

# Transmissible Mink Encephalopathy

*Mink Spongiform  
Encephalopathy, Mink Scrapie*

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the Center for  
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## Importance

Transmissible mink encephalopathy (TME) is a progressive and fatal neurodegenerative disease that affects ranched mink. Most or all of the adult animals on a ranch may be affected, and once an animal becomes symptomatic, death is inevitable. This disease is still poorly understood. It is very rare, with only a few outbreaks reported in the U.S. and other countries. Outbreaks seem to result from feeding contaminated food containing prions to mink; however, the origin of these prions is unknown. Recent evidence suggests they might be an unusual variant of the bovine spongiform encephalopathy (BSE) agent.

## Etiology

TME is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by unconventional disease agents. These agents are resistant to the treatments that ordinarily destroy bacteria, spores, viruses and fungi. They are generally thought to be prions, although a minority opinion suggests that TSEs may be caused by viruses or retroviruses. Prions are infectious proteins that appear to replicate by converting a normal cellular protein into copies of the prion. The cellular protein, which is called PrP<sub>c</sub>, is found on the surface of neurons. Pathogenic isoforms of PrP<sub>c</sub> are designated PrP<sup>Pres</sup>; PrP<sup>TME</sup> or PrP<sup>TSE</sup> are other names for this protein. Prions that cause different diseases (e.g. BSE or scrapie) are considered to be different strains of PrP<sup>Pres</sup>.

Mink seem to acquire the TME prion when they eat contaminated feed, but the origin of this agent is still unknown. TME could be caused by the scrapie prion, an agent found in sheep and goats, although this currently seems unlikely. Intracerebral inoculation of mink with U.S. (but not U.K) strains of scrapie can cause neurologic signs, but sheep tissues were not fed to mink in all TME outbreaks, and mink that were inoculated with scrapie prions by feeding did not become ill. Bovine spongiform encephalopathy (BSE), which occurs in cattle and some other species, may be a more likely source of TME. Epidemiological investigations suggest that some TME outbreaks were linked to feeding tissues from non-ambulatory (“downer”) or dead cattle, and mink infected orally with BSE prions develop neurologic disease. A recent study in a transgenic mouse line suggests that the TME agent most closely resembles L-type BSE, an atypical BSE agent that has been reported rarely in cattle. The L-type BSE (or “bovine amyloidotic spongiform encephalopathy”) prion has a lower molecular mass than the classical BSE prion. It may represent a spontaneously occurring prion, a strain of BSE or a different TSE agent found in cattle.

Strain differences have been reported in hamster-adapted TME prions. Hamsters inoculated with the HYPER (HY) strain become hyperexcitable and develop cerebellar ataxia, but hamsters inoculated with the DROWSY (DY) strain have only progressive lethargy. The DY strain remains pathogenic for mink, but the HY strain can no longer cause disease in this species.

## Species Affected

TME has been reported only in ranched mink; however, experimental infections can be established in other species. Raccoons are readily infected by oral as well as parenteral inoculation. Other species including striped skunks, ferrets, American sable (pine martens), beech martens, cattle, sheep, goats, hamsters and nonhuman primates (rhesus macaque, stump-tailed macaque, squirrel monkey) can be infected by intracerebral inoculation. Cattle, sheep, goats, hamsters, raccoons, striped skunks and squirrel monkeys are relatively easy to infect by this route, but the long incubation period in ferrets suggests that a species barrier exists. Nontransgenic mice are not susceptible to TME.

## Geographic Distribution

Several outbreaks of TME were reported in the United States between 1947 and 1985; no cases have been documented in the U.S. since that time. Many of the incidents occurred in Wisconsin, but ranches in Minnesota and Idaho were also affected during some years. TME has also been seen in ranch-raised mink in Canada, Finland, Germany and the former U.S.S.R.

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## Transmission

TME is thought to be transmitted orally. Outbreaks seem to occur when mink ingest prions in their feed. Studies in hamsters suggest that wounds on the tongue may facilitate the transmission of this agent. During an outbreak, the disease might be able to spread between animals in the same cage by cannibalism: TME prions have been reported in the mesenteric lymph node, spleen, thymus, kidney, liver, intestine and salivary gland of experimentally infected mink that had prions in the CNS. Nevertheless, mink-to-mink transmission is thought to be rare; in at least one outbreak, kits sharing a cage with their dam did not become infected. In addition, adult mink are usually housed individually in cages, making mink-to-mink transmission unlikely. TME is not known to be transmitted vertically, and mink born during one outbreak had no signs of disease the following year.

Whether TME prions can survive in the environment is unknown. Other prions have been reported to remain infectious for 2-3 years and possibly longer; however, TME does not seem to recur during subsequent years on the same farm.

## Incubation Period

The incubation period is 6 to 12 months in ranched mink. Experimental infections can become apparent as early as 5 months PI. Adult raccoons infected experimentally by the oral route become ill in approximately 10 months.

## Clinical Signs

Transmissible mink encephalopathy causes neurologic signs including behavioral changes. The early clinical signs can be subtle, and may include difficulty eating and swallowing, and changes in normal grooming behavior. Affected mink often soil the nest or scatter feces in the cage. Later, animals may become hyperexcitable and bite compulsively. Affected mink often carry their tails arched over their backs like squirrels. Incoordination, circling, clenching of the jaw, and self-mutilation (particularly of the tail) may also be seen. When death is imminent, mink tend to become somnolent and unresponsive; convulsions can occur but are not common. Once the clinical signs appear, TME is always progressive and fatal. Death usually occurs within 2-8 weeks.

In one experiment, mink inoculated orally with the classical BSE agent developed a fatal neurological disease that resembled TME; however, the animals tended to become unusually docile rather than aggressive.

Raccoons that are experimentally inoculated with TME prions develop neurologic signs including lethargy, abnormal responses to external stimuli, altered behavior and incoordination.

## Post Mortem Lesions [Click to view images](#)

No pathognomonic gross lesions are found in animals with TME; however, the carcass may be dehydrated and

the fat deposits can be depleted. The typical histopathologic lesions are confined to the central nervous system. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are pathognomonic. Astrocytosis can be seen, but amyloid plaques are not found.

## Morbidity and Mortality

TME is very rare, and has only been seen in ranched mink. Several outbreaks have been reported in the U.S. The first occurred in 1947, on a ranch in Wisconsin. Another facility in Minnesota that received animals from this ranch was also affected. Outbreaks were reported on five ranches in Wisconsin in 1961; in Idaho, Minnesota and Wisconsin in 1963; and on a single ranch in Wisconsin in 1985. In at least one case, multiple facilities were linked by a common food source. TME has not been reported in wild mink populations.

Only adult mink are usually affected; in at least one outbreak, kits housed with their dams and eating the same diet were completely spared. TME is always fatal once the symptoms appear. The mortality rate on a ranch can be as high as 60-90%; in one outbreak, all of the adult mink died. An outbreak may last several months, but the disease does not seem to recur.

## Diagnosis

### *Clinical*

Transmissible mink encephalopathy should be suspected in mink that develop progressive, fatal neurologic disease. Although TME has not been reported in raccoons, experimental infections suggest that this species could also be infected.

### *Differential diagnosis*

The differential diagnosis includes other neurologic diseases such as rabies, pseudorabies (Aujeszky's disease), lead or other toxicities, toxoplasmosis and other parasitic diseases, and nutritional diseases such as thiamine deficiency.

### *Laboratory tests*

Transmissible spongiform encephalopathies have traditionally been diagnosed by histopathology. Currently, disease is usually diagnosed by detecting prions in the central nervous system. Accumulations of prions can be found in unfixed brain extracts by immunoblotting (Western blotting) and in fixed brains by immunohistochemistry. Enzyme-linked immunosorbent assays (ELISAs) have been developed for some prions including BSE, but may need to be validated for TME. Serology is not useful for diagnosis, as antibodies are not made against prions.

### *Samples to collect*

**Before collecting or sending any samples from animals with a suspected exotic disease, the proper authorities should be contacted. Samples should only**

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**be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.**

An animal suspected of having TME should be killed and the head or brain removed for testing. In experimentally infected mink, prions have also been found in extraneural tissues including the salivary gland, intestine, mesenteric lymph node, spleen, thymus, kidney and liver, but only after prions are found in the brain. During necropsy, a standard neuropathologic approach should be followed to rule out other causes of disease.

## Recommended actions if transmissible mink encephalopathy is suspected

### Notification of authorities

TME is an exotic disease and must be reported promptly to state or federal officials.

Federal: Area Veterinarians in Charge (AVIC):

[http://www.aphis.usda.gov/animal\\_health/area\\_offices/](http://www.aphis.usda.gov/animal_health/area_offices/)

State Veterinarians:

<http://www.aphis.usda.gov/vs/sregs/official.html>

## Control

There is no vaccine or treatment for TME. Feed that may contain prions, particularly BSE or scrapie, should not be given to mink. Tissues from non-ambulatory cattle should be avoided in mink feed, unless the carcass was tested for BSE. Complete avoidance is generally necessary, as cooking or rendering cannot completely inactivate prions. Mink may be able to acquire TME by cannibalizing infected animals; however, because mink are typically housed in individual cages, this is unlikely to be a concern in most circumstances. Kits housed with their dam do not appear to become infected.

Because the TME agent may be related to BSE, scrapie or other ruminant prions, mink tissues are not allowed in ruminant feed in the U.S.

Although there is no evidence that the TME agent is transmitted to mink from the environment, contamination should be avoided whenever possible. Decontamination of prion-contaminated tissues, surfaces and environments is difficult. These agents are highly resistant to most disinfectants (including formalin), heat, ultraviolet radiation and ionizing radiation, particularly when they are protected in organic material or preserved with aldehyde fixatives, or when the prion titer is high. Prions can bind tightly to some surfaces, including stainless steel and plastic, without losing infectivity. Prions bound to metal seem to be highly resistant to decontamination. Few effective decontamination techniques have been published. A 1-2 N sodium hydroxide solution, or a sodium hypochlorite solution containing 2% available chlorine, has traditionally been recommended for equipment and surfaces. Surfaces should be treated for more than 1 hour at 20°C (68°F). Overnight disinfection is recommended for equipment. Cleaning before disinfection removes organic material that may protect

prions. Recently, milder treatments including a phenolic disinfectant, an alkaline cleaner (KOH with detergents), and an enzymatic cleaner combined with vaporized hydrogen peroxide have been shown to inactivate some prions. These disinfectants may be useful for items that cannot withstand harsher decontamination procedures. Physical inactivation of prions can be carried out by porous load autoclaving at 134-138°C (273-280°F) for 18 minutes at 30 lb/in<sup>2</sup>. Autoclaving items in water is more effective than autoclaving without immersion. Dry heat is less effective; hamster-adapted scrapie prions can survive dry heat at temperatures as high as 360°C (680°F) for an hour. A combination of chemical and physical decontamination can be more effective than either procedure alone; chemical disinfection should be carried out first, then the items should be rinsed and autoclaved. Anecdotal evidence suggests that decontamination of contaminated facilities is very difficult.

## Public Health

Although nonhuman primates develop neurologic disease after intracerebral inoculation of TME prions, there is no evidence that this agent can normally be transmitted to humans. However, caution is warranted with any poorly understood prion disease, particularly one that may be linked to BSE; ingestion of classical BSE prions can cause variant Creutzfeldt-Jakob disease (vCJD) in humans.

Veterinarians and laboratory workers should always take precautions when conducting necropsies on TME-suspects or handling tissues. Standard precautions include the use of protective clothing and the avoidance of penetrating injuries, contamination of abraded skin, and ingestion. A negative pressure laminar flow hood should be considered for tissue manipulations. Because prions may be able to survive in the environment for years and are difficult to disinfect, precautions should be taken to avoid contamination of surfaces and equipment. Disposable plastic-coated paper sheets can be used to protect tables and other surfaces. Disposable instruments and work clothing can also be used. No vaccine is available.

## Internet Resources

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.jsp>

United Kingdom. Department for Environment Food and Rural Affairs. Other TSEs.

<http://www.defra.gov.uk/animalh/bse/othertses/index.html#tme>

United States Department of Agriculture (USDA). Animal and Plant Health Inspection Service. Transmissible Mink Encephalopathy.

[http://www.aphis.usda.gov/lpa/pubs/fsheet\\_faq\\_notice/fs\\_ahtme.html](http://www.aphis.usda.gov/lpa/pubs/fsheet_faq_notice/fs_ahtme.html)

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