

REPORT OF THE COMMITTEE ON FOREIGN AND EMERGING DISEASES

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The Committee met on October 17, 2006, from 8:00 a.m. to 5:30 p.m, Salon F, Minneapolis Hilton Hotel, Minneapolis, Minnesota. Attendance varied through the day, from 50-200 attendees. Drs. Corrie Brown and Alfonso Torres presided and conducted the Committee meeting.

The Committee purpose statement was reviewed as well as protocol for membership on the Committee. Responses to 2005 resolutions were reviewed. The next edition of the Foreign Animal Diseases book was discussed. Planned publication date is early 2007.

The strategic plan to eradicate screwworm from the American continent was reviewed. Drs. Javier Ross, Dale Maki, and Gustavo Rodriguez, Regional Screwworm Eradication Program, International Service (IS), Animal and Plant Health Inspection Service (APHIS) reported on the status of their activities. Total losses from screwworm in the Americas are estimated as \$3.6 billion per year. Financial support is being solicited from a variety of organizations. A new plant is planned in Panama for next year to complement the capacity at Tuxtla Gutierrez. A few initiatives with Agriculture Research Services (ARS) are underway, including development of an all-male strain. Three take-home messages were highlighted:

- (1) Jamaica cannot fail where urban feral dog is preferred host;
- (2) Caribbean is the focus of most current efforts and;
- (3) All-male strain being developed by ARS will greatly facilitate efforts.

Learning from AI Panel

Dr. Aaron Scott, Centers for Epidemiology and Animal Health (CEAH), Veterinary Services (VS), APHIS, gave an overview of the National Avian Influenza Surveillance System. Data gathered includes passive reporting, active observational surveillance, active serologic surveillance, and active antigen surveillance. The testing that is being performed corresponds to a greater than 99% confidence for an Asian Highly Pathogenic Avian Influenza (HPAI) H5N1 outbreak in the 2 week window and 95% confidence in 7 to 10 days. Current surveillance could be augmented in the backyard and small volume, high-value poultry, where passive reporting is what we rely on primarily. In addition, targeted surveillance along flyways would be helpful.

Dr. Dan Sheesley, Deputy Administrator for International Services (IS), Animal and Plant Health Inspection Services (APHIS), reported on avian influenza activities. The mission of IS is to promote agricultural expertise that will serve to safeguard unintentional import of disease problems. A United States Department of Agriculture (USDA) International HPAI Coordination Group has been formed, with regional responsibilities. Dr. John Shaw coordinates the group. An APHIS Emergency Operations Center (AEOC) for domestic and international HPAI preparedness was formed in February 2006. APHIS and Foreign Agriculture Services (FAS) formed a "fusion group" to deliver USDA Foreign Assistance to the worldwide HPAI effort in June of 2006. Integrating efforts among all the various groups associated with HPAI has been challenging.

Dr. John Shaw, IS-APHIS, talked about international activities surrounding AI vaccination. He stressed that USDA does not make any recommendations regarding vaccine nor does it supply vaccine to any foreign government. There is a current initiative to create a specialized body of material regarding vaccination that can be delivered by non-specialists, e.g., attachés.

Dr. Bob Cook, Wildlife Conservation Society, described the Global Avian Influenza Network Surveillance (GAINS). He emphasized that wild birds are known to be reservoirs of low pathogenic avian influenza (LPAI), not highly pathogenic. However the

systems of sanitation in many markets create opportunities for spread and mutation of the virus. The role that wild birds play in HPAI spread was reviewed. In many developing countries, rearing of domestic fowl is outdoors and wild birds can land in these areas and pick up disease. GAINS was designed to promote preparedness, and insert more information about wild birds into the global information available on the epidemiology of HPAI. GAINS is a growing global network of monitoring sites, using many conservation organizations and a large cadre of volunteers. All information is open to the public, www.gains.org

The Committee's Time-Specific Paper, Atypical BSE – What it Means, was delivered by Dr. Linda Detwiler. This paper is presented in its entirety in these Proceedings following the Committee Report.

Educational Efforts for Foreign and Emerging Diseases Panel

Dr. Paula Cowen, Director, Professional Development Staff, VS-APHIS, reported on a decade of Smith-Kilborne. One sophomore veterinary student from each of the 28 schools of veterinary medicine is selected and all gather for a week-long course, first at Cornell University and then at Plum Island. Program has been successful in helping to inform students at all schools about University System of Georgia (USG) activities concerning foreign and emerging diseases and Smith Kilborne alumni can be found at all levels of government, academic, and private industry.

Dr. Sandy Amass, Purdue University, reported on the Graduate Certificate for Veterinary Homeland Security. It is a web-based, graduate level, distance learning program for individuals involved in animal emergency response. The first course started in May of 2006, and includes 47 students from many states, www.biosecuritycenter.org

Dr. Lee Myers, Assistant Commissioner for Animal Industry, Georgia Department of Agriculture, reviewed state-federal partnerships for training. Greater coordination at the federal level would help to close gaps and reduce overlap. In addition to state and federal entities, we need to continually include academia and private sector. Engagement and coordination among all would facilitate our progress.

Dr. Will Hueston, University of Minnesota, reviewed public health education at veterinary colleges. Public health information within the doctor of veterinary medicine curriculum is delivered in a variety of ways at the various colleges of veterinary medicine. Beyond the veterinary degree, there are an increasing number of options for pursuing an advanced degree in public health. Five years ago, 25 veterinarians and veterinary students were pursuing advanced public health programs. Today at least 225 veterinarians and veterinary students are enrolled in these programs. Options for studying public health are available in at least 17 colleges of veterinary medicine in North America.

Federal Programs on Foreign Animal Diseases Panel

Dr. Luis Rodriguez, Research Leader, Plum Island Animal Disease Center (PIAD), gave some of the research highlights from his unit. Thermography, an infrared technology, has been used successfully in Foot and Mouth Disease (FMD) vaccine and challenge studies. Research on empty viral capsid vaccines for FMD has progressed well, using several vectors. Biotherapeutics for emergency use, in the form of delivery

of interferons, was shown to protect pigs in the early phase of FMD infection, prior to the onset of immunity provided by the vaccine. The Global Foot-and-Mouth Disease Research Alliance (GFRA) has been formed to bring the world's primary FMD research laboratories (Australia, Canada, USA, UK) together and create synergy in addressing current gaps in countermeasures against FMD.

Dr. David Suarez, Research Leader, Southeast Poultry Research Laboratory–ARS, reviewed the work in his laboratory. Almost all research is focused on avian influenza and Newcastle disease. Research on AI includes, pathogenesis studies, molecular epidemiology, vaccines, diagnostics, mucosal immune response, immune variation between breeds and species, and viral changes affecting immune system. Research on New Castle disease virus (NDV) includes: pathogenesis, control including vaccines and diagnostics and biological and sequence characterization of new and emerging isolates.

Dr. Beth Lautner, Director, National Veterinary Services Laboratories (NVSL), reviewed progress on the construction and consolidation of the APHIS and ARS laboratories in Ames, Iowa. At NVSL, ISO 17025 accreditation is on target. Avian influenza has been a high priority for NVSL, with expanded testing and training of both US and international scientists. At Foreign Animal Disease Diagnostic Laboratory (FADDL), there were 638 foreign animal disease investigation accessions during 2006. The National Animal Health Laboratory (NAHLN), a partnership between USDA and state laboratories, has progressed significantly since its inception in 2002. A NAHLN Methods Technical Working Group is being developed.

Dr. Terry Nipp gave an update on research and education at the National Center for Foreign Animal and Zoonotic Diseases, Texas A&M University. Research on FMD involves investigation of anti-viral drugs for use in early infection, the role of natural killer cells in infection, and the development of rapid diagnostics. Research on AI focuses on improved diagnostic testing. A train the trainer flu school was developed, with pilot trainings completed in California, Tanzania, and Texas. Investigations on Rift Valley fever involve development of models, using environmental and animal population data. Carcass disposal is also an active area of development for the Center, with the use of Geographic Information System (GIS) and regulatory information to determine optimal sites.

Advanced Diagnostics and Expanded Capabilities for Foreign Animal Disease Detection and Surveillance, was presented by Dr. Pam Hullinger, Lawrence Livermore National Laboratories, Department of Homeland Security (DHS). During November and December of 2005, thirteen NAHLN laboratories and the NVSL and PIADC received training, "leave-behind" instrumentation, reagents and consumables to conduct the assay. These labs then participated in a nationwide interlaboratory comparison of the multiplexed assay, during which more than 3,000 blinded samples were analyzed and greater than 52,000 individual assays conducted. The overall assay success rate was greater than 92%.

A serotype-specific Polymerase Chain Reaction (PCR) for FMD was presented Dr. Eric Engelhard, Fair Isaac. The project has involved extensive comparisons of available sequences.

Integration of Efforts Panel

Dr. John Shaw, IS-APHIS, reported on USDA liaison efforts with World Organization for Animal Health (OIE) and Food and Agricultural Organization (FAO). With recent outbreaks, it became apparent that control of diseases requires infrastructure building, and this building must occur well in advance of any emergency. Agreements between USDA and FAO were signed recently, and three USDA animal health professionals are now in the Crisis Management Center in Rome. USDA personnel are now being deployed to help in other countries through FAO. Similar agreements with OIE were signed in June of 2006.

Dr. Kimothy Smith, Chief Veterinarian, Department of Homeland Security, talked about the National Bio and Agrodefense Facility (NBAF). Expression of interest was issued in January 2006, with 29 submissions received. An initial down selection to 14 consortia was announced in August 2006. Reviews and evaluations will be conducted through the next seven months, utilizing a committee approach. The Expressions of Interest (EOI) Committee consists of government employees from multiple agencies. Congress has appropriated \$23 million for NBAF site evaluation, Environmental Impact Statement and pre-construction design.

Dr. Bret Marsh, Indiana State Veterinarian, reported on state-federal partnerships that work. There were several examples. First, over the last decade there has been growth of cooperative programs federal funding that works through state programs, that allow states to function in support of federal programs. Second, the Interagency Personnel Agreement (IPA) has facilitated the work of numerous state animal health officials within the federal government, and this has helped each entity to understand the work of the other. Third, the National Safeguarding Review was a collaborative effort that led to several initiatives and positive changes within our approach to surveillance. Fourth, the NAHLN is a viable and integrated, functioning network that has greatly expanded diagnostic capabilities for animal diseases. Lastly, the National Veterinary Accreditation System might be the most durable and historic contribution to state-federal partnerships.

Mobile data collection – progress and prospects was presented by Dr. Bill Buisch who covered the possibilities for mobile data entry, handwriting recognition, and forms development.

National Veterinary Stockpile (NVS) was presented by Dr. Richard Nolan, VS-APHIS-USDA. The NVS was created as a result of Homeland Security Presidential Directive 9 (HSPD-9) and is modeled after the National Stockpile maintained for human diseases by the Center for Disease Control and Prevention (CDC). The NVS includes not only vaccines, but also contracts for vaccines, personal protective equipment (PPE) and antivirals.

Update on hemispheric eradication of FMD, by Dr. David Ashford, IS-APHIS-USDA, was an overview of the program and its progress. South America is the largest supplier of animal protein in the world and most outbreaks of FMD in the world due to illicit movement of animal products. Consequently, elimination of virus at the source is an efficient solution to avoiding hemispheric spread of FMD. The program has succeeded in greatly reducing the number of outbreaks but some problem pockets of infection remain. Vigilance at this stage is essential.

Atypical BSE: What is it and what is the significance

Linda A. Detwiler, Paul Brown, Lisa M. McShane, and Gianluigi Zanusso

For almost the entire two decades that BSE has been known in the world it was thought that there was only one “strain” that infected cattle and caused disease in some other species such as humans (Bruce et al., 1997; Hill et al., 1997; Casalone et al., 2004). We now know that there are other manifestations of prion diseases in cattle which have been termed atypical BSE. Atypical BSE is a study in progress with more unknowns than knowns. One of the most important of the unknowns is the significance of atypical BSE in regard to human and animal health.

Previous research in mice had suggested the existence of a number of scrapie strains. Historically, research involving the differentiation of Transmissible Spongiform Encephalopathy (TSE) strains was based on biological typing using panels of inbred mice inoculated with homogenates of infected tissues. If the mice developed a TSE it was characterized by length of incubation and lesion pattern in the brain. (Bruce et al. 1992; Bruce et al. 1994) More recently it has been determined that the human and animals variations may be biochemically differentiated on the basis of molecular mass of the protease resistant prion protein (PrP^{res}) and the degree of glycosylation (Collinge et al., 1996)

In 2004, cases of a bovine prion disease molecularly different than already documented as classical BSE were described by scientists in both Italy (Casalone et al., 2004) and France (Biacabe et al., 2004). In both countries the cattle were over 8 years of age. The Italian cases (11 and 15 years of age) originally named bovine amyloidotic spongiform encephalopathy (BASE) were characterized by an unglycosylated protein band with a lower molecular mass (thus named L cases) and the predominance of the monoglycosylated band. In addition, immunohistochemical detection of PrP^{res} in these cases found greater deposits in the cerebral cortex and thalamus versus the brain stem. The French cases found a higher molecular mass associated with the unglycosylated protein band and were called H cases (see figure 1). The different “strains” are now called atypical BSE.

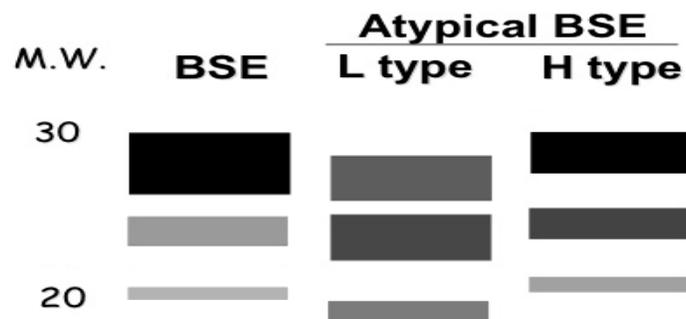


Figure 1. Comparison of Western Blot patterns from classical BSE and L and H atypical BSE. (Reprinted from Brown et. al. 2006)

Since these 2 publications additional cases of atypical BSE have been found in other countries. H cases have been detected in Canada, France, Germany, Japan, the Netherlands, Poland, Sweden, Switzerland and the United States. L cases have been diagnosed in Belgium, Denmark, France, Germany, Italy, Japan and Poland (Brown et al., 2006). The L cases in Belgium and Japan had additional differences (Yamakawa et al., 2003; De Bosschere et al., 2004). Two important points must be emphasized regarding the atypical BSE cases. Information regarding lesion pattern and PrP distribution is very limited as most cases were detected by the large scale surveillance programs which only required collection of the brain stem. In addition, if countries were using certain tests, some cases of atypical BSE may have been misdiagnosed or reported as negative. For example, if a country relied solely on immunohistochemistry to confirm positive ELISA screening test cases and did not use western blotting at all, the banding pattern differences would go unnoticed.

This may explain why the United Kingdom has not detected any cases of atypical BSE to date. The use of the western blot test was introduced to confirm BSE cases detected through passive surveillance only in 2000 and for active surveillance cases in 2001. The Department for Environment, Food and Rural Affairs (DEFRA) is conducting a retrospective study to examine if any of the cases diagnosed in the past did in fact have an atypical pattern.

When atypical cases were first reported there was some speculation that these may merely be protein accumulation disorders associated with old age. It has now been shown that both the L and H types of atypical BSE are at least experimentally transmissible. Homogenates from L cases have been transmitted to bovinized transgenic mice, humanized transgenic mice, *Cynomolgus* monkeys and 1 breed of cattle (Buschmann et al. 2006; Book of abstracts (2006), International Conference on Prion Diseases, Turin, Italy). H cases have been transmitted to bovinized transgenic (Tgbov) and ovinized transgenic mice (Béringue et al. 2006). The incubation times for atypical L cases of BSE were shorter in the Tgbov mice than classical BSE inoculated into Tgbov mice and the H cases had longer incubations.

There are several theories on the origin of atypical BSE:

- ❖ A variation or mutation of the classical BSE strain
- ❖ A different route of exposure or exposure at an older age
- ❖ A strain of Scrapie transmitted to cattle
- ❖ Sporadic or a spontaneous occurrence of BSE

At his point in time, there is no evidence to conclude that any of the theories are or are not a possibility. There is considerable interest in the sporadic theory. If a form of BSE were to occur naturally, this may suggest that certain control and prevention measure would have to remain in place indefinitely. Proving or disproving the occurrence of a relatively rare sporadic disease

poses a significant challenge. It would require between 3 and 4.5 million tests performed on brain samples randomly taken from cattle over 7 years of age in a country with no evidence of risk from orally acquired BSE. It is unlikely that any country would have the will or resources to perform such a study. Lacking this type of evidence, systematic surveillance over a long time period may provide evidence about the nature of atypical BSE.

As previously stated most of the characteristics of atypical BSE have not been defined. In addition to the origin, the risk to other cattle by means of natural transmission, the risk to humans and other animal species such as chickens and pigs is still unknown as is the distribution of infectivity throughout the body of a bovine. There is little information on clinical manifestation if it occurs at all in certain of the cases. Documented L cases have been diagnosed from samples taken from older “healthy” cattle presented for routine slaughter.

While additional surveillance and research is being conducted, it is important for policy makers to consider the implications of atypical BSE. They may need to rethink what populations are appropriate targets. It would probably be unwise to prematurely lessen or discontinue the current BSE protection measures.

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