, but the average was relatively high. This was rather surprising in view of the fact that feline babesiosis is an insidious, chronic disease. However, the data need to be treated with some caution, as the small numbers of cases seen in the non-endemic provinces may skew the mortality rates upward. This might also account for the high mortality in KwaZulu-Natal, where some practices see very few cases.

In conclusion, babesiosis is a significant problem of domestic cats in South Africa, affecting at least 3000 cats per year and presenting many challenges to the practitioner. Areas requiring further investigation are taxonomic status, identification of the vector, concurrent infections, chemotherapy, management of chronic symptomatic infections and complicated feline babesiosis.
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Appendix 1: Example of questionnaire used in the survey.

Feline babesiosis questionnaire

PRACTITIONER AND PRACTICE DETAILS

Practitioner: 

Practice name: 

Physical address: 

Postal Address: 

Province: Postal code: 

Tel: Fax: E-mail: 

PLEASE CIRCLE THE APPROPRIATE RESPONSE OR ANSWER IN THE SPACE PROVIDED

1a. Do you use stained blood smears to diagnose suspected feline babesiosis? 
   Always Usually Sometimes Never

1b. Do you routinely use stained blood smears to diagnose feline 'problem cases'? 
   YES / NO

2. Do you see cases of feline babesiosis in your practice? 
   YES / NO

If the answer is no, please stop here and return the questionnaire in the envelope provided. Negative responses are very important.
3. Is feline babesiosis a new phenomenon in your practice?
   YES/NO
   If yes, when did you first see it?

4. How many cases do you see per year? (please circle)
   <4  4–12  12–24  24–48  >48

5. During which month(s) do you see most cases? (please circle)
   Jan  Feb  March  April  May  June  July  Aug  Sept  Oct  Nov  Dec

6. What percentage of infections are contracted when the cat is taken on holiday with the owners?
   ...........................

7. Do you diagnose feline babesiosis more commonly in certain:
   Breeds?  YES/NO  If yes, specify: .................................................................
   Ages?   YES/NO  If yes, specify: .................................................................
   Sexes?  YES/NO  If yes, specify: .................................................................

8. What are the most common owner complaints? .................................................................

9. What are the most common clinical findings? .................................................................

10. What are the most common laboratory findings? ...............................................................;

11. Are the parasitaemias usually: .................................................................
    Low*  Moderate*  High*  Variable
    (*: Low – difficult to find; Moderate – not difficult to find but not striking numbers; High – striking numbers all over the smear)

12. The vector of feline babesiosis is unknown.
    What, in your opinion, is the most likely vector(s)? .................................................................

13. Which antibabesial drug(s) do you use? Please provide details (dose, frequency, duration of treatment)
    ........................................................................................................................................

14. What supportive treatment(s) do you give? (Include blood transfusions if you give them)
    ........................................................................................................................................

15. How would you rate clinical success of treatment? (percentage of cases)
    Poor*  %  Fair*  %  Good*  %  Not sure  %
    (*: Poor – no effect; Fair – moderate improvement; Good – clinical cure)

16. How well does treatment clear the parasites?
    No effect  Fair  Excellent  Not sure

17. What is the recurrence rate of:
    Parasitaemia with illness  ................. %
    Parasitaemia without illness ...................... %

18. Do you see asymptomatic babesiosis in cats (i.e a healthy cat with a B. felis-positive bloodsmear)?
    Often  Sometimes  Rarely  Never

19. Do you see complicated babesiosis in cats? (e.g. lung oedema, acute renal failure, cerebral signs etc.)
    Often  Sometimes  Rarely  Never
    Please list complications: .................................................................

20. What is the mortality rate overall? .............................. %

21. What is the average cost to the owner of an episode of feline babesiosis? .................................................................

22. Would you be interested in being involved in future research projects on feline babesiosis?
    YES/NO
    • What was the source of these responses? (please circle)
      Computerised records  Estimates from memory  Both

THANK YOU VERY MUCH FOR YOUR ASSISTANCE