Scrapie

Tremblante de Mouton,
Rida,
Traberkrankheit (trotting disease),
Gnubberkrankheit (nibbling disease),
Prúrigo lumbar

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Importance

Scrapie is a neurodegenerative disease, caused by a prion, that affects sheep, and less frequently, goats. Infected animals do not usually become ill for years; however, the clinical signs are progressive and invariably fatal once they develop. Scrapie can be transmitted between animals, either directly or via the environment, and infected premises are difficult to decontaminate. The presence of classical scrapie can result in trade sanctions, and many countries are conducting control or eradication programs. Breeding sheep for genetic resistance is an important tool in many of these programs; however, the understanding of resistance genes is still incomplete in goats.

As a result of increased surveillance, atypical (Nor98) scrapie prions have been detected in both sheep and goats. Atypical scrapie often occurs in sheep that are genetically resistant to classical scrapie. It has been reported in countries that do not have classical scrapie. Atypical/ Nor98 prions do not seem to be transmitted readily between animals in nature, and are rarely detected in more than one animal in a herd or flock. It is possible that they arise spontaneously in sheep, similarly to some genetic prion diseases in humans.

Etiology

Scrapie is a member of the transmissible spongiform encephalopathies (TSEs), a group of neurodegenerative disorders caused by prions, infectious proteins that seem 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. The pathogenic isoforms of PrP^{c} found in animals with scrapie are designated PrP^{res} ('res' refers to the proteinase K-resistant nature of prions, compared to normal PrP^{c}). Other names used for this protein are PrP^{Sc} ('Sc' for scrapie), PrP^{TSE} or PrP^{d} ('d' for disease-associated).

Classical scrapie is an infectious disease that can be caused by multiple strains of the classical scrapie prion. Atypical (or Nor98) scrapie prions were first detected in Norway in 1998, although they have also been found in older archived samples from Europe. Several lines of evidence, including the apparently sporadic nature of atypical/ Nor98 cases, and their relatively homogeneous distribution across small ruminant populations, have led to the suggestion that these prions may arise spontaneously, similarly to some diseases in other species (e.g., spontaneous Creutzfeldt-Jakob disease in humans). However, this agent can be difficult to detect, and some authors feel that additional research is still needed before this hypothesis is accepted. At one time, it was uncertain whether atypical scrapie was caused by one agent, or by different prions in different animals. Recent experiments suggest that most of these infections are caused by the same prion. One group reported that, in one experimentally infected animal, atypical/Nor98 changed into a phenotype indistinguishable from CH1641, an unusual classical scrapie strain that has some similarities to bovine spongiform encephalopathy (BSE) in immunoblots, while some other animals developed atypical/Nor98 scrapie.

Species Affected

Classical scrapie

Classical scrapie can affect domesticated sheep and goats, mouflon (*Ovis musimon*), and possibly other animals closely related to sheep and goats. An *in vitro* prion conversion test has suggested that bighorn sheep (*Ovis canadensis*) might be susceptible; however, this still needs to be confirmed by direct evidence of infection in these animals. Cattle and pigs were not susceptible to oral inoculation, although cattle have been infected by intracerebral inoculation, a route that bypasses normal species barriers to prions.

Squirrel monkeys (*Saimiri sciureus*) became infected when they were fed tissues that contained hamster-adapted scrapie prions; however, chimpanzees (*Pan troglodytes*), capuchin monkeys (subfamily Cebinae), cynomolgus macaques (*Macaca fascicularis*), and woolly monkeys (*Lagothrix* sp.) did not appear susceptible to oral inoculation. Mink (*Mustela vison*), rats, mice, hamsters, rabbits, various species of voles, and several primate species - chimpanzees, capuchin and woolly monkeys and marmosets (*Callithrix jacchus*) - have been infected experimentally by intracerebral

inoculation. Some of these studies (e.g., those in rabbits) used rodent-adapted scrapie prions rather than those from sheep or goats. Ferrets did not develop clinical signs after inoculation by an unspecified route, and cats were resistant to intracerebral inoculation. One study reported that sea bream (*Sparus aurata*) appeared to be susceptible to oral inoculation.

Atypical scrapie

Atypical (Nor98) scrapie has been reported in sheep and goats. Attempts to infect laboratory mice (non-transgenic) and bank voles by intracerebral inoculation were unsuccessful.

Zoonotic potential

There is no evidence that humans have ever been infected with scrapie. Epidemiological studies have found no links between scrapie and any human prion diseases. Most studies in animal models and *in vitro* systems also suggest that there is little or no risk to people; however, a few authors have speculated about the zoonotic potential of scrapie, based on the demonstration of disease after intracerebral inoculation in some humanized transgenic mice and nonhuman primates. One group reported that humanized mice were not susceptible to atypical scrapie prions by intracerebral inoculation

Geographic Distribution

Classical scrapie has been reported on all major continents and on many islands. Recent surveillance suggests that this disease is either absent or minimally present in some countries. However, small numbers of infected animals can be difficult to detect, and the World Organization for Animal Health (OIE) requires that a country conduct active surveillance, with a high probability of detecting low levels of scrapie, for at least 7 years before it can be considered scrapie-free. Australia and New Zealand, where scrapie was last reported in the 1950s, are widely recognized to be scrapie-free. Some countries perform little or no active surveillance for scrapie, and the presence or absence of this disease is uncertain.

Atypical/ Nor98 scrapie has been detected in most European countries, North America, New Zealand, Australia and some other nations. If it is a spontaneous genetic disease, it is likely to occur in all areas where small ruminants are found. The presence of atypical/ Nor98 scrapie does not affect a country's scrapie status for international trade.

Transmission

Infected animals carry the scrapie prion for life, and can transmit the agent even if they remain asymptomatic. Infections are thought to occur primarily by ingestion, but sheep can also be infected experimentally via the conjunctiva or nasal cavity, by injection into various body sites, and probably through abraded skin. Most sheep are thought to become infected from their dam, either at or soon after birth. Older animals can be infected, but are more resistant. The placenta can contain high levels of scrapie prions in some sheep (see **Genotype and Scrapie Susceptibility**, under **Control**), and licking or ingesting fetal membranes and fluids is thought to be an important route of infection in this species. Goats also have scrapie prions in the placenta, though in much smaller amounts. Milk from both sheep and goats is known to be infectious. One study demonstrated that, in sheep, both colostrum and milk from infected ewes can transmit scrapie One recent experiment suggested that prenatal transmission can occur in lambs derived by caesarian section and immediately separated from their dams, and highly sensitive techniques have detected small amounts of scrapie prions in fetal tissues of offspring from both subclinically infected and symptomatic sheep.

Highly sensitive techniques have found low levels of scrapie prions in the urine and saliva of symptomatic sheep; in the oral cavity of some subclinically infected sheep; and in feces from subclinical and symptomatic sheep. How much these sources contribute to transmission is still uncertain. Iatrogenic transmission is also possible. Prions have been detected intermittently in the blood of some animals, up to a year before the onset of clinical signs. Transmission via blood becomes increasingly efficient as the animal nears the clinical stage. Some animals were infected by two vaccines that had inadvertently been prepared with central nervous system (CNS) and lymphoid tissues from infected sheep. Most studies indicate that there is little or no risk of transmission in semen; however, one group detected scrapie prions and infectivity in the semen of sheep inoculated with one laboratory strain.

Epidemiological evidence suggests that sheep can be infected from contaminated environments, including pastures. One study recovered scrapie prions from various environmental sources, such as feed and water troughs, 20 days after infected sheep were removed. Prions were found both indoors and outside, although they seemed more likely to be recovered from metal objects (e.g., water troughs, metal gates) indoors. In another study, scrapie prions were detected on various surfaces, in ambient dust samples, and on pastures up to 30 m from the open ends of infected barns that had housed sheep a year earlier. In Iceland, scrapie recurred on some premises restocked 2-3 years after decontamination, and in one barn where small ruminants had been absent for 16 years. Prions can bind to soil, and persist for varying periods depending on the type of soil. They remain infectious for animals when bound to soil. Rodent-adapted scrapie prions were isolated from an experimentally contaminated soil sample after 3 years, and prions from sheep were still present for at least 18 months in some types of soils in the laboratory. Repeated cycles of wetting and drying are reported to decrease, though not necessarily eliminate, infectivity in soil. Prions can also remain infectious after passage through the digestive tracts of scavengers or predators; this has been demonstrated experimentally for coyotes and crows.

Scrapie prions in the tissues of sheep and goats

Scrapie prions occur in the CNS of sheep, but they have also been found in many tissues outside the CNS, including the peripheral nervous system, many lymphoid tissues, salivary glands, adrenal gland, and kidney; in the nerves or sensory structures (muscle spindles) of skeletal muscle; occasionally in various other tissues and organs; and in association with chronic inflammatory lesions caused by other pathogens. Whether an animal has prions outside the CNS may depend on factors such as its resistance to scrapie (e.g., its genotype), the stage of the disease, and possibly the prion dose. In some animals, there may be little or no accumulation outside the CNS.

A limited number of studies in goats have found scrapie prions in the CNS, retina, peripheral nervous system, adrenal gland, salivary gland, kidney, muscle, pancreas, liver and various lymphoid tissues including the spleen, lymph nodes, gut-associated lymphoid tissues (GALT), tonsil, and lymphoid tissues in the nictitating membrane and tongue. Lymphoid tissues can contain prions in both symptomatic and asymptomatic goats. Very small amounts of prions were also found in the nasal mucosa, associated with nerves.

Atypical scrapie

Epidemiological evidence suggests that atypical scrapie is either not a contagious disease in the field, or transmission occurs inefficiently and at a very low rate. Except in very large flocks, infections have only been identified in a single animal per flock or herd. However, laboratory experiments have demonstrated that atypical scrapie prions can be transmitted orally in newborn lambs. Highly sensitive tests found infectivity in the CNS and ileum of some of these lambs by 12 months, and some animals later developed neurological signs. In an ongoing experiment, there was no evidence of infection in lambs inoculated when they were 3-months old.

Atypical scrapie prions have mainly been found in the CNS. Highly sensitive bioassays have detected infectivity in lymphoid tissues, muscles and the peripheral nervous system of experimentally infected sheep, although prions were not found in these tissues with the standard techniques used to detect scrapie.

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, or ultraviolet, microwave 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.

Relatively few prion decontamination techniques have been published and confirmed to be effective for routine use. Some laboratories pre-treat tissues with formic acid to decrease infectivity before sectioning tissue blocks. A 1-2 N sodium hydroxide solution, or a sodium hypochlorite solution containing at least 2% (20,000 ppm) 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. 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, and sodium dodecyl sulfate plus acetic acid. These agents might be useful for items that cannot withstand harsher decontamination procedures.

Physical inactivation of prions can be carried out by porous load autoclaving at 134°C (273°F) for 18 minutes at 30 lb/in^2. Resistance to heat may vary with the specific prion, the degree of contamination and type of sample. 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. Dry heat is less effective than moist heat; some 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. It should be noted that even the harshest combination of chemical and physical disinfection is not guaranteed to destroy all prions in all types of samples.

Decontaminating contaminated facilities, especially sites such as animal pens, may be very difficult. In one study, genetically susceptible sheep became infected with scrapie prions after being placed in pens that had been pressure washed and decontaminated with high concentrations of sodium hypochlorite (20,000 ppm free chorine solution) for one hour, followed by painting and full re-galvanization or replacement of metalwork. Reports from an eradication program in Iceland indicated that scrapie recurred on some farms despite decontamination (500 ppm chlorine), power washing and no restocking for 2 years or more. Decontaminating soil contaminated with prions is currently impractical, although some agents, including an aqueous subtilisin-based enzymatic treatment (effective at ambient temperatures), appear promising in the laboratory. Incineration is commonly used for carcasses, but two studies found that composting may reduce or eliminate scrapie and other prions in tissues, while another suggested that soil microorganisms might degrade prions in buried carcasses.

Incubation Period

The incubation period for classical scrapie is estimated to be 2-7 years in most animals, with peak prevalence occurring at 2-5 years of age in sheep. Signs of illness are rare in animals less than a year old.

The incubation period for atypical scrapie is uncertain, but it is usually seen in older animals than classical scrapie. In the laboratory, however, some orally inoculated newborn lambs had neurological signs by 2 years of age.

Clinical Signs

Classical scrapie

The signs of classical scrapie can be variable in sheep, and may be influenced by factors such as the animal's susceptibility and the strain of the prion. The first clinical signs are usually behavioral. Affected sheep tend to stand apart from the flock and may either trail or lead when the flock is driven. Other common signs include hypersensitivity to stimuli, a fixed stare, ataxia and/or a high-stepping or unusual hopping gait. Animals may also develop tremors (especially of the head and neck), grind their teeth, have an impaired menace response or carry their heads low. Some animals may unexpectedly collapse when they are handled. Blindfolding may reveal incoordination, loss of balance or circling in an animal that is able to compensate for neurological deficits when it is able to see. Visual impairment is also possible, though uncommon. Many sheep become intensely pruritic, and may rub, scrape or chew at these areas. In a pruritic animal, scratching the dorsum or pressure over the base of the tail may cause a characteristic nibbling response or rhythmic head and body movements (the scratch reflex test). Loss of condition is common in the early stages, and significant weight loss or emaciation may be seen late. The fleece may be dry and brittle. Drinking behavior and urination can also change, with some sheep drinking small quantities of water often. Most animals die within a few weeks to several months after the onset of clinical signs.

Some goats have neurological and behavioral signs similar to those in sheep. However, pruritus seems to be less common; if it occurs, it is typically less intense and often localized over the tailhead or withers. Pruritic goats may nibble at affected body sites rather than rub, and the scratch reflex test is often negative. Many goats are reported to be difficult to milk. There are also reports of cases where the animal had only nonspecific signs (e.g., listlessness, weight loss and premature cessation of lactation). As in sheep, the disease is progressive and fatal, with death usually occurring within a few months.

Atypical scrapie

Incoordination and ataxia seem to be the most prominent clinical signs in sheep with atypical/ Nor98 scrapie. Pruritus appears to be minimal or uncommon, although it has been seen in some animals. Loss of body condition, anxiety, tremors, abnormal menace responses or a subdued mental status have been reported in some cases, but not others. Some cases of atypical scrapie have been found by routine surveillance in apparently healthy flocks or herds at slaughter.

Post Mortem Lesions

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There are no characteristic gross lesions in classical or atypical scrapie, although there may be nonspecific changes such as wasting or emaciation, and skin or wool lesions resulting from pruritus.

The histopathological lesions of scrapie are usually (though not always) bilaterally symmetrical. The characteristic lesions of classical scrapie are non-inflammatory spongiform changes, with neuronal vacuolation, in the CNS. Astrocytosis may be seen to a greater or lesser extent, and amyloid plaques may occur in some animals. Lesions are usually present in the brainstem of animals with classical scrapie, although they are not limited to this location. In contrast, animals with atypical/ Nor98 scrapie tend to have minimal or no spongiform lesions in the brainstem, although some animals may have lesions in more rostral parts of the CNS, such as the cerebellar cortex, cerebral cortex and basal ganglion.

Diagnostic Tests

Both classical and atypical scrapie can be diagnosed after death by detecting prions in the CNS. Prions can usually be found in the brainstem of animals with classical scrapie, and these animals are typically diagnosed by sampling the medulla oblongata at the level of the obex. Prions are much less likely to accumulate in this area in animals with atypical/Nor98 scrapie, and may be absent. Some animals with atypical/ Nor98 scrapie have had significant prion deposits in the cerebellar cortex, cerebral cortex, substantia nigra, thalamus and/or basal nuclei; however, the specific prion staining pattern differs between animals. Sampling both the cerebellum and medulla is more likely to detect both classical and atypical cases than sampling the medulla alone.

Classical scrapie can be diagnosed in live sheep by detecting prions in biopsies from the nictitating membrane (third eyelid test), palatine tonsil or rectoanal mucosa-associated lymphoid tissue. They have also been found sometimes in superficial lymph nodes. Third eyelid and rectal mucosa biopsies can be taken without sedation, using only topical anesthesia and restraint. Palatine tonsil biopsies require anesthesia, and are less practical for field use. In sheep and goats with classical scrapie, prions can sometimes be found in peripheral lymphoid tissues before they appear in the brain. The usual diagnostic tests have not, to date, found prions outside the CNS of animals with atypical scrapie.

Immunoblotting (Western blotting) and immunohistochemistry are the most specific assays for detecting prions. Immunoblotting can also distinguish atypical/Nor98 scrapie from classical scrapie. Various rapid tests for classical scrapie, based on enzyme-linked

immunosorbent assays (ELISAs), automated immunoblotting or other techniques, are available in some countries. Rapid tests allow large numbers of samples to be screened, and are often used in surveillance and slaughter testing. Some rapid tests can also detect atypical scrapie; however, their sensitivity varies. In autolyzed brains, scrapie may occasionally be diagnosed by finding characteristic prion fibrils, called scrapie-associated fibrils, with electron microscopy; however, this test has low sensitivity, and is no longer commonly used. Histological examination of the brain can be helpful in diagnosis (although it is not generally used as the sole confirmatory test), but some animals in the early stages of infection have few or no spongiform changes. A combination of tests may be used to certify flocks as scrapie-negative.

Highly sensitive assays, including protein misfolding cyclic amplification (PMCA) and quaking-induced conversion (QuIC) or real-time quaking-induced conversion (RT-QuIC), may be able to identify infected animals earlier than immunoblotting or immunohistochemistry. These techniques detect tiny amounts of prions by their ability to convert PrP^c (the normal cellular protein) into prions *in vitro*. They are mainly used in research at present, but are being investigated for possible diagnostic use in sheep and goats. Scrapie 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 for diagnosis, as antibodies are not made against prions.

Scrapie may need to be distinguished from BSE, which can infect sheep in the laboratory, and has been detected in rarely in naturally infected goats. In most cases, this can be accomplished with conventional prion tests. BSE is more difficult to distinguish from certain rare classical scrapie prions, such as CH1641. A limited number of assays such as PMCA, certain special types of immunoblots, PrPSc profiling or epitope mapping can differentiate the latter two agents.

Treatment

There is no treatment for scrapie or any other prion disease.

Control

Disease reporting

Veterinarians who encounter or suspect scrapie should follow their national and/or local guidelines for disease reporting. Scrapie is a reportable disease in many countries where it is endemic, especially when control programs are in place. Scrapie is reportable in the United States.

Prevention

Classical scrapie mainly seems to be introduced via animal movements, although other possibilities, such as exposure in contaminated feed (e.g., hay) have also been suggested. The risk of introducing scrapie can be reduced by maintaining a closed flock/ herd or minimizing outside purchases of stock. If replacement animals must be added, they should be from herds that test negative for this disease and are managed in a way that makes them unlikely to become infected. Milk and colostrum from potentially infected sheep or goats should not be fed to scrapie-free flocks. Selecting genetically resistant sheep (see below) as replacements and breeding rams may also be helpful in reducing the flock's risk of infection. Certification programs can help identify classical scrapie-free flocks.

In sheep flocks that have become infected, control measures can include removing animals that test positive in live animal tests, are at an elevated risk of infection and/or are genetically susceptible to scrapie. Lambs seem to become infected mainly from their dams, and removing the offspring of infected ewes may contribute to control. In addition, some countries cull members of the infected animal's birth cohort that were raised with it during the first year of life. Reducing exposure to high concentrations of prions (e.g., in the placenta) may reduce transmission within the flock. Breeding genetically susceptible, infected ewes to a resistant ram can decrease or eliminate prions in the fetal membranes and fluids (see genetic resistance, below). If a ewe of unknown scrapie status was not bred to a resistant ram, separating her from the rest of the flock before lambing, and until there is no vaginal discharge, may help protect other animals. Control is more difficult in herds of goats, where genetic resistance to scrapie is incompletely understood. Complete depopulation, followed by cleaning and disinfection, is sometimes used on infected farms, particularly in goat herds; however, decontamination of the farm is difficult and the disease may recur. Two studies suggest that it might be possible to derive a classical scrapie-free sheep flock from an infected flock by embryo transfer.

The components of official scrapie control/ eradication programs often include surveillance (e.g., at slaughter, on farms and in diagnostic samples sent to laboratories), flock/ herd certification programs, quarantines or depopulation of infected herds, tracing of infected animals, and programs to increase genetic resistance in sheep. A few countries have successfully excluded classical scrapie with import controls, although their sheep populations are genetically susceptible.

There are no control methods for atypical scrapie, which seems to occur sporadically and at low levels, and does not appear to spread readily between animals in the field.

Genotype and classical scrapie susceptibility in sheep

Sheep with that are genetically resistant to scrapie may either have no evidence of infection after exposure, or develop clinical signs after longer incubation periods than susceptible animals. The genotype also influences transmission. A genetically resistant fetus suppresses the appearance of prions in the placenta of an infected, scrapie-susceptible dam (except when a resistant fetus develops in the same uterine horn as a susceptible fetus). Breeding these ewes to a resistant ram can decrease the amount of prion contamination in the environment at lambing. Ewes with

resistant genotypes do not produce scrapie-positive placentas, regardless of the genotype of the fetus.

Polymorphisms in the PrP gene at codons 136, 154 and 171 play a major role in resistance to classical scrapie, although other PrP codons and other genes also seem to have some influence. At codon 136, alanine (A) is linked to resistance and valine (V) associated with susceptibility to some scrapie strains. Sheep with histidine (H) at codon 154 are relatively resistant to classical scrapie, with prolonged survival and a longer incubation period, while sheep with arginine (R) are more susceptible. Arginine (R) at codon 171 is linked to resistance, while glutamine (Q) and histidine (H) have been associated with susceptibility. The effects of some uncommon amino acids at codons 136, 154 or 171 are unknown. However, lysine (K) at codon 171 appeared to prolong the incubation time in the Barbado breed of sheep. The relative frequency of resistant genotypes can differ between sheep breeds, and this is thought to be a major influence on overall breed susceptibility to classical scrapie.

The five most common PrP alleles in sheep are A136R154R171 (abbreviated ARR), ARQ, AHQ, ARH and VRQ. Sheep with the ARR/ARR genotype are highly resistant to classical scrapie (cases are very rare); homozygous or heterozygous AHQ and heterozygous ARR animals usually have marginal susceptibility; and VRQ/VRQ, ARQ/VRQ and ARQ/ARQ sheep are expected to be most susceptible. Some countries use all three codons to classify sheep as susceptible or resistant, while the U.S. eradication program employs codons 136 and 171.

Genotype and classical scrapie susceptibility in goats

Scrapie resistance is still incompletely understood in goats; however, a number of polymorphisms that seem to influence resistance have been identified. Some alleles apparently linked to resistance include serine (S) or aspartic acid (D), rather than asparagine (N), at codon 146; histidine (H) rather than arginine (R) at codon 154; glutamine (Q) rather than arginine (R) at codon 211; and glutamine (Q) rather than lysine (K) at codon 222. K222, which seems to confer strong (but not absolute) resistance to classical scrapie, and has also been linked to resistance to BSE, has been proposed as a possible target for breeding goats. Some studies have also suggested that polymorphisms at codons 127, 142, 143 and 145 may influence susceptibility, although other studies found little or no effect for some of these codons. The influence of the animal's genotype might differ between goat populations and scrapie strains, and the effects of combined genotypes are still uncertain.

Genotype and atypical scrapie susceptibility in sheep and goats

Atypical/Nor98 scrapie often occurs in sheep that are genetically resistant to classical scrapie. Genotypes reported to be common in infected sheep include AHQ, ARR, ARH and ARQ. Animals with the VRQ genotype, which are very susceptible to classical scrapie, seem to be relatively resistant to atypical scrapie. Histidine (H) at the PrP gene codon 154 has been linked to increased susceptibility to atypical scrapie in both sheep and goats. Sheep with the ARQ genotype that have a phenylalanine (F) residue at codon 141 (AF141RQ) are reported to be more susceptible to atypical scrapie than ARQ sheep with leucine (L) at this position. Atypical scrapie has also been reported more often in ARR and ARQ genotypes with a leucine at position 141 (AL141RQ).

Morbidity and Mortality

Classical scrapie

Scrapie is always fatal once the clinical signs appear. Classical scrapie is most common in 2 to 5 year-old sheep, and signs of illness are rare in animals less than a year of age. The percentage of a flock or herd affected by scrapie varies, depending on the genotypes of the animals, flock management and other factors. If there are no control measures, the number of infected animals tends to increase over time, and clinical signs start to occur at a younger age. The annual mortality rate may be as high as 10-20% in some severely affected flocks with a high percentage of genetically susceptible sheep, but it is often lower. In some flocks or herds, many infected animals may be slaughtered for meat or culled before they show clinical signs.

Classical scrapie can be a significant problem in some areas, while other regions report few or no cases. The U.S. and E.U. both conduct control/ eradication programs. In the E.U., 17 countries reported classical scrapie in sheep between 2002 and 2012, and the average prevalence was 0.087%. The prevalence decreased over this period in some countries, but did not change significantly in others. In the U.S., the prevalence of scrapie has dropped from approximately 0.5%, in 2003, to 0.015% as of 2013.

Scrapie is much less common in goats than sheep; however, active surveillance programs have revealed that there may be significant numbers of infected goats in some areas. Between 2002 and 2009, surveillance programs in the E.U. identified approximately 3300 scrapie-infected goats (compared to about 15,000 infected sheep). The overall prevalence of infection was 0.098%, in the eight E.U. countries that reported goat scrapie in 2002-2012. However, most of these cases occurred in one country, and the average prevalence in the other seven countries was 0.02%. Surveillance of goats in the U.S., targeted at certain animal populations, suggested that the prevalence was < 0.1% in 2007-2008.

Atypical scrapie

Sheep and goats with atypical scrapie tend to be older than those with classical scrapie. While infections have been reported in all ages over 18 months (the lower age limit for testing in the E.U.), several studies found that more than half of all infected animals were more than 5 years old, and one study reported increasing prevalence with age. Typically, only a single animal is infected in each herd or flock, although additional cases are occasionally reported in large groups of animals. Atypical scrapie seems to be more common in sheep than goats; in 2009, a review reported that

908 infected sheep and 33 infected goats had been identified in the E.U. The prevalence of this disease appears to be relatively homogeneous across countries, consistent with an agent that may arise spontaneously. In a number of European countries, its prevalence ranged from < 0.1% to 1.4% in healthy slaughtered animals, and from 0.1% to 2.5% in fallen stock. Slaughter surveillance in the E.U. found an average prevalence of 0.06%. Some rapid tests used in slaughter surveillance do not readily detect atypical scrapie, and this disease might be underdiagnosed in some countries.

Internet Resources

European Commission. Control of TSEs (including BSE and scrapie)

European Union Reference Laboratory, TSE-LAB-NET (includes videos of animals with scrapie)

National Institute for Animal Agriculture. National Scrapie Education Initiative

Scrapie Canada

United States Department of Agriculture Animal and Plant Health Inspection Service [USDA APHIS]

USDA APHIS Scrapie Program

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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