# 7 Scrapie Flock Certification Program

This section provides information on the duties of the accredited veterinarian in the delivery of the Scrapie Flock Certification Program (SFCP).

## 7.1 The Disease

*Etiology*

1. While the precise cause of the disease is still a subject of significant research, abnormal prion protein is associated with the presence of disease.

*Susceptible Species*

2. Scrapie is a naturally occurring disease of domestic and wild (mouflon) sheep and goats.

*Distribution*

3. The disease was first reported in sheep over 250 years ago and in Canada in 1938. Scrapie is currently recognized in many sheep raising countries. New Zealand and Australia are notable as countries recognized free from the disease.

*Epidemiology*

4. Pregnancy appears to trigger the migration of abnormal prion protein to the reproductive tract. Birthing fluids and tissues, such as placenta, from infected females contain large quantities of the scrapie agent. Healthy animals become infected by eating or licking contaminated materials in the lambing or kidding environment. Newborn lambs and kids sharing the same contaminated environment (lambing pen) are extremely susceptible to infection. Adult females sharing the same environment are also at risk. Although scrapie is an infectious disease, it is not highly contagious. In contrast to some diseases such as foot and mouth, casual contact between animals and inanimate objects, such as vehicle tires, people or the wind, are not known to transmit scrapie.

   Abnormal prion proteins are extremely resilient to traditional approaches to disinfection, being very resistant to both chemical and physical inactivation and stable over a wide pH and temperature range. While they undergo a significant decrease in infectivity titre with time, they have been demonstrated to persist in the environment for periods of years. Reports from Iceland have suggested that environmental contamination or hay mites acting as mechanical vectors have resulted in the reintroduction of scrapie. This phenomenon has not been an epidemiological observation in North America.

   Several separate research studies on the potential of scrapie transmission by embryos have produced conflicting results. At present, there is inadequate information, other than pertaining to genetics, to negate embryo transfer or to provide advice on appropriate measures to mitigate the risk of scrapie transmission from an embryo of unknown genotype. There is no evidence to date that implicates semen in the transmission of scrapie.

*Genetic Effects*

Genetic makeup has been determined to be a significant factor in a sheep's susceptibility to infection with scrapie. At this time, a correlation between specific genetics and related scrapie susceptibility has not been determined for goats. Current experimental evidence indicates that there are different forms of the sheep prion proteins. Some forms are highly susceptible to the structural transformation to the abnormal form found in scrapie, while others are resistant to this change. As in all mammals, sheep are diploid organisms, so that all cells contain two copies of each chromosome and thus two copies of the gene that codes for the prion protein. Genes are made up of codons. A codon is a stretch of DNA that determines which particular amino acid will be included at a particular location of a protein (in this case the prion protein). The prion protein is composed of 256 amino acids; therefore there are 256 codons determining these amino acids. In the literature concerning susceptibility to various strains of scrapie, three codons are discussed: 171, 154 and 136. In North America, two of these codons are given primary importance: 171 and 136. The presence of an arginine ®) at codon 171 of the prion protein confers resistance to the prion protein undergoing the structural change associated with scrapie in North America. The presence of glutamine (Q) or histidine (H - treated the same as a Q) at codon 171 results in the prion protein being susceptible to the structural change associated with North American scrapie. An alanine (A) at codon 136 confers resistance to the prion protein undergoing the structural change associated with North American scrapie. The presence of valine (V) at codon 136 can produce susceptibility to structural change associated with North American scrapie. V at site 136 is linked with Q at site 171 such that R cannot be found at site 171 in combination with V at site 136.

Scrapie susceptibility as defined by the codons 171 and 136 are as follows:

Most susceptible 171QQ > 136AV171QR > 136AA171QR > 171RR Greatest resistance

It is still not known whether animals with these latter genotypes do not become infected with the scrapie agent or whether they are merely protected from developing the clinical signs of scrapie.

The specific amino acids and the sites that appear to confer susceptibility versus resistance vary with the strain of scrapie agent involved and the breed of sheep. Research indicates that QQ sheep are the most susceptible to scrapie infection. QR sheep are much less susceptible and RR sheep appear to be resistant. While the genetic profile for all sheep breeds present in North America has not been determined, the vast majority of positive cases of scrapie that have been genotyped in North America have been determined to be homozygotes for glutamine (QQ) at codon 171. Small numbers of QRs around the world have tested positive for scrapie. In these cases, the amino acids at a second codon (136) are examined and heterozygotes for alanine and valine at codon 136 appear to indicate greater

susceptibility among the QR population. Recent reports show a handful of RR positive scrapie cases, details regarding these cases are not currently available.

Recent science indicates that the genotype of the fetus may influence the migration and accumulation of abnormal prion in the placenta of an infected ewe. A 171QQ infected ewe carrying a 171QQ fetus would result in the accumulation of large quantities of abnormal prion, which is then shed during birth or abortion. The abnormal prion does not accumulate to a significant degree in the placenta of a fetus with a genotype 171QR or 171RR. This means that use of a 171 RR ram can prevent the shedding of abnormal prion at lambing even from infected ewes.

It is important for producers to understand that scrapie genotyping is NOT disease testing. A 171QQ sheep does not automatically have scrapie, just as it is not an absolute guarantee that a 171RR sheep cannot get scrapie. The CFIA has NO intention to mandate the Canadian sheep flock to breed for scrapie resistance. Scrapie genotyping is a tool that can be used in an overall plan to manage the risk of scrapie on a particular premises. Whether or not a particular producer can or should use scrapie genotyping is a decision based on individual factors such as: breed, prevalence of 171R within the flock, management of ewe flock, and current status of other breeding indices.

*Clinical Signs*

5. Clinical signs of scrapie rarely develop before the age of 18 months and are highly variable. The majority of cases are diagnosed in animals two to five years of age. As many animals do not show overt clinical signs until late in the course of the disease, significant transmission of the scrapie agent occurs prior to any visible indications of a disease problem. Clinical signs vary considerably, with wasting and debility with or without tremors and incoordination being more prominent features throughout the clinical course of cases of scrapie in Canada.

When present, the predominant nervous signs of scrapie are as follows:

- tremors and incoordination,
- a change in mental status (apprehension, teeth grinding, and aggression), and
- altered sensation (pruritus or itchiness, loss of wool, excoriation and inflammation of the skin, nibble reflex, and excessive licking).

*Differential Diagnosis*

Differential diagnosis to consider in the initial clinical stages of scrapie includes:

A. ectoparasites (lice, mites)
B. hypomagnesaemia
C. pregnancy toxemia (ovine ketosis)
D. rabies
E. listeriosis
F. maedi-visna
G. pseudo rabies (Aujeszky's disease)
H. sarcocystosis

*Laboratory Diagnosis*

6. Scrapie is diagnosed through the detection of the abnormal prion protein in brain or lymphoid tissue. Tissues to submit for diagnosis include: obex of brain, retropharyngeal lymph nodes, and 3rd eyelid from the live animal. Tissues are sent fixed in formalin and/or fresh frozen depending on test being applied for surveillance cases and the laboratory preference. Various testing techniques may be applied to the tissue; however, immunohistochemistry is the current gold standard testing technology for use on suspect cases. Abnormal prion protein is detectable as early as several months (eight), but consistently in animals over 12 months of age.

   Detection of abnormal prions in 3rd eyelid lymphoid follicles has good specificity; however, false negatives (eyelid negative, brain positive animals) are found. To maximize sensitivity, 3rd eyelid testing should be applied to animals with the genotype QQ171 that are over 14 months of age. The test is a useful screening tool for the presence of infection in a flock, but is not a reliable indicator of individual freedom from disease.

   Genotyping is a screening test that indicates a sheep's relative susceptibility for scrapie. When trying to find infection, sheep with the highest susceptibility are the subpopulation in which one is most likely to discover the disease.

*Immunity*

7. No immune response to scrapie prion protein has been detected.

*Public Health*

8. Scrapie is not known to be a human health hazard.