

Ranking control options for tropical theileriosis in at-risk dairy cattle in Tunisia, using benefit-cost analysis

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*Deceased. We dedicate this article to the memory of our colleague, Dr Jamila Laarif, a respected Tunisian veterinary microbiologist

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Summary

An economic evaluation of various control programmes against *Theileria annulata* infection was conducted on a sample of 49 Tunisian dairy farms where clinical cases of tropical theileriosis had been recorded during the summer. Indicators of morbidity and the prevalence of infection, as well as production and demographic indicators (recorded in the present survey or taken from secondary sources), were used to rank the potential costs and benefits of various control programmes for tropical theileriosis over a time horizon of 15 years. Three options were considered, i.e. vaccination with a local attenuated cell-line vaccine; partial barn upgrading, based on first roughcasting then smoothing all the walls of the animal premises (inner and outer surfaces); and applying acaricides to control the vector tick population on the cattle.

The most important loss from this disease, representing between 22% and 38% of the overall losses, is the loss in milk yield from carriers of *T. annulata*. Upgrading barns produced the highest mean benefit-cost ratio (1.62 to 3.71), while the ratios for vaccination and acaricides ranged from 0.20 to 1.19 and 0.32 to 0.88, respectively. However, the benefit-cost ratio of vaccination increased (from 1.65 to 5.41), when the costs due to carrier state infection, which vaccination does not prevent, were ignored. Upgrading barns is a sustainable eradication policy against tropical theileriosis, based on a single investment, and is environmentally friendly. This control option should be encouraged by national Veterinary Authorities in regions where tropical theileriosis is transmitted by a domestic endophilic tick.

Keywords

Benefit-cost analysis – Bovines – Control – Economic analyses – *Theileria annulata* – Ticks – Tunisia.

Introduction

Tropical theileriosis is a tick-borne disease caused by *Theileria annulata*, an Apicomplexa protozoan affecting cattle over a wide geographical area that includes three continents (southern Europe, Asia and North Africa). It is

transmitted by *Hyalomma* ticks. In several developing countries, *T. annulata* infection is considered a major threat to the development of the cattle industry. The disease, as well as the carrier state induced by *T. annulata*, causes significant production losses, due to mortality, the costs of treatment and the decline in milk yield and average daily

weight gain (34). As early as the 1920s, Sergent *et al.* (43) stated in Algeria that tropical theileriosis imposed a heavy economic burden.

Theileria annulata infection occurs in Tunisia in two endemic states: endemic stability and endemic instability (7, 13). In endemic stability, there is a high level of infection in a population; however, clinical disease is rare and mainly occurs during the first season of the disease. In endemic instability, only a proportion of the population becomes infected and immune, and clinical cases occur in different age classes and particularly in adult cattle. Endemic instability occurs more frequently in Tunisia (13) and accounts for the majority of clinical cases reported in those regions which are endemic for tropical theileriosis (13).

The state of endemic instability is divided into two endemic situations, according to the presence or absence of disease risk in cows (13, 15). Low endemic instability is characterised by the restriction of disease cases to heifers and bull calves, since all adults have already been exposed to *T. annulata* infection. High endemic stability is closely associated with pure-bred cattle herds and characterised by

a low prevalence of infection, even in older cattle. Cows also form part of the at-risk population.

At present, the control of tropical theileriosis is based on the use of attenuated cell-line vaccines and tick control measures that target the vector ticks (15). Vaccination with attenuated cell-line vaccines is an efficient measure leading to a dramatic reduction in disease incidence (9, 11, 40). In Tunisia, the vector tick for tropical theileriosis, *Hyalomma scupense* (formerly *H. detritum*), is a species that has two hosts and displays both domestic and endophilic behaviour. Immature instars of the tick occur on cattle from September to November, while the adult ticks, which can transmit *T. annulata*, appear on cattle from June to August (2, 43). *Hyalomma scupense* could be practically eradicated by upgrading barns and thus eliminating the ticks' shelter in the free stage of their life cycle. In practical terms, this upgrading could be achieved by roughcasting and smoothing all the interior and exterior walls of the barn (Fig. 1) (7). Alternatively, when applied properly according to an adequate treatment calendar, chemical acaricides sprayed on the cattle could interrupt the transmission of infection and control the vector tick population.

a) Nymphs can easily hibernate in the cracks of a roughcast wall



c) A hibernating *Hyalomma scupense* nymph in the wall



b) Once the wall has been smoothed, neither nymphs nor females can attach themselves to it



d) A *Hyalomma scupense* female laying eggs



Fig. 1

The interior and exterior walls of barns provide shelter for the free stage of the tick's life cycle

Ticks can be eradicated by roughcasting and smoothing these walls to destroy their shelter

Few reliable data are available on the economic performance of the methods currently used to control tropical theileriosis, despite their use in several endemic countries. The production losses due to *T. annulata* infection, and the economic benefits of vaccination, have been estimated in calves with primary infection under conditions of endemic stability in Tunisia (23). However, no economic analysis has been carried out on farms with high endemic instability, in spite of the frequency with which this occurs. It is estimated to affect 76.2% of at-risk farms in Tunisia (13). In this paper, the authors report the results of a cross-sectional survey on 49 dairy cattle farms where clinical cases of tropical theileriosis have been confirmed by routine laboratory diagnostics.

In the absence of other, external factors, tropical theileriosis remains a disease strongly associated with the state of the barns in which the cattle are kept. The barn environment influences the presence and size of the domestic vector tick population, *H. scupense*. Therefore, in Tunisia, control measures for tropical theileriosis are often targeted at farms which have recorded previous cases of clinical disease. A regulation establishing a farm register for all farms in the private sector was recently adopted. The enrolment strategy chosen by the authors for the present study should ensure that the farm sample is large enough to accurately represent the true risks of tropical theileriosis. Since the aim of this paper is to obtain results that represent, as far as possible, the actual general situation of tropical theileriosis in Tunisia, the authors applied a simulation model to the selected farms. The inputs for this model included a range of different variables:

- indicators of morbidity, mortality and infection prevalence recorded in other surveys in Tunisia, with similar epidemiological contexts
- individual production losses taken from secondary sources in Tunisia and India
- demographic data on the Tunisian cattle population.

Similar approaches have been used in other studies on the economic impact of livestock diseases (19, 36).

A benefit-cost analysis was then developed for these farms to assess the predicted benefits of three different control strategies for tropical theileriosis, namely:

- applying acaricides to cattle
- vaccination, using a Tunisian live attenuated vaccine
- upgrading barns.

The aim of this study was to rank these three control options in order to estimate their benefit-cost ratio under epidemiological scenarios that accurately represent the situation in Tunisia.

Materials and methods

Data resources

This survey was carried out during the 2004 summer season (from early July to late August) in the governorates of Sousse and Monastir, in eastern central Tunisia (Fig. 2). Both of these governorates are located in a semi-arid region. The combined population of these two areas is approximately 29,700 head of cattle (4.5% of the total Tunisian cattle population). Some 78.9% of the total number of cattle in the Sousse governorate, and 93.5% of those in the Monastir governorate, are housed on small farms with fewer than 20 females (cows and heifers) (45).



Fig. 2
Locations of the governorates of Ariana, Béja, Sousse and Monastir presented in this 2004 study of control options for tropical theileriosis in Tunisia

Blood samples from clinical cases of tropical theileriosis were collected in ethylene-diamine-tetra-acetic acid (EDTA) tubes by field veterinarians covering the study area and sent to the Parasitology Laboratory at the Centre Régional des Recherches Vétérinaires de Sousse (Tunisia). Here, the presence of *T. annulata* piroplasms was investigated on Giemsa-stained blood smears by standard microscopic examination at 1,000× magnification in immersion oil. Only those animals with typical symptoms of the acute form of tropical theileriosis (lymph node enlargement, anorexia and fever) and positive blood smears with more than 1% parasitaemia were included in the study. Animals presenting blood smears that tested positive for two or more haemopathogens were excluded from the survey.

A questionnaire was used to obtain data from the owners of the infected cattle, including information on herd structure, the age of the animals, and any previous health problems – in particular, clinical cases of tropical theileriosis, treated by field veterinarians. Information was collected on the infected animals, i.e. their:

- breed
- sex
- age
- physiological stage
- clinical signs
- milk yield before and after the clinical episode.

Information was also gathered on the presence of clinical cases of tropical theileriosis over the previous summer. The ages of the animals were ranked according to the number of tick seasons they had experienced: zero, if they were born after August of the preceding year; and one or more if they were born before August of the preceding year (10).

In cattle, *T. annulata* infection occurs in three forms:

- the clinical form, with typical signs of the disease
- the sub-clinical form, with mild fever and enlargement of the lymph nodes
- the carrier state, in which infected animals can transmit the parasite to vector ticks, without signs of disease (15).

All stages of the present study were carried out under the usual veterinary rules of practice for large animals.

Description of the economic analysis

A benefit-cost ratio was estimated with a time horizon of 15 years for the three control options being studied (16, 35, 41):

Benefit-cost ratio (BCR): $BCR = [\sum B_t / (1+r)^t] / [\sum C_t / (1+r)^t]$ where B_t is the benefit at year t , C_t is the cost at year t , r is

the discount rate and t is the number of years from the implementation of the control measure.

A discount was made for both costs and benefits, since they each have a time horizon longer than one year (18, 41). A discount rate corresponding to the nominal interest rate (0.4%) was used in the study. This was calculated as the difference between the nominal interest rate during 2007 (5%), minus the inflation rate during the same period (4.6%) (4). All costs and benefits have been expressed in Tunisian dinars (TND) (at 2007 values) and converted into euros according to the annual average exchange rate of 2007 (TND 1 = €0.6709) (4). The analysis was extended over a period of 15 years.

The baseline scenario corresponds to the absence of any control measures against tropical theileriosis, except specific and adjuvant treatment of clinically infected animals, as detailed below. The effect of the treatment was only considered in terms of disease cost (veterinary expenditure, abortion, milk yield, live weight decrease and mortality) during the disease and recovery phase. Data on these specific indicators are detailed below. Disease incidence and the prevalence of the carrier state considered in this analysis (Table I) are assumed to remain unchanged in the baseline scenario. Based on previous studies, the authors have assumed that clinical cases recorded in this survey will occur on the sample farms roughly every two to six years.

The economic analysis was carried out by comparing the baseline scenario with three control options.

Option 1: vaccination

This strategy consists of vaccinating all the animals in the herd, every two years, with a local attenuated cell-line vaccine, delivered in the field. While there is no cold chain, a specific delivery system is used, which confers a shelf life of at least four days (Table I). The effects of vaccination were estimated by reference to a Tunisian field trial, carried out on more than 2,000 cattle (8). Adverse vaccine reactions were observed in pure-bred lactating cows, but these were mild reactions that faded away without drug use. The cost of a single vaccination (including the price of a single dose plus vaccination fees) was estimated at TND 5 (€2.99). Over a two-year period, the benefits included:

- a decrease of 76% in clinical cases of tropical theileriosis
- a 100% reduction in lethal cases, assuming that all clinical cases were treated.

In contrast with the other two control options, vaccination is expected only to be effective against the occurrence of clinical infection, since it does not eliminate or prevent the

Table I
Parameters used to assess the costs and benefits of control options for tropical theileriosis in the surveyed animal sample

Item	Estimate	Reference
Epidemiological indicators		
Abortion rate in clinical cases	30% to 40%	12, 28
Mortality rate in treated animals	10% to 13.5%	1, 28, Darghouth ^{a)}
Mean percentage of dried-off cows (from September to November)	11.75%	OEP, 2007
Mean month of pregnancy	7th month	Estimated, present study
Infection losses		
Drop of weight gain in treated calves with clinical theileriosis over two months	14.7%	23
Losses in milk yield due to carrier state infection	1.4 litres	44
Market prices		
Value of a new-born calf	TND 400 to 600 (€239.39 to €359.09)	Range in market prices
Value of an adult animal	TND 1,500 to 2,000 (€897.72 to €1,196.96)	Range in market prices
Value of a heifer	TND 2,600 to 2,800 (€1,556.05 to €1,675.74)	Range in market prices
Value of a bull calf	TND 1,000 to 1,500 (€598.48 to €897.72)	Range in market prices
Value of a bull	TND 2,000 to 2,500 (€1,196.96 to €1,496.20)	Range in market prices
Market price of 1 kg live weight	TND 3.5 to 4 (€2.09 to €2.39)	Range in market prices
Mean market price of milk	TND 0.4 per litre (€0.24)	2007 wholesale price
Buparvaquone	TND 2.08 per millilitre (€1.24)	39
Long-acting oxytetracycline	TND 0.05 per millilitre (€0.03)	39
Veterinary consultation fees	TND 15 (€8.98)	CNOMVT, 39
Vaccine characteristics		
Reduction in incidence of clinical disease	76%	M.A. Darghouth ^{a)}
Duration of protection	2 years	M.A. Darghouth ^{a)}
Price of vaccination with the Tunisian live vaccine	TND 5 per injection (€2.99)	23
Parameters used for barn upgrading		
Mean ground surface requested for one adult cow	7 m ²	6
Mean ground surface requested for one calf	4 m ²	6
Mean height of barn walls	3 m ²	Estimated, present study

a) M.A. Darghouth, unpublished data.

OEP: *Office de l'élevage et des pâturages*

CNOMVT: *Conseil National de l'Ordre des Médecins Vétérinaires de Tunisie*

TND: Tunisian dinars

development of the carrier state in vaccinated cattle (7, 10, 14). However, to rank their financial effectiveness, the three control options were compared using the same production-loss parameters.

Nevertheless, if considering vaccination as a separate option, it might be justified to run an additional analysis purely on the costs of clinical cases of tropical theileriosis versus vaccination fees. A total of 633 animals could be

expected to be vaccinated with an overall cost of TND 3,165 (€1,894.19) every two years.

Option 2: upgrading barns by roughcasting and smoothing their wall surfaces

Roughcasting and smoothing all the outer and inner wall surfaces of cattle buildings and cleaning the surrounding areas could aid in eradicating the endophilic domestic vector tick, *H. scupense* (15). This, in turn, would lead to the virtual disappearance of clinical cases of tropical theileriosis in the following year. However, carrier animals would still remain on the farm until they died or were sold or culled. The authors assumed that these carrier animals would gradually disappear within two to six years. During this time, the authors estimated a constant average linear decrease each year in the proportion of carriers. The mean cost of roughcasting and smoothing the interior and exterior walls was determined as:

$$2Proughcast, \sum_{i=1}^n n_i h_i w_i$$

where *Proughcast* is the cost of one square metre of roughcast; *n* is the number of animals per age category; *h*, the height of the wall and *w* is the width of the surface needed per age category. The cost must then be multiplied by two, since both the inner and outer walls must be treated.

The yearly costs of roughcasting were estimated by considering the yearly costs of maintenance and the yearly decrease in the proportion of carrier cows. The benefits of roughcasting were evaluated each year over a time horizon of 15 years. These benefits were due to the eradication of clinical cases from the farm one year after roughcasting, and to the gradual culling of carrier cows at the end of their useful life, between the second and sixth year after upgrading the barns. The costs of culling were estimated as the difference between the market price of a heifer and the price of the culled cow.

Opportunity costs for cleaning the barns and their surroundings were not considered in the present study, since this simple task could be carried out by the farmers themselves, as a basic practice of good farming management.

Option 3: applying acaricides

This control option consists of spraying the cattle with an acaricide appropriate to the biology of the adult and immature stages of the vector tick (1, 46). The protocol adopted here aims to stop *T. annulata* transmission by:

- preventing infestation with adult ticks by spraying a Deltamethrin solution at 50 parts per million (Butox®

50‰, Intervet) over the animal's entire body surface every two weeks from June to August, i.e. seven treatments per summer. This protocol, which does not require a withdrawal period for milk under Tunisian regulations, has been shown to completely protect cattle against infestation with *Hyalomma* ticks (M. Kilani & A. Bouattour, unpublished data);

- interrupting the engorgement of immature stages of the tick by spraying acaricides onto the animals every three weeks from September to November. The authors have chosen to use Amitraz (Tactic®, Intervet), at a dilution of 0.25%, since this is the cheapest treatment, taking into account both the cost of the acaricide and the length of the withdrawal period (24 h only). The model assumes that farmers can save the milk collected over the withdrawal period to feed their calves, instead of using artificial milk. From September to November, the mean proportion of dried-off cows on small farms in Tunisia was estimated by the Office of Livestock and Pasture (unpublished data) to be 11.75%.

To estimate the opportunity costs of acaricide application, the authors estimated both the time needed to treat adult cattle and calves and the required volume of diluted acaricides by modelling acaricide application on the École Nationale de Médecine Vétérinaire farm (Sidi Thabet, Tunisia). In this model, the authors assume that the protocol described above will entirely prevent the occurrence of clinical theileriosis, and progressively eradicate carrier animals. The costs of this control option were estimated by adding the annual acaricide treatment costs to the remaining number of carrier cows, using the same approach as in the upgrading barns option. After culling all carrier animals at the end of their useful lives, the only cost of this control strategy is that of applying the acaricide. The benefits correspond to the savings generated by eradicating clinical cases and progressively culling carrier cattle. At the end of the sixth year, the costs from both clinical cases and carrier animals should be completely eradicated.

Calculating economic costs

To estimate the economic impact of tropical theileriosis, the authors collected a list of both infection and prevention costs. Data on several indicators were gathered from the literature, from market prices or were estimated by the authors. Market prices can vary due to many factors: the time of year, the region, the particular market, the balance between supply and demand, etc. For this reason, these prices were presented as a range (minimum and maximum) (Table I).

Losses due to clinical cases of theileriosis were estimated by adding the costs of treatment and veterinary fees, the

production losses (decreases in milk yield and live weight, abortions and reduced fecundity) and the losses caused by mortalities.

Treatment expenditures

The current therapeutic protocol used by field veterinarians is based on a single intramuscular injection of Buparvaquone, used as a generic speciality (Teldex ND, Medivet), at the conventional dose of 2.5 mg/kg, added to an intramuscular injection of long-acting oxytetracycline (Oxy-keel 20 L.A., ND, Kela), at the conventional dose of 20 mg/kg. The cost of the full treatment was estimated for each age category by adding the veterinary fees to the price of the two drugs.

Decrease in milk yield

Data on milk production before and after the disease occurrence were obtained from the farmers for each clinical case. The maximum daily losses in milk yield occur within the five days following diagnosis and represent 20% of the total losses, estimated over a period of 30 days. After this 30-day period, dairy production returns to normal (33). The daily drop in milk yield was determined by taking the difference between the milk yield before disease occurrence and the yield on the day of veterinary consultation. This figure was then multiplied by five (the number of days on which maximum production losses occur) and then again by five, to calculate the total loss over a period of 30 days. This is summarised in the following formula:

$$5 \times 5 \times P_{\text{milk}}, \sum_{i=1}^n \text{Milk}_{\text{before}} - \text{Milk}_{\text{after}}$$

where P_{milk} is the price of one litre of milk and $\text{Milk}_{\text{before}}$ and $\text{Milk}_{\text{after}}$ are the milk yield before and after the occurrence of the disease.

Decrease in live weight

Losses due to the decrease in live weight were considered only for calves, including bull calves. These losses were estimated at an average reduction in weight gain of 14.7% (23). In recovering adult animals, compensatory gain occurs and the original weight is regained (42). The mean losses due to live weight decrease were estimated as:

$$0.147P_{\text{weight}}, \sum_{i=1}^n w_i$$

where P_{weight} is the price of one kilogram of live weight and w_i is the estimated live weight per infected animal.

Abortion and reduced fecundity

The risk of abortion at an advanced stage of pregnancy ranged between 30% and 40% (12, 28). The average daily losses (in milk yield, and the decrease in the number of calves per lifespan) for a cow that has aborted have been estimated at TND 5 (€2.99) (F. Ouali, unpublished data). Losses due to abortion were calculated by adding the price of a new-born calf to the losses mentioned above:

$$M_{\text{aborted}} (C + 5 \sum_{i=1}^n P_{\text{days}_i}),$$

where M_{aborted} is the total number of aborted cows; C is the market price of one newborn calf and P_{days_i} is the number of pregnancy days of the cow i .

Mortality

In the Béja region (the governorate of Béja borders both sub-humid and humid regions), Darghouth *et al.* (12) reported a mortality rate of 10% for clinical cases of tropical theileriosis. In the Jedeida region (in the Ariana governorate, a semi-arid region [Fig. 2]), the mortality rate was estimated at 13.5% (28). The cost of mortality was estimated for each category group by considering the market price of one kilogram of live weight.

The percentages of carrier cows over more than two seasons of tropical theileriosis used in the study were taken from two previous serological surveys conducted in Sidi Thabet (Ariana governorate) and Amdoun (Béja governorate), on samples from farms representative of the study regions. The autumn seroprevalence in cattle, determined by indirect fluorescent antibody test to *T. annulata* schizont antigen, were estimated at 24.3% in Sidi Thabet (semi-arid sub-stratum) in 1996 (10), 38.4% in the Amdoun region (sub-humid sub-stratum) in 2000 and 8% in Amdoun in 2006 (10, 26).

The persistence of anti-schizont antibodies for long periods could be related to the development of a carrier state or to repeated infections (20, 38). However, since the animals were tested in autumn, after the disease transmission season, their seropositive status is more probably associated with the carrier state. Since seroprevalence in adults is expected to be an important determinant of the outcome of this economic analysis, a sensitivity analysis was considered for this parameter.

Carrier animals do not show any clinical signs; hence losses in this group are exclusively due to a fall in milk yield. The milk yield decrease in carrier cows has been estimated at 1.4 l per day, over a period of three months, in cross-bred cattle in India (44). Considering the standard lactation period of 305 days (21), the total mean losses in milk yield due to tropical theileriosis per lactating carrier

cow could then be extrapolated to 420 l. The mean proportion of dried-off cows through the year was estimated by the Office of Livestock and Pasture (unpublished data) to be 11.75%.

Based on previous observations and data reported by Darghouth (7), which indicated that, on average, individual animals are exposed to new infections of *T. annulata* every four years, in a region with high endemic instability, the authors assumed that clinical tropical theileriosis would occur at similar intervals on the farms under study. Accordingly, the economic losses caused by clinical cases during the summer of 2004 would only represent one quarter of the annual losses if the farms were not regularly sampled for the presence of clinical cases of tropical theileriosis. This interval between re-exposures was also subject to a sensitivity analysis, detailed below.

Sensitivity analysis

Owing to a lack of information about shape and data distribution, triangular distributions (with minimum, most likely and maximum values) were adopted for the epidemiological and economic indicators used to run the analyses (17, 30).

Autumn seroprevalences were obtained from three previous multicentric surveys carried out on herds with endemic instability for tropical theileriosis. These seroprevalences were used in the present study as estimators of the carrier state (7, 13, 26). The farms were ranked depending on their percentage of carrier animals, and data were fitted to the best function using the add-in Bestfit® (Palisade Corp., New York, USA) for Microsoft® Excel® (Microsoft Corp., Seattle, WA, USA). A sensitivity analysis (24) was then carried out by varying the proportion of carrier cows from 8.03% to 38.41% of the existing cows for the distribution function of this variable, fitted with the Bestfit® add-in software (7, 13, 26).

Because of the variable dependency between the periodic occurrence of clinical cases and the number of years over which the carrier cows were culled, on the one hand, and various other economic variables on the other, different runs of sensitivity analyses were conducted. Twenty-five scenarios were constructed, representing a combination of two sets of five scenarios (17):

- an occurrence of clinical cases every two to six years
- the culling of carrier animals within two to six years.

The time of culling depended on the age of the animal: a standard economic lifespan under Tunisian conditions is 6.44 years (25).

The sensitivity analysis was carried out for all 49 farms using the 25 scenarios. Five thousand iterations were run

in the model, using @risk® (Palisade Corp., New York, USA) for Microsoft® Excel® (Microsoft Corp., Seattle, WA, USA). As a result of the high number of outputs, minimum 5th percentile and maximum 95th percentile values were presented for each scenario.

Statistical analyses

An Excel for Windows® spreadsheet was used to construct the @Risk model. To test the significance of the various simulated economic indicators for the three control policies, a Tukey test for mean comparison was undertaken, using the SPSS 10.0 for Windows software package. A probability below 0.05 was used as a cut-off value between statistically significant and non-significant results (29).

Results

Epidemiology and clinical signs

Throughout the survey, a total of 100 suspected cases of clinical tropical theileriosis were received in the laboratory. Only 49 animals from 49 herds (one animal from each farm) which presented significantly positive blood smears to *T. annulata* alone were included in the survey (with parasitaemia above 1%). These farms had a total of 633 cattle and their demographic characteristics are presented in Table II. The overall morbidity from tropical theileriosis within the cattle population under study reached 7.74% (49/633). The other cases were either non-infected animals or those with mixed infections. (Cattle with mixed infections were dropped from the study to avoid over-estimating losses caused by *T. annulata* infection alone.) Previous clinical cases of tropical theileriosis during the preceding four years were reported from only 45% (22/49) of the farms, with a low frequency of disease cases. The majority of the affected herds (53%) were composed of fewer than ten animals. Almost all the diseased animals (92%) were exotic, pure-bred cattle (Holstein and Friesian). Clinical cases were mainly recorded in animals

Table II
Number of animals on 49 farms in a 2004 study of control options for tropical theileriosis in Tunisia

Statistical estimates	Category of animal		Total
	Adult cattle	Calves	
Minimum	6	6	–
Maximum	13	12	–
Mean (SE)	8.12 (10.3)	4.8 (6.4)	12.9 (15.4)
Total number	398	235	633

SE: standard error

with more than one summer season (84%; 41/49), and 55% (27/49) of such cases occurred in animals with three or more tropical theileriosis seasons. Animals born on the owners' farms represented 57% (28/49) of the diseased animals. The mean age of the diseased animals was 4.6 years over the whole sample and 5.3 years among adults. The majority of the cases (43/49) occurred in cows (88%). Only six cases were recorded in males, of which two were aged less than one year. Furthermore, 84% (41/49) of the diseased animals were lactating cows more than three years old.

Hyporexia, a fall in milk yield and fever were the most frequently observed signs, and were present in 84%, 76% and 65% of the animals, respectively. Farmers also consider these to be the most important signs of tropical theileriosis, justifying veterinary consultation whenever they are observed.

Disease costs

The simulated yearly mean costs due to clinical cases of tropical theileriosis and the carrier state could vary from TND 60.05 to TND 77.99 (€35.94 to €46.68) per cow (Table III). The most significant losses are caused by the drop in milk yield among carrier cows, which represents between 22% and 38% of the overall losses (Table IV).

The mean annual veterinary costs per clinical case were estimated at TND 64.32 (€38.50). Seven cows were pregnant, i.e. 17% (7/41) of the diseased cows. Dried-off cows (corresponding to cows in late pregnancy in this survey) represented 7% (3/41) of the total number of cows. The costs of abortion in pregnant cows were estimated to range between TND 48.60 and TND 51.40 (€29.09 to €30.76).

Table III
Fifth and 95th percentiles of simulated annual infection costs of tropical theileriosis in Tunisian dinars per infected or diseased animal, considering sensitivity analysis outputs

Cost	5th percentile in TND	95th percentile in TND
Milk yield losses in carrier cows infected with <i>Theileria annulata</i>	106.34 (€63.64)	245.83 (€147.13)
Mortality due to tropical theileriosis	157.86 (€94.48)	187.68 (€112.33)
Milk yield losses in diseased cows	81.43 (€48.73)	81.43 (€48.73)
Treatment of clinical cases of tropical theileriosis	64.32 (€38.50)	64.32 (€38.50)
Abortion in clinically infected females	48.60 (€29.09)	51.40 (€30.76)
Reduced weight gain in calves and bulls	14.21 (€8.50)	17.64 (€10.56)

TND: Tunisian dinars

Table IV
Fifth and 95th percentiles and mean of the estimated costs (in Tunisian dinars) due to *Theileria annulata* infection

Loss	5th percentile	95th percentile	Mean
Milk yield losses in carrier cows	22.49	37.92	29.88
Mortality costs	33.39	28.95	31.53
Milk yield losses due to clinical cases	17.22	12.56	14.85
Treatment costs	13.61	9.92	11.73
Losses due to abortion	10.28	7.93	9.12
Reduction in weight gain	3.01	2.72	2.88

Total mean yearly milk yield losses were estimated at TND 10.03 (€6.00) per cow. Estimated overall losses due to live weight decrease per bull calf were thought to range between TND 14.21 (€8.50) and TND 17.64 (€10.56), a total of €416.72 to €517.42 (Table III).

The fitting curve of the three seroprevalence simulations with Bestfit® led to an extreme value distribution (42.233; 10.235). The number of carrier cows was estimated (@risk risk analysis and simulation add-in) to vary between a minimum of 20 and a maximum of 119. Milk yield losses per cow were estimated to vary from 18.8 to 184.7 l of milk over a standard lactation of 305 days.

Control programme costs

Vaccination

The price of a single cell-line vaccine was estimated at TND 5 (€2.99) (23).

Upgrading barns by roughcasting and smoothing exterior and interior wall surfaces

The mean wall surface area to be roughcast at each farm was estimated at 277.7 m². The total cost for the roughcast of the 49 infected farms was TND 104,621.17 (€62,613.67), with a mean cost of TND 2,135.13 (€1,277.83) per farm. The authors assumed that the residual value of the roughcast after 15 years was 50% of its original value.

Spraying acaricides

A single acaricide treatment for one adult cattle beast would require approximately seven litres of diluted acaricide, which would take 3.52 minutes of labour to apply. The same treatment would use three litres for each calf and take 2.30 minutes of labour to apply. The quantity of acaricide and its cost per age category are presented in Table V. The total mean cost of acaricide control was estimated at TND 430.06 (€257.38) per treated farm.

Table V
Cost of acaricide tick control in Tunisian dinars

Season	Age category	Molecule	Cost per treatment in TND ^(a)	Acaricide cost in TND ^(a)	Labour cost in TND	Price of discarded milk in TND ^(b)
Summer	Calves	Deltamethrin	0.18 (€0.11)	302.05 (€180.77)	62.84 (€37.61)	–
	Adult cattle	Deltamethrin	0.43 (€0.26)	1,193.64 (€714.37)	164.60 (€98.51)	–
Autumn	Calves	Amitraz	0.15 (€0.11)	173.42 (€103.79)	44.88 (€26.86)	–
	Adult cattle	Amitraz	0.34 (€0.21)	685.33 (€410.16)	117.57 (€68.62)	22,526.80 (€13,481.84)

a) The costs of labour and discarded milk are considered in the calculation

b) Rather than being discarded, this milk could be used for feeding calves. Its annual mean value per farm was estimated at 112.8 Tunisian dinars (€67.51)

TND: Tunisian dinars

Indicators of economic efficiency

The sensitivity analysis was carried out by modifying several costs and epidemiological indicators. For the three tropical theileriosis control policies considered:

- the benefit-cost ratios are inversely proportional to the periodicity of the clinical cases
- the benefit-cost ratio is higher when the maximum values of infection costs are considered.

The benefit-cost ratio of roughcasting is higher than that for vaccination or acaricide application ($p < 0.001$). Vaccination is beneficial if using the maximum values of the benefit-cost ratio, and if the periodicity of clinical cases is two years.

However, since vaccination with an attenuated cell line does not affect the occurrence and persistence of carrier state infections, it is more useful to ignore the costs of the carrier state when assessing this option. When this approach was used, the predicted benefit-cost ratios of vaccination were always higher than one, for all the scenarios envisaged in the present study (Fig. 3).

The 5th and 95th percentiles of both benefit-cost ratios of the three control options were compared with the Tukey test. All the comparisons were statistically significant, except in the case of vaccination versus acaricide application (5th and 95th percentiles). The highest benefit-cost ratio was noted for roughcasting ($p < 0.001$). This control policy is not sensitive to the costs or epidemiological indicators described above, and can be implemented when any of the proposed scenarios occurs on a farm of endemic instability.

The benefits of acaricide application did not outweigh the costs under any of the scenarios.

For all three control options, the benefit-cost ratios were worst if a scenario with a periodicity of six years for clinical cases was envisaged, with a six-year culling period. The best economic indicators were expected with a periodicity of clinical cases of two years and the culling of carrier cows after two years.

Discussion

This study was undertaken in a region of Tunisia (the governorates of Sousse and Monastir, eastern central Tunisia) where high endemic instability could be expected to be dominant, according to the high number of tropical theileriosis cases annually reported in Holstein and Friesian cows. A parasitology laboratory is sited in Sousse (Centre Régional des Recherches Vétérinaires de Sousse), facilitating confirmation of clinical cases of tropical theileriosis. The typology of the distribution of clinical

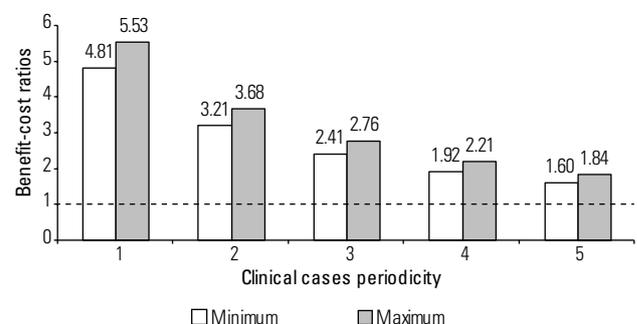


Fig. 3
Benefit-cost ratios of vaccination to control tropical theileriosis in Tunisia, considering the minimum and maximum overall values obtained by sensitivity analysis

This analysis was carried out considering exclusively those losses due to clinical cases of disease. Dotted line: threshold value (indifference point of decision-making where the benefits are equal to the costs)

cases among age categories (41 cows/49 diseased animals) and the breed characteristics (92% of clinical cases occurred in exotic dairy breeds) of the surveyed farms are indicative of the dominance of high endemic instability, as observed in other endemic regions of Tunisia (7, 13).

The majority of reported clinical cases occurred on farms with a mean number of 13 animals. Similar results were also reported in previous surveys in Tunisia (12), confirming that tropical theileriosis is principally a disease of small farms, whose owners either do not have the knowledge or the resources to improve the state of their barns to eliminate the domestic vector tick, *H. scupense*.

Previous cases of clinical theileriosis have only irregularly been reported by these owners. Since such previous cases were identified on only 45% (22/49) of the farms, this could reflect the long periodicity of the disease, due to the small number of animals per herd and limited infection risks in the high endemic instability state (7). The authors assumed a disease periodicity of two to six years in the farms under study. Accordingly, the corresponding predicted incidence should vary between 1.29% and 3.87%, reaching values very similar to those reported in longitudinal surveys on endemic instability in Tunisia (7, 13). The present study was conducted on farms with confirmed cases of tropical theileriosis, to provide a population of cattle at true risk of this disease. As explained earlier, several epidemiological, demographic and production indicators, taken from the present survey or extrapolated from secondary field sources in Tunisia and, in one case, from India, were applied to the cattle sampled here. This approach was used to design epidemiological scenarios representative of the Tunisian disease situation and aimed at assessing the financial effectiveness of various control options for tropical theileriosis.

The predicted overall losses due to *T. annulata* infection were estimated to range from TND 60.05 to TND 77.99 (€35.94 to €46.68) per cow. The overall costs of treatment of clinical tropical theileriosis were estimated to reach TND 64.32 (€38.50) per diseased animal, totalling between 10% and 14% of the overall losses. These expenses were dominated by drug costs, particularly those of Buparvaquone.

Although they are already significant, the overall costs of *T. annulata* infection estimated in this study are probably under-estimated, due to intangible losses (i.e. the impact of tropical theileriosis on the welfare of cattle and their owners; social problems due to falls in income caused by tropical theileriosis and increased reliance on imported animals and semen), and also to the exclusion from the present survey of mixed infections, i.e. of *T. annulata* with *Babesia* spp. or *Anaplasma marginale*, two other tick-borne pathogens infrequently reported in the study region (data not shown). These mixed infection cases were not

considered, partly because of the lack of data on their combined impact on production and partly because of the difficulty of assessing their respective contributions to disease and production losses. However, it is important to note that, even if mixed infections occur at an appreciable level, these under-estimations do not affect the significance of the study's conclusions and their relevance for animal health decision-makers.

In India, Minjaw and McLeod (34) evaluated the cost of treatment at US\$4.55 (TND 6.01; €3.60). This relatively lower treatment cost is probably due to the categories of treated cattle (predominantly calves in India) and the characteristics of their breeds (less heavy animals), as well as the cheaper costs of labour and drugs.

Losses in milk yield from clinically infected cows were estimated by comparing milk yields reported by the farmers during the five days before and after the occurrence of the disease. These losses have been estimated at TND 81.43 (€48.73) per diseased cow, corresponding to a drop of 203 l in milk yield. Such high losses emphasise the importance of early diagnosis and treatment of clinical cases of tropical theileriosis to reduce its economic impact. However, the potential losses caused by lactating cows being in the carrier state appear to be the most important. These have been estimated, using data available in the literature (44), to range from 22% to 38% of the overall costs evaluated on individual farms, according to the prevalence of infection. As a result of their potential significance, these losses should be systematically evaluated for the predominant cattle breeds and prevailing epidemiological contexts in Tunisia. Combining the sum total of milk losses caused by both the carrier state and the recovery phase of clinical theileriosis leads to significant overall falls in lactation: a fact which highlights the considerable importance of this disease in dairy cattle.

Tropical theileriosis in Tunisia could be controlled by any of these strategies:

- controlling the vector tick, *H. scupense*
- vaccinating with a Tunisian attenuated cell-line vaccine (7, 9, 13)
- upgrading barns, by roughcasting and smoothing exterior and interior wall surfaces and cleaning the surrounding areas, thus providing a more hostile environment for the free instars.

The purpose of this study was to measure the potential benefit-cost ratio of each of these control measures.

Upgrading barns produced the best benefit-cost ratio when all the losses caused by *T. annulata* were taken into account (Table VI). This control option appears consistently beneficial, with a benefit-cost ratio always higher than one,

Table VI
Benefit-cost ratios of control options against tropical theileriosis, considering the 5th and 95th percentiles and the mean of the sensitivity analysis

Control option	5th percentile	95th percentile	Mean
Partial upgrading of barns	1.62	3.71	2.49
Vaccination	0.20	1.19	0.51
Acaricide	0.32	0.88	0.54

even for the lowest infection prevalences considered in the present simulation. In reality, this ratio is probably even higher, since roughcasting also improves the general hygiene of the barns and reduces the impact of other diseases (e.g. infectious disease, lameness, mastitis). A similar trend in results was also observed in calves at risk of primary infection with tropical theileriosis on farms with endemic stability (22).

The comparative economic advantages of roughcasting, despite its higher implementation cost, are due to the eradication of the vector tick and thus the elimination of milk yield losses associated with the carrier state and with the recovery phase after treatment for the disease. The effectiveness of equivalent wall treatments is well illustrated by the absence of the infection in modern Tunisian cattle barns.

Vaccination was modelled using real data from actual studies maintained over at least two years (7), considering only the decrease in financial losses due to the clinical form of the disease. The attenuated cell-line vaccine is effective only against disease occurrence; it has no noticeable effect against the carrier state. In Turkey, the price of a single vaccination against tropical theileriosis is TND 9.50 (€5.69) (T. Karagenç, unpublished data). This is higher than the estimate used in this study, since the Turkish vaccine requires the use of a cold chain, which can add as much as 30% to its market price (3).

Since vaccination does not eradicate *T. annulata* infection, a partial budgeting analysis was carried out by estimating its benefit-cost ratio without considering infection losses due to the carrier state. This evaluation predicted a favourable benefit-cost ratio for all the envisaged scenarios, prompting the authors to recommend vaccination, especially when eradication of tropical theileriosis infection cannot be achieved, and/or the progressive upgrading of barns until the infection has effectively been eradicated. Mukhebi *et al.* (37) found similar benefit-cost ratios for various immunisation strategies against East Coast fever among grade and zebu cattle, when losses due to the carrier state were not taken into account. Morzaria *et al.* (36) have also shown that immunisation against East Coast fever is beneficial when the incidence of clinical cases is high (76 out of a cattle population of 160) with a long exposure period (nine months).

Of the three control options considered in this study, vaccination appears to be the most generally acceptable and, for this reason, could easily be implemented on the target farms (M.A. Darghouth and M. Gharbi, unpublished data).

As a result of the low tick burden on farms in a state of endemic instability (three to 50 ticks per animal) (31), the authors suggest chemical tick control as a prophylactic option, which could potentially lead to the interruption of disease transmission and the eradication of vector ticks. Veterinary Services also frequently recommend this control measure on small dairy farms where the barns have not been upgraded. Accordingly, the authors propose a strategy of acaricide application to prevent:

- adult ticks attaching themselves to cattle during the summer by using Deltamethrin at intervals corresponding to its remnant activity
- the detachment of engorged nymphs from the animals by using Amitraz every three weeks during the autumn.

The authors hypothesise that the alternative use, over 15 years, of the two molecules belonging to the distinct acaricide families will prevent the occurrence of resistance in the vector tick. Accordingly, in the present analysis, the authors have not addressed the development of acaricide resistance, which has never been reported in Tunisia.

In the authors' analysis, controlling ticks with acaricides is not beneficial; first because of the milk withdrawal associated with the application of Amitraz and, secondly, the cost of the acaricide. It is also important to note that chemical acaricide control of tropical theileriosis will certainly remain limited in practice, due to its low acceptability and poor compliance by animal owners (5, 27, 33), and also to its negative ecological impact.

The benefit-cost ratio approach adopted by this study could also be adapted to other North African farms, using the appropriate infection exposure and economic indicators. The economic importance of tropical theileriosis is emphasised by the losses it is predicted to induce in strategic outputs such as milk and meat. This is a typical example of an African disease acting as a constraint to farm profitability and to national self-sufficiency in meat and milk. The potential benefits of a sustainable tick vector eradication programme involving the upgrading of barns demand serious consideration of this control option, in addition to vaccination with *T. annulata* attenuated cell-lines. It would also be valuable to pursue other sustainable approaches that could interfere with the transmission dynamics of *T. annulata*, such as anti-tick vaccines. The combination of these control measures within an integrated strategy will probably represent the way forward for effective prevention of tropical theileriosis in the Tunisian and North African context.

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Competing interests

The authors have declared that no competing interests exist. ■

Classement des options de lutte contre la theilériose tropicale dans des élevages bovins laitiers à risque en Tunisie, en utilisant une analyse coûts-bénéfices

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Résumé

Plusieurs programmes de lutte contre *Theileria annulata* ont fait l'objet d'une évaluation économique en Tunisie, portant sur un échantillon de 49 élevages bovins laitiers ayant enregistré des cas cliniques de theilériose tropicale. Les coûts et les avantages potentiels, à un horizon de 15 ans, de plusieurs programmes de contrôle de la theilériose tropicale ont été comparés en utilisant des indicateurs de morbidité et de prévalence de l'infection, ainsi que des indicateurs de production et démographiques (relevés durant l'étude ou empruntés à des sources secondaires). Trois options de lutte ont été envisagées, à savoir : la vaccination avec un vaccin vivant atténué produit localement ; la mise aux normes des locaux d'élevage en appliquant un crépi et en lissant les surfaces intérieures et extérieures des murs des locaux d'élevage ; l'application d'acaricides afin de contrôler la population des tiques vectrices parasitant les bovins.

La baisse de la production de lait chez les vaches porteuses de *Theileria annulata* représente la part la plus importante (entre 22 % et 38 %) des pertes totales induites par ce parasite. La mise aux normes des locaux d'élevage était l'option présentant en moyenne le meilleur rapport coût-bénéfice (de 1,62 à 3,71), alors que la vaccination et l'application d'acaricides présentaient un rapport coût-bénéfice de 0,20 à 1,19 et de 0,32 à 0,88, respectivement. Néanmoins, le rapport coût-bénéfice de la vaccination augmentait (de 1,65 à 5,41) si l'on ne tenait pas compte des coûts induits par l'infection relevant de l'état de portage asymptomatique, contre laquelle la vaccination ne protège pas. La mise aux normes des locaux d'élevages constitue une stratégie d'éradication durable contre la theilériose tropicale, qui ne nécessite qu'un seul investissement. Les Services vétérinaires nationaux devraient encourager cette option de lutte dans les régions où la theilériose tropicale est transmise par une tique endophile domestique.

Mots-clés

Analyse coût-avantage – Analyse économique – Bétail – Bovin – Prophylaxie – *Theileria annulata* – Theilériose tropicale – Tique – Tunisie – Vache laitière. ■

Análisis de la relación costo-beneficio para jerarquizar distintos métodos de lucha contra la theileriosis tropical en vacas lecheras tunecinas expuestas al parásito

M. Gharbi, A. Touay, M. Khayeche, J. Laarif, M. Jedidi, L. Sassi & M.A. Darghouth

Resumen

Los autores describen un proceso de evaluación económica de distintos programas de lucha contra la infestación por *Theileria annulata* a partir de una muestra de 49 explotaciones tunecinas de producción lechera en las que se habían registrado casos de theileriosis tropical durante el verano. Para establecer una clasificación de los eventuales costos y beneficios de distintos programas de control en un horizonte temporal de 15 años se utilizaron indicadores de morbilidad y la prevalencia de la infección, así como indicadores de producción y demográficos (calculados para el estudio o tomados de otras fuentes). Se examinaron tres posibles métodos operativos de lucha: administración de una vacuna elaborada con un linaje celular local atenuado; mejora parcial de los establos, revocando y alisando todas las paredes (superficies interiores y exteriores); y aplicación de acaricidas para controlar las poblaciones de garrapatas que son el vector de transmisión al ganado.

De todos los prejuicios que acarrea la enfermedad, el más importante es la caída de la producción lechera en las vacas portadoras de *Theileria annulata*, que representa entre un 22% y un 38% del total de las pérdidas causadas por el parásito. La mejora de los establos deparó el mejor índice promedio entre beneficios y costos (1,62 a 3,71), mientras que la vacunación y el uso de acaricidas arrojaron cocientes de 0,20 a 1,19 y de 0,32 a 0,88, respectivamente. El índice correspondiente a la vacunación, sin embargo, aumentaba (de 1,65 a 5,41) si en el cálculo se obviaban los costos ligados a la presencia de animales únicamente portadores, parámetro sobre el cual no incide la vacunación. La mejora de los establos es un método sostenible de erradicación de la theileriosis tropical, que exige una inversión única y no tiene consecuencias negativas para el medio ambiente. En las regiones donde la enfermedad se transmite por una garrapata doméstica endofílita, las autoridades veterinarias deberían alentar este método de lucha.

Palabras clave

Análisis económico – Análisis de la relación costo-beneficio – Bovinos – Control – Ganado lechero – Ganado vacuno – Garrapata – *Theileria annulata* – Theileriosis tropical – Túnez.



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