

Feline Spongiform Encephalopathy

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Importance

Feline spongiform encephalopathy (FSE) is a neurodegenerative disease, caused by a prion, that affects members of the cat family. Once the clinical signs appear, this disease is invariably fatal. FSE is caused by the same agent that is responsible for bovine spongiform encephalopathy (BSE) in cattle. BSE was first reported in the 1980s, when it caused an explosive epidemic among cattle in the U.K. This disease eventually spread to many other countries. FSE was first reported in 1990, and was apparently transmitted to individual cats in BSE-contaminated food. As the BSE epidemic has declined, and controls have been placed on feeding high-risk bovine tissues to animals, FSE has become increasingly rare. However, this disease has a long incubation period and occasional cases may still occur in housecats and zoo animals.

Etiology

FSE is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by prions, infectious proteins that appear to replicate by converting a normal cellular protein into copies of the prion. The cellular protein, which is called PrP^c, is found on the surface of neurons. Pathogenic isoforms of PrP^c are designated PrP^{res} (The 'res' refers to the proteinase K-resistant nature of prions, compared to normal PrP^c). PrP^{Sc} or PrP^{TSE} are other names for this protein. Prions that cause different diseases (e.g., FSE or scrapie) are considered to be different strains of PrP^{res}. FSE is caused by the same agent that is responsible for BSE in cattle.

One TSE in a housecat, reported in 1998, was caused by a prion that was distinct from BSE. The authors suggested that this may have been a new type of FSE. No other infections with this prion have been reported in cats.

Species Affected

FSE has been documented in domesticated cats (housecats) and captive wild cats including cheetahs (*Acinonyx jubatus*), pumas (*Puma [Felis] concolor*), ocelots (*Leopardus [Felis] pardalis*), tigers (*Panthera tigris*), lions (*P. leo*), an Asian golden cat (*Catopuma temminckii*) and an Asian leopard cat (*Prionailurus [Felis] bengalensis*).

Cattle are the primary hosts for BSE, the prion that causes FSE. This agent has also been reported rarely in goats, as well as in exotic ruminants and lemurs in zoos. Experimentally, it has been transmitted by feeding to sheep, nonhuman primates, mink (*Mustela vison*) and European red deer (*Cervus elaphus elaphus*). The BSE factsheet has additional details about this prion in cattle and animals other than felids.

Zoonotic potential

Humans can develop variant Creutzfeldt-Jakob disease (vCJD) after eating BSE prion-containing tissues from an infected animal. However, there is no indication that humans have ever acquired this disease from cats.

Spongiform encephalopathies were reported simultaneously in a cat and its owner in 1998; however, the man was found to have the sporadic (genetic) form of Creutzfeldt-Jakob disease, rather than the BSE-associated form (vCJD), and the disease in the cat differed clinically from FSE. The prions isolated from both man and cat appeared to be similar, but differed from the BSE prion. It is not known whether these prions might have been transmitted between the man and the cat, whether both contracted the disease from a common source, or if the incident was due to chance. No other infections with this prion have been reported in cats.

Geographic Distribution

FSE has been found in some countries where BSE occurs, and in animals imported from these countries. Most cases have been seen in the U.K., but a few animals have been identified in other European countries and Australia. Most of the animals found outside the U.K., including the Australian case, had lived in the U.K. at one time and are thought to have been infected there. BSE has also been found in parts of North America, Asia and the Middle East, although no cats with FSE have been documented in these regions.

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Transmission

The BSE prion is thought to be transmitted to cats when they eat BSE-contaminated tissues from infected animals. Cooking or rendering does not destroy this agent. Experiments suggest that cattle and sheep are most readily infected during the first few months of life, but whether young cats are also more susceptible than adults is not known. Horizontal transmission has not been reported between cats, and is thought to be unlikely; however, infectivity has been found in the kidneys of some felids, and shedding in urine has not been ruled out. There is one report of possible maternal transmission, from a cheetah to one of its three offspring. The dam developed the first signs of FSE two months before giving birth and nursing the young cheetahs. Contaminated meat could not be completely ruled out as the source of the infection in the offspring; however, there had been every effort to avoid BSE-contaminated meat, and high-risk tissues such as neurological tissues were not fed. Prions have been transmitted iatrogenically in some other species (e.g., via contaminated surgical instruments or in blood transfusions), and iatrogenic transmission also seems possible in cats.

The distribution of BSE prions in the tissues of cattle and sheep

In cattle, the highest prion concentrations occur in the central nervous system (CNS) and ileum. Sensitive detection methods have also found this agent in lymphoid tissues associated with the jejunum and colon, spinal ganglia, peripheral nerves and adrenal glands, and in the optic nerve and retina. The accumulation of BSE in peripheral nerves, nerve ganglia and adrenal gland seems to coincide with or follow prion accumulation in the CNS. There have been rare reports of BSE prions or infectivity in other locations, such as the tonsils; bone marrow; mesenteric lymph nodes; the esophagus, abomasum and rumen of one animal (possibly in nerve endings); the tongue and nasal mucosa of cattle in the terminal stages of the disease; and even in concentrated saliva. These studies have generally used very sensitive techniques, found very small quantities of prions, and reported that these tissues contain prions only in animals with clinical signs. One such study detected low levels of BSE in sensory receptors (muscle spindles) of muscles but not myofibrils, and another reported this prion in one muscle sample (probably associated with the endings of the sciatic nerve); however, most studies have not detected BSE in muscles. In cattle, BSE prions do not seem to occur in the spleen or lymphatic tissues other than those associated with the gastrointestinal tract. One group reported evidence of BSE in a few plasma samples from cattle, but others have not detected these prions in bovine blood. Epidemiological evidence and transmission studies suggest that BSE is not transmitted in milk.

BSE prions seem to be more widely distributed in sheep than cattle. In experimentally infected sheep, these prions are readily found in many lymphoid tissues including the spleen, lymph nodes and gut-associated lymphoid tissue (GALT), as

well as in the CNS. Infectivity has also been reported in sheep blood. There is little information on goats.

Prion distribution in cats

In felids, BSE (FSE) prions have been found in the CNS, retina, optic nerve, peripheral nerves, spinal ganglia, adrenal gland, enteric nervous system of the small intestine (including the myenteric plexus) and some lymphoid organs, especially those associated with the GI tract. One study in housecats suggested that these prions accumulated in lymphoid tissues to a very limited extent: prions were sometimes found in the spleen and the ileum, but they were not detected in the lymph nodes, tonsil or thymus. However, some studies in cheetahs have detected these agents in various lymph nodes and the tonsils, as well as the spleen. Several groups found that the kidneys of housecats and zoo cats stained for prions by immunohistochemistry. This has frequently been interpreted as nonspecific staining, because it was also detected in uninfected cats. However, one group has confirmed the presence of infectious prions in the kidneys of cheetahs, using a mouse bioassay.

Prions in the environment

Prions in the environment are not thought to be significant in the epidemiology of BSE or FSE. Nevertheless, there have been concerns about their possible longevity in sources such as buried carcasses. In one study, infectivity was reported to persist for at least 265 days in sewage or phosphate buffered saline, under laboratory conditions. BSE prions detected by immunoblotting disappeared sooner than infectivity, and could not be found in sewage by 150 days. Other prions (e.g., the agents of scrapie and chronic wasting disease) can also persist in the environment for prolonged periods, and hamster-adapted scrapie prions have been shown to survive in the soil for at least 3 years. Prions are reported to remain infectious after passage through the digestive systems of birds (crows) and mammals (coyotes).

Disinfection

Complete decontamination of prion-contaminated tissues, surfaces and environments can be difficult. These agents are very resistant to most disinfectants, including formalin and alcohol. They are also resistant to heat, ultraviolet radiation, microwave irradiation 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. Hamster-adapted scrapie prions are commonly used to assess prion disinfection methods; however, some studies have reported that BSE prions are more resistant to decontamination (e.g., to heat) than other prions.

Few prion decontamination techniques have been published and confirmed to be effective for routine use. A 1-2 N sodium hydroxide solution, or a sodium hypochlorite solution containing 2% available chlorine (20,000 ppm), has

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traditionally been recommended for equipment and surfaces. Surfaces should be treated for more than one hour at 20°C (68°F). Overnight disinfection is recommended for equipment. Cleaning before disinfection removes organic material that may protect prions. Experimentally, some milder treatments have also been effective against certain prions, under some conditions. They include a specific phenolic disinfectant, various alkaline and enzymatic detergents (although the efficacy of specific agents within these classes varies), hydrogen peroxide gas plasma, radiofrequency gas plasma, sodium dodecyl sulfate plus acetic acid, copper plus hydrogen peroxide, and others. New commercial decontaminants have been developed for prions, though published tests of their efficacy vary. Some laboratories pre-treat tissues with formic acid (98%) to decrease infectivity before sectioning tissue blocks.

Physical inactivation of prions (e.g., on surgical instruments) can be carried out by porous load autoclaving at 134°C (273°F) for 18 minutes at 30 lb/in². Tissue films containing prions are more difficult to decontaminate by steam after they have dried, and human guidelines for surgical instruments recommend that, after use, they be kept moist or wet until decontamination is performed. The cleaning agent used before autoclaving should also be chosen with care, as certain agents (e.g., some enzymatic treatments) can increase the resistance of prions to steam sterilization. Some types of samples cannot be decontaminated effectively even at the recommended temperatures. For example, tissue macerates containing BSE were reported to require wet heat sterilization at $\geq 155^{\circ}\text{C}$ (311°F) for 20 minutes, and resisted even these temperatures if the sample was dehydrated. Dry heat is less effective than moist heat; hamster-adapted scrapie prions can survive dry heat at temperatures as high as 360°C (680°F) for an hour, and one group even reported that infectivity survived incineration at 600°C (1112°F). A combination of chemical and physical decontamination can be more effective than either procedure alone, and effective combinations of chemical agents (e.g., NaOH) and autoclaving have been published. Even the harshest combination of chemical and physical disinfection is not guaranteed to destroy all prions in all types of samples.

Anecdotal evidence and a recent study on scrapie suggest that decontaminating contaminated facilities, especially sites such as animal pens, can be very difficult. Incineration is commonly used for carcasses, but two studies found that composting may reduce or eliminate BSE and other prions in tissues, while another suggested that soil microorganisms might degrade prions in buried carcasses. In one of the two composting studies, BSE was found to be more resistant to decomposition than the prions that cause chronic wasting disease and scrapie.

Incubation Period

All transmissible spongiform encephalopathies have incubation periods of months or years. The incubation period for FSE in cheetahs is estimated to be 4.5 to 8 years. The incubation period in housecats has not been determined.

However, all housecats with FSE have been at least two years old, and most were between the ages of four and nine years.

Clinical Signs

The clinical signs of FSE are reported to develop gradually in housecats. Behavioral changes, such as uncharacteristic aggression, or unusual timidity and hiding, are usually seen initially. Gait abnormalities and ataxia are also common, and typically affect the hindlegs first. Affected cats often display poor judgment of distance. Some cats develop a rapid, crouching, hypermetric gait. Hyperesthesia is common, particularly when cats are stimulated by sound or touch. Some cats may have an abnormal head tilt, develop tremors, stare vacantly or circle. Excessive salivation, decreased grooming, polyphagia, polydipsia and dilated pupils have also been reported. In the late stages of the disease, somnolence is common and convulsions may occur. Similar clinical signs have been reported in zoo cats. Once the signs of FSE appear, this disease is relentlessly progressive and fatal. Death (or euthanasia due to debilitation) usually occurs within a few weeks to 3 months.

Post Mortem Lesions

No gross lesions, other than nonspecific changes due to illness, are found in cats with FSE. The typical histopathologic lesions are confined to the central nervous system. Neuronal vacuolation and non-inflammatory spongiform changes in the gray matter are pathognomonic.

Diagnostic Tests

No live animal test is available for FSE. This disease is usually diagnosed after death, by detecting prions in the CNS with immunoblotting or immunohistochemistry. In some cases, the diagnosis may be confirmed by finding characteristic prion fibrils (called scrapie-associated fibrils) with electron microscopy in brain extracts. This test has low sensitivity, but it may be useful in autolyzed brains. Histological examination of the brain can be very helpful (although it is not generally used as the sole confirmatory test), but some animals in early stages of the disease may have few or no spongiform changes.

Highly sensitive assays, including protein misfolding cyclic amplification (PMCA) and quaking-induced conversion (QuIC), are primarily available in research laboratories, at present. These techniques detect tiny amounts of prions by their ability to convert PrP^c (the normal cellular protein) into prions *in vitro*. They have mainly been investigated in ruminants with BSE and people with vCJD; however, one group used PMCA in conjunction with other assays to detect FSE prions in cheetahs. BSE can also be detected by inoculation into mice (rodent bioassays); however, an incubation period of several months makes this technique impractical for routine diagnosis. Serology is not useful, as antibodies are not made against prions.

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Treatment

There is no known treatment for diseases caused by prions, in any species including cats.

Control

Disease reporting

Veterinarians who encounter or suspect FSE should follow their national and/or local guidelines for disease reporting. BSE is considered exotic to the U.S., and state or federal veterinary authorities should be informed immediately.

Prevention

FSE can be prevented by not feeding tissues that may contain prions to cats. Complete avoidance is necessary, as cooking or rendering cannot completely inactivate these agents. Tissues that have a high risk of transmitting BSE (specified risk materials or SRM), such as the brain and spinal cord of cattle over a certain age, have been banned from pet food in many countries. Some countries also regulate SRM from small ruminants, and zoos no longer feed high-risk tissues to zoo cats. Controlling BSE in cattle and other ruminants also reduces the risk to cats. Iatrogenic transmission in blood transfusions or by surgical instruments must be avoided.

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 during procedures such as necropsies. Disposable plastic-coated paper sheets can be used to protect tables and other surfaces. Disposable instruments and work clothing may be used.

Morbidity and Mortality

FSE is always fatal once the clinical signs appear. Most of the cases in housecats occurred in 4-9-year-old animals, but cats as young as 2 years have been affected.

The BSE epidemic in cattle resulted from recycling tissues from infected cattle into ruminant feed supplements. Control measures, including surveillance of cattle and bans on ruminant tissues in ruminant feed, have significantly reduced the prevalence of BSE. The epidemic peaked in the U.K. in 1992, and a little later in other countries. BSE has now become uncommon or rare in many countries, including the U.K. The number of FSE cases has paralleled the BSE epidemic, and declined as this epidemic has been controlled. Nearly a hundred cases of FSE were diagnosed in housecats and approximately 20 cases in other felids, worldwide, between 1990 and 2007. The vast majority of the sick housecats (89) were found in the U.K., where 10-16 cats with FSE were reported each year between 1990 and 1994, 2-8 cases were reported yearly from 1995 to 1999, and no cases have been documented since 2001. Most cases, though not all, occurred in cats born before feed bans were established. Only five cases in housecats have been reported from other countries, including the most recent case, which occurred in Switzerland in 2003. Likewise, most of the zoo cats are

thought to have been infected in the U.K., although some became ill after they had been moved to other countries. The true incidence of FSE during the BSE epidemics is uncertain, as it may have been underdiagnosed or underreported. Some sources estimate an annual incidence, at the height of the U.K. epidemic, of 10-15 cases per million cats. One survey of clinically suspect cases from 1990-1997 (mainly in the U.K.) found that none of 192 cats had histopathological evidence of this disease, and prions were found in only one of 173 cases examined for these proteins. A retrospective study revealed no evidence of FSE in 286 cats that died of neurological disorders before 1990. More recent surveillance conducted in Italy found no FSE cases in 110 samples from cats with neurological signs.

Public Health

Because people are susceptible to BSE by ingestion, precautions are advisable when conducting necropsies on FSE-suspects or handling tissues, particularly high-risk tissues such as the CNS. BSE is generally classified as a BSL 3 pathogen.

Internet Resources

[U.K. Department for Environment Food and Rural Affairs. Exotic species and domestic cats: TSE surveillance statistics](#)

[World Organization for Animal Health \(WOAH\)](#)

[WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals](#)

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