Other vector-borne parasitic diseases: animal helminthiases, bovine besnoitiosis and malaria


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Summary
The parasitic diseases discussed elsewhere in this issue of the Scientific and Technical Review are not the only ones to make use of biological vectors (such as mosquitoes or ticks) or mechanical vectors (such as horse flies or Stomoxys flies). The authors discuss two major groups of vector-borne parasitic diseases: firstly, helminthiasis, along with animal filariasis and onchocerciasis, which are parasitic diseases that often take a heavy toll on artiodactyls throughout the world; secondly, parasitic diseases caused by vector-borne protists, foremost of which is bovine besnoitiosis (or anasarca of cattle), which has recently spread through Europe by a dual mode of transmission (direct and by vector). Other protists, such as Plasmodium and Hepatozoon, are also described briefly.

Keywords

Introduction
A large number of parasitic diseases are associated with arthropods. They include:

– pathologies associated with arthropods themselves: pediculosis caused by lice (Insecta, Pediculicidae); allergies, dermatitis and scabies associated with mites (Arachnida); tungiasis associated with chigoe fleas (Insecta, Siphonaptera); and blood loss and dermatitis associated with the bite of many arthropods, which are regarded as ectoparasites

– parasitic diseases caused by pathogens transported passively by arthropods: amebiasis, cryptosporidiosis, and helminthiasis of various types, often associated with flies (Insecta, Diptera) or cockroaches (Insecta, Blattoptera)

– pathologies associated with pathogens whose life cycle involves a blood-sucking arthropod: these are vector-borne diseases.

The major parasitic diseases in the latter group (trypanosomosis, theileriosis, leishmaniosis and babesiosis) are discussed elsewhere in this issue of the Scientific and Technical Review. This article describes other vector-borne parasitic diseases of animals and humans, including helminthiasis, besnoitiosis and malaria.

Helminthiasis
Helminthiasis covers a large number of different pathologies of which only a few involve an insect as vector. The vector-borne helminths (transmitted by mosquitoes such as Anopheles and Mansonia, as well as by flies of the Muscidae family) belong to the order Spirurida, suborder Spirurina and families Filariidae and Onchocercidae (Table I).

Filariasis
Three filarial worm species are known to cause non-zoonotic human lymphatic filariasis: Wuchereria bancrofti, Brugia malayi and B. timori (1). There is no animal reservoir for these forms of human filariasis, which are not examined in this article. Animal filariasis includes a number of pathologies, as outlined below (2, 3).

Arterial filariasis of camelids
Arterial filariasis of camelids, caused by the growth of the filarial worm Dipetalonema evansi in blood vessels and lymph nodes, is a disease that is specific to the dromedary and camel and can cause significant losses. In the 1990s, the prevalence was estimated at 5% in Egypt and 41% in Iran, where the parasitic disease is still rampant.
As yet, little is known of the life cycle of *D. evansi*. The mosquitoes *Aedes caspius* and *Ae. detritus* appear to be its main vectors. The microfilariae are ingested by *Ae. caspius* during a blood meal on an infected dromedary; the parasites then migrate to the mosquito's chest muscles, where they continue to develop. Ten days later, infective larvae are present in its proboscis, ready to infect a new host at a future blood meal.

The main clinical signs in camelids are hyperthermia (39–40°C), loss of appetite, weight loss, pale mucous membranes and enlarged testicles and scrotum. In the case of massive infection, death may ensue.

Diagnosis is based on the observation of clinical signs, epidemiology and the presence of mosquito vectors. Confirmation is by the detection of microfilariae in blood.

Treatment is based on subcutaneous administration of ivermectin. Sanitary prophylaxis is based on avoiding contact between camels and mosquitoes (by sending animals into desert areas during mosquito outbreaks).

**Bovine and equine parafilariasis**

Parafilariasis is caused by the development of the filarial worms *Parafilaria bovicola* and *P. multipapillosa* in cattle and equids, respectively. The parasites develop in the subcutaneous and intramuscular connective tissue and both forms of the disease are characterised by the formation of skin nodules that become haemorrhagic (streaks of blood on the skin, hence the label ‘summer bleeding’).

The cattle form of the disease is found mainly in Africa, Asia and Europe. In the late 1970s, a prevalence of 36% was observed in the Transvaal (South Africa). The equine form of the disease is present in North Africa, eastern and southern Europe, Asia and South America, with a prevalence of up to 41% in Iran. These pathologies can prevent draught animals from working and have a major economic impact because they reduce the value of hides and carcasses.

The *Parafilaria* life cycle involves Muscidae: different species of *Musca* in cattle (*M. lusoria* and *M. xanthomelas* in the tropics, *M. autumnalis* in Europe) and different species of *Haematobia* in horses. In flies, the first-stage larvae of filarial worms become infective (third-stage larvae) in 10–20 days, depending on the temperature. At their next meal, flies will deposit the larvae on bleeding wounds or on the conjunctiva when feeding on tear fluid. The larvae then migrate to their development site on the skin. In vertebrates, the development period can be around 300 days.
(experimental infection) for *P. bovicola* and 9–13 months for *P. multipapillosa*.

The clinical signs occur during the hot season in tropical countries and in late spring and summer in temperate countries. Subcutaneous nodules 0.5–1.5 cm in diameter appear on the neck and back. They contain worms and it is the females of *Parafilaria* that pierce the skin to lay their eggs. There is a close correlation between the parasite’s egg-laying during hot weather and fly outbreaks.

Diagnosis is based on the seasonal occurrence of bleeding skin nodules. Confirmation is by the detection of eggs and microfilariae in the blood. A serological test (enzyme-linked immunosorbent assay [ELISA]) has been developed for *P. bovicola* (4, 5).

The following treatments are available:

- for cattle: ivermectin, nitroxynil, levamisole and fenbendazole
- for equids: metrifonate, diethylcarbamazine, fenbendazole, ivermectin and moxidectin.

Sanitary prophylaxis is based solely on fly control.

**Bovine stephanofilariasis**

Bovine stephanofilariasis is caused by a filarial worm of the genus *Stephanofilaria*. Several species are known in Asia, Japan and North America. The most important is *S. assamensis*, high prevalences of which are observed in India, Bangladesh and Uzbekistan.

Little is yet known of the life cycles of these different species. Muscidae, such as *M. conducens* and *M. planiceps* (Indian subcontinent), *Haematobia irritans* and *Stomoxys calcitrans*, are thought to be the main vectors. Flies become infected when taking a blood meal in lesions. The filarial larvae develop in the flies’ chest muscles before migrating to the proboscis as infective larvae. Vertebrates become infected during a meal by an infected fly. The microfilariae complete their development in the dermis of the vertebrate host.

The clinical signs are inflammation of the dermis, with irritation and itching. The lesions quickly become ulcerative and are active mainly in the rainy season owing to high humidity. The lesions are commonly found on the back or limbs of animals (cattle, goats, buffaloes). In the case of the species *S. zaheeri* (buffaloes in India and Pakistan), the lesions are concentrated on the ear pinna. This is a seasonal disease, with the lesions becoming inactive during the dry season.

Diagnosis is based on the location and appearance of the lesions, coupled with their seasonal occurrence. Filarial worms can be detected by microscopic examination of scrapings from lesions.

Treatment is based on ivermectin and/or levamisole. Sanitary prophylaxis is based on fly control.

**Onchocerciasis**

Onchocerciasis is a parasitic infection caused by nematodes of the genus *Onchocerca*. Several species parasitic to humans and domestic animals are present throughout the world (6). Cattle, equids and camels can be infected and the vectors are *Culicoides* (Diptera: Ceratopogonidae) or black flies belonging to the genus *Simulium* (Diptera: Simuliidae). The disease is characterised by the formation of skin and subcutaneous nodules caused by the development of *Onchocerca* in ligaments and in skin and subcutaneous tissue.

**Bovine onchocerciasis**

Bovine onchocerciasis is caused by many different species of *Onchocerca* and has a cosmopolitan distribution. It has a major economic impact because it reduces the value of hides and carcasses.

Female *Onchocerca* are viviparous and lay first-stage larvae (microfilariae) which migrate into the dermis of the vertebrate host. The vectors – different species of the genera *Culicoides* and *Simulium* – become infected during a blood meal from infected cattle. The microfilariae move to the chest muscles of insects where they undergo two successive moults. The third-stage larvae then migrate to the insect’s proboscis, which they leave during the vector’s blood meal to enter the host tissue through the bite wound. The development of the different species of filarial worms in cattle varies and little is known about it.

The clinical signs differ widely depending on the species of *Onchocerca* involved, and the disease is often asymptomatic. This makes clinical diagnosis very difficult and confirmation is only possible by detecting adult filarial worms in intradermal nodules or microfilariae in dermal lymph. Serological tests by indirect haemagglutination and ELISA exist.

Treatment is possible using ivermectin, diethylcarbamazine or levamisole. Sanitary prophylaxis is based on vector control.

**Equine onchocerciasis**

Equine onchocerciasis is caused by three species: *Onchocerca cervicalis*, which localises to the cervical ligament; *O. reticulata*, which localises to the suspensory ligament of the fetlock; and *O. raillieti*, a parasite of the subcutaneous
tissue of the donkey. Infection is characterised by tendinitis, nodule formation and dermatitis.

*Onchocerca cervicalis* and *O. reticulata* are found worldwide, while *O. raiilieti* is parasitic only to donkeys in Africa.

The cycle of these parasites involves different *Culicoides* species as vectors (*C. nebulosus, C. parroti, C. obsoletus, C. variipennis* and *C. robertsi*). The third-stage larvae migrate to the host following a bite by the vector and grow to adulthood at the predilection sites.

The clinical signs are dermatitis associated with the microfilariae of *O. cervicalis*. However, *O. reticulata* is more pathogenic, owing to chronic inflammation of the suspensory ligament of the fetlock, preventing horses from running.

Clinical diagnosis is based on the observation of seasonal dermatitis, presence of potential vectors (*Culicoides* sp.), location of lesions and possible lameness. Confirmation is by the detection of microfilariae in a skin biopsy.

Treatment is with ivermectin, avermectin B1 and diethylcarbamazine, which are active against the microfilariae. Sanitary prophylaxis is based on *Culicoides* control.

**Onchocerciasis of camelids**

Onchocerciasis of camelids is very similar to equine onchocerciasis. It is caused by the presence of *O. fasciata* in the subcutaneous tissue of the head and neck of dromedaries. It is present in Africa, the Near East and Middle East. Dromedaries infected with *O. gutturosa* have been observed in Australia and Sudan.

**Other forms of onchocerciasis**

Other forms of livestock onchocerciasis are classed as helminthiasis of the circulatory system, with the microfilariae circulating in blood vessels and sometimes found far from the site of the adult worms. This is the case with aortic onchocerciasis of cattle caused by *O. armillata*. The nodules form in the intima and the cycle involves *Simulium* spp. (*Diptera, Simulidae*) as vectors. It is a common disease of cattle in Africa and Asia.

This is also the case with elaeophorosis of artiodactyls, which has a cosmopolitan distribution. It is caused by several species of the genus *Elaeophora*, which develop in the heart, coronary arteries and other arteries. The cycle involves horse flies (*Diptera, Tabanidae*) as vectors, particularly species of the genera *Tabanus* and *Hybomitra*.

One species of *Onchocerca* infecting wild pigs has been described as zoonotic in Japan (6).

**Other forms of filariasis**

In addition to the livestock filariasis described above, many other forms of filariasis can infect wildlife. For example (7, 8):

- Filariasis transmitted by mosquitoes: *Wuchereria halimentani* has been reported to cause filariasis in apes from Borneo, but most mosquito-borne filarial worms belong to the genus *Brugia*, which infects carnivores (*B. pahangi* in Malaysia, *B. patei* on Africa’s eastern coast, *B. ceylonensis* in Sri Lanka, *B. guyanensis* and *B. baeveri* in the Americas), non-human primates (*B. malayi, B. pahangi* in Southeast Asia) and tree shrews (*B. tupaia* in Southeast Asia). The genus *Dirofilaria*, several species of which are parasitic to carnivores (*D. immitis*, the agent of heartworm disease of dogs, with cosmopolitan distribution, *D. repens*, *D. reconditum*), also has many *Culicoides* as vectors. Some of these filarial worms can accidentally infect humans and cause lung damage (*D. immitis*) or subcutaneous lesions (*D. repens, D. tenuis*). Other filarial diseases of the canine vascular system are caused by *Acanthocheilonema reconditum* and *A. dracunculoides*. *Culicoides* are also responsible for transmitting *Setaria* (including *S. labiato-papillosa* and *S. digitata* in cattle), filarial worms parasitic to reptiles (*Oswaldofilaria* of agamas and chameleons), *Folyella* of amphibians, and filarial worms of birds (*Cardiofilaria* spp.).

- Filariasis transmitted by biting midges (family *Ceratopogonidae*): Biting midges transmit filarial worms of the genus *Mansonella*. These worms are parasitic to apes in Africa, including gorillas and chimpanzees, which become infected with *M. gorilla* and *M. rodhaini (= vanhoofi)*, respectively. Together with the human parasite *M. perstans*, these parasites could be considered a species complex. Biting midges also transmit filarial worms of birds, such as *Chanderella chitwoodae* (possible vectors: *C. stilbezzioides* and *C. travisi* in Canada) and filarial worms of amphibians, such as *Icosiella neglecta* of European frogs (vector: *Forcipomyia velox*).

- Filariasis transmitted by ticks: Filariasis caused by *Cercopithifilaria* spp., a dermal microfilaria of carnivores, is transmitted by *R. sanguineus* (9).

**Besnoitiosis**

**Aetiological agent**

Bovine besnoitiosis, also known as elephantiasis, anasarca of cattle or cutaneous sarcosporidiosis, is caused by the protozoan *Besnoitia besnoiti*, which has a coccidian life cycle. This parasite belongs to the phylum Apicomplexae,
order Eucoccidioridae, suborder Eimeriorinae and family Isosporidae. It is a coccidian parasite whose development cycle is heteroxenous, involving a classic intestinal cycle with schizogony, followed by gamogony (production of oocysts) in the feline definitive host (cat; lynx suspected). Cattle are the intermediate hosts (10, 11).

Epidemiology

Most outbreaks of bovine besnoitiosis occur on the African continent, mainly in the south. Outbreaks have also been reported in Israel, Kazakhstan, the People's Republic of China, India and Venezuela. In Europe, the disease is endemic in Spain, Portugal and France. Cases have also been described in Africa. In France, outbreaks were formerly concentrated in the south-west, particularly the Pyrenean foothills stretching from the eastern Pyrenees to the departments of Aude and Ariège. However, in 1990, scattered outbreaks began to occur in Hauts-Pyrénées, Massif Central and the southern Paris Basin (Deux-Sèvres). In 2001, a major outbreak developed in the Alps and, in 2003, the disease spread westwards and to the Pays de la Loire region.

While the definitive hosts are mainly the domestic cat and lynx (12), other wild mammals are suspected: fox, genet, wild cat. There are many potential intermediate hosts: wild and domestic ungulates (impala, wildebeest, zebu, sheep, goat, cattle) (13), rodents (gerbil, muskrat, vole), warthogs and birds. However, the disease is expressed only in the most susceptible animals: domestic cattle and goats. The other intermediate hosts are reservoirs and play an epidemiological role, especially in Africa (14, 15).

Epidemiological surveys show a seasonal aspect of the disease, which appears in France in summer, from July to September (16). Although animals of any age can be infected, the clinical signs are observed mainly in young animals, although not in those under the age of six months (17). Several authors note the epidemiological importance of summer pastures in the transmission of infection. Bigalke (18) demonstrated the contagious aspect of besnoitiosis by placing cattle with cysts alongside healthy cattle. The transmission rate was close to 100%.

Modes of transmission

The definitive hosts shed into their faeces oocysts that infect intermediate hosts (12). In the intermediate host, sporozoites released from the oocysts penetrate the intestinal mucosa and invade the endothelial cells of blood vessels where they become tachyzoites that go on to invade most tissues. In the skin (fibroblasts and histiocytes), the tachyzoites multiply in the form of bradyzoites, causing thick-walled globular cysts (1–2 mm in diameter) that can remain in cattle for around ten years. Contamination of the feline definitive host would appear to be from eating the tissue of infected cattle. The most common mode of transmission is from infected cattle to healthy cattle. Indeed, the bradyzoite-bearing cysts are present in large quantities in the skin, mucous membranes, connective tissue, etc. Bradyzoites from these skin cysts can be transmitted from infected to healthy cattle mechanically by blood-sucking insects (horse flies, Stomoxys flies) or by the use of a dirty needle for group injections. Vector transmission explains the strong seasonality of besnoitiosis and plays a major role in the disease's epidemiology (16, 19, 20).

Clinical signs

The clinical picture has three phases (19):

– a phase of uncharacteristic hypertermia: after an incubation period of six to ten days, acute hypertermia (40–42°C) occurs, which lasts for two to three days before decreasing; severe congestion, shortness of breath and nasal discharge are present

– a phase of oedema, which can last from one to two weeks: the oedema occurs on the head, dewlap and dependent regions; anoxia is common

– a final phase of cutaneous expression: alopecia and scleroderma are present and can last for several months, giving the typical 'elephant skin' appearance that is highly visible on the inner thigh; cracks form at the joints, resulting in cachexia and the death of animals diagnosed late.

Diagnosis

Clinical diagnosis is difficult during the first phase of the disease. The clinical signs are more suggestive of an infectious – particularly respiratory – disease. During the second phase, in areas where the disease is known, oedema of limbs, head and dependent parts is a very telling warning sign. During the scleroderma phase, skin thickening and wrinkling, hair loss and sometimes shedding of skin are highly characteristic signs. In addition, the presence of cysts in the sclera of the eye is a pathognomonic sign. These cysts also make it possible to detect healthy carrier animals, in which they are the only visible sign.

Laboratory diagnosis includes the following elements (14):

– direct detection of the parasite by microscopic examination of skin scrapings or shavings and by histological examination of conjunctival or skin biopsies (hematoxylin and eosin staining), or by polymerase chain reaction (PCR) (21)

– available serological methods include: indirect immunofluorescence (22), ELISA and Western blot (23, 24).
Control measures

Treatment consists chiefly of administering sulphonamides (25) as early as possible, but the results are not completely satisfactory. It is often coupled with symptomatic treatment for the animals' welfare: anti-inflammatories, diuretics.

In South Africa, there is a vaccine that confers immunity for around four years. Although the vaccine reduces the clinical signs, the animals remain asymptomatic carriers.

In disease-free areas

Ideally, serological testing should be conducted prior to introducing animals into disease-free areas. If a clinical case occurs in these areas, it is best to euthanase the animal as soon as possible (25).

In endemic areas

All sick animals should be culled, even those that have recovered (as they are still considered to be carriers), as well as animals with cysts. However, this may be difficult to implement when the number of infected animals is high.

The only way to prevent transmission of the parasite is vector control. Measures must be taken to control populations of horse flies (Diptera, Tabanidae), which are active only outside buildings, and populations of Stomoxys flies (Diptera, Muscidae), which are active both inside and outside buildings (14, 25, 26, 27).

Malaria

Aetiological agents

Malaria is a protozoan disease, caused by a species of Plasmodium, which is transmitted by vectors of the genus Anopheles (Insecta, Diptera, Culicidae). The taxon Plasmodium belongs to the kingdom of Protozoa, phylum Apicomplexa (Sporozoa), class Coccidea and order Haemosporidida. It is characterised by a heteroxenous life cycle, with schizogony in a vertebrate vector and sporogony in an invertebrate vector (blood-sucking Diptera). The genus Plasmodium is very diverse, with over 100 species described (28, 29), which are found in mammals, birds and reptiles.

Currently, around 40% of the world’s inhabitants, most of them living in the poorest countries on the planet, are exposed to malaria (1 million deaths per year).

Plasmodium parasites of animals are transmitted by members of the family Culicidae. Anopheles spp. are the vectors of parasites of non-human primates (apes, lemurs) (30). They are also the vectors of most Plasmodium parasites of other mammals: rodents (P. berghei), bats, etc. However, Plasmodium parasites of birds are transmitted by mosquitoes of the subfamily Culicinae (genera Aedes, Culex, Culiseta, etc.). In the case of amphibians and reptiles, the natural vectors of Plasmodium do not seem to be mosquitoes but rather other Diptera of the suborder Nematocera (Phlebotominae and Ceratopogonidae, etc.).

Epidemiology

The malaria parasite enters the body of the host when an infected mosquito takes a blood meal. The parasite then undergoes a series of transformations throughout its complex life cycle until it finally takes a form that is able to infect a mosquito once more.

More than 422 different species of the genus Anopheles have been described, 68 of which are associated with malaria. Of these, 40 species are acknowledged as the main vectors and 28 as secondary vectors (31). The chief factor governing the ability of an Anopheles species to act as a Plasmodium vector is the frequency with which it feeds on its hosts. In Anopheles, blood meals and egg-laying (oviposition) alternate, forming the gonotrophic cycle.

A female Anopheles mosquito cannot transmit Plasmodium until the parasite’s sporogonic cycle is complete, which takes at least eight days. With malaria, it is the ‘old’ females that are dangerous, and this determines the control methods (30, 32).

Clinical signs

In primates such as Macaca or Presbytis, the clinical signs of Plasmodium knowlesi malaria (zoonotic) appear in a few days. As a rule, malaria is accompanied by fever, asthenia, dehydration, lowered blood pressure, cyanosis and anaemia. Left untreated, the infection can prove fatal. Malaria can kill by destroying red blood cells (anaemia) and clogging the capillaries carrying blood to the brain (cerebral malaria) or other vital organs.

Diagnosis

Specific diagnosis includes the detection of parasites in blood, titration of serum antibodies to Plasmodium and detection of Plasmodium RNA/DNA in whole blood (PCR) (33, 34).

Control measures

Zoo primates and humans are treated with the same molecules (chloroquine, atovaquone, etc.), which raises a number of ethical issues in the face of growing resistance to anti-malarial agents.
Other vector-borne protists

*Hepatozoon canis* causes canine hepatozoonosis in Europe. It is a protozoan transmitted to dogs by the ingestion of an infected vector (35). *Rhipicephalus sanguineus* is its main vector in Europe. The clinical signs vary widely and its diagnosis is based on detecting the parasite in a blood smear.

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**References**


