Haemoparasitic diseases of bovines*

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Summary: The various aspects of the haemoparasitic diseases of bovines, with the exception of trypanosomes, are briefly discussed. These diseases have a global distribution and are transmitted by ticks, whereas anaplasmosis is also transmitted by blood-sucking flies.

Babesiosis is caused by Babesia divergens, B. bovis, B. bigemina, B. major, B. ovata and B. occultans. Babesia bovis is the most pathogenic species followed by B. bigemina. Babesia beliceri and B. jakimovi have been described from the USSR.

Theileriosis with a high mortality is caused by T. parva and T. annulata; T. orientalis, T. tauronagi and T. mutans are not pathogenic or only mildly so. T. velifera is apathogenic.

Heartwater is caused by Cowdria ruminantium and anaplasmosis by Anaplasma marginale.

The economic importance of tickborne diseases is considerable, but there is a need for good cost-benefit analyses.

The epizootiology is briefly discussed. Various factors such as climate and vegetation are important in the distribution of the tick vector. Enzootic stability, based on many factors, is widespread.

Control of tickborne diseases is based on tick control, vaccination, treatment with antibiotics or chemotherapeutic drugs, and the introduction of tick resistant animals.

Exotic cattle are very susceptible to tickborne diseases.


INTRODUCTION

This review of the haemoparasitic diseases of bovines (with the exception of trypanosomes) is based on the submitted country reports. It is supplemented by references from the literature, in order to place the reports in a broader perspective and to indicate new trends.


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Haemoparasitic diseases have a global distribution, stretching from the polar circle to the equator. This is due to the fact that their vectors, ticks and blood-sucking flies, also have a global distribution.

Some of the haemoparasitic diseases are caused by rickettsiae and there is general agreement that anaplasmosis is caused by two species: one is the virulent *Anaplasma marginale*, the other the mild *A. centrale*. Heartwater, another rickettsial disease, is caused by *Cowdria ruminantium*. Apathogenic or mildly pathogenic rickettsial parasites, like *Eperythrozoon* and *Ehrlichia* have a world-wide distribution. Locally pathogenic species (e.g. *Ehrlichia ondiri* and some strains of *E. bovis*) have been reported, but will not be considered further here.

Haemoparasitic diseases such as theileriosis and babesiosis are caused by protozoa. Some confusion exists about the names of the aetiological agents causing these diseases. At a meeting such as this, where different names have been used in the reports for the same aetiological agent, it is therefore imperative to reach an agreement about the aetiology of the diseases we are discussing.

### AETIOLOGY

Classification of *Babesia* and *Theileria* species is based on the following criteria:

— Morphology of the parasite in the red blood cell, lymphocyte (for *Theileria*) and tick vector.
— Tick vector responsible for their transmission.
— Host in which the parasite is found.
— Severity of clinical symptoms.
— Localisation of the parasite in the various organs.
— Cross-protection or its absence between two species.
— Antibody titres, measured in different serological tests, using homologous and heterologous antigens.

Useful as these criteria may be, they are by no means fixed and have led to great confusion at the species level. It is beyond the scope of the present article to discuss in detail the advantages and disadvantages of the different classification criteria.

The reader is referred to the review article by Hoyte (1976) for the different aetiological agents of *babesiosis*.

Since he wrote his review, three or perhaps four new species in cattle have been described, e.g. *B. ovata* by Minami and Ishihara (1980) mentioned in the reports of South Korea and Taiwan. *B. occultans* was described from South Africa (Gray and de Vos, 1981). Although not mentioned in the report of the USSR, Krylov (1981) also recognises *B. beliceri* as a separate species. He regards *B. jakimovi* described by Nikolski et al. (1977) from Siberia as identical with *B. bigemina*.

In addition Hoyte (1976) lists:

— *B. bovis*, with the junior synonyms of *B. argentina*, *B. berbera* and *B. colchica*. The report from the USSR still uses the name *B. colchica*. So far no serological comparative studies have been done with *B. colchica* and the other three species.
— B. major.
— B. bigemina.
— B. divergens.

Uilenberg (1981), Uilenberg et al. (1982) and Morel and Uilenberg (1981) made the following aetiological classification of theileriosis:

— T. parva, with the lawrenci and bovis types, causing a severe disease in cattle in southern and eastern Africa.

— T. mutans, transmitted by the African Amblyomma species, causing mild or no disease in cattle. Through ticks, it has been introduced from the mainland of Africa into Madagascar and the Caribbean area.

— T. velifera, a non-pathogenic species, which has the same distribution and vectors as T. mutans.

— T. taurotragi, an African parasite of the eland antelope (Taurotragus oryx), which is also infective to cattle. It usually causes subclinical or mild reactions, but disease occasionally occurs.

— T. annulata is highly pathogenic to cattle but mild in buffalo, causing Mediterranean or tropical theileriosis. It has been transmitted by several species of Hya lømma ticks. Country reports mention its occurrence in the USSR and Sri Lanka where in the latter it is said to be transmitted by H. isaiaci.

— T. orientalis, which Morel and Uilenberg (1981) consider as the only valid name (and not T. sergenti) to describe the benign Theileria of cattle in Eurasia. It has been introduced in Australia and described from Africa (Becerra et al., 1983) and Europe. They are transmitted by ticks belonging to different Haemaphysalis species. The theileriosis reported from several countries on the American continent and Cuba appear to be closely related to these parasites. The name T. orientalis will perhaps have to give way to Theileria buffeli (Neveu-Lemaire, 1912), if the identity of the benign Theileria of cattle proves to be the same as that of the buffalo (Bubalis bubalis). The name of T. buffeli in the Australian report is therefore perhaps a correct older synonym for T. orientalis and T. sergenti mentioned in the reports of the USSR, Korea and Sri Lanka. It is possible that T. orientalis is more pathogenic in the Far East than in Australia, America or Europe. In view of the above it is, however, unlikely that T. mutans occurs in Sri Lanka, Taiwan, Cuba or Sicily as mentioned in their reports.

ECONOMIC IMPORTANCE

Losses due to haemoparasitic diseases fall into different categories e.g. direct losses due to death of the animal and lower production, or indirect losses (quarantine measures, tick control, vaccination and restriction in cattle movements).

It is estimated that if ticks and babesiosis became re-established in the USA, annual losses of up to US$ 500 million would occur to the cattle industry (McCosker, 1981). This author also mentions that the total estimated annual losses in Queensland and New South Wales, attributed to ticks, tickborne diseases and their control, amount to US$ 7.8 million per annum.

Tanzania reports that of the 10,000 cases of B. bigemina found annually, about 10% of the animals die. It also reports that 46% of its calf losses are due to T. parva.
Sweden estimates that the total annual losses due to *B. divergens* are in the order of US$ 2.5 million per annum.

Cost-benefit analysis for the control of tickborne diseases is, however, extremely difficult. McCosker (1981) is of the opinion that the losses attributable to babesiosis alone, are not sufficiently great to justify eradication, if the ticks are not eradicated as well.

Lawrence and McCosker (1981), in a workshop on the control of theileriosis, are of the opinion that there is insufficient evidence to evaluate the costs and benefits of total dipping compared with less intensive control measures, or no control at all. They strongly recommend that research should be undertaken to investigate the economic aspects of control measures against tickborne diseases.

**DIAGNOSIS**

The diagnosis of the haemoparasitic diseases is based on clinical signs, herd history, presence of vector, etc.

A definitive diagnosis can be made only if the causal organism has been found and properly identified (see also under "Aetiology"). Stained blood smears are used for the diagnosis of babesiosis, theileriosis and anaplasmosis. Lymph-node and spleen smears are used to find the development stages of theileriosis within lymphocytes.

Brain smears are used to identify *C. ruminantium* and *B. bovis* in capillaries. The latter can also be found in the capillaries of kidney and spleen.

A great variety of serological tests have been used for various purposes.

Control programmes are based on the assumption that a positive test indicates that parasitic antigen is still present in the animal.

Serological tests have also been used to differentiate between *Babesia* species (Zwart and Brocklesby, 1979). There is a great need to use such tests to confirm statements made in country reports about the occurrence of certain parasites.

Monoclonal antibodies have been used to differentiate between various stocks of *T. parva* (Irvin *et al.*, 1983).

**EPIZOOTIOLOGY**

**Distribution**

Babesiosis, theileriosis, anaplasmosis and heartwater are transmitted by various tick species. Each tick species has its own requirement as far as temperature and humidity range is concerned. Vegetation plays an important role, because it will determine to a great extent a microclimate where the ticks can moult and lay their eggs.

Potential microclimates, far beyond the present distribution of certain tick species, exist in different parts of the world.
The introduction and establishment in the Caribbean area of the African tick *Amblyomma variegatum*, in combination with the aetiological agent of heartwater (Uilenberg, 1983), should serve as a warning that the distribution of ticks is by no means static.

*A. marginale* can also be transmitted by blood-sucking insects. This is the case in the USA, where it can occur independently of the main tick vectors.

This is contrary to the Australian experience. For insects to transmit *Anaplasma* there must be a large number of biting flies present at the same time as animals experience high parasitaemia. The transmission must occur within minutes, because *Anaplasma* does not survive any longer in a mechanical vector.

Man can also serve as a mechanical vector when performing vaccinations and (minor) operations without proper precautions.

*B. bigemina, B. bovis* and *A. marginale* have common tick vectors and often occur together (see reports from Australia, Latin America and Asian countries).

*B. bovis* is economically more important than *B. bigemina* (see reports from Uruguay and Australia), but *B. bigemina* is more prevalent in nature.

Vertical transmission of *A. marginale, B. bovis* and *B. bigemina* has been described (see report from Cuba), but its role should be further evaluated.

**Resistance**

Age resistance plays a role in most tickborne diseases which is independent of colostral antibodies.

The reports from Australia and Sweden mention this factor for babesiosis, Uilenberg (1983) mentions it for heartwater, but for *T. parva*, it has not been definitely established (Young, 1981). Age resistance, perhaps in combination in some cases with maternal antibodies, is reflected in the reduced number of clinical outbreaks in young animals (see the reports from Sweden and Australia). It is also used to vaccinate young animals with virulent material. This will then cause little or no symptoms.

Breed differences are important in the susceptibility of cattle to tickborne diseases. Cattle of European origin are usually highly susceptible, and many importations of these breeds have ended in failure.

Zebus (*Bos indicus*) are more resistant to tickborne diseases. They are also able to reduce the number of ticks on their skin, and hence the number of blood parasites invading them. Their resistance is, however, by no means absolute and, occasionally, heavy losses are reported in native cattle (see report from Senegal).

**Occurrence of clinical cases**

Outbreaks of clinical illness do not occur uniformly in tick-infected areas due to the differences in genetic or age resistance of the cattle, variations in tick populations, numbers of infected ticks and established control methods.

Mahoney (1974) and Ross and Mahoney (1974) have reviewed the epidemiological principles in the control of babesiosis in cattle. Where the inoculation rate of *Babesia* is adequate to ensure that all calves are infected while they are protected by
age resistance and colostral immunity, clinical babesiosis is rare and enzootic stabili-
ty is achieved.

In Australia, some parts of Cuba and Latin America, the strategic use of acaricides to control ticks, combined with the introduction of zebus (*Bos indicus*), vaccination and good management has led to a state of enzootic stability as far as babesiosis and anaplasmosis are concerned.

In Africa, where heartwater and theileriosis can occur side by side with babesiosis and anaplasmosis, enzootic stability is far more difficult to reach. In Zimbabwe a strategy to control tickborne diseases based on a thorough knowledge of the various vectors of bovine haemoparasitic diseases and sero-epidemiological surveys has been proposed (Norval *et al.*, 1983, 1984).

**CONTROL**

**Vector control**

Tick vector control with the aid of acaricides is widely used in the tropics and subtropics. The development of acaricide resistance and residue problems in meat and milk, has prompted research workers to investigate new control methods such as vaccination against ticks. No country report, however, mentions any practical application under field conditions.

In Europe (see country reports from Yugoslavia, Romania, USSR) cultivation of the land has resulted in an ecological system which is unfavourable for the tick vectors, leading to the disappearance of tickborne diseases. Zero grazing, which is also used in intensive dairy units in tropical and subtropical countries, has a similar effect.

**Immunisation**

Before any immunisation is attempted, it is essential to know whether different strains exist that do not cross-protect against each other.

Irvin *et al.* (1983) used monoclonal antibodies to distinguish three different groups of *T. parva*, which also differed in cross-immunity tests.

Little is known as to whether such differences also exist between *T. annulata* strains (Ozkoc and Pipano, 1981). Evidence from countries in South-East Asia and South America shows that cattle immunised with the Australian vaccine strains against *B. bovis* and *B. bigemina* have adequate immunity to the local strains (McCosker, 1981).

Uilenberg (1983, and personal communication) found good protection between various heartwater isolates from Africa and the Caribbean area.

Antigenetically different strains of *A. marginale* have been reported. The mild *A. centrale* does not always protect against *A. marginale*, according to the report from Cuba.

Immunisation is mainly used after the importation of susceptible exotic cattle into an enzootic area, and for indigenous cattle at risk in an unstable enzootic situa-

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The Australian method of *Babesia* immunisation using a standardised dose of an attenuated strain of *Babesia* is reported from Australia, Sweden, Sri Lanka and Latin American countries.

With chemoprophylaxis, a suitable drug offers protection for a certain period. For example, imidocarb will protect for at least 33 days (Callow and McGregor, 1970). Exposure of the animals to *Babesia* parasites during this period will stimulate the immune systems. If the challenge is too high, there is a risk of clinical reactions. Development of a poor immunity if the challenge is too low is also possible. The development of drug resistance against imidocarb cannot be excluded (Dalgliesh and Stewart, 1977).

Surveillance and treatment is another method that has been used widely (McCosker, 1981). This method can be modified by using the blood of a donor animal, to infect the herd and treat when necessary.

*Babesia* antigens from cell cultures of *B. bovis* show promising results in limited field experiments (Country report, Mexico; Smith and Ristic, 1981; Timms and Stewart, 1984).

Surveillance and treatment with tetracyclines has been used widely for preventing anaplasmosis (see reports from Latin American countries).

Imidocarb has also been used as a prophylactic drug, but is unreliable. *A. centrale*, which causes only mild clinical reactions in cattle but protects to some extent against *A. marginale* has been used in Latin America, South East Asia and Africa. Its use in the USA is not allowed.

The use of other attenuated vaccines (Ristic, 1981) is limited but good results are reported from Mexico.

An inactivated vaccine has been prepared, but its efficiency is doubtful (Ristic, 1981) and no countries have reported its use under field conditions.

Immunisation of cattle with virulent material, followed where necessary by chemotherapeutic treatment (tetracyclines), is the only method available for cow-driosis (heartwater) at the moment (Uilenberg, 1983). Young animals show an innate resistance and often do not require any treatment.

A culture-derived schizont vaccine against *T. annulata* is the only vaccine used on a large scale (see report from the USSR). A similar vaccine based on cultured lymphocytes infected with *T. parva* has no practical application because large numbers (10^8 infected cells) have to be used. This is probably due to the fact that the recipient animal will destroy the inoculated parasite containing lymphocytes if they belong to a different major histocompatibility antigen. If donor lymphocytes and recipient animals have the same histocompatibility antigens, only 100 cells are needed (Morrison *et al.*, 1981).

Experimental field studies have shown that cattle can be vaccinated either against *T. annulata* or *T. parva* by inoculating them simultaneously with sporozoites and a long-acting tetracycline (Irvin and Gill, 1981).
Treatment

For a review of old and new drugs used against babesiosis, see Kuttler (1981). Country reports mention various drugs under their trade names, but the two drugs now widely used are:

— 4.4’-diamidinodiazoaminobenzene diaceturate with the approved name diminazene aceturate, known under the trade names Berenil® and Ganasag®;
— 3-3’-bis (2-imidazolin-2-yl) carbanilide dihydrochloride or dipropionate with the approved name imidocarb and the trade name Imizol®.

Tetracyclines are effective against anaplasmosis (Ristic, 1981) and early stages of heartwater (Uilenberg, 1983). These drugs have also been used for eliminating A. marginale carrier status (Ristic, Rogers and Dunster, 1984). Imidocarb in a high dose has been used for curative treatment of anaplasmosis.

Tetracyclines have been used in the “infection and treatment” method against theileriosis (Dolan, 1981). An effective development in the treatment of clinical theileriosis has been the development of quinone compounds, one of which (Clexon®) is on the market. It is active against T. annulata and T. parva. A quinazolinone compound, halofuginone hydrobromide was found to be effective against theileriosis (Dolan, 1981) and has been used extensively under the trade name Sternorol® to prevent poultry coccidiosis. It is probably too toxic to be used for the treatment of theileriosis under field conditions.

Good results of supportive therapy for treating T. annulata infections are mentioned in the report of the USSR. This consists of blood transfusions, mineral and vitamin supplementation.

Appendix

53rd GENERAL SESSION OF THE O.I.E.
RESOLUTION No. XIV

HAEMOPARASITIC DISEASES OF BOVINES
(with the exception of trypanosomiasis)

CONSIDERING THAT

the world-wide dissemination of haemoparasitic diseases, transmitted by ticks, seriously hinders agricultural development, particularly in tropical countries, and calls for the urgent setting up of international control measures;

it is recognised that several techniques have shown potential for alleviating the tickborne disease problems by various control methods;

advances in recent years in the field of serology and immunisation have indicated their promise of providing improved survey and control methods of tickborne diseases;
it is also appreciated that these techniques cannot always be supported because of various restraining factors such as insufficient knowledge of the cost/benefit ratio, lack of the necessary funds and shortage of experienced personnel,

THE COMMITTEE

RECOMMENDS THAT

1. The search be intensified for the *in vitro* cultivation of haemoparasitic parasites as a source of purified antigens for serological purposes and vaccines.

2. More emphasis should be given to international reference banks for *in vitro* comparison of stocks of various parasites. The relationship between characters determined by *in vitro* techniques of different stocks and cross-immunity in cattle should be explored further, so that suitable stocks for immunisation can be selected on the basis of these characters.

3. Wherever possible, before a country starts a control programme of haemoparasitic diseases, scientific data should be collected concerning the biology of the transmitting ticks, the genetic resistance of the cattle involved and a cost-benefit analysis.

4. More studies should be carried out on the epizootiology of theileriosis and cowdriosis and the threat which the latter poses for the American mainland.

5. The economy of the control of haemoparasitic diseases be further evaluated.

6. Emphasis should be given to the study of naturally acquired host resistance and artificially induced immune responses to ticks for the development of alternative methods of tick control.

7. A variety of tick and tickborne disease training programmes be developed.

8. Member Countries remain constantly alert to the danger of diseases transmitted by ticks, resulting from the uncontrolled importation of exotic breeding animals for livestock improvement programmes.

*(Adopted by the International Committee of the O.I.E. on 24 May 1985.)*

**REFERENCES**


Reports submitted to the 53rd General Session, May 1985:

1. ANON. — Haemoparasitic diseases of bovines - Australia.
2. ANON. — Haemoparasitic diseases of bovines in the Republic of Korea.
3. ANON. — Situation des maladies hémoparasitaires des bovins au Mexique.
4. ANON. — Present aspects of babesiosis in cattle in Romania.
5. ANON. — Hémoparasitoses bovines au Sénégal.
7. ANON. — Haemoparasitic diseases of bovines (with the exception of trypanosomiasis) - USA.
8. ANON. — Haemoparasitic diseases of cattle in Tanzania (other than trypanosomiasis).
10. CHRISTENSSON D. — Haemoparasitic diseases of bovines in Sweden.


12. LEE R.C.T. & TSAI-CHUN LIN. — Investigation and control of haemoparasitic diseases of bovines in Taiwan ROC.


15. STEPANOVA N.I. — Les hémoparasitoses bovines en URSS.