

Appendix 4—Transmission and Genetics of Scrapie

Sheep and goats are typically infected with scrapie as young lambs or kids through contact with the infected placenta or birth fluids from infected ewes or with contaminated lambing areas but not necessarily mother to offspring. Age seems to provide some protection; however, a few animals may become infected as adults. Rams get scrapie, but infected rams are not known to transmit scrapie.

The agent can enter the body by ingestion, ocular exposure, or contact with abraded skin or mucus membranes. The incubation period is typically 2-to-5 years. Animals infected at or near birth typically die by 72 months of age. Likewise, animals infected after weaning typically die at more than 72 months; however, this does not always hold true for valine associated scrapie discussed below, particularly in VVQQ sheep. Scrapie is always fatal—no treatment or vaccine is available.

Due to their genetic make-up, some sheep are more susceptible to scrapie and some are more resistant to the disease. The genes that control susceptibility/resistance can be identified by blood test known as genotyping or DNA testing.

A. General Information about Genotyping

1. The animal's genotype never changes, so it can be tested at any age.
2. Under most circumstances, one test during the animal's life is adequate to determine its genotype (susceptibility/resistance to scrapie.) In the case of exposed sheep, USDA currently requires two tests to minimize any chance of error in sampling, labeling, or testing.
3. The genotype test measures only an animal's susceptibility/resistance to scrapie, not whether it has scrapie. The third eyelid biopsy test can be used to detect scrapie infection in some animals.

B. Basic Facts about Sheep Genetics and how Genotyping is used to Determine Scrapie Resistance/Susceptibility

1. Out of the many sheep genes scientists have identified, one pair affects scrapie susceptibility as well as the disease's incubation time. That gene is the prion protein gene (PRNP).
2. Each sheep has two copies of the PRNP gene; one derived from each parent.
3. In uninfected sheep, the PRNP gene produces the normal cellular prion protein molecule

known as PrPc. In scrapie infected sheep, the abnormal prion protein, PrPsc or prions, is found. Prions are closely associated with scrapie infectivity and may be the causative agent.

4. Genes are made up of codons. Each codon instructs the body's cells to put a specific amino acid at a particular location when building a protein molecule.
5. Since PrPc is composed of 256 amino acids, these locations are numbered from 1 to 256.
6. Two codons, 136 and 171, are particularly important to scrapie susceptibility in the United States.
7. Codon 171 can give instructions to insert the amino acid Histidine (H), Glutamine (Q), Lysine (K), or Arginine (R) at a position 171 of PrPc. The letter in parentheses is the single letter biochemical abbreviation for each amino acid. For regulatory purposes, H, Q, and K are treated the same and will be represented as Q throughout the remainder of this discussion. At codon 171, R is very important because it produces the greatest scrapie resistance.
8. Codon 136 can give instructions for either Alanine (A) or Valine (V) to be the amino acid at 136 of PrPc. The presence of V at 136 makes AV QR sheep susceptible to the valine associated scrapie strain. The valine associated strain is relatively uncommon in the U.S. and only appears to infect sheep that have V at codon 136.
9. As previously stated, sheep have two copies of the PRNP gene, one from each parent that can produce one of four possible combinations of amino acids at codons 136 and 171 as shown below in Table 1.

**Table 1 –
Amino Acid Combinations Indicating Susceptibility/Resistance**

	Location	
	Codon 136	Codon 171
Amino	A	R
Acid	V	Q*
	V	Q*
		R**

* Q = Q, H, or K at codon 171

** This combination is very rare and has not been identified in the United States.

10. Producers need to be familiar with the six common genotypes and their corresponding amino acid combinations to understand genotyping for scrapie resistance. Based on what is now known, the following genotypes at codons 136 and 171 (shown below in Table 2) are used to determine the scrapie susceptibility of sheep by USDA.

**Table 2 –
Common Genotype Susceptibility/Resistance Combinations**

1. AA RR – Sheep that are resistant.
2. AA QR – Sheep that are rarely susceptible.
3. AV QR – Sheep that are susceptible to some scrapie strains*.
4. AA QQ – Sheep that are highly susceptible.
5. AV QQ – Sheep that are highly susceptible.
6. VV QQ – Sheep that are highly susceptible.

*These strains are believed to occur with low frequency in the United States.

At this time, no resistant genotypes have been conclusively identified in goats. There is some preliminary literature suggesting that lysine (K) at codon 222 may be resistant; however, K at codon 222 is uncommon in U.S. goats tested to date. All goats, therefore, should be assumed to be susceptible.

11. Official genotype tests -
APHIS will only recognize the results of genotype tests as official if:
- a. The blood is drawn by an accredited veterinarian or a State or Federal animal health official;
 - b. The sheep is officially identified;
 - c. The sample is submitted with a VS Form 5-29 or State equivalent; and
 - d. The laboratory has been approved by APHIS.