Theileriosis in Cattle and Small Ruminants

Theileriasis

Theileria parva: East Coast Fever, Corridor Disease, January Disease, Zimbabwean Tick Fever

Theileria annulata: Tropical Theileriosis, Mediterranean Coast Fever, Mediterranean Theileriosis

T. buffeli/orientalis group: Theileria-Associated Bovine Anemia, Oriental Theileriosis

T. lestoquardi: Malignant Ovine (or Small Ruminant) Theileriosis

T. luwenshuni, T. uilenbergi: Cervine Theileriosis

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Importance

Protozoa in the genus *Theileria* are tick-borne parasites that have been found in many species of mammals. More than a dozen species of *Theileria* occur in cattle, water buffalo, sheep and goats. Some tend to circulate with few or no clinical signs, but others can cause serious illnesses with high morbidity and mortality rates, especially in naive animals. The two organisms with the greatest economic impact in cattle are *Theileria parva* and *T. annulata*, which cause East Coast fever/ corridor disease and tropical theileriosis, respectively. *T. lestoquardi, T. uilenbergi* and *T. luwenshuni* are the most virulent species in sheep and goats. In addition to causing direct losses, highly virulent species of *Theileria* can limit the movement of livestock between countries and are a constraint on the importation of new breeds or improved stock. The widely distributed *T. orientalis/ T. buffeli* group is classed among the less pathogenic species of *Theileria*, but members of this group have caused a number of outbreaks among cattle in New Zealand, Australia and other countries since 2010.

Etiology

Cattle

At least 15 species in the genus *Theileria* (phylum Apicomplexa, order Piroplasmida) infect domesticated ruminants. The two most virulent organisms in cattle are *Theileria annulata*, which causes tropical theileriosis, and *T. parva*, which causes East Coast fever. East Coast fever has other names in some regions, and some authors prefer to call this disease East Coast fever when it is caused by *T. parva* strains circulating in cattle, and corridor disease when the causative organisms are normally maintained in African buffalo. Although there are some differences in how cattle- or buffalo-adapted strains behave initially in cattle, both cause the same clinical signs, and buffalo-derived strains can adapt to cattle after serial passage.

Other organisms known to infect cattle include *T. velifera, T. taurotragi, T. mutans, Theileria* sp. (buffalo) and the *T buffeli/ orientalis* group. While all of these species are much less virulent than *T. parva* or *T. annulata*, *T buffeli/ T. orientalis* group can cause oriental theileriosis, which is also called *Theileria*-associated bovine anemia (TABA). The taxonomy of the *T buffeli/ T. orientalis* group and the number of species it contains are currently unresolved. At one time, three separate organisms - *T. orientalis, T. buffeli* and *T. sergenti* - were recognized in different parts of the world. These organisms are now thought to be the same species, which is called either *T. orientalis* or *T. buffeli* in current publications; however, some authors have argued that there may be 2 or more valid species. *T. sinensis*, which may or may not be a separate species, also belongs to the *T. buffeli/ T. orientalis* group. The *T. orientalis/ T. buffeli* group is abbreviated as *T. orientalis* in this factsheet. *T. orientalis* has 11 genotypes, types 1-8 and N1, N2 and N3. Types 1-3 are often referred to as the Chitose, Ikeda and Buffeli genotypes, respectively. Most recent outbreaks of oriental theileriosis have been caused by the Ikeda (type 2) genotype, although other genotypes can also cause disease.

Small ruminants

Clinical theileriosis in sheep and goats is usually caused by *T lestoquardi* (formerly *T hirci*), *T. uilenbergi* or *T. luwenshuni*. The disease caused by *T lestoquardi* is called malignant ovine theileriosis or variants of that name (e.g., malignant sheep theileriosis, malignant small ruminant theileriosis). A similar illness caused by *T. luwenshuni* and *T. uilenbergi* has been termed cervine theileriosis, as these agents also infect some cervids. Other species of *Theileria* that infect small ruminants, typically without clinical signs, include *T. separata, T. ovis, T. recondita, Theileria* sp. OT3 and *Theileria* sp. MK.

Species Affected

T. parva affects cattle and water buffalo (*Bubalus bubalis*). African buffalo (*Syncerus caffer*) and cattle are important reservoir hosts for this organism. Waterbuck (*Kobus* spp.) are also susceptible to infection. *T. annulata* affects cattle, yaks and water buffalo. It can also infect sheep and goats, but does not cause significant illness in these

animals. Small ruminants have very few *T. annulata* piroplasms in the blood, and have little or no importance in transmitting this agent to ticks. Cattle, yaks, water buffalo and African buffalo can be infected with *T. orientalis*. Nucleic acids of this organism have also been detected in eland (*Taurotragus oryx*) and bushbuck (*Tragelaphus* sp.). *T. mutans* has been found in cattle, water buffalo, African buffalo and bushbuck, while *T. velifera* and *Theileria* sp. (buffalo) have been detected in cattle and African buffalo. *T. taurotragi* has been recognized in cattle, eland and bushbuck, but African buffalo do not seem to be susceptible to this organism.

T. lestoquardi, T. luwenshuni and *T. uilenbergi* affect sheep and goats. *T. luwenshuni* and *T. uilenbergi* have also been found in subclinically infected sika deer (*Cervus nippon*) and red deer (*Cervus elaphus*), and *T. luwenshuni* was detected in asymptomatic roe deer (*Capreolus pygargus*) and Mongolian gazelles (*Procapra gutturosa*). Although the nucleic acids of *T. lestoquardi* have been reported in cattle, all attempts to establish experimental infections in this species, to date, have failed. One report described the apparent isolation of this organism from a fatal case of theileriosis in a cow, but the recovered organism was not pathogenic in sheep and it might have been misidentified. Other species of *Theileria* found in small ruminants, typically without clinical signs, include *T. separata, T. ovis, T. recondita*, *Theileria* sp. OT3 and *Theileria* sp. MK. *Theileria* sp. OT3 nucleic acids have also been detected in red deer, roe deer and chamois (*Rupicapra rubicapra*). *T. ovis* was found by PCR in a cow in China and a chamois in Spain. Other species of *Theileria* have also been reported in wild ungulates, including African buffalo and cervids, but are not known to infect domesticated ruminants.

A few reports have found nucleic acids from cattle or small ruminant *Theileria* in other mammals. Clinical theileriosis seems to occur in camels, and the nucleic acids of *T. annulata*, *T. mutans* and *T. ovis* have been detected in this species by PCR. However, none of these organisms has been definitively linked to clinical cases in camels. *T. annulata* has been found by PCR in asymptomatic dogs from several countries, and one report described *T. orientalis, T. luwenshuni* and *T. ovis* nucleic acids in sheepdogs in the Middle East. *T. sinensis* and *T. parva* were found by PCR in < 2% of healthy captive lions (*Panthera leo*) in Africa. *T. luwenshuni* was detected by PCR in a number of hedgehogs in China. Reports of *Theileria* spp. found by PCR alone should be viewed with caution, as the genomes of some species can be very similar and tests designed to amplify some organisms have occasionally amplified other species.

Zoonotic potential

There is no evidence that the species of *Theileria* found in ruminants affect humans. One study that detected *T. luwenshuni, T. ovis* and *T. orientalis* in sheepdogs by PCR did not find any evidence of these organisms in the dogs' owners.

Geographic Distribution

T. parva (East Coast fever/ corridor disease) occurs in sub-Saharan Africa. Other organisms that have been reported mainly or exclusively from Africa include *Theileria* sp. (buffalo), *T. velifera* and *T. taurotragi*. *T. mutans* has been documented in Africa and many other locations around the world; however, some of the organisms outside Africa were later found to be other species of *Theileria* (e.g., *T. orientalis*), or the presence of *T. mutans* could not be confirmed in recent PCR-based surveys. *T. annulata* (tropical theileriosis) occurs in southern Europe, the Middle East and parts of Asia. *T. orientalis* is widespread; it has been reported from Europe, Asia, Africa, North and South America, Australia and New Zealand. *T. sinensis* has been documented in Asia (China) and Africa.

T. lestoquardi and *T. ovis* have been found in Asia, the Middle East and parts of Africa and Europe. *T. uilenbergi* has been reported from China, while *T. luwenshuni* has been described in parts of Asia, Europe and the Middle East.

Transmission

Theileria are transmitted by ticks acting as biological vectors, and can be transmitted transstadially. Transovarial transmission is not thought to occur. Genera of ticks reported to act as vectors include *Rhipicephalus* (*T. parva, T. taurotragi, T. ovis, T lestoquardi*), *Hyalomma* (*T. annulata, T lestoquardi, T. separata*), *Haemaphysalis* (*T. orientalis, T. uilenbergi, T. luwenshuni*) and *Amblyomma* (*T. mutans, T. velifera*).

Theileria spp. enter the body as sporozoites in the saliva of a feeding tick. Ordinarily, *T. parva* and *T. annulata* only mature after an infected tick attaches to a host, and the tick must be attached for a few days before these organisms are transmitted. However, *T. parva* can develop to the infectious stage in ticks on the ground if environmental temperatures are high. These organisms may enter the host within hours of attachment. Inside the mammalian host, *Theileria* undergoes a complex life cycle involving the replication of schizonts in leukocytes and development of piroplasms in erythrocytes. Piroplasms infect ticks when they feed on the animal's blood. *Theileria* can also be transmitted mechanically via blood (e.g., on re-used needles) and possibly by biting flies and sucking lice (*Linognathus vituli*).

Ruminants, including animals that recover, can carry some species of *Theileria* for months or years. Transplacental transmission has been documented for several species of *Theileria*, including *T. annulata* and *T. orientalis* in cattle and *T. lestoquardi* in sheep and goats. The frequency of vertical transmission might differ depending on whether the dam is acutely infected or a carrier. *T. orientalis* has been found in colostrum by PCR, but one attempt to infect calves orally with colostrum was unsuccessful.

Disinfection

Disinfection is not important in the control of theileriosis. If needed, an agent effective against protozoa should be selected.

Incubation Period

The incubation period for East Coast fever is 7-12 days in experimentally infected animals, although some cases might appear as late as 3 weeks. The incubation period for tropical theileriosis is approximately 1-3 weeks.

Clinical Signs

Cattle and water buffalo

East Coast fever/ corridor disease (*T. parva*) is characterized by fever, generalized lymphadenopathy, anorexia, loss of condition and, in some animals, nasal discharge and/or diarrhea. Petechiae and ecchymoses may be found on the conjunctiva and oral mucous membranes, and milk yield usually decreases in lactating animals. Corneal opacity, exophthalmia and skin lesions (nodules, hemorrhagic or ulcerative lesions, erythematous papular rashes) have been reported occasionally. Terminally ill animals often develop pulmonary edema, with severe dyspnea and a frothy nasal discharge. Some animals have poor productivity after recovery and their growth is stunted. Although ocular signs including corneal opacity sometimes resolve with treatment, permanent loss of eyesight is possible. *T. parva* can also cause a fatal condition called "turning sickness," where infected cells block capillaries in the central nervous system and cause neurological signs.

Tropical theileriosis (*T. annulata*) generally resembles East Coast fever, but these parasites also destroy red blood cells, causing anemia and, in some cases, jaundice or hemoglobinuria. Petechiae are often found on the mucous membranes, and hemorrhagic diarrhea may be seen in the late stages. Some animals abort. In at least two cases, newborns appeared normal at birth but developed clinical signs within a few days, probably from infections acquired *in utero*. Neurological signs have been documented in some terminally ill water buffalo, but turning sickness does not seem to be a feature of tropical theileriosis in cattle.

Other species of *Theileria* tend to be carried asymptomatically, although some can cause anemia or other clinical signs, especially when there are exacerbating factors such as coinfections. The Ikeda genotype of *T. orientalis* has recently caused a number of outbreaks in cattle, with clinical signs of fever, lethargy, inappetence, lymphadenopathy, anemia, jaundice, diarrhea and reproductive losses including stillbirths and late term abortions. Although many animals recover, some cases are fatal. Similar clinical cases, accompanied by generalized depigmentation of the skin, were reported in water buffalo infected with *T. orientalis* of the type 7 genotype. *T. taurotragi* was recently suggested to be the cause of a neurological disease, which is locally called ormilo disease, among cattle in Tanzania.

Sheep and goats

The clinical signs in small ruminants infected with *T. lestoquardi* are similar to other forms of theileriosis, and may include fever, anorexia, weight loss, lymphadenopathy, respiratory signs (coughing, nasal discharge, dyspnea), anemia, icterus and diarrhea. Reproductive losses including abortions may be seen. Similar signs have been reported in sheep infected with *T. luwenshuni* or *T. uilenbergi*.

Experimental infection of sheep and goats with *T. annulata* resulted in only mild to moderate clinical signs, with fever and lymphadenopathy in some cases. The signs were milder in goats than sheep.

Other species

African buffalo seem to be infected subclinically by various species of *Theileria*, but whether this is always the case in naive individuals is unclear. *T. taurotragi* can be found in healthy wildlife, but it was thought to have caused a fatal illness in eland that was characterized by generalized lymphadenopathy and, in some animals, wasting, severe terminal diarrhea or severe respiratory distress.

Post Mortem Lesions

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Petechiae and ecchymoses are often found on the serosal surfaces of internal organs, and the body cavities may contain serous fluid. Signs of icterus may be observed in some carcasses. The lymph nodes and spleen are usually enlarged in acute cases. The liver may also be larger than normal, and white foci of lymphoid infiltration (pseudoinfarcts) may be detected in the liver and kidneys. The gastrointestinal tract can have signs of hemorrhagic gastroenteritis, particularly in the small intestine and abomasum. Interlobular emphysema and severe pulmonary edema are common in cattle that die of East Coast fever. The lungs are hyperemic and full of fluid, and a frothy exudate may be found around the nostrils and in the trachea and bronchi. Pulmonary edema also occurs in small ruminants infected with *T. lestoquardi*, and it has sometimes been reported in animals affected by other species of *Theileria*. The gross lesions in turning sickness include congestion, hemorrhages and areas of malacia in the brain.

Diagnostic Tests

In live animals, theileriosis can be diagnosed by finding piroplasms or schizonts in Giemsa-stained thin smears from blood or lymph node biopsies, respectively. The organisms are usually rod-shaped or oval in blood smears, although other forms can be seen. Piroplasms may be absent or uncommon in animals with acute illnesses caused by some organisms, such as buffalo-derived *T. parva* in cattle. At necropsy, schizonts can be detected in impression smears from many internal organs of sick animals, such as the lungs, lymph nodes, spleen and liver. The number of piroplasms is typically too low to be detected in the blood of carriers.

PCR is often used in diagnosis, and can identify *Theileria* in the blood of both carriers and clinical cases. Some tests can distinguish the species of *Theileria*, while

others are specific for the genus. Species-specific PCR assays may occasionally amplify closely-related species of *Theileria*. This seems to be a particular issue with *T. lestoquardi* and *T. annulata*. One survey also found that a PCR test for *T. taurotragi* amplified what appeared to be a variant of *T. mutans* in African buffalo. These situations can be clarified with other tests, such as PCR-RFLP to distinguish *T. lestoquardi* and *T. annulata*. Other genetic tests, such as reverse line blotting assay (RLB), may be available in some areas, though they are mainly used in research. Loop mediated isothermal amplification (LAMP) assays have been published. *In vitro* culture is possible for some (but not all) species of *Theileria*; however, this technique is usually employed only in research.

Antibodies to *T. parva* and *T. annulata* can be detected with ELISAs, indirect fluorescent antibody test (IFA) or other serological assays. These tests may not be sensitive enough to detect all infected cattle, and cross–reactions can occur between some species of *Theileria*. The use of serological tests in diagnosis is more common in areas where molecular tests such as PCR are not widely available.

Treatment

Sick animals can be treated with antiparasitic drugs such as buparvaquone. Combinations of drugs have been used in some outbreaks. Antiparasitic drugs are most effective in the early stages of theileriosis, and severely affected animals may die despite intensive care. Organisms can persist in animals that recover. Drug-resistant organisms have been reported.

Control

Disease reporting

Veterinarians who encounter or suspect theileriosis should follow their national and/or local guidelines for disease reporting. The most pathogenic species in cattle and small ruminants (i.e., *T. annulata*, *T. parva*, *T. lestoquardi*, *T. luwenshuni* and *T. uilenbergi*) are all exotic to the U.S. and must be reported to state or federal authorities immediately upon their diagnosis or suspicion.

Prevention

Theileriosis is not transmitted by casual contact. If an organism was introduced recently, it might be eradicated by stamping out (i.e., movement controls, culling of infected animals), together with measures to prevent its establishment in ticks.

In endemic areas, exposure can be reduced with acaricides and other methods of tick control such as rotational grazing. The transfer of blood between animals must be avoided. Vaccines are available for East Coast fever and tropical theileriosis in some countries. Attenuated live vaccines are used for tropical theileriosis, but animals are vaccinated against East Coast fever by concurrently administering several strains of *T. parva* and an antibiotic (usually a long-acting tetracycline). This generally results in a mild or inapparent infection followed by immunity, and the animal becomes a carrier. The possibility of introducing live vaccine organisms into areas where they are not endemic is a concern.

Morbidity and Mortality

The severity of theileriosis varies with the species of *Theileria*, strain and dose of the organism, and host factors such as immunity and concurrent illnesses. Breed-related differences in susceptibility have been reported in cattle. The effect of coinfections with less pathogenic species of *Theileria* seems to be complex. While coinfections may increase the severity of some illnesses, some organisms seem to protect cattle from *T. parva*.

In endemic regions, outbreaks of East Coast fever and tropical theileriosis tend to occur when susceptible animals are moved into the area. They may also be seen in situations where exposure has changed, such as when tick control measures have stopped. The case fatality rate for untreated East Coast fever/ corridor disease can approach 100% in fully susceptible taurine, zebu or sanga cattle. In contrast, morbidity rates can be close to 100% in indigenous cattle but the mortality rate is usually low. Water buffalo are said to be as susceptible to East Coast fever as cattle, although there is relatively little information published about this species. The mortality rate for tropical theileriosis is reported to be 40-90% in newly introduced cattle but < 5% in some indigenous animals.

The morbidity rate in small ruminants infected with *T. lestoquardi* can approach 100%, with reported mortality rates of 46-100%. Clinical cases seem to be more severe in sheep than goats. As in cattle, infections can be milder in indigenous animals. Limited information is available for *T. luwenshuni* and *T. uilenbergi*, but morbidity rates in sheep and goats ranged from 19% to 65% in different regions of China, with mortality rates of 18-75%. The most severe infections occurred in lambs and animals that had come from other areas. In the U.K., an outbreak in a flock of sheep that appeared to be caused by *T. luwenshuni* resulted in 25 deaths. All of the affected sheep grazed in a field that had an unusually large number of ticks and were severely infested; the rest of the flock was apparently unaffected.

Most other *Theileria* in domesticated ruminants tend to be carried with few or no clinical signs. However, *T. orientalis* has caused a number of outbreaks in cattle since 2010, especially in New Zealand and Australia. The illness tends to be more serious in young calves and pregnant or recently calved animals. One study estimated the overall case fatality rate to be approximately 17% and cumulative mortality < 0.5% during outbreaks caused by the Ikeda genotype of *T. orientalis* on New Zealand farms. However, some farms were more severely affected, with cumulative mortality rates greater than 5%. A genotype N2 organism caused a severe outbreak with a high case fatality rate on a water buffalo dairy in India. Outbreaks caused by *T. orientalis* have often occurred after animals were moved from one region to another.

Internet Resources

Food and Agriculture Organization of the United Nations (FAO). Manual on Meat Inspection for Developing Countries

The Merck Veterinary Manual

United States Animal Health Association. Foreign Animal Diseases

World Organization for Animal Health (WOAH)

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

WOAH Terrestrial Animal Health Code

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