Contagious Equine Metritis

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Importance

Contagious equine metritis (CEM) is a highly communicable venereal disease of horses, caused by the bacterium *Taylorella equigenitalis*. This disease can spread widely from a single asymptomatic carrier, particularly a stallion. Infected horses do not become systemically ill or die, but reproductive success is reduced. Additional economic impacts include the cost of pre-breeding tests and treatment in endemic areas, as well as screening before importation into CEM-free countries.

Excluding *T. equigenitalis* from a country can be challenging. Control programs have significantly reduced the incidence of this disease in Thoroughbreds, which were severely affected by outbreaks in the 1970s; however, it also occurs in other breeds, and identifying carriers can be difficult. *T. equigenitalis* is fastidious and can be difficult to culture, and serological tests are useful only in mares and for short periods. In addition, some recent strains circulate with only mild clinical signs. In the U.S., an outbreak in 2008-2010 may have resulted from the importation of an infected horse 8 years earlier. Similarly, *T. equigenitalis* appears to have circulated for some time before the 2011 outbreak in South Africa, although the country was thought to be CEM-free. Thus, contagious equine metritis should be a diagnostic consideration even where this organism is thought to be absent.

Etiology

Contagious equine metritis is caused by *Taylorella equigenitalis*, a fastidious microaerophilic gram-negative coccobacillus in the family Alcaligenaceae. Only one serotype is known; however, there are two biotypes, one sensitive and the other resistant to streptomycin. Streptomycin-resistant strains were common in the past, but most of the currently circulating strains are streptomycin-sensitive. *T. equigenitalis* strains can differ significantly in virulence.

The closely related organism *Taylorella asinigenitalis* seems to be associated mainly with donkeys. *T. asinigenitalis* can cause clinical signs in some experimentally infected (horse) mares; however, no symptomatic infections have been reported in naturally infected equids, as of 2015, and this organism is currently considered to be nonpathogenic. At present, its major significance is that it must be distinguished from *T. equigenitalis* during diagnostic testing.

Species Affected

Horses appear to be the only natural hosts for *T. equigenitalis*, although donkeys have been infected under experimental conditions. Attempts to infect cattle, pigs, sheep and cats were unsuccessful, but some laboratory rodents could be infected for relatively short periods by intrauterine inoculation.

Donkeys are thought to be the major hosts for *T. asinigenitalis*, but this organism has also been isolated from a small number of mares and a few stallions. Most of these horses appear to have been infected during contact with donkey jacks, especially during breeding.

Zoonotic potential

There is no evidence that *T. equigenitalis* infects humans.

Geographic Distribution

The geographic distribution of *T. equigenitalis* is difficult to estimate accurately. This organism has been detected at times in Europe, North and South America, Africa and Asia and on some islands. In some countries, it may be absent or rare in some breeds of horses (e.g., Thoroughbreds) due to control programs, but present in others. Some nations reported to have eradicated contagious equine metritis include certain European countries, the U.S., Canada, Australia and Japan.

T. asinigenitalis has been detected in North America (the U.S.) and Europe (e.g., France, Sweden, Italy), and probably exists in other areas.

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Transmission

T. equigenitalis is transmitted mainly during mating. It can also be spread by infected semen during artificial insemination (AI) or introduced to the genital tract on fomites. The risk of infection appears to be lower in mares bred by AI than natural service, and one study reported that the antibiotics in semen extenders significantly decreased infection rates. Transmission risks associated with embryo transfer are incompletely understood.

Stallions are the most common source of the infection. In untreated stallions, *T. equigenitalis* can persist for months or years on the reproductive tract, where it may be detected in the urethral fossa and its associated sinus, the distal urethra, the exterior of the penis and prepuce, and occasionally in the pre-ejaculatory fluid. Up to 20-25% of mares can also carry *T. equigenitalis* after they recover from acute disease. The vast majority of carrier mares maintain *T. equigenitalis* on the clitoris, particularly in the clitoral sinuses and fossa, but a few carry it in the uterus. Carriage is typically shorter in mares than stallions (often a few weeks to months); however, there have been cases where mares carried the organism for years. Foals born to infected mares can also maintain *T. equigenitalis* on the external genitalia, and may become long-term asymptomatic carriers.

There is no evidence that *T. equigenitalis* survives long-term in a free-living form in the environment. However, this organism has been reported to persist, at least for short periods, in some free-living amoebae (e.g., *Acanthamoeba castellanii*).

Disinfection

T. equigenitalis is susceptible to most common disinfectants, including chlorhexidine, ionic and nonionic detergents, and sodium hypochlorite (400 parts per million).

Incubation Period

The incubation period is 2 to 14 days; most infections become apparent 10 to 14 days after breeding.

Clinical Signs

Infected stallions display no clinical signs. Mares can develop metritis and become temporarily infertile, although they have no systemic signs. Some of these infections are subclinical; the only sign may be a return to estrus after a shortened estrus cycle. In other cases, a mucopurulent, grayish-white vaginal discharge develops a week or two after breeding; in severe cases, the discharge is copious. Mixed bacterial infections may result in a gray to yellow exudate. Variable degrees of endometritis, cervicitis and vaginitis can sometimes be found if the reproductive tract is examined with a speculum. Infertility usually lasts a few weeks, with the discharge often disappearing in a few days to two weeks. Long-term effects on reproduction have not been reported; however, some mares can carry *T. equigenitalis* for a time. Carriers are usually asymptomatic, although a few mares may have an intermittent vaginal discharge.

Most infected mares do not conceive. Those that do, usually give birth to a normal full-term foal, which may carry the organism asymptomatically. Some infected mares have an intermittent vaginal discharge during the pregnancy, while others do not. Abortions also occur, but appear to be rare.

T. asinigenitalis has not been reported to cause disease in donkeys or horses under natural conditions; however, some experimentally infected mares developed cervicitis and metritis, with vaginal and cervical discharges. These mares had a shortened estrus cycle and failed to conceive. The clinical signs were milder than in mares infected with *T. equigenitalis.*

Post Mortem Lesions

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The most severe lesions are usually found in the uterus. The endometrial folds may be swollen and edematous, and a mucopurulent exudate may be apparent. Edema, hyperemia and a mucopurulent exudate may be seen on the cervix. Salpingitis and vaginitis also occur. The lesions are most apparent approximately 14 days after infection, then gradually decrease in severity over the next few weeks. They are not pathognomonic for contagious equine metritis.

Diagnostic Tests

Microscopic examination of the uterine discharge may reveal numerous gram-negative coccobacilli or bacilli (present individually or arranged end-to-end) and large numbers of inflammatory cells. *T. equigenitalis* is often pleomorphic and may exhibit bipolar staining.

Contagious equine metritis can be diagnosed by isolation of the causative organism from the genital tract, or with polymerase chain reaction (PCR) assays. Samples collected from mares include vaginal discharges from clinical cases; or swabs of the clitoral fossa and its sinuses from suspected carriers, with the addition of cervical and endometrial swabs if the animal is not pregnant. If possible, carrier mares should be cultured during estrus, particularly during the first part of the cycle. In stallions, swabs are taken from the urethral fossa and sinus, distal urethra, and external surface of the penis and the prepuce. The pre-ejaculatory fluid may also be sampled. For optimal success, carriers should be sampled on more than one occasion, at intervals of 7 days or more. No systemic antibiotics should be used for at least 7 days, or topical antibiotics for 21 days, before a sample is taken for culture. If an infected mare conceives, *T. equigenitalis* may also be found on the placenta, on the genital tract of some normal foals, and in multiple sites in aborted fetuses. The fragility of the organism dictates special transport conditions (e.g., transport in Amies medium.) and rapid transfer to the laboratory.

PCR (where available) can be used directly on clinical samples, and some assays can distinguish *T. equigenitalis*

from *T. asinigenitalis*. Culture should be performed by a laboratory experienced in isolating *T. equigenitalis*; this organism is fastidious and difficult to grow. It can be isolated on chocolate (heated blood) agar. Additives (e.g., Timoney's medium) are often incorporated to suppress the growth of commensal organisms, which may otherwise prevent its recovery. Some media take advantage of the resistance of certain *T. equigenitalis* strains to streptomycin; however, streptomycin-sensitive biotypes are now more common, and isolation should not rely solely on such media. Colonies usually become visible in 3-6 days, although they may rarely take up to 2 weeks to appear. *T. equigenitalis* colonies can be identified by PCR, biochemical tests, identification with immunological techniques and molecular genotyping (e.g., 16S rRNA gene analysis). Immunological methods for identification can include slide agglutination, latex agglutination and immunostaining. Rare cross-reactions with *Mannheimia haemolytica* have been reported in some tests. *T. equigenitalis* and *T. asinigenitalis* react identically in biochemical tests, and cross-react in some serological assays. Tests that could distinguish these two organisms in published reports have been based on PCR, 16S rRNA sequencing, loop-mediated isothermal amplification methods, multilocus sequence typing (MLST) and indirect immunofluorescence. *T. equigenitalis* can be genotyped for epidemiological purposes with molecular tests such as pulsed-field gel electrophoresis (PFGE). A MLST scheme was described recently.

Because carrier stallions can have few organisms, cultures from these animals may be unsuccessful. For this reason, stallions may be bred to test mares and these mares tested for *T. equigenitalis*.

Serology is unreliable as a diagnostic tool, but it may be helpful as an adjunct screening test. Serological tests include complement fixation, rapid plate agglutination, enzyme-linked immunosorbent assay (ELISA), passive hemagglutination and agar-gel immunodiffusion. Antibodies can be found in acutely infected mares beginning 7 days after infection; however, in some animals, they may be undetectable for up to 2 to 3 weeks. Antibodies persist for up to 6 to 10 weeks after the primary infection, then disappear. Complement fixation can detect infected mares 21-45 days after they have been bred to a suspected carrier stallion, but this test becomes unreliable thereafter. Carrier mares may or may not be seropositive. Stallions do not produce detectable antibodies to *T. equigenitalis*.

Treatment

In carriers, *T. equigenitalis* may be cleared by washing the external genitalia with disinfectants (e.g., chlorhexidine), combined with local antimicrobial treatments such as nitrofurazone, silver sulfadiazine or gentamicin ointment. Particular care should be taken in the washing of the clitoral fossa and sinuses. Systemic antibiotics might also be recommended in some animals. Treatment may need to be repeated in some cases in both mares and stallions, and the optimal length of treatment is undefined. Surgical excision of the clitoral sinuses (which can be difficult to expose for topical treatment) may eliminate the organism in mares that do not respond to treatment, but this is uncommon and it is rarely used. Some mares can also clear the infection on their own; however, this is unpredictable and may take several months or more in some cases. Acutely infected mares may or may not be treated with antibiotics; it is unclear whether treated mares eliminate the organism more rapidly.

Similar treatments could eliminate *T. asinigenitalis* from donkeys and horses in one study.

Control

Disease reporting

Veterinarians who encounter or suspect contagious equine metritis 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

In countries free from contagious equine metritis, horses are screened for *T. equigenitalis* during importation. Infected animals must be treated and test negative before they are released into the community. The fastidious nature of the organism complicates its detection.

Where this disease is present, it is controlled by breeding only from stallions and mares that have been tested for the organism and are known not to be carriers. Control programs have generally been based on the UK's Horserace Betting Levy Board's Code of Practice (www.hblb.org.uk/codes.htm), which is reviewed and updated annually. Samples are generally taken from all stallions at the beginning of the breeding season, and from mares according to the risk that they carry this organism. Mares with clinical signs, including those that return to estrus prematurely, should be investigated. Good hygiene, decontamination of potential fomites, and sanitation during breeding are also important. While fomites associated with breeding are the primary risk, other objects, such as sponges used to groom multiple horses, might also transfer the organism. There is no vaccine.

T. equigenitalis has been eradicated from some countries by surveillance/ testing, quarantine of infected animals, treatment and a moratorium on breeding from infected animals.

Morbidity and Mortality

The transmission rate during natural service varies between animals and over time, but it can be very high in some instances. In some cases, nearly every mare mated to an infected stallion will become infected. Approximately 30-40% of infected mares are estimated to develop clinical signs. Most mares recover without incident, but some continue to carry *T. equigenitalis*, usually asymptomatically. Fatal infections have not been seen.

Immunity after an infection is not complete, and mares can be infected repeatedly during a short period of time. The first infection is usually the most severe; infertility and clinical signs are less likely to occur during later bouts of the disease, and some mares conceive.

Internet Resources

Canadian Food Inspection Agency. Contagious Equine Metritis
http://www.inspection.gc.ca/animals/terrestrial-animals/diseases/reportable/cem/eng/1356159688621/1356159810186

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.html

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

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS).
http://www.aphis.usda.gov/

USDA Contagious Equine Metritis
http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth/sa_animal_disease_information/sa_equine_health/sa_hot_issues/ct_contagious_equine_metritis

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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*Link is defunct