Putting Science into Animal Science Projects

Area: Using Genetics (advanced members)

Activity: Eradicate Scrapie in Sheep through Genetic Selection

Goal: Provide advanced members with the information and tools they need to breed scrapie resistance into a flock of sheep.

Materials Needed: Eradicate Scrapie in Sheep through Genetic Selection packet

Part 1 – Background Information (for advanced members and instructor)
Part 2 – Breeding for Scrapie Resistance (for advanced members and instructor)
Part 3 – Activity Worksheet (for advanced members)
Part 4 – Answer Key for Worksheet (for instructor)

How to do the Activity:

Use Part 1 to discuss scrapie with members. Use leading questions as you share the information:

- Why is eradicating scrapie from the United States important?
- What steps would you take to eradicate scrapie?
- Encourage members to learn more about scrapie
    - http://www.aphis.usda.gov/animal_health/animal_diseases/scrapie
    - Many universities have reliable information on scrapie as well
    - Caution members that scrapie in the United States and scrapie in the United Kingdom are different types. Websites from the UK may share information that is not relevant here, especially where genetic resistance is concerned.

Use Part 2 to discuss how genetics can be used to develop scrapie resistance. Use leading questions after you explain the information:

- Should the USDA require all breeding sheep in the United States to be genetically tested for scrapie resistance and mandate the removal of all QQ animals?
- Under the current program, when is it mandated that QQ animals be removed from a flock?
    - (When an animal has been identified as a positive in a flock and the flock is in the process of depopulation.)
- How can QR animals be used successfully in a sheep breeding program by increasing scrapie resistance and decreasing scrapie susceptibility in the flock?
- Why does the delay in scapie disease onset make its eradication challenging?
    - (Sheep that have scrapie and look phenotypically (visually) superior will have been in production for 1-4 years, potentially infecting other susceptible ewes and lambs in the flock.)
- Scrapie is considered an infectious disease with susceptibility determined genetically. Does this aid or impede the scrapie eradication goal?

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- Why would Dr. Wagner caution producers not to cull genetically superior females who are productive, based just on their genotype at codon 171?

Using the provided Part 3 activity worksheet, give your advanced members the opportunity to demonstrate what they learned in Part 2.

The provided Part 4 answer key helps you explain the worksheet answers.

Conclusion:
By completing this activity, 4-H members have been able to explore some concepts of science. They have asked questions, answered questions, gained some factual knowledge, and have hopefully been encouraged to ask more questions. *How else might this _____? What if _____ were done? Why did I get these results?* As they expand their knowledge with Inquiry Based Learning, they are learning life skills that they will use again and again as capable adults.

Eradicate Scrapie in Sheep through Genetic Selection

Part 1 – Background Information

Scrapie is an infectious disease of sheep (and goats) that affects the central nervous system and is ultimately fatal. The disease is classified as a transmissible spongiform encephalopathy (TSE). Some TSE's in other species include bovine spongiform encephalopathy (BSE, Mad Cow Disease), Creutzfeldt-Jakob Disease (CJD) in man and chronic wasting disease (CWD) in deer and elk. There is evidence that CJD may be contracted through consumption of meat from cattle with BSE. Therefore, there is concern about all TSE's. The United States Department of Agriculture (USDA) implemented a Scrapie Eradication Program in an effort to eliminate scrapie from the United States sheep and goat populations.

To contract scrapie a susceptible animal must come in contact with the disease agent. The scrapie agent is thought to be spread most often from ewe to offspring, ewe to ewe and to other lambs through contact with the placenta and placenta fluids from infected ewes. Signs of scrapie usually do not appear until 2-5 years after an animal is infected. This delay in disease onset makes the goal of eradicating scrapie very challenging.

Researchers have discovered that **susceptibility** of sheep to scrapie has a genetic component. The infectious material in scrapie appears to be a particular form of a prion protein molecule found in normal, healthy sheep. They have discovered that certain genotypes resist the alteration of the normal prion protein to a scrapie prion.

The genotype of sheep at codon 171 affects the animal's susceptibility to scrapie. (A codon is a stretch of DNA which codes for a single amino acid). The amino acids coded at codon 171 include glutamine (Q) and arginine (R). Since genes occur in pairs, sheep have two protein prion genes at this codon. Each gene

can be the same (homozygous) in which case the sheep will produce only one type of prion protein. If the genes are different (heterozygous), then two types of prion proteins are produced. Thus, at codon 171 each sheep is QQ, QR or RR.

A considerable body of evidence exists indicting that RR sheep virtually never develop clinical scrapie. The frequency of heterozygous (QR) sheep developing scrapie is also very low. In contrast, the QQ genotype is associated with scrapie susceptibility both in experimental studies and in naturally occurring scrapie. It is possible to have sheep genetically tested for their genotype at codon 171. This information may be used to genetically breed scrapie resistance into a flock.

It is important to note that a sheep with a QQ genotype is not guaranteed to develop or to be a carrier of scrapie. To be a carrier of scrapie, a sheep must be exposed to the scrapie prion proteins. Scrapie is not generally considered to be a genetic disease, but rather an infectious disease with susceptibility determined genetically. Therefore, a QQ sheep is considered susceptible to scrapie and is only a potential carrier if exposed.

Sheep producers should strive to increase scrapie resistance without losing superior genetics meeting their production goals in the process.

Part 2 – Breeding for Scrapie Resistance

Most flocks contain a combination of QQ, QR and RR sheep. Producers should develop a breeding plan to work toward a flock of RR sheep. This plan needs to start with the current genetics of the flock. Here are some suggestions on how to work toward an RR flock (reprinted from *Scrapie and Codon 171, Part 2: The painless way to RR* by Bob Wagner from Gene Check, Inc., used with permission).

We will begin with some comments/rules about selecting for "R" in sheep:

1. Determine the genotype of (test) all rams you intend to use or purchase. No matter what other testing you do, it is absolutely necessary to test rams. If you know the genotypes of the rams, you can make "worst case" predictions for the genotypes of the offspring (see Rule #2).

2. Do not cull good females based on codon 171 genotype. Because we are dealing with a trait ("R") that behaves in a dominant fashion, that is, only one copy of the gene is necessary to convey resistance to scrapie, any ewe can produce resistant offspring provided she is bred to a resistant ram. If a QQ animal is bred to an RR animal, all of the offspring will be QR resistant.

To understand how this works, it is important to remember that a sperm or an egg contains only one copy of each chromosome. This means an RR sheep will produce only R sperm or eggs, a QQ sheep will produce only Q sperm or eggs and a QR sheep will produce both Q and R sperm or eggs (in roughly equal numbers).

How can you predict the genotypes of offspring? An easy way is to use a Punnett square. In these squares, the sperm and egg genotypes of the sire and dam are shown outside the square on the top and left respectively. Inside the box are the potential genotypes of the offspring. The inside genotypes are formed by combining the genotypes of the sperm and egg above and to the left of each individual inside box.

A Punnett square of a RR x QQ mating will look like this:

		Sire	
		R	R
Dam	Q	QR	QR
	Q	QR	QR

Note that every inside box is QR. 100% of the offspring of a RR x QQ cross will be QR.

Even if you only use a QR ram on QQ ewes, half the offspring will be resistant (QR). The Punnent square:

		Sire	
		Q	R
Dam	Q	QQ	QR
	Q	QQ	QR

These are the only really important rules, everything else is a matter of individual preference and almost everything depends on individual circumstances. Everyone should begin by following Rule #1 and testing all rams that have been or will be used to sire replacements or that you intend to purchase. Let's consider two possible outcomes to testing your rams:

1. You are loaded with "R" (nothing but QR and RR rams). It is probably a good idea to begin testing all of your lambs to begin selecting for RR replacements. Remember, once you are breeding RR rams to RR ewes there is no reason to continue testing since such a cross can produce only one kind of offspring. The Punnent square:

		Sire	
		R	R
Dam	R	RR	RR
	R	RR	RR

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2. You have no “R” or almost no “R” in your rams. In this case you need to begin looking for a ram with some “R”. There are several ways to go about this: (1) if you have any “R” at all in your current rams, you can consider concentrating on their offspring for future rams, (2) you can test your best ewes and see if there is enough “R” in them to allow you to produce QR rams to use on the rest of the ewes or (3) you can begin looking for good QR or RR rams to purchase.

Buying some “R” may be simplest, but can also be expensive. Although there will be increasing numbers of RR rams available today they are still in short supply and can be pricey. However, if you find an RR ram that you would love to use even if he weren’t RR, he is probably worth the money and will certainly save you money in the long run by minimizing the amount of testing you will need to do. On the other hand, no one should sacrifice other good traits just to get an RR ram. In other words, if the ONLY reason you are considering using a ram is because he is RR, you probably shouldn’t use him. Fortunately, there are a lot of good QR rams available. Even before anyone was testing, QR sheep made up about 40% of the black face sheep population in North America, so you should be able to find plenty of QR rams that complement your breeding program.

If you are: (a) starting with QR rams, (b) suspect that you have very little “R” in you ewes and (c) are relatively patient, it probably makes most sense to test only rams and a limited number of ewe lambs for at least a couple of years. You may want to test those good lambs that you might consider keeping or selling in order to avoid selling any “R” too early in the game.

In the second year of using QR rams you should begin making some RR sheep. If you breed the QR offspring of your first QR ram (at least half will be QR) to another QR ram, ¼ of the offspring will be RR and only ¼ will be QQ. The Punnett square:

		Sire	
		Q	R
Dam	Q	QQ	QR
	R	QR	RR

One key message is that you should be extremely careful to keep the positive traits you have worked to breed into your sheep. It is not necessary to give up important qualities just to get “R” into your sheep. Remember how hard it is to get good quality sheep (much harder than getting an “R” into a sheep!) If you sacrifice quality to get an RR, you may take longer to reach the goal of good RR sheep than if you kept the quality high and added the “R” more slowly. Patience may be a good idea.

There are circumstances where the advice to be patient may not be best. In particular, if your sheep have had scrapie or have been exposed to scrapie, it may be best to get “R” into your sheep in a hurry (and even consider culling QQ sheep). When you need resistance in a hurry, a good RR ram may be

worth whatever you need to pay for him. If you can't get an RR ram, you may want to test most of your lambs to be certain you keep only resistant replacements. Under these circumstances, it is also important that you only sell resistant animals for breeding purposes.

It is very important to remember that, if one of your sheep ever dies with scrapie on someone else's farm, your flock will be considered a trace back or source flock. By far the safest approach for anyone selling sheep is the policy contained in the Michigan Scrapie Risk Reduction Program: sell no QQ sheep except for slaughter.

Building a scrapie-resistant flock is both desirable and possible without any loss of the god genetics currently in every sheep breed. Codon 171 genotype should not be used as a tool for culling but rather as a tool for selection. In a nutshell: keep your productive females – just be sure you breed them to produce resistant offspring. And to be really safe, only sell QR or RR sheep for breeding stock.

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Part 3 – Worksheet Using Scenarios

You have taken market lambs in 4-H for many years. You decide to try raising your own market lambs and have purchased five ewes. You want to build a scrapie resistant flock, so you purchased a ram that was tested to be QR. You do not know what the genotypes of your ewes are and decide not to spend the money to find out.

What are the possible genotypes of offspring from breeding your ram to the ewes?

1. If a ewe is RR:
   - What percentage of lambs will be RR? _____
   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

2. If a ewe is QR:
   - What percentage of lambs will be RR? _____
   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

3. If a ewe is QQ:
   - What percentage of lambs will be RR? _____
   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

You enjoyed your first years' experience raising lambs and decide you want to continue raising lambs. You are going to keep your QR ram and decide to test your best ewes and most promising ewe lambs for genotype at codon 171. The test results are as follows:

Ewe 241 is QR	Ewe 244 is QR	Ewe 245 is QQ
Ewe lamb 260 is QR	Ewe lamb 263 is QR	Ewe lamb 266 is QQ
Ewe lamb 267 is RR		

1. You want to keep your flock size at five ewes.
   - Which ewes /ewe lambs will you cull? _____
   - Which ewes/ewe lambs will you keep? _____

2. If all five of the ewes you kept in your flock have twins next year:
   - What percentage of lambs will potentially be RR? _____
   - What percentage of lambs will potentially be QR? _____
   - What percentage of lambs will potentially be QQ? _____

3. Plan a breeding program for year three which will assure that your entire flock is either QR or RR.

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PUNNETT SQUARES FOR WORKSHEET CALCULATIONS

Ram

Ewe

Ram

Ewe

Ram

Ewe

Ram

Ewe

Ram

Ewe

Ram

Ewe

Ram

Ewe

Ram

Ewe

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Part 4 – Answer Key for Worksheet

1. If a ewe is RR:
   - What percentage of lambs will be RR? 50
   - What percentage of lambs will be QR? 50
   - What percentage of lambs will be QQ? 0

		Ram Q	Ram R
Ewe	R	QR	RR
	R	QR	RR

2. If a ewe is QR:
   - What percentage of lambs will be RR? 25
   - What percentage of lambs will be QR? 50
   - What percentage of lambs will be QQ? 25

		Ram Q	Ram R
Ewe	Q	QQ	QR
	R	QR	RR

3. If a ewe is QQ:
   - What percentage of lambs will be RR? 0
   - What percentage of lambs will be QR? 50
   - What percentage of lambs will be QQ? 50

		Ram Q	Ram R
Ewe	Q	QQ	QR
	Q	QQ	QR

You enjoyed your first years' experience raising lambs and decide you want to continue raising lambs. You are going to keep your QR ram and decide to test your best ewes and most promising ewe lambs for genotype at codon 171. The test results are as follows:

Ewe 241 is QR	Ewe 244 is QR	Ewe 245 is QQ
Ewe lamb 260 is QR	Ewe lamb 263 is QR	Ewe lamb 266 is QQ
Ewe lamb 267 is RR		

1. You want to keep your flock size at five ewes.
   - Which ewes /ewe lambs will you cull? Ewe 245 and Ewe lamb 266
   - Which ewes/ewe lambs will you keep? Ewes 241 & 244 and Ewe lambs 260, 263 & 267
     You would cull the QQ ewes because of their lack of scrapie resistance.

2. If all five of the ewes you kept in your flock have twins next year:
   - What percentage of lambs will potentially be RR? 30
   - What percentage of lambs will potentially be QR? 50
   - What percentage of lambs will potentially be QQ? 20

		Ram Q	Ram R
Ewe	R	QR	RR
	R	QR	RR

		Ram Q	Ram R
Ewe	Q	QQ	QR
	R	QR	RR

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Potential genotypes from QR ram and RR ewe:

2 RR
2 QR
0 QQ

Potential genotypes from QR ram and 4 QR ewes:

4 RR
8 QR
4 QQ

20 Total potential offspring genotypes:

6 RR ÷ 20 total = .30 or 30%
10 QR ÷ 20 total = .60 or 60%
4 QQ ÷20 total = .20 or 20%

3. Plan a breeding program for year three which will assure that your entire flock is either QR or RR.

- Option 1: Cull your QR ram and purchase an RR ram. All offspring from an RR ram will be scrapie resistant (QR or RR).

- Option 2: Keep your QR ram and test all potential replacement ewes. Cull all QQ ewes. Keep all RR ewes (as long as they have the traits you want in your flock). Keep good QR ewes and continue testing replacement ewes. You would not need to test any potential replacement ewes from your RR ewes.

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   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

2. If a ewe is QR:
   - What percentage of lambs will be RR? _____
   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

3. If a ewe is QQ:
   - What percentage of lambs will be RR? _____
   - What percentage of lambs will be QR? _____
   - What percentage of lambs will be QQ? _____

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   - What percentage of lambs will potentially be RR? _____
   - What percentage of lambs will potentially be QR? _____
   - What percentage of lambs will potentially be QQ? _____

3. Plan a breeding program for year three which will assure that your entire flock is either QR or RR.