African Animal Trypanosomiasis

Nagana, Tsetse Disease, Tsetse Fly Disease, African Animal Trypanosomosis

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Importance

African animal trypanosomiasis is a parasitic disease that causes serious economic losses in livestock from anemia, loss of condition and effects on reproduction. Losses in cattle are especially prominent. Animals other than livestock, including dogs, can also be affected. Untreated cases can be fatal, and the mortality rate is high in some outbreaks. The causative agents mainly circulate in parts of Africa that contain the biological vector, the tsetse fly; however, they can also be found in nearby regions due to mechanical transmission and the movement of infected animals. One organism, *Trypanosoma vivax*, has become established in South America, where it is mainly transmitted by biting flies acting as mechanical vectors. Tsetse fly control programs in Africa can help reduce the incidence of African animal trypanosomiasis, as well as other forms of trypanosomiasis that affect both humans and animals.

Etiology

Trypanosomes are protozoan parasites in the family Trypanosomatidae. African animal trypanosomiasis is caused by those organisms that are transmitted by tsetse flies but do not ordinarily affect humans. The three most important species are *Trypanosoma congolense* (subgenus *Nannomonas*), *T. vivax* (subgenus *Duttonella)* and *T. brucei* subsp. *brucei* (subgenus *Trypanozoon*). There are three variants of *T. congolense*, called the savannah, forest and kilifi (or Kenya Coast) types. African animal trypanosomiasis can also be caused by *T. (Nannomonas) simiae*, *T. (Pycnomonas) suis*, *T. (Nannomonas) godfreyi* and *T. (Duttonella) uniforme*, and possibly by additional unnamed trypanosomes.

Two related parasites, *T. brucei* subsp. *gambiense* and *T. brucei rhodesiense*, cause human African trypanosomiasis, which is also known as sleeping sickness. The primary distinction between this disease and African animal trypanosomiasis is that these two organisms can evade the innate resistance humans possess against other tsetse-transmitted African trypanosomes.

Species Affected

The organisms that cause African animal trypanosomiasis have been found in many species of mammals, including all domesticated animals and some free-living or captive wildlife. Wildlife known to be susceptible to infection include ruminants such as South American white-tailed deer/ cariacou *(Odocoileus gymnotis)*), duikers (*Cephalophus* spp.), antelope and African buffalo (*Syncerus caffer*), as well as wild equids, felids, warthogs (*Phacochoerus* spp.), capybaras (*Hydrochoerus hydrochaeris*), elephants, nonhuman primates and various rodents. Cattle are reservoir hosts for *T. congolense*, *T. vivax* and *T. b. brucei*, but other animals including small ruminants, pigs and some wildlife (e.g., African buffalo) are also thought to maintain these organisms. Clinical cases have been seen in a number of species including cattle, sheep, goats, pigs, camels, horses, donkeys, water buffalo, alpacas, llamas, dogs, cats and captive wild ungulates. Laboratory rodents and rabbits can be infected experimentally with trypanosomes, but not with all species and strains.

T. congolense, *T. vivax* and *T. b. brucei* have a wide host range among domesticated animals, although there could be some differences in their host preferences or virulence for different species. *T. godfreyi*, *T. simiae* and *T. suis* are mainly known to affect pigs. *T. simiae* has also been detected in sheep, goats, cattle, camels, horses and wildlife. Very little is currently known about *T. suis*, which is suspected to be carried in wild African suids. Attempts to infect goats, sheep, calves, donkeys, cats, dogs, rabbits and laboratory rodents with this organism were unsuccessful.

Reptiles and birds carry their own species of trypanosomes, but *T. vivax* DNA was detected by PCR in crocodiles and monitor lizards (*Varanus ornatus*) in Africa. Whether this organism can become established in reptiles or is only inoculated transiently by insects remains to be determined.

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Zoonotic potential

Humans are normally not susceptible to the trypanosomes that cause African animal trypanosomiasis. The trypanolytic activity of apolipoprotein L-I (apoL-I), found in human blood, is thought to be the major innate defense mechanism. Genetic defects in apoL-I have been detected in some people who were infected by trypanosomes not expected to be pathogenic for humans (e.g., *T. evansi*, which causes surra). Partial resistance of *T. vivax* and *T. congolense* to human serum has also been demonstrated in the laboratory under certain conditions.

A very small number of human infections caused by *T. b. brucei*, *T. vivax* and *T. congolense* have been reported. Most cases were not fully described, and many are very old and not definitive, as they were diagnosed by the parasite's morphology alone. For instance, a case reported to be caused by *T. vivax* dates from 1917. One infection with *T. b. brucei* occurred after accidental inoculation in a laboratory, and one of 7 volunteers infected with this organism in the 1940s became infected for 3 weeks. Two clinical cases of sleeping sickness in people infected with *T. b. brucei* or *T. congolense* were diagnosed by PCR-based confirmation of the organism's identity. In the latter case, the person was infected with both *T. congolense* and an unidentified subspecies of *T. brucei*, which might have been one of the usual agents of sleeping sickness in humans (i.e., *T. b. gambiense* or *T. b. rhodesiense).* Therefore, the contribution of *T. congolense* to the illness, if any, is uncertain. Although the risk to humans seems to be minimal, precautions are recommended when handling blood, tissues and animals infected with the agents of African animal trypanosomiasis.

Geographic Distribution

Trypanosomes transmitted by tsetse flies are endemic in a part of sub-Saharan Africa called the tsetse fly belt, which occurs approximately between latitudes 10°N and 20-30°S. A few species of tsetse flies have also been detected in parts of the southwestern Arabian peninsula. Trypanosomes, particularly *T. vivax*, can spread beyond the tsetse fly belt by animal movements and transmission through mechanical vectors. *T. vivax* has become established in parts of South and Central America and the Caribbean, which are free of tsetse flies.

Transmission

Tsetse flies (*Glossina* spp.) are biological vectors for the trypanosomes that cause African animal trypanosomiasis and transmit these organisms in their saliva. Trypanosomes must develop for one to a few weeks in the fly before they reach the infective stage. *T. vivax* has the shortest cycle. Trypanosomes can also be transmitted by mechanical vectors including surgical instruments, needles, syringes and other biting flies. Mechanical transmission is thought to be most significant for *T. vivax*, which is transmitted primarily by this route in South America. Tabanidae (horseflies) and stable flies (*Stomoxys* spp.) are thought to be the most important vectors in this region.

Animals infected with trypanosomes can become chronic carriers, and inapparent infections can be reactivated if the animal is stressed. Transplacental transmission has been reported. The possibility of venereal transmission was suggested by the detection of *T. vivax* nucleic acids in the semen of experimentally infected goats and the demonstration that another trypanosome (*T. cruzi*, the cause of Chagas disease) can be transmitted venereally in mice. However, it remains to be proven.

Trypanosomes do not survive for long periods outside the host. *T. brucei* may remain alive for a few hours in blood, and for up to a few days if it is refrigerated under certain conditions (e.g., in blood with adequate oxygen).

Disinfection

T. brucei is susceptible to a number of disinfectants including 0.05% sodium hypochlorite, 70% ethanol, 2% formaldehyde, 0.05% glutaraldehyde and 0.1% hand soap. Trypanosomes are also inactivated by a temperature of 50°C (122°F).

Incubation Period

Incubation periods from 4 days to approximately 8 weeks have been reported in ruminants. More virulent isolates seem to have a shorter incubation period, often 2 weeks or less. In one study, all dogs developed clinical signs within 2 weeks after inoculation with trypanosomes.

Clinical Signs

Cattle, sheep and goats can be infected with or without clinical signs. Most clinical cases in ruminants are chronic, but acute disease, which may be fatal within weeks, can also be seen. The first sign may be a localized swelling (chancre) at the site of the fly bite, but this usually remains unnoticed. The primary clinical signs are an intermittent fever, signs of anemia (e.g., pale mucous membranes, lethargy), lymphadenopathy and weight loss. Hypoglycemia may be seen in the acute stage. Over time, the animals can lose condition and become progressively emaciated, often with concurrent signs such as decreases in milk yield. They can have a decreased appetite, and may develop neurological signs, dependent edema (including submandibular edema), cardiac lesions, diarrhea and keratitis/ corneal opacity. There may also be abortions, premature births, perinatal losses and damage to the male reproductive organs (e.g., orchitis, epididymitis), with reduced semen quality. Trypanosomes can cause immunosuppression, and concurrent infections may complicate this disease. Sudden deaths have been reported in small ruminants, and deaths are common in untreated animals with chronic clinical signs. Animals that recover clinically may relapse when stressed.

An acute hemorrhagic syndrome has been seen sporadically in cattle infected with some isolates of *T.*

vivax, mostly in East Africa. This condition might be mediated by antibodies directed against red blood cells. Affected animals have enlarged lymph nodes and signs of severe anemia, and they develop widespread visceral and mucosal hemorrhages, particularly in the gastrointestinal tract. In one outbreak, the main hemorrhagic sign was bleeding from the ears. Weight loss can be severe. This syndrome can be rapidly fatal.

There is limited information about trypanosomiasis in species other than cattle, sheep and goats, but the clinical signs are reported to be similar. Anemia, weight loss and other typical signs, including neurological signs, were seen in some pigs, while other pigs have had mild illnesses or asymptomatic infections. *T. simiae* is reported to cause a hyperacute illness in this species, with death often occurring within 48 hours of the initial signs. Severe illnesses and deaths have been seen infrequently in horses, while most infections in donkeys seem to be mild or asymptomatic. Donkeys did not develop clinical signs after inoculation with a South American *T. vivax* isolate pathogenic for goats. There are very few reports of clinical trypanosomiasis in wildlife, but illnesses have apparently been seen in captive Artiodactyla, and *T. b. brucei* caused systemic signs, orchitis and several deaths in experimentally infected red-fronted gazelles (*Gazella rufifrons*).

Both acute and chronic clinical cases, as well as subclinical infections, have been described in dogs. The signs in naturally and/or experimentally infected dogs have been similar to those in ruminants, and included neurological signs or keratitis/ corneal opacity in some cases. A few unusual cases have also been seen. In addition to other signs, one dog presented with seizures and severe hypoglycemia that was refractory to treatment with glucose and oral sugar supplementation but responded to elimination of the trypanosomes. Two dogs had clinical signs that included acute hemorrhagic vomiting and diarrhea. Bloody diarrhea was also seen in some experimentally infected dogs; however, these animals were inoculated intraperitoneally, which could have resulted in atypical signs. Several sudden deaths were reported in naturally infected dogs. Other animals died during the course of the illness, especially during episodes of cardiovascular collapse or other events. A few dogs with clinical signs recovered spontaneously, and some dogs were treated successfully with antiparasitic drugs. Relapses have also been reported in treated dogs, and corneal opacity may be permanent.

Post Mortem Lesions

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The gross lesions are nonspecific. The lymph nodes and spleen are enlarged in the acute stage, and petechiae are frequently found on serosal surfaces, particularly in the peritoneal cavity. The lymph nodes may be enlarged, normal or atrophied in more prolonged cases; they are not usually enlarged in chronically infected animals. Serous atrophy of fat and evidence of anemia are common, and subcutaneous edema, excessive fluid in the body cavities and pericardial sac, pulmonary edema and an enlarged liver may also be seen. The carcass may be wasted or emaciated. Some trypanosomes can directly damage tissues, resulting in lesions such as keratitis or cardiac damage (e.g., myocarditis). Immune complexes also cause inflammation and damage in a variety of tissues including the kidneys and blood vessels.

Diagnostic Tests

A presumptive diagnosis can be made if trypanosomes are observed by direct microscopic examination of blood, lymph nodes (e.g., smears of needle biopsies), edema fluid or tissues collected at necropsy. Organisms are most likely to be found in the blood during the initial stages of the infection. They are less likely to be detected in chronically ill animals, and are almost never seen in healthy carriers. Samples for microscopy can include unstained wet blood films and thick or thin smears stained with Giemsa or other agents. Wet films are examined by light microscopy (condenser aperture, phase-contrast or interference contrast), using 400x power to detect the motile trypanosomes. Thick or thin blood films should also be examined at high magnification. Thick films are more likely to detect trypanosomes when their numbers are low, but parasite morphology is easier to observe in thin films. Parasite concentration techniques, such as mini anion–exchange chromatography, hematocrit centrifugation, the quantitative buffy coat method and the dark-ground/phase-contrast buffy coat technique, can increase the probability of detecting the organisms. The trypanosome's morphology can provide a presumptive species identification, but some species cannot be distinguished by this method, and unusual morphologies have occasionally been reported. Animals can be infected concurrently with more than one species of trypanosome. Pathogenic species must be distinguished from avirulent organisms such as *Trypanosoma theileri*.

Polymerase chain reaction (PCR) assays on blood or tissue samples can identify trypanosomes at the genus, species or subspecies level. The World Organization for Animal Health (OIE) currently recommends the use of species-specific PCR tests; however, these tests may miss organisms other than *T. vivax*, *T. congolense* and *T. b. brucei*. The internal transcribed spacer (ITS-1) PCR technique can amplify multiple species of trypanosomes, followed by gel electrophoresis to distinguish these organisms by the size of the amplified fragment. It can recognize infections with less commonly identified species, as well as the 3 major organisms. However, the OIE notes that sequencing is often necessary to confirm the organism's identity and ITS-1 PCR is not used routinely for diagnosis. Loop-mediated isothermal amplification (LAMP) tests are in development for livestock, and have been used to detect clinical cases in dogs in Africa. Antigen detection techniques have been described but were found to

be unreliable. Some newer antigen-detection methods in development may be promising.

In vitro cultivation can be used to isolate some species of trypanosomes, though it is not employed for routine diagnosis. Not all pathogenic species will grow *in vitro*, and nonpathogenic trypanosomes can readily overgrow the culture. Animal inoculation of rats or mice is rarely employed for diagnosis except in unusual circumstances.

Serology is mainly used in surveillance and for identifying infected animals before transport to trypanosome-free areas. The indirect fluorescent antibody test and ELISAs are generally used in cattle. Cross-reactions can occur between the various trypanosomes causing African animal trypanosomiasis. These tests can also cross-react with nonpathogenic trypanosomes (e.g., *T. theileri)* and trypanosomes that cause other diseases (e.g., *T. evansi*).

Treatment

A small number of drugs have been licensed as veterinary treatments for trypanosomiasis. Diminazene aceturate and isometamidium chloride are used most often, but resistance to these agents is common in some regions. Various systems to maximize effectiveness and reduce the development of resistance, such as alternating drugs that are unlikely to induce cross-resistance, have been proposed for livestock. Drug resistance or inadequate treatment (or poor quality drugs) can result in clinical cure but persistence of the infection.

Some of the drugs used in livestock, especially isometamidium chloride, have been employed in clinical cases in dogs. Agents used to treat trypanosomiasis in humans (e.g., pentamidine) were used in a few cases when other drugs were unavailable. Two dogs recovered after treatment with pentamidine, although one later relapsed. Treatment is most effective when begun early in the course of the disease.

Control

Disease reporting

Veterinarians who encounter or suspect African animal trypanosomiasis should follow their national and/or local guidelines for disease reporting. In the U.S., this disease should be reported immediately to state or federal authorities.

Prevention

Although most of the organisms that cause African animal trypanosomiasis can only become established where tsetse flies are present, *T. vivax* has become endemic in some areas where it is transmitted mechanically by other insects. Stamping out (e.g., quarantines, movement controls and the euthanasia of infected animals), combined with vector controls, may be able to eliminate this organism from a disease-free area if its introduction is recognized promptly.

In Africa, trypanosomiasis can be controlled by reducing or eliminating tsetse flies with traps, insecticides and other means, and by treating infected animals. The specific control methods may differ depending on the epidemiological importance of various livestock species and wildlife in a region, and the predominant species of tsetse flies. A tsetse fly eradication campaign, the Pan African Tsetse and Trypanosomosis Eradication Campaign (PATTEC), is being conducted in Africa. Its eventual goal is to eliminate tsetse flies from the continent, and with them, to eliminate most animal trypanosomes. Whether this is realistic is currently uncertain; however, trypanosomes were cleared or mostly cleared from limited areas in the past.

The selection of trypanotolerant breeds (see Morbidity and Mortality) can lessen the impact of African animal trypanosomiasis. Good nutrition and the management of concurrent illnesses are also helpful. Chemoprophylaxis is sometimes used to protect susceptible livestock. Chemoprophylaxis with isometamidium also reduced the nmber of clinical cases in trypanosome-naive dogs introduced to Africa, together with the use of deltamethrin-impregnated collars.

Morbidity and Mortality

T. vivax and *T. congolense* are considered to be the major pathogens in ruminants, while *T. b. brucei* is thought to be of lesser significance. The acute hemorrhagic syndrome caused by some *T. vivax* strains has a mortality rate of 6-35%, but, in general, *T. vivax* is considered to be less pathogenic for cattle than *T. congolense*. Some of the savannah type strains of *T. congolense* are among the most virulent isolates. Other trypanosomes are poorly understood; however, *T. simiae* caused high mortality in some pigs.

Morbidity and mortality rates for African animal trypanosomiasis are influenced by an animal's general health, as well as the strain and dose of the infecting organisms. In susceptible cattle or small ruminants, some strains can result in 50-100% mortality within months, especially when poor nutrition or other factors contribute to debilitation. Infections with other organisms may be subclinical or mild, and can be followed by spontaneous recovery. In Africa, trypanosomiasis is now mostly a disease of high morbidity but low mortality in regions where sick animals are treated with trypanocidal drugs. Epizootics with high morbidity and mortality rates can be seen occasionally when susceptible livestock are introduced into endemic regions or when tsetse flies spread into an area where cattle are naive. However, such outbreaks seem to be infrequent. In South America, clinical cases seem to be mild and mortality low in many areas, but periodic outbreaks can be seen in some regions. Perinatal mortality due to abortions and neonatal deaths can exceed 50% in some outbreaks, even if mortality rates in adults are not

high. Chronically affected animals may be slow to recover after treatment.

Some breeds of African cattle and small ruminants are genetically resistant to the development of clinical signs, a phenomenon known as trypanotolerance. Trypanotolerant breeds include West African Shorthorn (which may also be known as Muturu, Baoule, Laguna/ Lagune, Namchi, Samba/ Somba or Dahomey) and N'Dama cattle, Djallonke and Red Maasai sheep, and West African Dwarf and Small East African goats. Some trypanotolerant breeds tend to self-cure and eliminate the organism; others may remain persistently infected but maintain productivity and show few or no signs of illness. Trypanotolerance is not absolute, and resistant animals may require treatment in areas where the challenge intensity is very high. Trypanotolerance varies with the pathogen, and some breeds are susceptible to the strains of *T. vivax* that cause hemorrhagic disease.

Trypanosomiasis in dogs is incompletely understood. Some dogs living in endemic regions seem to be infected without significant clinical signs, but clinical cases have been described, and the number of recognized cases in Africa seems to be growing. Of 148 French military dogs sent to Africa with only vector control as protection from trypanosomiasis, 13% became infected and 3.4% died of trypanosomiasis. The infection rate decreased to 2% when dogs were protected by both chemoprophylaxis and deltamethrin-treated collars. Reported infection rates among dogs born and raised in Africa range from < 10% to 30%. Many clinical cases in dogs have been caused by *T. congolense*, although other organisms were also found.

Internet Resources

The Merck Veterinary Manual
http://www.merckvetmanual.com/

United States Animal Health Association. Foreign Animal Diseases
http://www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

World Health Organization. The Pan African Tsetse and Trypanosomiasis Eradication Campaign – PATTEC
http://www.who.int/trypanosomiasis_african/partners/pattec/en/

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

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