TICK-BORNE DISEASE TREATMENT

Author : Hany M Elsheikha

Categories : Vets

Date : August 24, 2009

Hany M Elsheikha concludes his two-part article on ticks and tick-borne diseases, and explains how the future of vaccine development looks exciting

IN part one (*VT* 39.19), the author discussed the biology, ecology, and veterinary significance of the most prevalent tick species in the UK, *Ixodes ricinus*.

In this second part, the author focuses on the pathogenic agents transmitted by *I ricinus* and presents treatment options for diseases caused by these pathogens.

Disease vector

Ticks play an indirect role in the transmission of infectious agents, such as viruses, bacteria, protozoa and helminths, which are common to both humans and animals. Their important role in disease transmission is reinforced by ticks having a worldwide distribution and being adaptable to any kind of environment or host.

Transovarian (adult female to egg/larva) and trans-stadial (larva to nymph, nymph to adult) transmission are the mechanisms by which *I ricinus* can contribute to the survival and maintenance of pathogen populations and facilitate transmission to susceptible hosts. Transovarian transmission of *Babesia divergens* from adult *I ricinus* ticks to larvae does occur and is believed to be important in maintaining the life cycle of other tick-borne viral and rickettsial pathogens.

Trans-stadial transmission occurs following the acquisition of other pathogens, such as *Babesia*. In trans-stadial transmission, nymphs and adult ticks infected in a previous life stage emerge infective

after moulting, and subsequently transmit disease to other hosts during feeding. The most important disease organisms transmitted to animals by *I ricinus* are:

- *Anaplasma phagocytophila* (tick-borne fever of ruminants, formerly known as Ehrlichia);
- *Borrelia burgdorferi* (causative agent of Lyme disease);
- *B divergens* (causes redwater fever in cattle);
- *Staphylococcus aureus* (tick pyaemia of sheep); and
- louping-ill virus (causes encephalitis in sheep and grouse).

I ricinus ticks are not host-specific and feed on different host species. They have non-specific feeding habits-not only feeding on species that are reservoirs for multiple tick-borne pathogens (such as small mammals), but also humans. Therefore, these non-specific feeders are more important as vectors of human disease than host-specific ticks, which are less likely to bite humans.

Pathogens of human diseases transmitted by *I ricinus* include:

- *Anaplasma phagocytophilum* (causes granulocytic anaplasmosis in humans);
- *Rickettsia conorii* (boutonneuse, or Mediterranean tickbite fever);
- *Coxiella burnetii* (Q-fever);
- *Francisella tularensis* (tularaemia);
- *B burgdorferi* and tick-borne encephalitis; and
- Tettnang, Eyach and Uukuniemi viruses.

Treatment of diseases transmitted by *I ricinus*

Treatment of human diseases transmitted by *I ricinus* is out of the scope of this article; therefore, treatment options are limited to *I ricinus*-borne diseases of relevance to animal health and welfare in the UK.

- **Tick-borne fever or anaplasmosis**

– Tick-borne fever (TBF) is a febrile disease of domestic and free-living ruminants in the UK and

other European countries.

– It is caused by the bacterium *Anaplasma phagocytophilum* (Figure 1).

– The disease affects cattle, sheep and horses; in dogs, anaplasmosis leads to fever, anorexia, joint pain and swelling.

– The disease suppresses the immune system in young lambs, predisposing infected animals to other infections, such as loupingill and tick pyaemia.

– As there is no colostral protection and immunity builds up as animals age, young animals are at the greatest risk of disease in endemic areas.

– Diagnosis is based on clinical signs, history of exposure to ticks and microscopic examination of blood smears.

• Treatment

– Short-acting oxytetracyclines are the most effective option.

– If dairy cattle are treated with oxytetracyclines within a few days of infection, the pyrexia is reduced quickly and milk yield restored.

– Other antibiotics, such as penicillin, streptomycin and ampicillin, do not prevent relapses.

– Sulfamethazine has also proved useful.

• Comments

– Treatment with long-acting tetracyclines may be used as a prophylactic measure in enzootic areas.

• Borreliosis (Lyme disease)

– This is a common tick-borne zoonotic disease of dogs (it rarely appears in cats).

– Lyme disease is caused by the spirochaete bacterium *B burgdorferi* (Figure 2).

– The disease causes fever, lameness, arthritis, renal failure and meningitis.

– There is no persuasive evidence that *B burgdorferi* infection is transmitted in utero in dogs.

– Once an animal contracts Lyme disease, urgent treatment with antibiotics is required.

– Diagnosis is based on history of tick exposure, clinical signs and a demonstration of borrelial infection, using either direct (isolation, PCR) or indirect (serology) antibody-based tests.

• Treatment

– Doxycycline (10mg/kg) or amoxicillin (20mg/kg) are the drugs of choice.

– Other effective drugs include azithromycin, cephalexin, amoxicillin, tetracycline, penicillin G and chloramphenicol.

– NSAIDs may also be used for symptomatic treatment.

• Vaccination

– There is no vaccine against borreliosis for dogs in the UK.

• Comments

– Doxycycline should not be used in very young animals because it can cause staining of the teeth.

– If the disease is untreated, nervous system, arthritic or other complications may develop weeks or months after the infection.

– Treatment of some later complications of Lyme disease may require antibiotics to be given by injection for several weeks.

– The disease may recur, with intervals of weeks to months, but should respond to antibiotic treatment each time.

– Full recovery may take some time, as damaged tissue takes time to heal, especially in the chronic stage of the disease.

– Antibiotic therapy does not eliminate the *B burgdorferi* bacteria responsible for Lyme disease, but it does suppress the bacteria so that symptoms subside.

• Babesiosis (redwater fever)

– In the UK, babesiosis is often caused by *Babesia divergens* (Figure 3).

– *B divergens* is a serious pathogen for cattle in the UK and northern Europe.

– It is an intraerythrocytic protozoan parasite that is transmitted and spread between cattle by the tick *I ricinus*.

– This disease is usually first reported in May or June, when its tick host becomes active.

– *B divergens* produces a disease syndrome similar to *B bigemina* and *B bovis*; however, the cerebral form is rarely seen.

– Redwater fever is often only noticed at the onset of haemoglobinuria, when the disease is at an advanced stage.

– It not only causes significant losses to the cattle industry, but can also infect immunocompromised humans, with serious consequences.

– Diagnosis is based on clinical signs, history of exposure to ticks and microscopic examination of blood smears.

• Treatment

– Mild cases may recover without treatment.

– More severe babesiosis cases require treatment, and imidocarb dipropionate is the drug of choice. This is often best combined with a preventive treatment for the unaffected cattle.

– Therapy and blood transfusions will generally save an affected animal, even at an advanced stage of the disease.

• Vaccination

– Live vaccines have proven effective and reasonably safe, particularly when vaccination was restricted to cattle less than a year old, when they still have natural resistance to the disease. However, live vaccines have several limitations, the most obvious being that the vaccine itself may cause babesiosis unless its virulence can be controlled.

– A vaccine is not yet available in the UK.

• Comments

– Imidocarb is most toxic when given intravenously; therefore, intramuscular or subcutaneous administration is generally recommended.

– Imidocarb is associated with residue problems, especially when used for chemoprophylaxis,

which has led to the withdrawal of imidocarb in several European countries.

– Long-acting oxytetracycline against bovine *B divergens* infections has no therapeutic effect if given after the parasitaemia has become patent. Despite this, continuous prophylactic administration allows sufficient numbers of parasites to multiply for antibodies to be produced while clinical effects are absent.

– The use of continuous oxytetracycline administration is too costly and risky due to the likelihood of resistance development in bacterial pathogens.

– Trials to control *B divergens* infection in calves by stimulating concurrent non-specific immunity failed[1].

• ***Staphylococcus aureus***

– Tick pyaemia in sheep is caused by the bacterium *S aureus*, an inhabitant of the normal skin, which enters the bloodstream by the biting action of the blood-sucking nymphal stage of the tick *I ricinus*.

– This disease affects lambs born in, or introduced to, a tickinfested area, at the time tick activity is at its greatest (usually in the spring).

– There is evidence that tickborne fever infection, which causes profound leucopaenia, may predispose tick pyaemia.

– This disease can result in skin abscesses, but in immunosuppressed animals (such as those with tick-borne fever), the bacteria can spread into joints and the spinal column, causing arthritis or even paralysis.

– Lambs may be affected by both tick pyaemia and joint-ill, especially if the ewes are in poor condition and have insufficient colostrum.

– Diagnosis is based on history and postmortem, and a bacterial culture of the infected joint.

• Treatment

– Parenteral administration of penicillin or tetracycline can be effective, provided the lesions are not too advanced.

– Severe cases should be euthanised.

• Comments

– Local treatment of affected joints is often disappointing because, by the time lesions are noticed, irreversible damage to the joint may have occurred.

– Long-acting antibiotics, to which particular strains of *S aureus* agents are sensitive, can be used prophylactically, although care should be taken not to underdose to avoid the development of bacterial resistance.

– Both benzathine penicillin and long-acting tetracyclines are effective against *S aureus*, while the latter are also effective against the rickettsial agent of tickborne fever.

• **Louping-ill**

– Louping-ill (ovine encephalomyelitis, infectious encephalomyelitis of sheep, trembling-ill) is an acute viral disease, primarily of sheep, caused by a neurotropic single-strand RNA flavivirus.

– It is characterised by a biphasic fever, depression, ataxia, muscular incoordination, tremors, posterior paralysis, coma and death.

– Louping-ill is a tick-transmitted disease, the occurrence of which is closely related to the distribution of the sheep tick *I ricinus*, which requires an environment with a high relative humidity.

– Louping-ill can affect sheep of all ages and can infect a range of hosts (it is an important disease in grouse).

– It is endemic in rough, upland areas in Scotland, northern England, Wales and Ireland.

– Colostrum will protect lambs in areas where ewes have been exposed to the virus and, therefore, clinical signs will generally be seen in weaned lambs. Young lambs that have not received sufficient colostrum are also susceptible to disease, as are naïve sheep of any age brought into an endemic area.

– Although cases of louping-ill can occur at any time of year, the disease is most prevalent during periods of maximal tick activity

– between April and June, and again in September.

– Diagnosis is based on clinical grounds, history of an introduction to tick-infested pastures in an endemic area, serological assays and reverse transcription PCR.

– Louping-ill virus is transmissible to humans.

• Treatment

– No specific treatment for louping-ill virus infection is effective. Unlike sheep, cattle affected by louping-ill may respond favourably to good nursing and symptomatic treatment.

– If there is evidence that susceptible animals have been exposed to the disease, administration of the louping-ill antiserum within 48 hours of exposure to the infection is recommended.

– Recumbent animals must be euthanised.

• Vaccination

– A formalin-inactivated commercial vaccine is available that has been used successfully for many years in endemic areas.

– Two doses of vaccine, with an interval of two to eight weeks between injections, is recommended to achieve optimal protection against natural infection.

– Vaccination of pregnant ewes during the last trimester is advocated to ensure lambs receive maximal levels of passively acquired antibodies and are protected during the initial critical months of life.

Conclusions

Despite the veterinary and zoonotic importance of tickborne diseases (TBDs), relatively little research has been carried out on the ticks and diseases associated with them, and many questions regarding tick epidemiology and the host's response remain unanswered.

A better understanding of the species' biology and hostparasite interactions may lead to improved control mechanisms and new trends in TBD management. Development of acaricide resistance is a serious problem in the control of several TBDs, although the real extent of the problem is unknown.

Characterisation of the tick genomes will have a great impact on the discovery of new protective antigens. The future of tick vaccine development research is exciting because of new and emerging technologies for gene discovery, vaccine formulations and delivery methods. Any control strategy should be based on knowledge of the local tick ecology, which would improve the efficiency of the control programme, reduce the risk of acaricide resistance and environmental pollution, and cut costs considerably.

Summary

• Ticks are distributed worldwide and impact on human and animal health, as well as food animal production.

• Ticks can transmit various diseases to several animal species and humans.

• *I ricinus* is a good example of a tick vector with multiple pathogens affecting companion animals, livestock and humans.

• Apart from the use of antimicrobials against TBD, prevention is based mainly on adequate tick control.

• For economic and animal welfare reasons, the best option is to take preventive measures, rather than treat TBD.

• Ideal control strategies should be directed towards both tick control and the blocking of pathogen transmission.

• Integrated control (identification of risk areas, tick control, chemoprophylaxis and vaccination) should be considered in endemic TBD areas.

Reference

- Brocklesby D W and Purnell R E (1977). Failure of BCG to protect calves against Babesia divergens infection, *Nature (London)* **265**: 343.

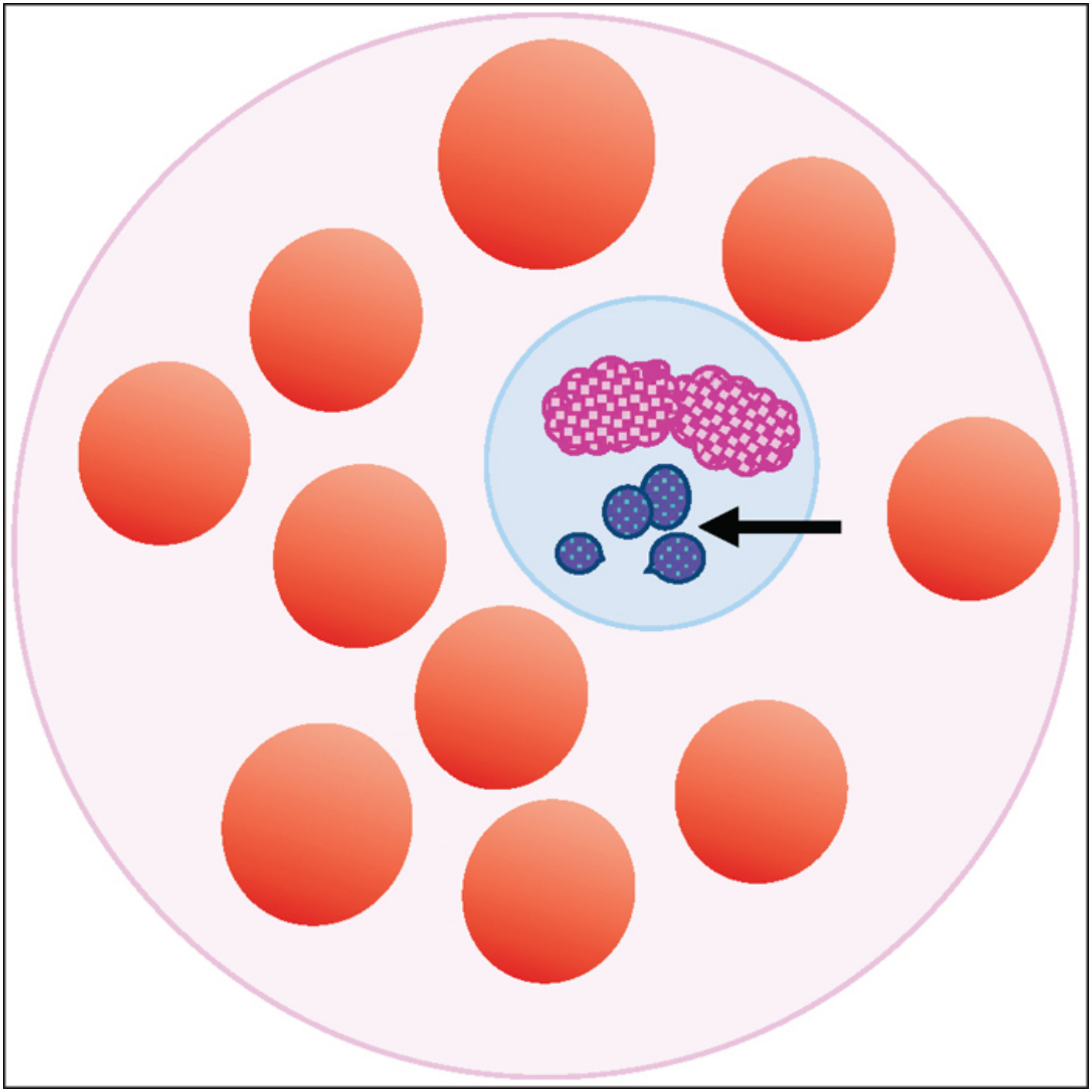

Figure 1. Illustration of a peripheral blood smear demonstrating variably sized basophilic inclusions, representing a cluster of* Anaplasma (Ehrlichia) phagocytophilum *(arrowed) contained within vacuoles in the cytoplasm of a leukocyte.

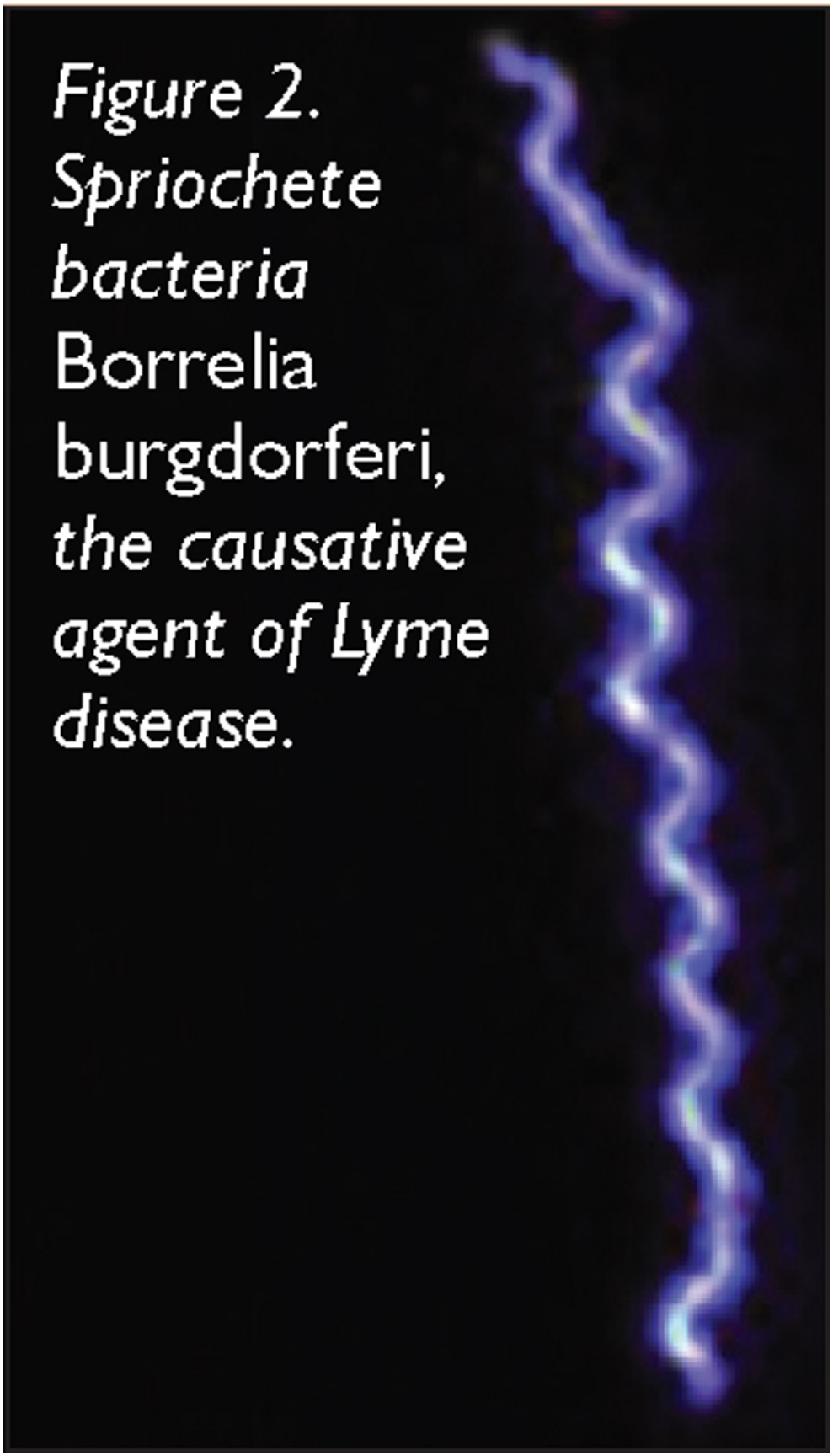
Figure 2.
Spriochete
bacteria
Borrelia
burgdorferi,
the causative
agent of Lyme
disease.

Figure 2. Spriochete bacteria* Borrelia burgdorferi*, the causative agent of Lyme disease.

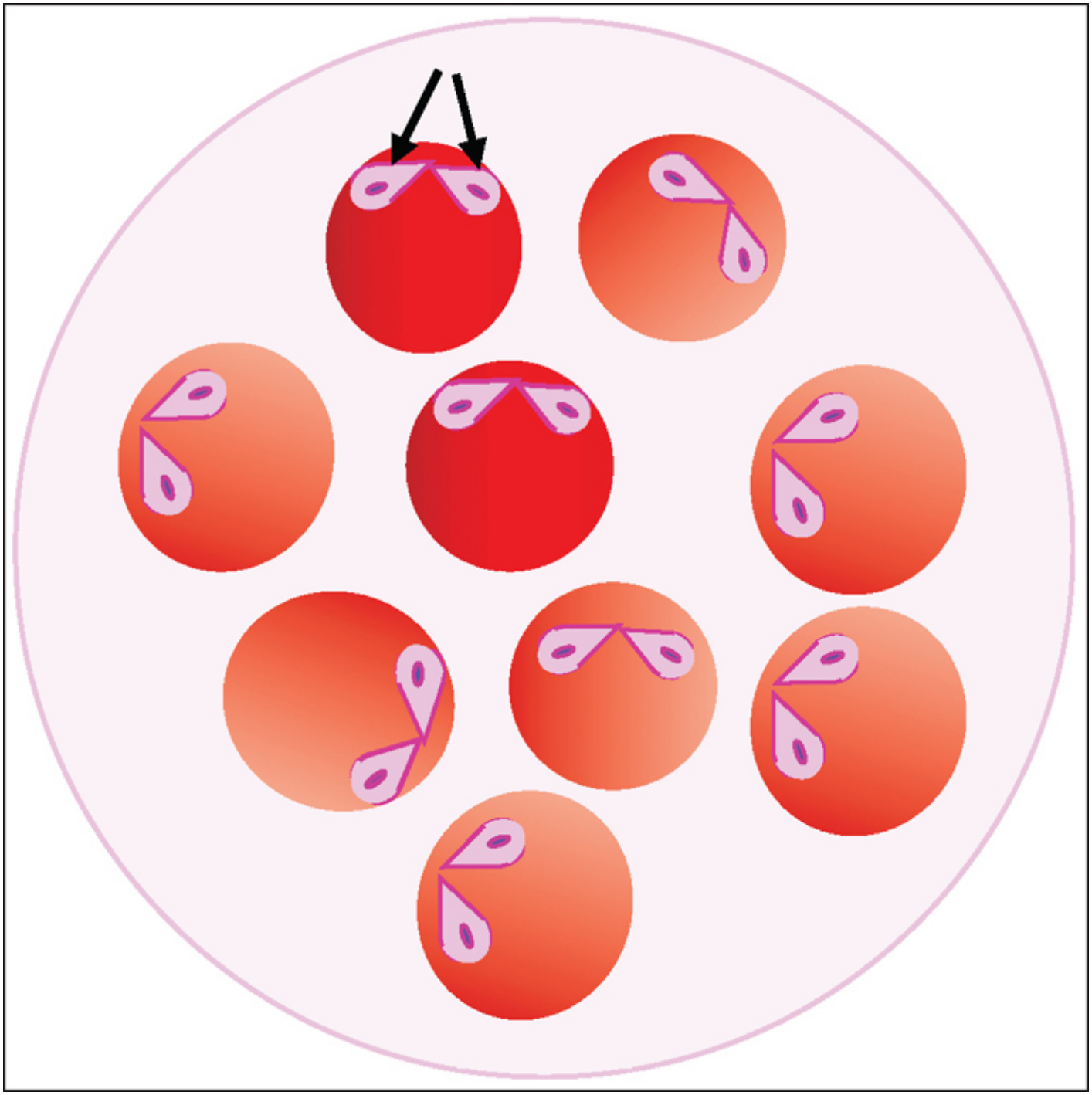

Figure 3 (right). Illustration showing the intraerythrocytic protozoan* Babesia divergens *in a blood smear. Merozoites are pear shaped (arrows) and often occur in pairs, joined at the tip, which is a result of binary schizogony.