Differential *Bos taurus* cattle response to *Babesia bovis* infection

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Abstract

Bovine babesiosis is a tick-borne disease caused by *Babesia* spp. haemoprotozoans. The disease is of great importance at tick enzootic unstable areas and hampers cattle production in several developing countries. The available immunisation alternatives are pre-immunisation and attenuated vaccines. Despite being efficient and protective, they are unsafe as they use cattle blood cells as inoculum and may potentially spread other diseases. Another alternative to help in babesiosis control would be the identification of genetically resistant cattle to *Babesia bovis* infection. The objective of this work was to phenotype cattle based on primary response against *B. bovis* infection. Two-hundred and forty half-sib Hereford and Aberdeen Angus heifers (120 animals from each breed), 12–18-month-old naïve cattle, originated from a tick-free area in Southern Brazil, were used in the experiment. Animals were monitored following an inoculation with $1 \times 10^7$ *B. bovis* parasitised erythrocytes. Results showed three different phenotypes: 1—-'susceptible', animals with babesiosis clinical signs that received treatment to avoid death; 2—-'intermediate', animals with clinical signs: parasitaemia, $\geq 21.5\%$ reduction in packed cell volume (PCV) and increase in body temperature when compared to their pre-challenge physiological parameters, no specific treatment was needed as animals self recovered from the disease, and 3—-'resistant', animals without clinical signs that showed *B. bovis* presence in blood smears, $<21.5\%$ PCV reductions, with little or no increase in body temperature and no need for babesiosis treatment. The frequencies of each phenotype were: 45.4, 26.7, and 27.9%, respectively, demonstrating the existence of phenotypic variation for *B. bovis* in *Bos taurus* cattle.

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1. Introduction

Bovine babesiosis is a tick-borne disease caused by intra-erythrocytic haemoprotozoans of the *Babesia* spp. genus. *Babesia bovis* and *B. bigemina* are the main parasite species, with *B. bovis* being the most pathogenic species. Babesiosis causes important economic losses and hampers cattle production in several developing countries. Cattle raised at tick enzootic unstable areas, such as Southern Latin America (Nari, 1995), where the *Boophilus microplus* vector presence is not constant throughout the year, is the most affected. This haemoparasite causes abortion, weight loss, and frequent cattle deaths during disease outbreaks. A surveillance study showed that Southern Brazilian farmers lose, in average, six animals per property per year (SEBRAE/SENAR/FARSUL, 2005) due to babesiosis.

Among farmers, adoption of immunisation alternatives such as pre-immunisation and attenuated vaccines is low (9.1 and 7.9%, respectively; SEBRAE/SENAR/FARSUL, 2005). Despite the fact that attenuated vaccines are efficient and offer reasonable long-lasting protection, if manufactured under rigorous quality control, they are unsafe because cattle blood cells are used as inoculum and may potentially spread other diseases as happened in the past with pre-immunisation procedures. Recombinant vaccines are still being studied and no commercial products are available in the market.
Field observations during Babesia outbreaks and experimental inoculation challenge trials have shown that a small percentage of naïve infected cattle was unaffected by this haemoparasite. These observations suggest that cattle resistance to Babesia spp. infection may exist, in this case selection of resistant animals could be an alternative strategy to help farmers on babesiosis control.

Host genetic resistance against haemoparasite infections has been studied for Plasmodium spp. in mice (Foote et al., 1997; Burt et al., 2002; Fortin et al., 2001; Hernandez-Valladares et al., 2004) and humans (Livingstone, 1984; McGuire et al., 1994; Rihet et al., 1998; Wattavidanage et al., 1999), and for Trypanosoma spp. in cattle (Kemp and Teale, 1998, 2005; Hanotte et al., 2003; Murray et al., 2004; Kemp and Teale, 2005) and mice (Kemp et al., 1997; Nagayasu et al., 2002). As B. bovis shares similar biological characteristics with Plasmodium falciparum, malarial studies may bring relevant insights into cattle genetic resistance to B. bovis infection. Anaemia is a common synhom in Babesia, Plasmodium and Trypanosoma infections, thus comparative studies in host response to these parasites may hold important clues for host-resistance against babesiosis.

Thus far, cattle non-specific immune response against B. bovis infection has been attributed to age- or breed-related factors (Mahoney, 1972). In general, young cattle has been described as less susceptible to Babesia infections than adult cattle, and Bos indicus less susceptible than Bos taurus. However, the specific resistance of naïve adult cattle to B. bovis infection within B. taurus populations has not been measured, and information is confined to few unpublished field reports or vaccination trials. Therefore, the objective of this work was to measure cattle primary response against a B. bovis infection in naïve B. taurus to investigate the existence of cattle resistance to B. bovis infection.

2. Material and methods

2.1. Animals

The study was performed at South Embrapa Cattle & Sheep Research Centre (Bage, RS, Brazil, located at 31°S 54°W). Two hundred and forty naïve B. taurus heifers were challenged with a B. bovis virulent strain. The animals were 12–18-month-old, from two different breeds (120 Hereford and 120 Aberdeen Angus), and were originated from a tick-free region (Santa Vitoria do Palmar, RS, Brazil, located at 33°S 53°W). Four challenges were performed in groups of 60 animals each.

2.2. B. bovis challenge

Cattle were subcutaneously inoculated with $1 \times 10^7$ B. bovis virulent strain parasitised erythrocytes and all individuals were daily monitored for body temperature, packed cell volume (PCV) and parasitaemia from 7 to 30 days post-challenge (dpc). The inocula used in the challenges were planned to induce a clinical primary reaction to allow identification of different cattle responses against B. bovis infection. The experiment steps are presented in Fig. 1.

The B. bovis virulent strain (6558 B. bovis RS 06/05/94) used in this experiment was kindly donated by Dr. Raul Kessler from Embrapa Beef Cattle Research Centre, Campo Grande, MS, Brazil. Stocks of this strain were cryopreserved, biologically re-activated by primo-infection in splenectomised calves, and erythrocyte counts and parasitaemia percentage were determined in order to obtain standard inocula at each challenge. As challenges were performed with 6 months period interval, each challenge had its own re-activation process.

Fig. 1. Experimental schedule showing steps used in Babesia bovis challenges. Time for each step is shown in grey as day post-challenge (dpc).
Prior each challenge, body temperature and packed cell volume were measured at 3 different days in order to obtain normal physiological parameters, and thin peripheral blood smear slides were also analysed. All animals were weighed before challenge and at treatment day and blood sera were collected before and after challenges to test for anti- \textit{B. bovis}, anti- \textit{B. bigemina} and anti- \textit{Anaplasma marginale} IgG by indirect fluorescence antibody test (IFAT; IICA, 1987). Blood sera were analysed in two-fold dilutions, starting from 1:80. Parasitaemia and IFAT measurements were undertaken to confirm cattle naïve status.

During challenge, body temperature, packed cell volume and parasitaemia were daily monitored and PCV results were expressed as percentage reduction in packed cell volume when compared to their normal physiological values. Thin peripheral blood smears were fixed on methanol and stained in Giemsa-May Grünwald (IICA, 1987). Blood slide exams were performed on optical microscopes, 100×, with immersion oil. Parasitaemia levels were calculated when numbers of \textit{B. bovis} parasitised erythrocytes were >5 in the whole blood slide (>200 microscopic fields examined), otherwise animals were recorded as positive for \textit{B. bovis} presence.

2.3. Phenotyping criteria

Treatment decision was based upon babesiosis signs, such as important PCV reductions and/or high parasitaemia levels, and behavioural alterations (apathy, loss of condition or nervous disorders). All animals were phenotyped in three different groups (resistant, susceptible or intermediate) according to individual performance throughout the challenge. Babesiosis treatment was the criterion used to classify animals as susceptible. Cattle were phenotyped as resistant or intermediate based on their PCV reduction levels, the threshold used to phenotype animals as resistant was PCV reduction <21.5%.

2.4. Statistical analyses

Normal physiological parameters of body temperature, body weight (BW) and PCV at pre-challenge levels were analysed by fitting phenotype and challenge as fixed effects. During challenge body temperature variation was analysed by fitting either phenotype or challenge as fixed effects and pre-challenge body temperature and body weight averages as covariates. As fixed effects and pre-challenge PCV and body weight averages as covariates. General linear models were also used to analyse day at first parasitaemia detection, days of patent parasitaemia, day at maximum PCV reduction and days between first parasitaemia and maximum PCV reduction. Chi-square test was used to analyse weight loss among susceptible animals. All analyses were done in SAS software using GLM and Freq/chisq procedures.

3. Results

3.1. Cattle phenotypes to \textit{B. bovis} infection

The results showed three different phenotypes: 1—‘susceptible’, animals that needed specific treatment to avoid death; these animals presented ≥ 18.5% reduction in packed cell volume with severe behavioural alterations; 2—‘intermediate’, untreated animals with ≥ 21.5% reduction in packed cell volume, without behavioural alterations, and 3—‘resistant’, untreated animals without clinical signs of babesiosis that showed parasitaemia, <21.5% PCV reductions and with little or no increase in body temperature. The frequencies for each phenotype were: 45.4, 26.7, and 27.9%, respectively.

3.2. Pre-challenge

All animals tested negative for parasitaemia and specific anti- \textit{B. bovis}, anti- \textit{B. bigemina} and anti- \textit{A. marginale} IgG serology prior each challenge, confirming their naïve status for these three tick-borne disease parasites. Body weight was significantly higher in resistant animals, followed by intermediate and susceptible individuals (Table 1; \( P < 0.05 \)). Packed cell volume was significantly higher in intermediate phenotypes when compared to resistant and susceptible phenotypes (Table 1; \( P < 0.0001 \)). Pre-challenge body temperature did not differ among phenotypes (\( P > 0.05 \)).

3.3. During challenge

3.3.1. Among challenge variation

Body temperature significantly differed among challenges (Fig. 2). There was a similar trend in challenges 3 and 4, with body temperatures slightly increasing from 7 to 10 dpc, showing a decrease later on. Challenge 2 had a different behaviour, showing the lowest body temperature patterns, never reaching their pre-challenge normal physiological temperatures (Fig. 2), and challenge 1 showed an intermediate behaviour.
Table 1

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Pre-challenge</th>
<th>During challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body weight (kg)</td>
<td>Body temperature (°C)</td>
</tr>
<tr>
<td>Resistant</td>
<td>188.00 ± 2.83&lt;sup&gt;a&lt;/sup&gt;</td>
<td>39.65 ± 0.04</td>
</tr>
<tr>
<td>Intermediate</td>
<td>182.36 ± 2.88&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>39.76 ± 0.04</td>
</tr>
<tr>
<td>Susceptible</td>
<td>178.15 ± 2.23&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39.75 ± 0.03</td>
</tr>
</tbody>
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P < 0.05 for Pr > P

Within column means with different superscripts are significantly different to at least the 5% level of probability.

Variations in packed cell volume were also different among challenges, showing greater reductions from 7 to 12 dpc (Fig. 3). Among challenges, the strongest reductions occurred in challenge 3, at 8–9 dpc, showing the best recovery in PCV from 13 dpc onwards.

During challenges, all animals tested positive for *B. bovis* on thin peripheral blood smear slides, except one. Positive *B. bovis* slides were detected from 4 dpc onwards and parasitaemias as high as 0.05% were observed from day 7. From 22 dpc onwards, only *B. bovis* presence was detected.

### 3.3.2. Among phenotypes variation

As far as phenotypes are concerned, intermediate animals showed higher body temperature averages at the beginning of the experiment (7–8 dpc) when compared to resistant and susceptible phenotypes (Fig. 4). Resistant animals showed lower body temperatures at 11–12 dpc, when compared to intermediate and susceptible individuals. Resistant cattle also showed the lowest ($P < 0.001$) PCV reduction among the phenotypes (Fig. 5). Resistant animals presented PCV recoveries from 17 dpc onwards. Packed cell volume reduction averages for intermediate and susceptible animals were significantly different from each other, except at 7–10, 15, 17, 20–21, and 23 dpc. Intermediate animals maintained packed cell volumes at around −17% but reached stability from 13 dpc onwards. On the other hand, susceptible animals also maintained their PCV values, but at lower levels of around −21%, but decreasing even further at 18–19, 22, and 24 dpc (Fig. 5). There was not significant difference in maximum increase in body temperature between phenotypes, however, maximum PCV reduction was greater in susceptible, followed by intermediates and resistant animals (Table 1).

All animals (except one) showed patent parasitaemia: 38.9% of the individuals showed parasitaemia levels between 0.01 and 0.23% and the remaining (61.1%) showed *B. bovis* presence. Parasitaemia levels of 0.01–0.1, 0.01–0.2 and 0.01–0.23% were observed in resistant, intermediate and susceptible phenotypes, at a

![Fig. 2. Body temperature variation during Babesia bovis infection in the four different challenges (1, 2, 3, and 4). The asterisks in dpc suggest statistical significance levels ($^aP < 0.05$, $^bP < 0.01$, and $^cP < 0.001$). Different superscripts indicate significantly different means.](image)
Fig. 3. Packed cell volume variation during *Babesia bovis* infection in the four different challenges (1, 2, 3, and 4). The asterisks in dpc suggest statistical significance levels ($^*P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$). Different superscripts indicate significantly different means.

Fig. 4. Body temperature variation during *Babesia bovis* infection in resistant (□), intermediate (○) and susceptible (▲) cattle. The asterisks in dpc suggest statistical significance levels ($^*P < 0.05$, $^{**}P < 0.01$, and $^{***}P < 0.001$). Different superscripts indicate significantly different means.

Fig. 5. Packed cell volume variation during *Babesia bovis* infection in resistant (□), intermediate (○) and susceptible (▲) cattle. The asterisks in dpc suggest statistical significance levels ($^{***}P < 0.001$). Different superscripts indicate significantly different means.
frequency of 18.3, 28, and 53.8%, respectively ($\chi^2 = 7.1; P = 0.03$). Since patent parasitaemia was not normally distributed and more than 60% of the observations did not vary (B. bovis presence), number of days with patent parasitaemia (dpp) was used instead to analyse parasitaemia data. Animals varied from 0 to 16 dpp and phenotypes were significantly different ($P < 0.0001$), with resistant and intermediate animals having higher averages (Table 2). Day at first parasitaemia detection did not differ between phenotypes; days between first parasitaemia detection was lower in resistant animals (Table 2).

The fact that susceptible animals were removed from the experiment after the day of treatment lead to the decrease in observation numbers for this phenotypic group by the end of the experiment. This reduction in numbers can be noted in the increase in standard errors towards the end of the challenge period (Figs. 1–4).

Babesicidal treatments were administered in susceptible cattle from 8 to 27 dpc, with 75% of the treatments occurring up to 18 dpc. Although treated animals were removed from the experiment, monitoring continued in order to assure health recovery. During this post-treatment monitoring, 33% of these animals took from 1 to 9 days to recover at least 50% of their PCV levels, after treatment; 33% took from 10 to 26 days, and 34% up to 30 days. After treatment, 11.1, 2.8 and 0.9% of the susceptible animals had to be treated once, twice and three times again, respectively. These animals also showed liveweight variation from –40 to +25 kg due to B. bovis infection. This variation was related to number of days with patent parasitaemia before treatment, animals with more than 5 dpp were among those with higher weight losses (Fig. 6).

Phenotype frequencies also differed between breeds, showing that 39.2, 23.3, and 37.5% of Aberdeen Angus cattle used in this experiment were classified into

![Graph showing liveweight variation during B. bovis challenge](image)

Fig. 6. Liveweight variation during B. bovis challenge (>2, –8 < kg ≤ 2, and ≤8 kg), according to patent parasitaemia length (≤3, 4 and 5, and >5 days).
susceptible, intermediate and resistant phenotypes, respectively. Results for Hereford cattle were: 51.7, 30.0, and 18.3% ($\chi^2 = 11.86, P < 0.01$).

Post-challenge indirect fluorescence antibody test (IFAT) showed that all intermediate and resistant animals tested positive (≥1:160 titre) for specific anti-B. bovis IgG, confirming seroconversion. A small percentage (2.9%) of the susceptible animals showed 1:80 titres and 1.9% tested negative for specific anti-B. bovis IgG (Fig. 7). The animal described earlier as having negative parasitaemia showed seroconversion (1:1280 titre). Deaths were not recorded as result of babesiosis clinical signs.

4. Discussion

As expected, B. bovis infection caused reductions in packed cell volume and increments on body temperature during experimental challenges (Figs. 1–4). Variations in PCV reduction were significantly different between phenotypes, however, the average for maximum PCV reduction of susceptible animals was lower than the figures observed by Kessler et al. (1987), which was of 52%. Variations in body temperature did not differ between phenotypes ($P > 0.05$; Table 1) and, in overall, they were lower than results observed by Kessler et al. (1987), who found 2 °C increase in body temperature. In fact, these authors used a different strain at an inoculum of $1 \times 10^8$, what could explain the stronger reaction observed in the latter experiment.

Sharp declines in PCV are often seen in haemoparasitic infections. Cattle response to Trypanosoma congolense infection usually takes 3 days between first parasite detection and 16–17% PCV reductions (Buza et al., 1995). Our results agree with this rapid decrease in PCV. Susceptible animals took 5.5 days from first B. bovis detection to an average of 29.5% in PCV decrease, showing how acute B. bovis infection is when compared to T. congolense in cattle.

Challenge was a significant fixed effect for body temperature and packed cell volume variations. The inocula used was as standard as possible, however, as B. bovis frozen stabitate re-activation was performed in four different processes, at different times and in different splenectomised calves, slight variations around the inoculum used ($1 \times 10^7$ of B. bovis parasitised erythrocytes) might have altered cattle infection levels among challenges.

Although Callow and Pepper (1974) recommended that either body temperature, PCV or parasitaemia would be sufficient to evaluate cattle susceptibility to B. bovis, our results showed that susceptibility could not be determined by body temperature nor parasitaemia. Packed cell volume reduction was undoubtedly the major trait to take into consideration to determine babesiosis severity. Therefore, the threshold used to distinguish between untreated animals (resistant and intermediate phenotypes), was based on their PCV variations throughout the experimental challenge. Resistant animals presented lower PCV reductions with one peak during monitoring, while PCV reductions of intermediate individuals tended to plateau at levels slightly lower than maximum PCV reduction. Considering these profiles, 21.5% in PCV reduction
was the cut-off that separated these two phenotypes. Babesiosis treatment was the criterion used to classify animals as susceptible. Most of susceptible animals (93.6%) showed important PCV reductions (>21.5%), agreeing with intermediate animal profiles. Nonetheless, seven heifers (6.4%) were treated before their PCV reductions reached 21.5%, in these situations extreme alterations in behaviour (listlessness, anorexia, and roughened coat) indicated these animals had to be treated. These subjective babesiosis-related behavioural alterations are well described as pathological signs of this disease (Mahoney, 1973; 1977; 1979) and must be taken into consideration during clinical evaluation. Packed cell volume reductions are the main trait to consider when deciding on specific treatment, however, perception of babesiosis-related behavioural signs are also important on treatment decision. Behavioural signs are often observed in severe babesiosis even before the onset of parasitaemia and important PCV reductions.

Parasitaemias were generally low and variable, it happened that animals detected with *B. bovis* presence 1 day showed negative blood slides in the following day. This transient presence of the parasite is one of the hallmarks of the disease. The higher frequency of susceptible animals with parasitaemia levels (53.76%) and at higher levels (from 0.01 to 0.23%) might have been the main causes to the abrupt PCV decrease in these animals. Reductions in packed cell volumes are directly related to erythrocytic sequestration and destruction due to haemoparasite multiplication. Intermediate animals behaved like susceptible individuals, having similar parasitaemia levels (of up to 0.2%) and important PCV reductions. However, the frequency of animals with parasitaemia levels were lower (27.96%) than the observed in susceptible animals, yet intermediate animals reaction to *B. bovis* infection was as strong as in susceptible animals. This demonstrates that even at lower levels of parasitaemia (*B. bovis* presence), this haemoparasite is able to reduce PCV.

As a consequence of strong PCV reductions, susceptible animals presented the shortest period of days with patent parasitaemia (4.93 days) because they soon needed specific treatment. After susceptible animals, intermediate individuals showed the second highest drop in maximum PCV levels, however, these animals supported *B. bovis* infection for longer (7.48 dpp). Resistant animals also had a long struggle against *B. bovis* infection (6.65 days) but they were faster from first parasitaemia detection to maximum PCV reductions (3.8 days), reaching lower PCV reductions (14.98%). It is noteworthy that three resistant

(and one intermediate) animals had their parasitaemias detected after maximum PCV reduction occurred. These results demonstrate that the immune system of resistant animals might have been able to control parasite multiplication faster than the other two phenotypes, consequently leading to significantly less pronounced PCV reactions (Fig. 5). On the other hand, the immune system of susceptible individuals was unable to overcome parasitaemia nor PCV reductions, causing the development of severe babesiosis and the need for specific treatment.

All animals, except two susceptible animals, had seroconversion, i.e., developed specific anti-*B. bovis* IgG titles ≥ 1:80. It would be expected that animals with high parasitaemias would show higher anti-parasite IgG titles, however, babesicidal treatment of susceptible animals might have arrested parasite multiplication, blocking development of immune responses and consequently lowering specific anti-parasite IgG titles. Interestingly, resistant animals were able to control parasitaemia and PCV levels, without hampering parasite multiplication. As a result, *B. bovis* infection took its course, allowing the development of anti *B. bovis* IgG titles ≥ 1:320, levels compatible with strong immunological responses, in 97.02% of resistant animals. These observations indicate that the development of a protective immunity does occur in animals that undergo infection, which is in agreement with the “coinfected immunity” statement made by Sergent et al. (1924), that remains valid up until now.

This experiment also led to unexpected results: (1) Resistance to *B. bovis* infection in *B. taurus* cattle has not been reported in the literature. Earlier field observations suggested that there is a ≈10% frequency of resistant animals in a Holstein Friesian population (Ana Maria Sacco, personal communication), however, the frequency of resistant animals observed in this experiment was higher (27.9%). (2) Our initial hypothesis was that *B. taurus* response to primary *B. bovis* infection would either be clinical (babesiosis) or sub-clinical (babesiosis). In this sense, the existence of an intermediate phenotype was an interesting finding. Although this group had high parasitaemia levels and PCV reductions as susceptible individuals, intermediate animals had no need for specific treatment. These results indicate that, despite these animals had been severely affected by *B. bovis* infection, intermediate individuals were capable of controlling infection as well as resistant animals.

How resistant and intermediate animals were able to control PCV reduction is yet unclear. Reduction in PCV is a consequence of parasite multiplication inside the
erythrocytes. It has been suggested that more than one mechanism might control haemoparasite infections: through parasite multiplication control and anaemia development control (Naessens, 2006). It is well known that macrophages act as the first line of defense against B. bovis multiplication (Brown, 2001), so it could be hypothesised that resistant animals were capable of producing higher activation of these phagocytic cells and their secretory products during early infection. Increased expression of nitric oxide and of inflammatory cytokines such as IL-12, IFNg and TNFa may also help to control B. bovis infection (Goff et al., 2001). Control of anaemia development, mediated by haemopoietic system cells, has been suggested to be, along with parasitaemia control, one of the major mechanisms for ‘trypanotolerance’ in B. taurus N’Dama cattle (Traill et al., 1991; Naessens et al., 2002; Murray et al., 2004; Naessens, 2006). At this point, it can be speculated that animals with resistant and intermediate responses against B. bovis infection can also be under these same mechanisms of control.

This was the first report that demonstrates differential B. taurus primary response to B. bovis infection, measured and characterised in large number of individuals from commercial herds, and it demonstrated that naïve Hereford and Aberdeen Angus cattle, breeds predominantly raised in Southern Brazil, vary in response to B. bovis infection. According to Mahoney (1973) only two non-specific factors seem to be importantly associated to babesiosis resistance: age and breed. The experimental animals used here were naïve B. taurus 12–18-month-old heifers born to non-immune dams, i.e., without age and breed non-specific resistance-related factors, therefore the differences reported in cattle response to B. bovis infection are truly due to variations in susceptibility within Hereford and Aberdeen Angus populations.

Young cattle with less than 9 months of age have been reported to have milder B. bovis infections when compared to responses in adults (Mahoney, 1973; Levy et al., 1982; Montealegre et al., 1985; Goff et al., 2001). Maternal antibody was first thought to be the cause of such resistance. Levy et al. (1982) found that a calf sera-antibody independent component was able to control parasite multiplication. Later, Goff et al. (2001) demonstrated that calf serum and splenic cells expressed interleukin (IL)-12 earlier than IL-10. Interleukin-10, an anti-inflammatory cytokine, down-regulates the synthesis of other pro-inflammatory cytokines, like IL-12, IFNg and TNFa, that are essential to build cattle immune response against B. bovis infection.

B. indicus catte and B. indicus × B. taurus crosses have been extensively reported to be more resistant to Babesia infection than B. taurus cattle (Kelley, 1943; Daly and Hall, 1955; Francis and Little, 1964; Francis, 1966; Johnston, 1970; Mahoney, 1973; Johnston et al., 1978; De Vos, 1979; Mahoney et al., 1981; Aguirre et al., 1990; Bock et al., 1997). Callow (1977) even stated that all European breeds raised in Australia seemed to be susceptible to B. bovis. Likewise, B. indicus cattle and their crosses have been extensively reported to be more resistant to tick infestation than B. taurus (Francis and Little, 1964; Francis, 1966; Gomes et al., 1989; Frisch, 1990, 2000; Frisch et al., 2000, to name a few). As most of babesiosis experiments used ticks to challenge cattle with this haemoparasite rather than needle B. bovis inoculation, lower transmission rates through the vector might have decreased B. bovis inoculation results in B. indicus.

Field babesiosis outbreaks are very frequent in Southern Brazil when tick numbers increase in the environment (February–April), causing high mortality among naïve cattle. The standard procedure is to treat all animals to avoid further deaths. An early statement that >50% of mortality rate is frequent in B. taurus naïve cattle during babesiosis outbreaks (Wright, 1991) is in agreement with the results obtained here, where 45% of cattle would really need babsicidal treatment (susceptible individuals). Have farmers had previous information on their animals phenotypes for selection purposes, they would be able to reduce cattle deaths and costs with tick-borne disease treatments. At the same time it would maintain the pathogen in the population, allowing natural immunisation of young cattle against B. bovis.

In order to allow breeding programmes to select cattle based on their responses to B. bovis infection, the different levels of susceptibility to B. bovis infection must be made by phenotype-molecular marker association studies. This is the next necessary step to be dealt with in our future research projects.

5. Conclusions

We have demonstrated that variation in naïve B. taurus cattle primary response against B. bovis infection does exist. Resistant animals showed lower parasitae-mia levels and PCV reductions, however, they were indeed able to build humoral response against the infection.

The behaviour of intermediate animals during infection was very similar to susceptible individuals, however, intermediate animals were able to recover
from babesiosis without the help of specific treatment. Susceptible animals, on the other hand, were unable to recover without babesicidal treatment.

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