

REPORT OF THE COMMITTEE ON SCRAPIE

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The Committee met on October 13, 2009 at the Town and Country Hotel, San Diego, California, from 12:30-5:00 pm. At least 18 members and 22 guests were present.

Chuck Palmer reviewed the Committee's 2008 resolution which urged the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS) to request adequate funding for the National Scrapie Eradication Program budget. The response from USDA-APHIS-VS indicated that they would be reconsidering all disease program funding requests and needs, and would be prioritizing its overall budget accordingly.

Diane Sutton, USDA-APHIS-VS, gave the following update of the scrapie eradication and certification program:

In Fiscal Year 2009 the Scrapie Eradication Program focused on: (1) cleaning up infected and source flocks utilizing a genetic based approach; (2) tracing and testing exposed animals and animals in exposed flocks; (3) expansion of regulatory slaughter surveillance (RSSS) to new collection sites; (4) producer education, (5) ID compliance; (6) implementing the National Scrapie Surveillance Plan, (7) working through the World Organization for Animal Health (OIE) to remove Nor98-like scrapie from the scrapie chapter and development of a policy for handling Nor98-like cases in the US, and (8) development of a proposed rule to revise 9 CFR parts 54 and 79.

Scrapie Flock Certification Program

As of July 31, 2009, there were 1,830 flocks participating in the Scrapie Flock Certification Program (SFCP). Of these flocks 543 were certified flocks, 1,241 were complete monitored flocks, 41 were export monitored, and 5 were selective monitored flocks.

National Scrapie Surveillance Plan Implementation

The National Scrapie Surveillance Plan is posted at http://www.aphis.usda.gov/vs/nahss/sheep/national_scrapie_surveillance_plan_08192008.pdf. The plan provides a comprehensive review of scrapie surveillance in the US, explains the basis for implementing state-of-origin sampling targets and ultimately flock level surveillance, and establishes minimum targets for FY 2009 and 2010. In FY 2009 Area Action Plans were developed to help meet State-of-origin sampling and ID compliance targets identified by the National Scrapie Surveillance Plan. This activity resulted in increased sampling in states not meeting plan targets.

Infected and Source Flocks

Thirty-three percent fewer newly infected and source flocks were identified in FY 2009 through July compared to the same month in FY 2008 (chart 1). As of July 31, 2009, there were 21 scrapie infected and source flocks with open statuses. In FY 2009, 21 new source flocks and 8 new infected flocks had been reported; 26 flocks had completed a clean-up plan and been released. The ratio of infected and source flocks released to newly identified infected and source flocks for FY 2009 = 0.9 : 1.

Positive Scrapie Cases

As of July 31, 2009, 65 positive cases in sheep or goats were reported by the National Veterinary Services Laboratories (NVSL); 34 were field cases and 31 were Regulatory Scrapie Slaughter Surveillance (RSSS) cases collected between October 1, 2008 and July 31, 2009 and confirmed by August 20, 2009. Field cases are positive animals tested as part of a disease investigation including

potentially exposed, exposed and suspect animals. Twenty cases of scrapie in goats have been confirmed by NVSL since implementation of the regulatory changes in FY 2002. The most recent positive goat case was confirmed in July 2009 and is epidemiologically linked to the same herd in Michigan as the positive goat cases that were found in FY 2008. The positive goat was a pet animal quarantined as part of the FY 2008 investigation. No additional animals were exposed.

Regulatory Scrapie Slaughter Surveillance (RSSS)

RSSS started April 1, 2003. It is a targeted slaughter surveillance program which is designed to identify infected flocks. Samples have been collected from 223,452 animals since April 1, 2003: this total includes 695 rectal biopsies collected in Texas as part of a surveillance pilot project. There have been 415 NVSL confirmed positive animals since the beginning of RSSS. As of July 31, 2009, 34,193 samples, including 513 rectal biopsies, have been collected in FY 2009. Thirty one samples collected in FY 2009 have tested positive for scrapie; 28 of these were from black-faced sheep and 3 from mottled-faced sheep. Two of these RSSS cases originated from a source flock identified at the end of FY 2008. Four other animals originated from flocks containing other RSSS positive sheep. There was an 11% decrease in percent positive black face sheep sampled at slaughter (.18 to .16%) between FY 2008 and FY 2009 as of July 31, 2009 if multiple positives from the same flock are excluded (chart 2). RSSS was designed based on the findings of the Center for Epidemiology and Animal Health (CEAH) Scrapie: Ovine Slaughter Surveillance (SOSS) study. The results of SOSS can be found at <http://www.aphis.usda.gov/vs/ceah/cahm/Sheep/sheep.htm>.

Scrapie Testing

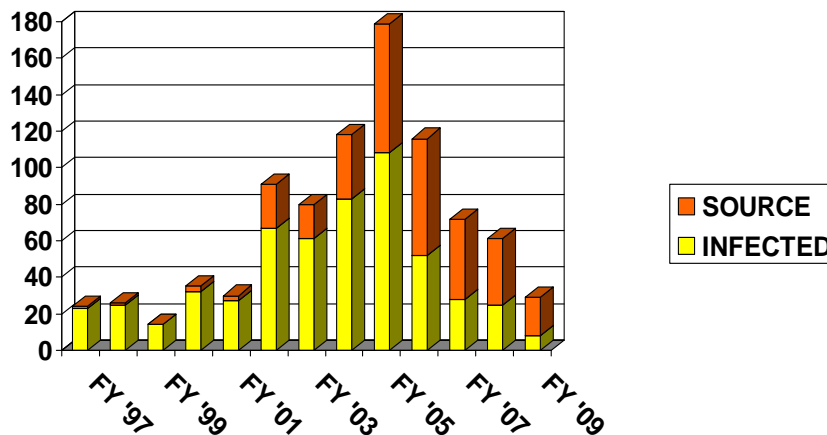
As of July 31, 2009, 36,524 animals have been sampled for scrapie testing: 34,193 RSSS samples (number includes 513 rectal biopsies from Texas), 1,663 regulatory field cases, and 668 live-animal biopsies .

Animal ID

As of September 1, 2009, 160,294 sheep and goat premises had been assigned identification numbers in the Scrapie National Generic Database and 126,123 premises had received official ear tags.

Chart 1

**Infected and Source Flocks
New Statuses by Year
FY 1997 – 2009***

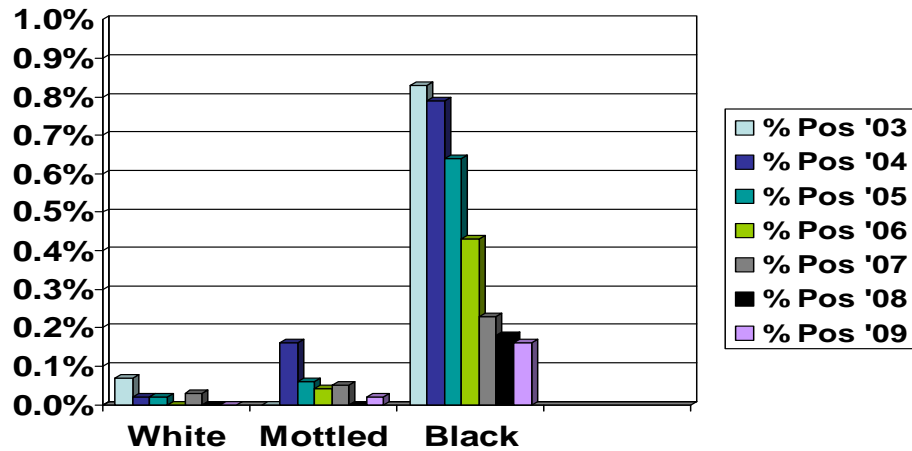


*Through July 31, 2009

Chart 2

**Percent of RSSS Samples that Tested
Positive for Classical Scrapie by Face Color during each
Fiscal Year (2003 – 2009*)**

Positive animals from same flock removed (black and mottled).



* Through July 31, 2009—does not include Nor98-like scrapie cases found through RSSS (2 in FY 2007 and 1 in FY 2008)

Scrapie Eradication Program Educational Materials

Cindy Wolf, University of Minnesota, College of Veterinary Medicine

Dr. Wolf presented information on new and updated educational materials that have been developed in conjunction with USDA-APHIS and the National Institute for Animal Agriculture (NIAA). This included a new reference CD "A Guide to the National Scrapie Eradication Program for Veterinarians", as well as the following materials:

- ABCs of Genetic Based Flock Clean-up and Monitored Plans for Classical Scrapie Infected, Source and Exposed Sheep Flocks, brochure 2009, English & Spanish
- A Guide to the National Scrapie Eradication Program for Veterinarians, CD 2009
- Why Eradicating Scrapie in US Goats is so important, PowerPoint available on CD Nov 2009.
- Identification Requirements of the National Scrapie Eradication Program for Sheep, PowerPoint available on CD 2008
- Goat Identification: Visual & Electronic, PowerPoint available on CD 2008
- Genotyping: A Tool for controlling classical scrapie, PowerPoint available on CD 2008
- Role of Market & Dealer in the Eradication Program poster
- Sheep Identification poster
- What You as a Producer Need to Know
- Requirements for Going to 'the Show'
- Sale and tagging record book

These educational resources can be ordered by contacting the NIAA at: 13570 Meadowgrass Dr, Suite 201, Colorado Springs, CO 80921, Ph: 719-538-8843 Fax: 719-538-8847, or online at scrapie@animalagriculture.org. They can also be viewed in their entirety at www.eradicatescrapie.org.

ARS Research Update

Katherine O'Rourke, USDA-(Agriculture Research Service (ARS))

With the continuing progress of the joint federal-state-industry scrapie eradication program in reducing the prevalence of classical scrapie in sheep, ARS is investigating potentially minor sources of infection, including scrapie in goats and scrapie in sheep of minor prion genotypes. USDA APHIS and the state regulatory agencies in Colorado and Michigan have submitted live goats with scrapie exposure and these animals have provided the first reports on prion accumulation in the placenta of infected does

as well as insights into diagnostic strategies and genetic resistance. In the very small number of goats examined, the placenta was positive only in the terminal year of the disease, in contrast to sheep scrapie in which the placenta is usually positive at one year of age. At least one kid born to a doe with a positive lymphoid biopsy but with a negative placenta, has become lymphoid biopsy positive. This suggests that other sources of infection might occur in goats. Experimental feeding of milk and experimental transmission of blood from experimentally infected does will be initiated in the next year of the project. Rectal lymphoid biopsies in goats showed very low levels of abnormal prion protein in young goats and antemortem diagnosis is challenging. Genetic changes at prion protein positions 146 and 222 are potential candidates as resistance genes. Experimental challenge of goats was initiated last year and goats will be observed for at least 7 years.

Sheep with a genetic change at prion protein 112 have been reported to have a prolonged incubation time. In the small numbers of animals available, rectal biopsies were observed to be positive at approximately 24 months, rather than the 14 months observed with sheep without the mutation. Sheep with experimental administration of Nor98-like scrapie had negative placentas at year one and are clinically normal at 1.5 years; these ewes will be bred again for lambing at 2 years post-inoculation.

Update on transmissible spongiform encephalopathies (TSE) of sheep and goats

Linda Detwiler

Mississippi State University

Dr. Detwiler highlighted scientific papers that were presented at the recent Prion 2009 presentations given at this meeting. There is still considerable debate over the specific nature meeting held in Greece September 23-25, 2009. This included recent publications as well as overviews of the agent. The biggest discrepancy is that evidence of infectivity does not correlate to the detection of the abnormal form of the prion protein (PrP^{Sc}). Multiple studies have demonstrated infectivity (some with significant levels) in certain tissues with no or low levels of PrP^{Sc}.

Protein misfolding cyclic amplification (PMCA) is a relatively new technique that greatly increases sensitivity in detecting the presence of prions. PMCA functions on the principle that a prion (PrP^{res}) acts as a seed or template that actively recruits normal prion protein and alters the conformation. PMCA uses sonication cycles to amplify the reaction between the PrP^{res} seed and normal prion protein (PrP^C). PMCA reactions seem to be able to amplify minuscule quantities of preexisting PrP^{res} seeds. Currently PMCA is used in research settings. There is discussion about its use as a commercial test.

As science advances there have been breakthroughs in obtaining information regarding the tissue distribution of infectivity in a scrapie infected sheep and the routes of agent shed. It has now been well established that scrapie and experimental BSE in sheep can be efficiently transmitted in blood (Houston et. al., 2008). In a study designed to look at the risks associated with human blood transfusions and vCJD, sheep experimentally infected with BSE were used as the model. This study found that all blood components (platelets, buffy coat, and nonleucoreduced plasma) would transmit the disease to recipients. Furthermore, it appears that transmissions occur irrespective of volume, plasma content and white cell count. Blood and products may transmit infection as early as 30% of the incubation. Thus far, sheep receiving leucodepleted product are still free from evidence of clinical disease. (survival time between 600-800 days). (*McCutcheon et al, Prion 2009*)

There have been 3 recent publications that demonstrate colostrum, milk and milk components (cream, casein-whey, cellular pellets) from certain genotypes of scrapie-infected sheep transmit infectivity. (Konold et. al., 2008; Lacroux et. al., 2008; Maddison et. al., 2009)

Atypical scrapie continues to be detected throughout Europe, in the US and Canada. In some countries of Europe the vast majority of cases are atypical versus classical. In Europe, a twelve-country study (Fediaevsky et.al., Prion 2009) was conducted to determine the extent of the contagious nature. Questionnaires were used to collect country level data on 1) control measures, 2) results of active surveillance and 3) testing resulting from outbreak control. Prevalence data was modeled using linear regression mixed models and meta-analysis. Mean prevalence for abattoir surveillance was 6 cases per ten thousand and 8 cases per ten thousand in fallen stock. Meta analysis on data from 11 countries found the probability of detecting secondary cases of atypical scrapie in positive flocks similar to the probability observed in animals for healthy slaughter. Also, the probability of detecting secondary cases of scrapie in flocks infected with classical scrapie was significantly higher than the probability of detecting secondary cases in atypical scrapie positive flocks (OR=32.4, CI95%: 20.7-50.7). These results suggest

that atypical scrapie is not contagious or has a very low level of transmissibility under natural conditions compared to classical scrapie.

A study was also conducted in Norway to determine the potential contagiousness of Nor 98 scrapie. Animals from 7 flocks with classical scrapie and 58 flocks with atypical scrapie were examined. There were multiple secondary cases of scrapie in the flocks with classical disease. There was only one of the 58 atypical flocks that had another positive. The other case in this flock happened to be the mother of the index case. (The flock size was very small) In this study not all flocks totally were completely depopulated. The results indicate that atypical scrapie is clearly less contagious, if at all.

There are a number of issues to keep on the radar screen in regard to the TSEs:

- Atypical scrapie – What are the risks to other species?
- What is the actual level of vCJD and what are the real risks associated with the contamination of the human blood supply?
- Is there a subclinical (carrier) state in humans with vCJD?; if so are these individuals a continuing risk to the blood supply?
- Most likely there will be newly emerging TSEs?
- Transmission between species is unpredictable hence there needs to be surveillance for emerging disease.

Regulatory Program Changes for Scrapie

Diane Sutton

USDA-APHIS-VS

Dr. Diane Sutton then highlighted some upcoming regulatory changes that may affect the scrapie program. These include a new VS Memo which provides the option for states to manage Nor98-like scrapie cases as a pilot project, thereby eliminating the need for depopulation in these flocks. She also mentioned revisions had been drafted for the scrapie sections (Parts 54 and 79) of the Code of Federal Regulations (CFR) which include:

- Giving the Administrator authority to relieve requirements for sheep and goats exposed to scrapie types, such as Nor98-like, that do not pose a significant risk of transmission
- Increasing flexibility in how investigations can be conducted and allow the epidemiology in a specific flock to be given more consideration in determining flock and animal status
- Adding genetic-based approach to regulation
- Making goat ID requirements for interstate movement similar to sheep in preparation for slaughter surveillance in goats
- tightening up the definition of slaughter channels
- expanding individual ID requirement to all sexually intact animals, unless moving as a group lot (allows mixed-source groups moving in slaughter channels under 18 months)
- Limiting use of tattoos and implants to animals not moving through concentration points and not in slaughter channels
- Establishing recordkeeping requirements similar to current UM&R compliance guidance
- Establishing surveillance requirements for consistent states

These proposed rules will likely be available for public comment sometime during FY2010. USDA is also developing a proposed rule to update the import requirements for sheep and goats, their embryos, and products and for exotic ruminants not addressed in other rulemaking, to mitigate risks from scrapie and BSE.

Overview of Nor98-like scrapie

Bradd Barr, California Animal Health and Food Safety Laboratory

Dr. Barr gave an overview of Nor98-like scrapie and discussed diagnostic testing. He reviewed the literature and detailed how Nor98-like scrapie, also referred to as atypical scrapie, differs from classical scrapie in several ways. The evidence suggests that Nor98-like scrapie is clinically, pathologically, biochemically, and epidemiologically unrelated to classical scrapie. Furthermore, Nor98-like scrapie may not be contagious and may, in fact, be a spontaneous degenerative condition of older sheep. He also presented information showing that the BioRad Elisa test is currently the most sensitive test for diagnosing Nor98-like scrapie.

Case Review Nor98-like Scrapie in the United States

Kris Petrini

Minnesota Board of Animal Health

Dr. Petrini reviewed the findings of the six cases of Nor98-like scrapie that have been diagnosed in the United States and compared them to findings from European cases. None of the sheep that were diagnosed with Nor98-like scrapie in the United States exhibited clinical signs and only one animal per flock was positive. The animals from three of the flocks had already been euthanized or slaughtered when Nor98-like scrapie was diagnosed and the remaining three were depopulated. With more and more evidence that Nor98-like scrapie does not transmit readily from animal to animal, if at all, the need for depopulation in affected flocks is questionable. Petrini also recapped recent literature which supports the idea that Nor98-like scrapie may result from a spontaneous degenerative condition.

Proposed VS Memo on Nor98-like scrapie

Jim Logan

Wyoming State Veterinarian

Dr. Logan talked about the proposed VS Memo regarding Nor98-like scrapie. A discussion on how to handle these cases in the United States followed. One concern that was brought up is that even if animals from flocks diagnosed with Nor98-like scrapie are not required to be depopulated, producers may lose the ability to market their animals. The Committee also discussed diagnostic testing for scrapie. ELISA tests have a greater sensitivity for finding Nor98-like scrapie than the IHC test, which is currently being used in the United States. It is therefore likely that cases of Nor98-like scrapie may be going undetected in the United States. However, since the sensitivity of the IHC test for classical scrapie is better than the ELISA, Dr. Sutton said that there is no plan to use the ELISA test in the scrapie eradication program in the immediate future.

Committee Business:

The possible benefits of passing a resolution to address concerns about Nor98-like scrapie in the current regulatory program was discussed. However, since USDA-APHIS has already approved a VS Memo which addresses the immediate concerns, and since the proposed CFR rule changes will allow the administrator more flexibility to deal with Nor98-like scrapie, the Committee did not feel a resolution was necessary at this time.