Dourine

Covering Disease, Morbo Coitale Maligno, Slapsiekte, El Dourin, Mal de Coit, Beschalseuche, Sluchnaya Bolyezn Lappessa Dirressa

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Importance

Dourine is a serious, often chronic, protozoal disease of equids that is usually acquired by venereal transmission. Inflammation and edema of the genitalia is prominent, but neurological signs and progressive emaciation are also common, and the case fatality rate is high. No vaccine is available, and the long-term efficacy of treatment is uncertain.

Etiology

Dourine is caused by the protozoan parasite *Trypanosoma equiperdum* (subgenus *Trypanozoon*, Salivarian section). Strains of this organism appear to differ in pathogenicity.

T. equiperdum is very closely related to both Trypanosoma brucei, one of the causative agents of African trypanosomiasis, and T evansi, which causes surra, and whether it should be considered a distinct species is controversial. While T. equiperdum has a narrower host range than T. evansi and T. brucei, these three organisms can cause similar illnesses, though dourine also has prominent lesions related to its route of transmission. Some genetic analyses suggest that T. equiperdum and T. evansi evolved independently from *T. brucei* while losing the ability to be transmitted by tsetse flies. Unlike T. brucei, these two organisms are mostly monomorphic (they do not change from the slender forms replicating in mammalian hosts to the short, stumpy form that infects tsetse flies); they proliferate only asexually (sexual reproduction occurs in the tsetse fly) and are thus less variable than T. brucei; and they have partially or completely lost some of the genetic elements found in T. brucei. However, the genetic distance between T. brucei and T. equiperdum or T. evansi is sometimes less than the difference between T. brucei isolates from different geographic areas. Various naming systems have been proposed as a result, including some that consolidate all three parasites under a single Trypanosoma species, either T. brucei or T. evansi, though there is, as yet, no consensus.

Species Affected

Dourine mainly affects horses, donkeys and mules, which seem to be the only natural reservoirs for *T. equiperdum*. Zebras have tested positive by serology, but there is no conclusive evidence of infection in this species. In 2023, one group reported finding protozoa identified as *T. equiperdum* by PCR in some cattle and water buffalo in Indonesia, though it remains possible that this organism was actually *T. evansi* with a genetic element not thought to occur in *T. equiperdum*.

In laboratory studies, it has been difficult to infect healthy animals with *T. equiperdum* isolated directly from equids, but mice immunosuppressed with glucocorticoids are more susceptible, and some rabbits can be infected by intratesticular inoculation. Isolates that have been passaged through rodents can acquire a broader host range. Sheep, goats, dogs, rabbits, rats and mice can be experimentally infected with mouse-adapted strains, and may develop clinical signs, and sheep have also been inoculated intravenously with rat-passaged strains. Despite this, ruminants do not seem to be susceptible to isolates from equids, and an attempt to inoculate dogs with organisms from horses also failed.

Zoonotic potential

There is no evidence that T. equiperdum can infect humans.

Geographic Distribution

Diagnosing dourine can be difficult, especially where its close relatives *T. evansi* or *T. brucei* are also present, and its current distribution is unclear. Research papers and reports to the World Organization for Animal Health (WOAH, formerly OIE) suggest that this organism remains endemic in some parts of Africa, Asia, the Middle East and Latin America, with relatively recent documentation of its presence in Mongolia, Iran, Venezuela and some African countries. It is particularly likely to remain undetected in impoverished agricultural regions that have large numbers of equids but limited diagnostic capabilities. While dourine was also established in many other parts of the

world in the past, including in North America and Europe, eradication programs eliminated the organism from these areas. It has also been eradicated from these regions when it was re-introduced, most recently in Italy in 2011.

Transmission

Unlike other trypanosomal infections, *T. equiperdum* is thought to be transmitted almost exclusively during breeding. The organism occurs in the genital secretions of both sexes, and while transmission from stallions to mares is more common, mares can also infect stallions. Some equids, particularly donkeys, can be asymptomatic carriers, and *T. equiperdum* can occur in semen before animals develop clinical signs. It can periodically disappear from the genital tract, with the animal becoming noninfectious for weeks to months. Noninfectious periods are more common late in the disease.

Occasionally this organism might infect animals through other mucous membranes, such as the conjunctiva. Vertical transmission from the mare to the foal has been documented, though it seems to be uncommon. Whether this happens before or during birth, or through the milk, is unclear; however, *T. equiperdum* is known to occur occasionally in milk as well as in the genital tract. Animals that become infected when they are sexually immature can transmit the organism when they begin breeding. While mechanical transmission via arthropod vectors is theoretically possible, there is currently no evidence that it plays any role in transmitting *T. equiperdum*.

T. equiperdum is reported to be unable to survive for long outside a living organism. The related organism *T. brucei* remained viable for up to 6 days in blood under certain carefully controlled laboratory conditions.

Disinfection

There is limited need for disinfectants, due to the fragility of trypanosomes in the environment, and no studies have examined the disinfectant susceptibility of *T. equiperdum* specifically. The closely related organism *T. brucei* can be inactivated by various agents including 0.05% sodium hypochlorite, 70% ethanol, 2% TriGeneTM, 0.1% hand soap, 2% formaldehyde and 0.05% glutaraldehyde. Exposure to 50°C (122°F) is reported to kill 100% of *T. brucei* trypomastigotes.

Incubation Period

The incubation period ranges from a few weeks to several years.

Clinical Signs

Dourine varies from a chronic, relatively mild condition that persists for years to a more acute illness that may last only 1-2 months, and in rare cases, can progress to the end stage in as little as a week. Subclinical infections are also possible. The clinical signs often develop gradually. The initial sign is usually a mucopurulent discharge from the urethra of stallions or vagina of mares, followed by edema of the prepuce and glans penis or vulva, respectively. There may also be inflammatory changes such as orchitis or vulvitis and vaginitis, and some animals can have genital vesicles or ulcers, which may leave permanent white scars called leukodermic patches when they heal. Thickened, semitransparent patches on the vaginal mucosa may be noted in some mares. Genital lesions may be accompanied by polyuria or other signs of discomfort, and pregnant mares infected with more virulent strains sometimes abort.

Genital edema can disappear and reappear, with the extent of the permanently thickened, indurated tissue becoming greater each time. Sometimes the edema spreads to involve the ventral abdomen, perineum and even the legs, especially the hindlegs. Occasionally ventral edema might be noted without obvious involvement of the genitalia, most likely because the genital lesions have already resolved. Swollen udders in mares may exude serum-like or cloudy, whitish secretions. Eventually, the genital region, perineum and udder may become depigmented.

Some animals also develop edematous patches called "silver dollar plaques" on the skin. Silver dollar plaques can be up to 10 cm in diameter, occur most often over the ribs, and are usually visible for several days before disappearing. While they have been called pathognomonic for dourine, similar lesions can be found occasionally in surra, caused by *T. evansi*. Other types of cutaneous lesions have also been reported. During an outbreak in Italy in 2011, horses were reported to have variable wheals and plaques, which were smaller than typical silver dollar plaques, lasted for hours to days, and waxed and waned in different parts of the body. Pustular dermatitis was also described in this outbreak.

Other signs may include intermittent fever, anemia, and ocular lesions, particularly conjunctivitis and keratitis, which may lead to corneal opacity and blindness. Ocular lesions can sometimes be the first sign observed in an animal. Neurological signs may develop soon after the genital edema or weeks to months later, and can be caused either by invasion of the CNS or peripheral neuritis. Facial paralysis, which is generally unilateral, may be seen in some animals, and ptosis of the lower lip is common. A common presentation in animals with CNS involvement is initial restlessness and weight shifting from one leg to another, often followed by progressive weakness, stiffness and lameness especially in the hindlegs, incoordination and eventually paralysis. More subtle signs such as incoordination/ inability to mount, seen only during mating, have also been described in experimentally infected animals. During outbreaks in Italy, the neurological signs were not accompanied by sensory dysfunction.

The clinical signs of dourine often wax and wane, with relapses sometimes precipitated by stress. This can occur several times before the animal either dies or apparently recovers. Animals that decline often experience progressive loss of condition and emaciation, though the appetite remains good. Whether any animals can recover permanently is controversial.

Post Mortem Lesions

Loss of condition and/or signs of cachexia are common in animals with dourine, the perineal region may be depigmented, and some animals may have swelling of the ventral abdomen and legs, with gelatinous exudates under the skin. Chronic lymphadenitis may also be apparent, especially in the abdominal cavity, with enlarged, soft and possibly hemorrhagic lymph nodes. In stallions, the scrotum, sheath and testicular tunica are often thickened and infiltrated, with signs of chronic orchitis. In severe cases, the testes may be embedded in sclerotic tissue and unrecognizable. A gelatinous infiltrate may also thicken the vulva, vaginal mucosa, uterus, bladder and mammary gland of mares. Some mares have been reported to have endometritis, with congestion and/or hemorrhages in the mucosa.

There are usually few or no gross lesions in the CNS, though perineural connective tissues may be infiltrated with edematous fluid, the spinal cord is sometimes surrounded by a serous infiltrate or contains small hemorrhages, and a soft, pulpy or discolored spinal cord may be noted in animals with paraplegia, particularly in the lumbar or sacral regions. There are a few reports of lesions in internal organs, such as pinpoint white lesions in the liver or congestion of the spleen, though such lesions seem to be minimal and inconsistent in naturally infected animals. However, some experimentally infected horses had increased synovial fluid in the joints and yellowish fluid in the thoracic and abdominal cavities, probably as the result of hypoproteinemia.

Diagnostic Tests

Dourine is usually diagnosed by serology, combined with clinical signs, and supported by evidence from histopathology. However, the currently available serological tests cannot determine that an animal's antibodies are specifically caused by exposure to *T. equiperdum*, due to the close relationship between it and some other trypanosomes. Thus, epidemiological evidence of insect-independent transmission is also helpful, as it can help distinguish dourine from African animal trypanosomiasis and surra, which are transmitted by tsetse flies or mechanically by biting insects, respectively.

The complement fixation (CF) test is the prescribed serological test for dourine in international trade, while indirect fluorescent antibody tests can help resolve equivocal cases or false positives caused by the anticomplementary effects of equid serum. Anticomplementary effects are particularly common in samples from donkeys ELISAs, radioimmunoassay, and mules. counter immunoelectrophoresis and agar gel immunodiffusion (AGID) tests have also been used at times, though the latter three assays are considered outdated in modern laboratories. Newer tests described in the literature include a lateral flow immunoassay and a chemiluminescent immunoblot. Equids infected with T. equiperdum can also react in serological tests for other trypanosomes, such as the card agglutination test for T. evansi (surra).

Organisms occasionally be detected may microscopically in tissues or exudates, though they cannot be distinguished morphologically from T. evansi and are usually present in very small numbers, making them difficult to find. Sites that sometimes contain T. equiperdum include the edematous fluids of the external genitalia; vaginal or preputial washings, swabs or scrapings; aspirates from silver dollar plaques; and various other samples such as lymph, mammary gland exudates, conjunctival swabs and cerebrospinal fluid. Parasites are most likely to be found soon after the animal becomes infected or, in lesions such as silver dollar plagues, when those lesions first appear. Repeated sampling may be helpful, and immunostaining can help visualize the organisms. On rare occasions, T. equiperdum can be found in thick blood films, but it is present very transiently and only early in the infection. The chance of success can be improved by concentration techniques such as capillary tube centrifugation or mini anion exchange centrifugation. One study detected T. equiperdum by impression smears in various organs of experimentally infected horses, including the liver, heart and kidney, at necropsy.

PCR can be used to diagnose dourine, though the currently used tests usually identify the organism only to the level of the subgenus *Trypanozoon* and cannot distinguish it from other agents such as *T. evansi*. Some genetic assays used in research might be more specific; however, detailed genetic analyses may need to be done, which is usually impractical for diagnosis.

Treatment

Dourine has been treated with various anti- trypanosomal drugs in endemic regions, including combinations of drugs that might be more effective than single agents. It is still uncertain whether any treatment can completely eliminate *T. equiperdum*, though some reports appear promising, with treated animals eventually becoming seronegative. Treatment only seems to be effective in animals without CNS invasion; case reports and laboratory studies suggest that animals with parasites in the CNS will probably relapse, even if there appears to be initial improvement. Whether this would be also be true if drugs with better penetration into the CNS are employed is unclear, but such drugs are generally considered too expensive for veterinary use, particularly in large animals.

Treatment may not be allowed in countries that are dourine-free.

Control

Disease reporting

Veterinarians who encounter or suspect dourine should follow their national and/or local guidelines for disease reporting. In the U.S., state or federal veterinary authorities should be informed immediately.

Prevention

To prevent dourine from being introduced into a herd or dourine-free region, new animals should be quarantined and tested by serology. While *T. equiperdum* does not survive long in the environment, good hygiene and sanitation are advisable at assisted matings to avoid any crosscontamination to other animals via fomite-mediated transmission. When dourine is found in an area, quarantines and the cessation of breeding can prevent transmission while infected animals are identified. This disease can be eradicated from a herd, using serology to identify infected equids. Infected animals are typically euthanized, though lifetime isolation may also be a possibility.

Stallions have sometimes been castrated in an attempt to prevent them from spreading *T. equiperdum*, but geldings can still transmit the disease if they display copulatory behavior. There does not seem to be any way, at present, to preserve the genetic potential of valuable breeding stallions. One study found that single-layer centrifugation decreased the number of parasites in semen samples; however, while samples with fewer trypanosomes appeared to be cleared of the organism, those with larger initial parasite concentrations remained infectious even when parasites could not be detected by visual examination or PCR in the pellet.

Morbidity and Mortality

The severity and duration of dourine can be influenced by the virulence of the strain and the health of the horse (e.g., nutritional status, concurrent illnesses) and existence of stressors that may precipitate a relapse. Although some animals progress to the terminal stages of this disease within a month or two, experimentally infected horses have survived up to 10 years. Donkeys, mules and native ponies tend to be more resistant than horses.

The mortality rate in untreated cases has been estimated to be 50-70%, but there are also reports of spontaneous recoveries. However, apparent recoveries have been questioned by some, in view of the long course of the disease and the waxing and waning clinical signs. Some authors feel that nearly all cases are eventually fatal.

Internet Resources

The Merck Veterinary Manual

<u>United States Animal Health Association. Foreign Animal</u> <u>Diseases</u>

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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*Link is defunct