ARS and Partners Set Their Sights on Scrapie in Goats

PEGGY GREB (D1360-1)

Microbiologist Katherine O'Rourke and molecular biologist Tom Truscott obtain tissue from a goat for use in a new test for scrapie.

Goats are tough, spirited animals. But they're no match for scrapie, a form of transmissible spongiform encephalopathy. In goats—and sheep—the degenerative disease causes tremors, lip-smacking, weight loss, a hopping gait, and other peculiar symptoms. Scrapie-afflicted animals cannot be cured, and they eventually die.

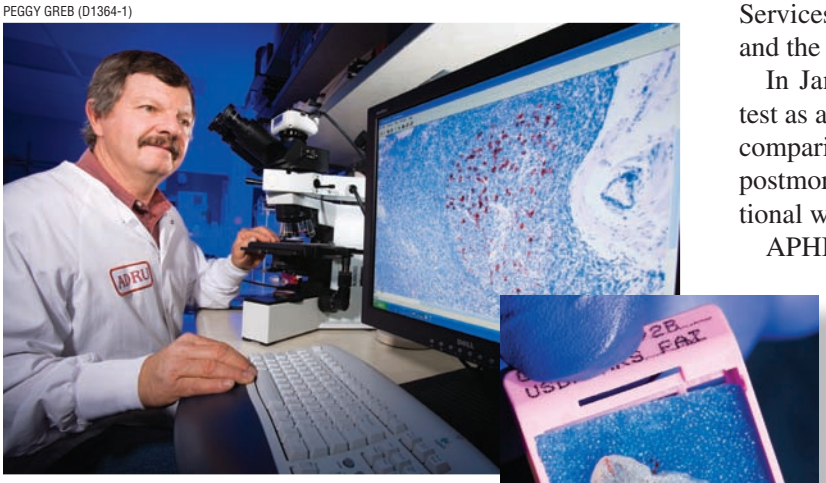
Since 2001, USDA's Animal and Plant Health Inspection Service (APHIS) has coordinated an accelerated National Scrapie Eradication Program to eliminate the disease from U.S. sheep and goats. But transmission routes, progression, and genetic underpinnings of scrapie in goats are poorly understood. Low occurrence rates, underreporting, and the inconvenience and cost of tissue testing make eradication challenging.

The good news is that a new, live-animal test to detect scrapie is being applied to goats. There's also an ongoing study of goat genes that might confer resistance to the disease.

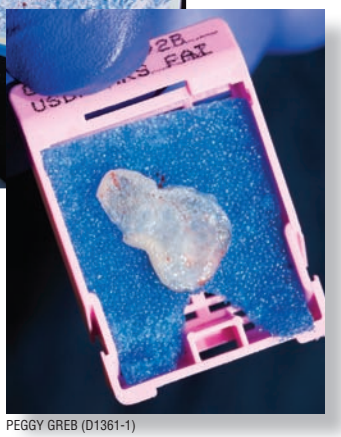
Building on Early Successes

The new method, known as the "rectal mucosal-associated lymphoid tissue (RMALT) test," is based on the currently used third-eyelid test. Developed by the Agricultural Research Service and Washington State University (WSU), the third-eyelid test has been used by APHIS and state veterinarians since 2002 as an official test to detect scrapie in sheep. It involves snipping a tiny piece of lymphoid tissue from the animal's nictitating membrane, or third eyelid, staining it with antibodies, and examining it under a microscope. Lymphoid tissue is used because it tends to collect malformed proteins called "prions," which are thought to cause scrapie.

PEGGY GREB (D1364-1)



Tom Truscott views a live-animal test for scrapie. The red areas indicate the presence of the scrapie prion protein.



Inset: **The live-animal test requires removal of a small snip of tissue after a local anesthetic is applied.**

PEGGY GREB (D1361-1)

Researchers in Norway and Scotland modified the method for a different site: lymphoid tissue in the lining of the animal's rectum. The rectal biopsy has also been used in deer, elk, sheep, and now goats. It's quick to perform and relatively painless to the animal—thanks to a dab of local anesthetic.

"Rectal biopsy also allows for more repeat samples from an individual animal when needed," says ARS microbiologist Katherine I. O'Rourke, a member of the scrapie research team, which includes APHIS Veterinary Services (VS) and Wildlife Services, the National Park Service, Colorado State University, and the Canadian Food Inspection Agency.

In January 2008, APHIS-VS approved use of the RMALT test as a scrapie-detection tool after large-scale validation trials comparing its accuracy (87 percent) to third-eyelid biopsies and postmortem examinations of tissue from infected sheep. Additional work on the accuracy of the test in goats is under way.

APHIS has incorporated the RMALT test into the National Scrapie Eradication Program. Current users are mainly federal and state veterinary personnel.

Setting the Stage for Selective Breeding

A key facet of scrapie prevention in sheep flocks involves use of selective breeding to increase the number of sheep with the version of the prion protein gene (dubbed "R171") that confers resistance. For now, goat producers don't have that option. Despite searches by ARS and WSU scientists at Pullman, as well as at other labs, the R171 prion gene version has never been found in goats. But there are several different gene variants in goats, some of which might confer resistance to scrapie.

No one has confirmed genetic resistance in goats thus far, but some tantalizing leads are emerging.

"In sheep, the discovery of resistance genes was key to developing a broadly accepted eradication program. If scrapie is found in a flock, only the genetically susceptible sheep are removed, allowing the producer to maintain quality animals," says O'Rourke. "As we learn more about goat genetic resistance, we hope the same approach can work for them."

Towards that end, ARS Pullman geneticist Stephen White is leading a team of ARS and university scientists to characterize the prion protein gene of goats and identify important gene variants in individuals and breeds. The Pullman team has so far examined the prion protein gene sequences from 446 goats representing 10 breeds, 8 of which have never been genetically characterized for their potential scrapie response.

The team's analysis found four gene variants (R143, S146, H154, and K222) in the genes of Boer, Nubian, Saanen, Toggenburg, and a few other goat breeds. These gene variants were relatively rare or absent in animals that developed scrapie in previous outbreaks, which suggests these gene variants might help the animals in some way. A fifth variant (M142) was found mainly in Alpine and Toggenburg goats, and it is known to delay incubation of scrapie from infection to clinical disease. More work is needed to demonstrate true resistance for any of these genetic variations, notes the team in a paper published in the September-October 2008 issue of *Genetic Selection Evolution.*

Putting Together the Pieces

In related work, the Pullman scientists are monitoring six goats from a Michigan farm with a known history of scrapie infection. In March, two of the infected goats, named "Nutmeg" and "Meeko," gave birth to three kids, providing the scientists with an unprecedented look into parent-to-offspring transmission of scrapie and inheritance of genes affecting the animal's response to the disease.

PEGGY GREB (D1365-1)

Molecular biologist Jim Reynolds extracts DNA for genetic testing to see which goats might have increased resistance to scrapie.

PEGGY GREB (D1363-3)

Geneticist Stephen White studies goats with a version of the prion gene that might confer increased resistance to scrapie.

"We learned that—unlike in sheep—the goat placenta is not a very reliable indicator of the scrapie status of the dam," says O'Rourke. "We'll do some more research to determine why this is, and how it affects transmission in a herd."

Genetic testing revealed that Meeko's kid is genetically susceptible, which allows for monitoring of scrapie's onset and development during the animal's life. Nutmeg gave birth to twins—one genetically susceptible and the other with a variation that may eventually prove to confer resistance.

Besides their university colleagues, ARS's Pullman team, led by Donald P. Knowles, has collaborated closely with APHIS-VS to formulate a strategy aimed at helping the U.S. goat industry to eliminate scrapie. The current effort takes a multipronged approach that includes early detection through slaughter surveillance and reporting of clinical suspects, flock management and selective breeding in sheep, scrapie-free flock certification, and producer outreach and education.

"In support of the eradication effort led by APHIS and industry, ARS will continue to do research on genetic resistance, diagnostic testing, and transmission modes," says O'Rourke. "Prevention is always a more desirable route than removal of infected animals or exposed animals. So research on resistance genetics and transmission modes will be especially important contributions."—By **Jan Suszkiw,** ARS.

This research is part of Animal Health, an ARS national program (#103) described on the World Wide Web at www.nps.ars.usda.gov.

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