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Animal Health MATTERS

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South Dakota State University

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Head/Director's Message
David H. Zeman, DVM, PhD

High Containment Facility Needs of the ADRDL: an update

As your Director of the SD Animal Disease Research and Diagnostic Laboratory (ADRDL), I have spoken to you in recent years about significant national and international trends that are impacting the way state animal health laboratories conduct business. A variety of rising risk factors have increased the likelihood that state animal health laboratories will be significantly involved with animal disease outbreaks of high consequence, many of which are also human diseases. Some of these outbreaks may be accidental introductions of dangerous diseases into our service region, while others may be malicious introductions of foreign or manipulated pathogens. The following rising risk factors and synergistic opportunities seem to make this the ideal time to seriously assess our situation:

- Rising Risks due to Globalization of Animal Agriculture
- Rising Risks due to Agroterrorism
- Rising Risks due to Changing Societal Expectations
  - The environment and EPA regulations
  - Public/Community health and agricultural hazard control
  - Employee health hazards
- Synergism with the VSD, ABS College and SDSU Research Programs
- Synergism with State and Local High-Technology Economic Development
- Synergism with Federal/State Diagnostic Networks (NAHLN, FERN, LRN)

In response to these trends, many state animal health laboratories have already built high containment facilities (BSL3) to handle pathogens of high consequence and of zoonotic concern. Currently the ADRDL has no high containment diagnostic or research space. A stakeholder committee has been formed by animal industry stakeholders to study and find solutions to this issue for South Dakota. Co-chairs of the committee are Christine Hamilton (Christianson Land and Cattle Company) and Dr. Dan Farrington (retired DVM industrial researcher). They will work with key representatives of all friends of animal health in the state, to keep the ADRDL on the cutting edge of the ever-changing disciplines of diagnostic medicine and disease research.

Diagnostic News - SDSU ADRDL

Classical Swine Fever Surveillance (Hog Cholera) at the SDSU ADRDL:

The ADRDL has recently obtained a $75,000 cooperative agreement grant from the USDA to conduct Classical Swine Fever (CSF) surveillance. This disease, also known as Hog Cholera, is of high interest to the US swine industry. The program is coordinated by the National Animal Health Lab Network (NAHLN). ADRDL diagnosticians have been asked to test tissues from as many sick or dead pigs as possible, as they are submitted to the diagnostic laboratory for other routine disease investigations. There will be no charge to our clients for this passive surveillance activity.

To encourage testing activity, practitioners will receive a financial reward for their efforts. For any routine disease investigation a $50 credit per pig (up to 3 pigs per case; cannot exceed maximum bill for the case) can be applied to that diagnostic bill if appropriate specimens for CSF testing are included with your submission. Appropriate specimens to qualify for the credit are:

- Any age sick or dead pig from any of our clients (not restricted to SD clients)
- Must submit dead pigs with tonsils or collect and submit a fresh tonsil during an on farm necropsy
This is a tremendous opportunity to participate in an important surveillance activity and receive free diagnostic support at the same time. In most cases, the credit will cover all or at least most of the diagnostic investigation expenses for any of your routine morbidity and mortality investigations such as scours, pneumonia, CNS, or sudden death syndromes. We look forward to receiving fresh tonsils with your submissions and dead pigs submitted to the ADRDL. The program will continue until December 31, 2007 or until funds are depleted.

Questions: Call Dr. David Zeman at 605-688-5172 or email at David.Zeman@sdstate.edu

Biopsy Service Changes at the ADRDL – Effective July 1, 2007

As part of our ongoing efforts to optimize diagnostic services at the ADRDL, we have instituted some changes to the Biopsy Service which will take effect on July 1.

The most important change is that lab schedules have been modified to ensure that a written diagnostic report will be faxed to the submitter within 24 hours of our receipt of the sample. This report will include a morphologic diagnosis, or at least our initial impression of the lesion pending additional stains, and additional interpretation as indicated. After the case is finalized, we are also available for phone consultation during regular business hours at no additional charge.

Another change is that a team of veterinary pathologists will rotate through the service, giving a high priority to expertise and shortened turn-around time. Each case will be assigned to one team member, with challenging cases reviewed by all. Team members are Dr. David Zeman, Dr. Tanya Graham, and Dr. David Knudsen.

David Zeman DVM, PhD, DACVP is a veterinary graduate of Oklahoma State University and PhD graduate of Louisiana State University, where he also completed his veterinary pathology residency. He joined the ADRDL in 1986, and is now laboratory director. He was designated South Dakota veterinarian of the year in 2003 by the SDVMA, and laboratory diagnostician of the year in 2006 by the American Association of Veterinary Laboratory Diagnosticians (AAVLD). He particularly enjoys infectious disease investigations and tumor biopsies.

Tanya Graham DVM, DACVP graduated from Oklahoma State University in 1994, then completed her residency in veterinary pathology at Texas A&M and then joined the pathology faculty at OSU. She then worked as a diagnostic pathologist at the University of Pennsylvania for two years, and moved to the ADRDL in 2000. She is associate director of the laboratory, and section head of Histopathology and Immunohistochemistry. Currently, her interests beyond routine diagnostic pathology include avian pathology and regulatory diagnostic medicine.

David Knudsen DVM, MS, DACLAM is a 1982 graduate of Colorado State University and was in mixed animal practice for three years before completing residencies in veterinary pathology and laboratory animal medicine at University of Missouri – Columbia. After five years on staff at University of California – Davis, he was a private consultant in veterinary and comparative pathology for pharmaceutical and biotechnology companies before joining the ADRDL in 2002 as a diagnostic pathologist and section head for Clinical Pathology.

As in the past, a typical biopsy case accession includes processing and examination of up to 3 masses or samples from the same patient, up to 2 special stains as needed, written report plus phone consultation as needed, and return of the shipping container with fresh formalin, for a single case charge of $20 plus a $8 case generation fee. There is no additional charge for decalcification, but an additional day for processing is generally required. Biopsy shipping containers, which include a small jar of formalin and a slide mailer for cytologic samples, are available for a nominal initial fee.

Holiday hours:
September 3 – Labor Day
October 8 – Native American Day
November 12 – Veteran’s Day Observance

Listing of Pharmacies Offering Compounding Services for Veterinarians – April 2007
Compiled by Regg Neiger, DVM PhD

Animal Pharmacy
66 West Avenue
Canandaigua, NY 14424
Phone: (800) 663-5261
Local Phone: (585) 394-4930
Fax: (585) 396-7264
CIDRV Research Looks at New HIV Drug

Researchers with the SDSU Center for Infectious Disease Research and Vaccinology (CIDRV) have won a major grant to study a new drug for treating HIV.

The National Institutes of Health has awarded $389,000 to help SDSU scientists research the mechanism of action of a drug called bevirimat. A company called Panacos Pharmaceuticals Inc. makes the drug.

HIV, or human immunodeficiency virus, is a virus that causes acquired immunodeficiency syndrome, or AIDS, in humans. The immune system begins to fail in patients with AIDS, leaving them vulnerable to life-threatening infections. The Joint United Nations Programme on HIV/AIDS and the World Health Organization estimated that about 39.5 million people were living with AIDS at the end of 2006.

Principal investigator Feng Li, an associate professor with the CIDRV, said there are already three classes of drugs being used to treat HIV. Li and his co-investigator, SDSU assistant professor Philip Hardwidge, will study a compound that is the first in a new class of anti-HIV drugs called "maturation inhibitors." Li said the drug interferes with virus particles called "virions" by not allowing the core of the virion to assume its mature conical shape.

Some researchers say virions can be compared to spacecraft in that they transport the genome of the virus from cell to cell and protect it in inhospitable environments. The new drug attacks HIV by disabling the virions -- it leaves them too immature and imperfectly formed to infect another host cell, and so the infection dies. Importantly, Li said, the drug may help deal with the issue of drug resistance, the leading reason that treatments fail for HIV patients.

"We do have the situation where, whenever people get infected with HIV, that transmitted HIV strain likely already has developed resistance to approved drugs. The new inhibitor we are working on could really provide a new option for treatment in overcoming resistance," Li said. "This inhibitor is different from all the other approved drugs."

Hardwidge said the goal of the two-year SDSU study is to characterize as precisely as possible what the drug does and also to examine viral resistance as it relates to the drug.

"We have a novel compound, but at a molecular level, how this compound functions is not absolutely clear yet. If
we understand that better, we may be able to improve the efficacy of the drug, we may be able to modify it so that HIV is less prone to evolve resistance against it," Hardwidge said. "With all of these compounds it's crucial to understand precisely how they're acting in order to make them the best drugs they can be."

Li said unlike other drugs, bevirimat does not attack the HIV viral enzymes, which may undergo modification readily as new strains of the virus develop. Instead, it will attach a part of the virus structure protein that is highly conserved among different viral strains.

That approach gives doctors a new tool to treat drug-resistant strains of HIV, and it also suggests the new compound may remain effective longer in the fight against HIV.

David Zeman, head of SDSU's Department of Veterinary Science, said the new grant is one example of how the governor's 2010 Centers of Excellence are beginning to produce results for South Dakota. Both Feng Li and Philip Hardwidge were recruited about two years ago to fill positions in the Center for Infectious Disease Research and Vaccinology. Both scientists maintain positions in both the SDSU Department of Veterinary Science and the SDSU Department of Biology/Microbiology.

The center fosters research leading to the development of novel therapeutic and diagnostic technologies and products for infectious diseases in humans and domestic animals.

Hardwidge added that the project illustrates one way that SDSU is looking beyond its borders to address major issues important to science.

"We're pleased with the federal funding for this project and we appreciate SDSU's support for basic biomedical research," Hardwidge said.

Sources: SDSU AgBio Communications, Yankton Press and Dakotan

Research Spotlight:
Dr. Ying Fang

Dr. Ying Fang joined the faculty of the SDSU Veterinary Science Department and the Center for Infectious Disease Research and Vaccinology in 2005. She holds a bachelor’s degree in Biology, masters degrees in Entomology and Microbiology, and a PhD in Veterinary Microbiology from SDSU.

Dr. Fang’s research has focused on the molecular characterization of porcine reproductive and respiratory syndrome virus (PRRSV) and applying that knowledge in the development and evaluation of vaccines and diagnostic assays for PRRSV. The laboratory has successfully constructed a full-length cDNA (complementary DNA) infectious clone of European-like Type 1 PRRSV that recently emerged in the US. Current efforts are directed towards the use of this reverse genetics system to study PRRSV pathogenesis and develop the next generation of genetically engineered PRRSV vaccines.

As a member of the SDSU Hybridoma Facility, she is directing the establishment of a panel of monoclonal antibodies against PRRSV non-structural proteins. A collaborative project also involves developing monoclonal antibodies against Severe Acute Respiratory Syndrome (SARS-CoV) nucleocapsid protein, and the study of the basic mechanism of nucleocapsid protein function in the pathogenesis of SARS.

Dr. Fang’s current projects include:
1. Genetic marker development in the Nsp2 region of a European-like PRRSV: implication for future recombinant marker vaccine development. PRRS continues to plague the pork industry worldwide. To control this disease, there is a great need for new generations of PRRS vaccines. One of the key steps in development of these new vaccines would be to include markers for diagnostic differentiation of vaccinated animals from those naturally infected with wild-type virus. Such vaccines would greatly benefit PRRS elimination, since it would be possible to assess the effectiveness of MLV vaccines. In this project, a full-length cDNA infectious clone of a European-like PRRSV isolate was constructed as a viral backbone. Then a marker was inserted into the unique deletion site of the Nsp2 region of the infectious clone as a means to identify vaccinated animals using routine serology. In the third step, conserved epitopes in the Nsp2 region were deleted so that the immune response to a wild-type virus could be detected in vaccinated pigs.

2. In vivo evaluation of genetic markers in the Nsp2 region of PRRSV: Implications for future recombinant marker vaccine development. Two Nsp2 mutant viruses have recently been constructed. Previous work resulted in the development of Nsp2 epitope-based differential ELISA assays. The goal of this study is to observe how these Nsp2 marker viruses behave in the live animal, and to study the potential of using the Nsp2-specific ELISAs to identify and differentiate vaccinated animals from naturally infected animals.

3. Accurate ELISA test development for PRRSV serology: Evaluation of cysteine protease domains of Nsp2 as potential diagnostic targets. The overall goal of this study is to characterize the PRRSV cysteine protease (CP) domain and the conserved epitope of Nsp2 along with the serological response to these antigens.
The cysteine protease domain (CP) of PRRSV Nsp2 was evaluated as a potential new antigen for sensitive, specific and differential diagnostic ELISA tests. Antibody to the CP domain could be detected as early as 14 dpi, and the CP-based ELISA detected the antibody response to diverse field strains.

4. Production of monoclonal antibodies against the PRRSV non-structural proteins. In order to produce new, safe, and effective vaccines and antiviral drugs against PRRS, a thorough understanding of the basic biology of the virus is needed. Since PRRS research began, a great deal of knowledge has been revealed about PRRSV’s structural proteins, but very little is known about PRRSV’s non-structural proteins (Nsps). Nsps play roles in mediating replication and transcription of the structural proteins of the virus. This makes them attractive targets for the development of antiviral drugs. One of the key reagents to study protein structure-function and design antiviral intervention strategies is the monoclonal antibody (mAb). Since the first development of mAbs thirty years ago, thousands of bioscience researchers worldwide rely on them to understand the structures, functions, and interactions of complex biomolecules. MAbS also contribute tremendously to in vitro diagnostic tests and in vivo therapeutic uses in clinical medicine. Previous work has built up a large panel of mAbs against PRRSV structural proteins, but no mAbs have been made against PRRSV Nsps. Therefore, the aim of this work is generating a full panel of mAbs against all Nsps of Type 1 and Type 2 PRRSV. This project will provide basic key reagents for study of the fundamental biology of PRRSV Nsps. The proteins and mAbs produced will be good candidates for future development of diagnostic assays.

5. The Role of PRRSV Nonstructural Protein 2 in Viral Replication. This is another study that looks at non-structural proteins (Nsps) in PRRSV. As previously mentioned, Nsps play roles in viral replication. In particular, Nsp2 has been shown to encode a putative cysteine protease, and in cell culture, it’s been shown that a cysteine protease inhibitor can block viral replication. In addition, Nsp2 is a very immunogenic protein that induces an earlier immune response than that of PRRSV structural proteins, suggesting that Nsp2 may be involved in the modulation of host immunity. This makes it attractive for development of antiviral drugs and vaccines. This study will focus on elucidating the basic properties of Nsp2 in viral replication. From this research, a cell-free model system for the study of PRRSV Nsps will be created, which can be used for high throughput screening of anti-PRRSV drugs. Better characterization of Nsp2 will allow the design and development of antiviral drugs, which directly target the virus and do not depend on the host immunity. These would be extremely valuable as a means to protect certain genetic breeding herds and seed stock herds, such as boar studs. In addition, altering Nsp2 function in PRRS viruses may be a means for production of attenuated vaccine viruses.

6. The role of PRRSV non-structural protein 1 and 2 in host immunity. The overall goal of this project is to understand the basic functions of PRRSV Nsp1 and Nsp2 in viral pathogenesis and host immunity. PRRSV infection typically induces a rapid, robust host humoral antibody response that is comprised predominantly of non-neutralizing antibodies. In contrast, anti-viral innate and cell mediated immune responses initially remain at a fairly low level. When anti-PRRSV neutralizing antibodies do appear, the response is slow and titers remain low. Many pathogens, in order to evade the immune system, will initially present non-protective but immunodominant epitopes to the host immune system, which decoy or dysregulate the ability of the immune system to focus on more protective targets, and subsequently, suppress a more protective immune response, resulting in semiprotective immunity.

Recent studies from Dr. Fang’s laboratory revealed that swine mount an immediate non-neutralizing antibody response to Nsp1 and Nsp2. The antibody response to Nsp1 and Nsp2 is greater than that to any other PRRSV protein, and lasts more than 120 days, which indicates the immunodominant nature of these proteins. This strong, immediate non-neutralizing humoral response induced by Nsp1 and Nsp2 suggests that these proteins may be involved in modulation of the host immune system. Therefore, in this proposed study, it is hypothesized that PRRSV Nsp1 and Nsp2 function as immune modulators to decoy the ability of the immune system to focus on more protective targets. This study will provide basic knowledge for future development of more effective and broadly protective second-generation PRRSV vaccines.

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Extension News - SDSU ADRDL

National Animal Health Monitoring System (NAHMS) to Study Beef Industry in 2007-08

The U.S. Department of Agriculture’s (USDA) NAHMS conducts national studies on the health and management of the U.S. livestock, poultry, and aquaculture populations. These studies are designed to meet the information needs of the industries and other stakeholders – as identified by people working with these industries.

In 1993, NAHMS conducted the Cow/Calf Health and Productivity Audit (CHAPA). CHAPA provided baseline information on U.S. beef cattle inventories, health and management practices, forage nutrient content, and animal
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selenium deficiency status. The Beef ’97 study built on the results of CHAPA. Objectives of the Beef ’97 study included describing trends in health issues affecting the U.S. beef herd and acquiring national prevalence estimates of Mycobacterium paratuberculosis (Johne’s disease) exposure and infections with bovine leukosis virus.

NAHMS Beef 2007-08 Study
The NAHMS Beef 2007-08 Study will continue to address the priority issues of the U.S. beef cattle industry and other stakeholders. Twenty-four States will participate in Beef 2007-08. These states represent 79.4 percent of U.S. beef herds and 87.8 percent of U.S. beef cows. The Beef 2007-08 Study will:

• Describe trends in beef cow-calf health and management practices,
• Evaluate management factors related to beef quality assurance,
• Describe record-keeping practices on cow-calf operations,
• Determine producer awareness of bovine viral diarrhea (BVD) virus and management practices used for BVD control,
• Describe current biosecurity practices and producer motivation for implementing or not implementing biosecurity practices and,
• Determine the prevalence and antimicrobial resistance patterns of potential food-safety pathogens.

By gathering reliable and valuable information on the U.S. beef cattle industry, the Beef 2007-08 Study will help to

• Educate the producers and practitioners of tomorrow
• Help policymakers and industry make informed decisions,
• Measure the impact of disease,
• Evaluate the potential impact of diseases affecting beef cattle and/or human health,
• Assist researchers and private enterprise to identify and focus on vital issues related to beef cattle health and productivity, and
• Conduct economic analyses of the health and production of the U.S. beef industry.

Participation in all NAHMS studies is voluntary. Randomly selected producers will be contacted by representatives from USDA’s National Agricultural Statistics Service from October through November, 2007. An on-site questionnaire will be administered, and eligible producers will be asked to participate in the second phase of the study. Producers that choose to continue in the study will be visited by veterinary medical officers (VMOs) and/or animal health technicians (AHTs) who will administer questionnaires and collect biological samples from January through March, 2008. VMOs and/or AHTs will make a second contact from July through August, 2008.

Testing Options
Results from tests on biological samples will be provided to participating producers at the conclusion of the study.

BVD Virus
Goal: Estimate the percentage of calves persistently infected with BVD virus by testing ear notch samples. The study will also help to identify factors associated with herds having persistently infected calves.

Food-Safety Pathogens
Goal: Estimate the prevalence of specific food-safety pathogens such as Salmonella and E. coli O157 via testing of fecal samples.

Confidentiality
Because NAHMS’ studies rely on voluntary participation,APHIS protects the privacy of every participant. Only those collecting the data know the identity of the respondent. No name or address is ever recorded in any APHIS database. No data will be reported on any individual or in a manner that would allow the identification of an individual.

Pieces and Parts

• Extension Publication Spotlight:
  1. Raising Cattle “Naturally”: The Significance of Animal Health (ExEx 11020). “Naturally raised” cattle programs generally prohibit the use of antibiotics, ionophores, and growth promotants. This publication outlines some of the more common health ailments encountered in raising cattle for the natural market, along with management recommendations to minimize these problems when the usual medications used for prevention or treatment may not be available to be used.
  2. How to Capture High Calf Prices (ExEx 5055). Producers in South Dakota market a high proportion of the state’s calf crop shortly after weaning. Generally, the largest volume of sales occurs during October and November with the calves commonly weighing 500–600 lb. This publication provides suggestions for producers who will be selling calves on how to capture the relatively high prices currently available.
  3. Livestock Risk Protection: Insuring Calves (ExEx 2058). Historically high cash prices for calves, general price volatility, and concern that prices could move lower may lead producers to insure calf prices. Livestock Risk Protection (LRP) is an insurance program that covers a single peril: lower prices. This publication explains how LRP works and outlines considerations for its use.

These publications, among many others, are available for free at: http://agbiopubs.sdstate.edu.
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- Dr. Young Named Research Coordinator for Veterinary Science Department. Dr. Alan Young has been named Research Coordinator for the SDSU Department of Veterinary Science. In making the announcement, Dr. David Zeman, Veterinary Science Department Head, said, “Dr. Young is an excellent team player and a natural leader, who brings forth positive constructive ideas to an issue. I look forward to working with him and all of the department researchers as we grow our research program to maximize service to our stakeholders.” The VSD Research Coordinator's role is to work closely with the department head and faculty on management and strategic issues relative to the department’s research program. In this role, Dr. Young replaces Dr. David Francis, who will focus on his responsibilities with the Center for Infectious Disease Research and Vaccinology.

Student News - SDSU Veterinary Science Department

SDSU Pre-Veterinary Students Accepted to Veterinary Schools

Four South Dakota State University pre-veterinary students have been accepted to veterinary schools for Fall 2007:

- Christine Ferderer, Baltic, SD – Kansas State University
- Nathan Runke, Willmar, MN – University of Minnesota
- Loni Schumacher, Eureka, SD – Oklahoma State University
- Kim Wellendorf, Ida Grove, IA – Iowa State University

Congratulations and good luck to these students as they embark upon their professional education.

Calendar of Events

August 12-15, 2007
South Dakota Veterinary Medical Association Annual Meeting
Ramkota Inn, Sioux Falls, SD
Large and small animal sessions: Future of the ethanol industry/use of co-products; drug use and the VCPR in dairies and beef herds; latest on Johne’s disease; food animal diagnostics; companion animal emergency care, orthopedics; SDSU case reports, much more.
605-688-6649 or www.sdvetmed.org

August 1-3, 2007
North Dakota Veterinary Medical Association Annual Meeting
Doublewood Inn, Bismarck, ND
http://www.ndvma.com

August 2-4, 2007
Academy of Veterinary Consultants Summer Meeting
Embassy Suites Hotel, Kansas City, MO
http://www.ave-beef.org/

August 16, 2007
George A. Young Swine Health and Management Conference
Marina Inn, South Sioux City, NE.
http://georgeyoungswineconference.unl.edu/

September 13-14, 2007
Iowa Veterinary Medical Association Annual Meeting
Scheman Center, Ames, IA
http://www.iowavma.org/

September 15-18, 2007
Allen D. Leman Swine Conference
RiverCentre, St. Paul, Minnesota
http://www.cvm.umn.edu/outreach

September 15-18, 2007
Central Veterinary Conference
Bartle Hall, Kansas City, MO
http://www.thecvc.com

September 20-22, 2007
American Association of Bovine Practitioners
Vancouver Convention & Exhibition Centre, Vancouver, BC
http://www.aabp.org/meeting/default.asp

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