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## Coming Events

SPA Conference for Veterinarians
September 9–10, 1999
*Presenters: Twig Marston and Rodney Jones, K-State Research and Extension Specialists*

9th Annual Equine Fall Conference on Nutrition and Colic
October 22–23, 1999
*The featured speaker will be Dr. Kent Thompson, Manager, Purina Equine Nutrition and Research*

8th Annual Mid-Western Exotic Animal Medicine Conference
October 23–24, 1999
*Topics include the surgery, medicine and captive management of birds, reptiles, and small exotic mammals. An optimal wet-lab on "Surgical Techniques in Birds" will be presented by Dr. Avery Bennett.*

# Vaccination of Pregnant Cows With Modified Live Virus Vaccine is Not Without Risk

*by JEROME C. NIETFELD*
*Veterinary Diagnostic Laboratory, Department of Diagnostic Medicine/ Pathobiology*

Several times I have heard veterinarians recommend vaccinating pregnant cows with modified live virus (MLV) vaccine. Usually, the veterinarians are discussing herds with chronic problems associated with bovine virus diarrhea (BVD). Many feel that vaccination in late pregnancy will stimulate high colostral antibody titers at calving and the calves will be protected for the maximum time. They feel that kill vaccines do not stimulate as high a titer as MLV vaccines and recommend using MLV BVD vaccine, even though several modified live BVD vaccine viruses have been shown to be capable of crossing the placenta and infecting the fetuses of nonimmune dams. The theory is that in herds with BVD problems, the cows will be immune to BVD and MLV BVD vaccine will not cause a problem. However, it is rare to find a MLV BVD vaccine that does not also contain modified live infectious bovine rhinotracheitis (IBR). For at least 20 years it has been known that most MLV IBR vaccines can infect the fetus and may cause abortion in nonimmune cows. Because of concerns about possible abortions, most MLV IBR-BVD vaccines carry the following warning: "Do not use in pregnant cows or in calves nursing pregnant cows." Even though one might vaccinate pregnant cows on multiple occasions and see no adverse consequences there is always a risk that one or both of these vaccine viruses might cause abortion. In each of the past two years we have seen an example of this. In both cases pregnant cows were vaccinated because of past problems with BVD in the calves.

This spring, we received four submissions from the same herd, with each submission containing tissues from two to three aborted fetuses. In each case the fetal tissues were virus isolation and/or fluorescent antibody positive for IBR virus and the fetal livers contained multifocal, random necrosis which is almost pathognomonic for fetal IBR infection. Approximately 120 cows had been vaccinated with a combination vaccine containing modified live IBR, BVD, parainfluenza-3 and bovine respiratory syncytial viruses. Approximately 30 days after vaccination the cows began to abort. About 45 days after the initial abortion between 50 and 60 cows had aborted or given birth to stillborn calves or weak calves that died soon after birth. A similar incident occurred last year. A veterinarian vaccinated between 35 and 40 pregnant cows. A month later a cow aborted. The fourth fetus that was aborted was submitted to the Kansas State Veterinary Diagnostic Lab and IBR virus and lesions typical of IBR virus infection were found. Both experimentally and in reported outbreaks of IBR abortion following vaccination with MLV vaccine, a 30- to 60-day interval between virus inoculation and abortion is typical. Remember that vaccination of pregnant cows with MLV vaccines that warn against such vaccination is not without risk.

Thank you to the Pfizer Animal Health Group, Livestock Division, Cattle Products Group for financial assistance in publishing this newsletter.

# Neonatal Calf Diarrhea

*by JOHN RAGSDALE, DVM*
*Pathology Resident*
*Department of Diagnostic Medicine/*
*Pathobiology*

Calf diarrhea can be caused by a variety of pathogens including viral, bacterial, and parasitic agents. Viral agents include bovine coronavirus (BCV), bovine rotavirus and bovine viral diarrhea virus (BVD). Bacterial agents include but are not limited to *Escherichia coli*, *Salmonella* sp. and *Clostridium perfringens*. Parasites include but are not limited to *Cryptosporidium parvum*, *Eimeria* sp. (Coccidia), and, occasionally, *Giardia* sp.

The following is a list of the samples taken for diagnosis and the diagnostic tests performed on each sample:

## Histopathology

Intestinal samples should be approximately 1 inch long and flushed with formalin or partially opened to allow adequate fixation of the villi. Samples should be taken of the duodenum, mid-jejunum, distal jejunum, ileum, colon, abomasum, spleen, mesenteric lymph node, liver, and other tissues as indicated. *The distal jejunum, ileum, and colon are the most important intestinal samples.*

## Bacteriology

Five to eight centimeter long sections of the middle to distal jejunum, ileum, and mesenteric lymph node (for *Salmonella*) should be submitted for aerobic culture. Other tissues can be submitted depending on the history and/or lesions. Small intestine can be submitted for anaerobic culture in cases of sudden death or postmortem findings suggestive of clostridial enteritis.

## Fluorescent Antibody

Five centimeter long sections of ileum should be submitted for BVD, BCV, and rotavirus. A similar length of colon should be submitted for BCV only.

## ELISA

Five ml of colonic contents should be submitted for fecal ELISA test for BCV and rotavirus. The FA and ELISA tests are both performed due to the fact that differences in the stage of disease and the degree of postmortem autolysis can cause one or the other of these tests to be negative in a given case.

## Parasitology

Fecal flotation can be performed in-office or five ml of colonic contents can be submitted for *Cryptosporidium*, coccidia and *Giardia.*

## Virus Isolation

If desired, pooled samples of ileum, mesenteric lymph node, and spleen can be submitted for virus isolation for BVD.

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# Drug Residue Scenario

*by G.L. STOKKA DVM,*
*TOM EDWARDS DVM,*
*J. VAN BOENING BS*

A steer is sent to the processing plant after treatment for respiratory disease with a label dose of beef cattle approved antibiotic. The steer is part of a pen of 100 animals. The withdrawal time for this steer had not been observed, and, due to an oversight, was sent to the processing facility. Who is responsible, the veterinarian who prescribed the drugs, the employee that administered the product, or the feedyard?

The truth to this matter is that it could be one or all persons described above, and is most likely the result of a communication error or simple oversight by everyone involved. The FDA defines the safe concentration of a drug as the maximum allowable concentration for total residues of toxicological concern in tissues. The United States Department of Agriculture's (USDA) Food Safety and Inspection Service (FSIS) is responsible for monitoring and surveillance of red meat and poultry. Surveillance activities undertaken by FSIS focus on obtaining tissue samples from individual animals or lots that are suspected to contain violative drug residues based on clinical signs or herd history. Testing may also result from decisions by FSIS inspectors that are based on regional guidelines and direct antemortem and postmortem observations. Moreover, it is used to follow up on producers and owners who have been identified as marketing animals with residues above regulatory guidelines.

When a producer or owner is identified, they are sent a letter explaining the violative residues. They are then placed on a list at FSIS and will not be removed from the list until their products are residue free for a number of years. If subsequent violations are discovered by FSIS, they will call upon the Animal Plant Health Inspection Service (APHIS) for an on-farm visit to get to the source of the problem. APHIS will assess the situation and alert the proper authorities if action is warranted.

Dr. Ron Kelly of the Food Safety and Inspection Service in Lawrence, Kansas, offers that, by far, most violations are the result of miscommunication or simple oversight by producers, ranch hands, and veterinarians. Additionally, he contends that those tagged with a violation are generally concerned and usually do not have future infractions. He recommends that accurate detailed records be kept at all levels of management to protect yourself and to always follow the label instructions for withdrawal times. If the veterinarian has questions on extra label use withdrawal times they should contact FSIS or FDA to ensure a proper withdrawal time is allowed.

Immediate action should be taken after discovering an animal carrying an improper withdrawal time has been sent to the processing plant. Time is of the essence to prevent the meat or tissues from entering the food supply. The following guidelines could be used in the event such a case occurs:

1. Contact (A)"Head Buyer" or (B)"Quality Control" of the packing plant to which the cattle were sent and explain the situation. This should include detailed information such as: customer; day of shipment; lot #; pen #; head count; sex; product administered dosage, route of administration and withdrawal time remaining.
2. Contact the FSIS inspector in charge at the plant or the FSIS district office as to the nature of the problem.
3. Contact a representative from the company that manufactured the product. In particular, an individual with knowledge pertaining to product metabolism, distribution and elimination.
4. Acquire all feedlot health records from the cattle in question.

Establishing a conference call between all parties involved will serve to address questions/concerns and the course of action required.

# Notes on Giardia

*by ROBERT RIDLEY*
*Department of Diagnostic Medicine/ Pathobiology*

Veterinarians are not in universal agreement concerning the pathogenicity of *Giardia* sp. in companion and food animals, although documented cases of *Giardia* being a primary pathogen exist. Unlike the situation in dogs and humans, in which *Giardia* cysts are shed intermittently, in dairy calves the cysts appear to be shed continually over a rather long period of time. Reports of the prevalence of *Giardia* in dairy calves in some herds have been reported to be approximately 80% in calves 2 to 4 weeks of age, and 47% of calves with diarrhea had high *Giardia* cyst counts in fecal exams. In another study, up to 100% of young animals having diarrhea were shedding *Giardia* cysts in their feces.

Animals with severe *Giardia* infections can eliminate as many as 5 million *Giardia* cysts per gram of feces. The prepatent period of *Giardia* is about 1 week, so animals usually start to shed *Giardia* cysts during their second week of life. Heavy infections usually occur between 2 weeks and 2 months of age. Immunity does develop, but it develops slowly. The cysts are quite resistant to environmental extremes, but they are susceptible to drying, so exposure to direct sunlight will kill them over time. Stalls, pens, hutches, etc., usually remain severely contaminated, and cysts in those areas are the source of infection to new calves.

Fresh feces, preferably rectal samples, should be obtained for diagnosis of *Giardia*. If giardiasis is suspected in puppies, samples should be collected for three successive days. One sample from calves, if they are between two and 8 weeks of age, should be sufficient. Feces should be floated in zinc sulfate solution having a specific gravity of 1.18. Other levitation solutions will float the cysts, but distort them severely making recognition difficult. Lugol's or Dobell's iodine stain makes morphological detail much easier to see, and helps distinguish *Giardia* cysts from yeasts, pollen, lipid droplets, etc. Trophozoites may be observed in stained saline smears of fresh feces, but will not survive transit. *Giardia* trophozoites must be distinguished from other motile flagellates, especially trichomonads, which often occur in diarrhetic stools. Iodine staining is helpful. Immuno-diagnostic kits (ELISAs) utilizing monoclonal or polyclonal antibodies for diagnosing giardiasis are available, but are expensive and most are very time consuming. Most of those diagnostic tests have sensitivities and specificities approaching 100%, but take about 90 minutes to run. These kits sell for about $175; individual tests cost about $6 for the reagents. There is one kit (ProsPectT Rapid Giardia; Alexon, Inc.) that requires only 1 minute to run, but the sensitivity is only 90% and a single test costs about $15. Even given its price and lack of sensitivity, this kit probably makes the most sense for practices that run only one or two tests at a time. Two companies which formerly marketed diagnostic kits (Meridian, Inc. and Trend, Inc.) are no longer manufacturing their kits.

Fresh fecal specimens submitted to the Veterinary Diagnostic Laboratory for suspected *Giardia* should be sent overnight in specimen containers, and packed with "Polar Packs", "Insul-Ice" or something similar.

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# Starting at the Beginning:

## Keeping Biological Source Animals TSE-Free Through Proactive Regulation

*By JOHN HONSTEAD, D.V.M., M.S.*
*Veterinary Medical Officer*
*Food and Drug Administration*
*Center for Veterinary Medicine*
*Division of Animal Feeds*
*Presented at the Institute for International Research conference:*
*TSEs: Managing Risk in Mammalian Organs, Cells and Sera*
*March 15–16, 1999, San Diego, California*

### Introduction

Many of the thousands of FDA-regulated drugs, biologics, devices and foods used on or in humans and animals contain ingredients that are of bovine origin. For human drugs, 80% have at least one component from cattle. The best way to assure that these materials are safe from the agent causing bovine spongiform encephalopathy (BSE) is to assure the United States remains free of BSE. This article will briefly summarize basic information on transmissible spongiform encephalopathies (TSE), review the current BSE situation in the United States, and describe FDA efforts to protect U.S. cattle from BSE.

### Characteristics of TSE Diseases

TSE's are fatal diseases of humans and animals caused by the accumulation of a specific protein in the brain of affected individuals. They are characterized by progressive degeneration of the central nervous system (CNS) with a long incubation period, a shorter clinical course of neurological signs, and 100-percent death rate. Post-mortem histopathology of brain tissue from victims of TSE's reveals bilaterally symmetrical degenerative changes in gray matter and neuronal vacuolation. Animal TSE's include sheep scrapie, BSE, transmissible mink encephalopathy, feline spongiform encephalopathy, and chronic wasting disease of deer and elk. TSE's in humans include Creutzfeldt–Jakob disease, Gerstmann–Straussler–Scheinker syndrome, kuru, and fatal familial insomnia. In the United States, naturally occurring TSE's of animals have been reported in sheep, goats, mink, elk, and deer.

The cause of TSE's is unknown. Proposed causes of TSE's are the infectious protein or prion theory, an unconventional virus, and Spiroplasma, among others. Resistance of the agents to physical and chemical agents that destroy nucleic acid have essentially ruled out conventional microbiological agents as the only cause. The mode of transmission of the TSE's is also not understood. As a measure of infectivity, laboratory animals are inoculated with TSE tissue, generally through intracerebral injections, and observed for signs of disease.

### Bovine Spongiform Encephalopathy

BSE is a TSE of cattle in Europe transmitted orally through feed containing protein from rendering BSE-infected cattle. Cows with BSE have a prolonged incubation period of 2 to 8 years. BSE was first recognized as a distinct disease of cattle by researchers of the British Ministry of Agriculture, Fisheries, and Foods (MAFF) at Weybridge, England, in November 1986.

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The clinical signs of BSE last several weeks and begin with subtle changes in the normal behavior of the cow such as a change in the milking order, separation from the rest of the herd while at pasture, disorientation, staring, and excessive licking of the nose or flanks. This is followed by gait and postural abnormalities, increased reaction to sound, light and touch. The disease progresses with stumbling, falling and eventually the inability to stand. It ends with coma, seizures and death.

BSE has not been detected in cattle in the United States. Intensive efforts are in place by USDA both to determine whether the disease exists in the United States and to prevent its entry by prohibiting the importation of BSE-infected cattle or feed. There is, nevertheless, a small risk that the disease could occur in the United States as it has in a number of countries in addition to the United Kingdom (UK).

## Creutzfeldt–Jakob Disease (CJD) in Humans

Sporadic CJD is a typical TSE of humans with no known cause or risk factors, and exists throughout the world with an incidence of approximately one case per million population. The average age is 56 years, and clinical symptoms start with changes in sleeping and eating patterns, and often include confusion, inappropriate behavior, and lack of coordination, and proceed to coma and death.

In April 1996, British scientists reported a previously undetected new variant of CJD (nvCJD) in young patients with symptoms and histopathologic lesions different from sporadic CJD. Clinically, nvCJD begins with a psychiatric presentation, including depression, anxiety, nightmares and hallucinations followed by memory impairment with dementia in the late stages. The clinical course may last up to 2 years. Recent evidence has shown a strong association between BSE and the occurrence of a new form of CJD (new variant CJD). The prion protein in the nvCJD brains is the same prion protein found in cattle with BSE, leading UK scientists to state that exposure to the BSE agent is the most plausible explanation for these findings though the exact route of exposure is unknown. There are currently 35 cases of nvCJD in the UK, and one in France.

## BSE epidemic in the UK

Since BSE was first diagnosed in the United Kingdom in December 1986, more than 174,000 cattle have been diagnosed with the disease. The epidemic peaked in 1992 with 1,000 cases per week and is currently down to 80 cases per week. BSE has also been reported in native cattle in France, Switzerland, Netherlands, Belgium, Portugal, Luxembourg, the Republic of Ireland, and Northern Ireland.

Epidemiological studies have characterized the outbreak of BSE in the UK as a foodborne epidemic. The only common factor in the cattle with BSE is that feed containing meat and bone meal was fed to the affected animals. Two possible hypotheses as to the original source of this agent were consistent with the epidemiological findings—that it was the agent of scrapie itself, or that it was a cattle-adapted strain of a scrapie-like agent.

## FDA BSE Regulation for U.S. Feeds

Even though BSE has not been diagnosed in cattle in the United States, information and theories on TSE diseases raise concern that there might be a very small risk that BSE could occur in the United States. If BSE does occur, the consequences would be severe and the cost would be very high. U.S. cattle would be at risk for disease, and the human population could be at risk for nvCJD. The causative agent could be transmitted and amplified through feeding of certain processed animal proteins to cattle resulting in an epidemic. The greatest risk for cattle, given the prolonged incubation period of 2 to 8 years, would be unrecognized amplification in the cattle population, resulting in greater animal exposure. The announcement of the possible link between new variant-CJD and BSE, and new information about the origin and ecology of the BSE agent has caused increased concern about BSE regulation in the United States.

Processed animal proteins had been safely fed to animals for many years before the BSE outbreak, and, except for BSE, FDA was not aware of data indicating this practice is not safe. Therefore, the FDA rule utilized scientific data regarding the difference between animals with TSE's and animals with no natural TSE, mammalian tissues with no TSE agent contained in them or processing that reduces the BSE threat. The FDA BSE rule reduces the threat of undetected amplification of BSE by banning mammalian tissues known to be a TSE risk from ruminant feed, but allows feeding of safe tissues.

## Materials Affected by the Ban

The FDA BSE regulation prohibits the use of protein derived from mammalian tissue, with some exemptions, in feed for ruminant animals. The basis for the inclusion of only protein in the regulation is that only protein portions for feed. I will use the term "prohibited materials" to describe nonexempt mammalian proteins, and I will use the term "non-prohibited materials" to mean all other proteins.

The basis for exemption of pure swine or pure equine proteins is that these species have never been found to have a naturally-occurring TSE. We are aware that 1 pig out of 10, inoculated with BSE developed TSE lesions. We do not believe that this represents an event that occurs naturally in pigs. Pigs were no doubt exposed quite routinely in the UK during the BSE epidemic before the feed bans, and no pigs came down with a TSE. Blood and blood products, milk and milk products, and gelatin were exempt for the reason that none of these have been shown scientifically to play a role in transmitting BSE. The WHO considers all of these to be of no risk for BSE based on scientific information. Plate waste was exempt because meat from the United States is a low risk material for BSE—plate waste contains a small proportion of meat (2%) and high moisture requiring addition of 50 to 60% corn or soybeans for extrusion of animal feed. The initial cooking for human use would reduce the amount of any TSE agent present and the second heating and high pressure for animal feed often at 1,900 to 4,000°F would reduce it even more.

## Industries Affected

Renderers, protein blenders, feed manufacturers, distributors including haulers, and individuals that are responsible for feeding ruminants are directly affected in this regulation. The BSE regulation covers mammalian protein materials from renderer to the animal feeder including all the operations between. The rationale for this goes back to a MAFF calf study demonstrating that 1 gram of BSE infected brain fed one time to calves will cause them to get BSE. The minimum dose to transmit BSE orally in bovines is, therefore, believed to be less than 1 gram.

The entry of prohibited mammalian proteins into rendering establishments is the first point of control for this regulation. Renderers are defined as anyone that processes slaughter byproducts, animals unfit for human consumption or meat scraps. This includes traditional renderers, renderers that blend animal protein products, those who collect slaughter byproducts and minimally process them, and those who collect and distribute slaughter byproducts to firms other than renderers.

Renderers can either separate or not separate prohibited and nonprohibited materials. For those that do not separate, all prohibited materials must be labeled:

"Do not feed to cattle or other ruminants"

Records such as invoices or similar documents must be maintained to track the materials through their business, made available

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to FDA and state inspectors for copying and inspection, and kept for 1 year. Renderers that separate prohibited and nonprohibited material must label the prohibited material, maintain records, obtain nonprohibited material from single species slaughter facilities, and provide for measures to avoid commingling or cross-contamination of prohibited and nonprohibited materials.

There are many businesses that handle mammalian proteins between renderers and animal feeders including protein blenders, feed manufacturers, and distributors, including haulers. These processors and haulers can either separate or not separate prohibited and nonprohibited materials. For those that do not separate, all prohibited materials must be labeled: "Do not feed to cattle or other ruminants"

Records must be maintained to track the materials through their business, made available to FDA and state inspectors for copying and inspection, and kept for 1 year. Protein blenders, feed manufacturers, distributors including haulers that separate prohibited and nonprohibited material must label the prohibited material, maintain records, and provide for measures to avoid commingling or cross-contamination of prohibited and nonprohibited materials.

In order for the regulation to be fully effective, individuals and establishments that are responsible for feeding ruminants must ultimately handle feed properly, and be held accountable. They must maintain all feed invoices and copies of labels for feeds that contain animal protein, make them available to FDA and state inspectors for copying and inspection, and keep records for one year.

Retail Pet foods were exempted from the labeling requirements of the regulation because once manufactured and packaged for sale as pet foods, they are unlikely to be fed to ruminants. Once pet food is damaged or otherwise unfit for pet use, the material must be handled according to the regulation like any other mammalian protein since it could be diverted to ruminant feed.

## Role of Processing

The production of animal feeds involves several physical processes such as heat and pressure applied over time. When sufficient heat and pressure are applied to BSE-infected materials for a sufficient time, a decrease in infective titer is seen as measured by bioassay in susceptible mice. When the conditions are very severe, the final product may not have any detectable infectivity remaining. However, processing cannot assure complete removal of BSE agent from feed materials as demonstrated by research on rendering processing. When this is coupled with the fact that very small amounts of BSE agent can cause disease orally in cattle, a dilemma arises in a BSE-free country that utilizes rendered ruminants for ruminant feeds. It becomes apparent that processing alone cannot be counted on to stop undetected amplification if BSE occurred undiagnosed at any time in the future. Processing must be combined with controls over source materials for ruminant diets to assure complete safety from BSE.

## The Role of Feed Testing

A provision of the FDA feed regulation provides for exemption from certain requirements if the feed is tested for BSE agent using an FDA-validated test. To date, no such test exists, but this provision may stimulate research and development in the future.

The UK is presently using an ELISA test for ruminant proteins to enforce its mammalian-to-farm animal feeding ban. FDA is reviewing a polymerase chain reaction test developed in Italy for consideration as a regulatory tool. It is currently focused on the identification of bovine mitochondrial DNA that survives rendering, but may be able to be modified to identify mammalian material. FDA is also reviewing a feed microscopy method that identifies mammalian meat and bone meal using the presence of characteristic bone chips, hair and horn. In the future, test information may be used to focus inspectional efforts.

## Impact of FDA BSE Regulation

The ultimate impact of the regulation has been a reformulation of ruminant feeds to exclude prohibited materials, and labeling of non-ruminant feeds that contain prohibited materials. There has been a small decline in the price of mixed-mammalian meat and bone meal. Many inquiries have been received by FDA from the feed and animal feeding industries regarding the requirements and methods for complying, indicating a genuine concern for compliance. To date, FDA and state feed officials have conducted approximately 2500 inspections of the operations covered by the regulation. Analysis of the data shows that approximately 75% of those inspected had no violations. FDA is working with its partners to evaluate the nature of the violations and find solutions to correct them.

## Conclusion

Although the risk of BSE in the U.S. is small, the consequences would be severe and the cost would be very high, should it be diagnosed. More U.S. cattle would be at risk for disease, and the human population could be at risk for nvCJD. The FDA BSE regulation requires identification and control of prohibited mammalian proteins from the renderer through processing and transportation, and prohibits their feeding to ruminants. The provisions and requirements of the regulation are based on current science. Because BSE is an emerging disease, the scientific base is limited, and should be expanded through research.

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# Interaction of Cattle Health/Immunity and Nutrition

American Society of Animal Sciences
*© J. Anim. Sci. (77:1120–1134)*

*by M.L. GALYEAN, L.J. PERINO, AND G.C. DUFF*

The usual means of assessing the health of newly received beef cattle susceptible to bovine respiratory disease (BRD) are subjective, typically involving visual evaluation aided by minimal clinical measurements. Recent evidence based on the occurrence of pneumonic lung lesions at slaughter indicates a need for more accurate methods of diagnosing BRD. Inadequate passive immune transfer at birth may be an important risk factor in susceptibility to BRD, suggesting the need for management to improve passive transfer success rates. Preweaning management and vaccination practices offer opportunities for beef cattle producers to improve the immune status of newly weaned calves and decrease postweaning BRD. Feeding diets with higher levels of concentrate typically improves performance by newly weaned or received cattle, as does feeding diets supplemented with protein; however, limited data suggest that increasing concentrate and protein in receiving diets increases the rate and severity of subjectively determined BRD morbidity. Research with receiving diet concentrate/protein level relative to humoral and cell-mediated immune function coupled

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with indicators of health and performance is needed. Supplemental B vitamins are sometimes useful in receiving diets, but the effects have been variable, presumably reflecting differences in stress and associated feed intake responses. Vitamin E added to receiving diets to supply ≥ 400 IU/animal daily seems beneficial for increasing gain and decreasing BRD morbidity; however, further dose titration experiments are needed. Supplemental Zn, Cu, Se and Cr can alter immune function of newly received calves, and some field trials have shown decreases in BRD morbidity rate with supplementation; however, several experiments have shown no performance or health/immune benefits from supplementation of these trace minerals. Formulation of receiving diets should take into account decreased feed intake by highly stressed, newly received beef cattle and known nutrient deficiencies, but fortification of such diets with trace minerals beyond the levels needed to compensate for these effects is difficult to justify from present data.

# Antibacterial Products May Worsen Problem in Resistant Bacteria

*Doctor US Guide to Medial & Other News, Memphis, TN*

In a paper published in the April 16, 1999, Journal of Biological Chemistry, Charles Rock, Ph.D., and Richard Heath, Ph.D., researchers in the biochemistry department of St. Jude Children's Research Hospital, find that the use of antibacterial products may actually make drug-resistant strains of bacteria more prevalent. The use of popular antibacterial products such as soaps and body washes introduces an antibacterial compound called triclosan into the environment. Triclosan interacts with bacteria and, as is their nature, the bacteria develop resistance to the compound. The accumulation of triclosan in the environment could lead to the emergence of drug-resistant bacteria, Rock said. As a result, the very antibacterial products designed to kill the bacteria would become ineffective.

"We consider this to be a serious public health concern," Rock said. These findings are important because it has been widely reported that triclosan acts as a nonspecific agent that attacks bacterial membranes and kills indiscriminately, much like a bomb. If triclosan works in this way, then it is unlikely that bacteria could devise a way to develop resistance. On the contrary, the St. Jude study shows that triclosan interferes with a specific biochemical process inside bacteria. Thus, bacteria can and do find a way to develop resistance. Rock reported in a paper published in September that it was possible for E. coli bacteria to develop a resistance to triclosan. Rock showed that triclosan inhibited an enzyme in fatty acid biosynthesis produced by a gene called fabl and that mutations in the fabl gene caused resistance to triclosan.

In this latest paper, the St. Jude team explains how this resistance occurs. The researchers pinpointed that the formation of a specific complex (Fabl-NAD+-triclosan) accounts for the effectiveness of triclosan as an antibacterial agent. If the formation of this complex is prevented, bacteria can become resistant to triclosan. Rock's group has identified a specific mutation in the fabl gene that prevents the formation of this complex and, thus, creates resistance to triclosan. "The ability of E. coli to acquire genetic resistance to triclosan and related compounds through mutations in the fabl gene suggests that the widespread use of this drug will lead to the appearance of resistant organisms that will eventually compromise the usefulness of triclosan, and other antibacterials that interact with the same target," Rock said. Rock also points out that there is little or no evidence that the inclusion of triclosan in most antibacterial products offers any additional protection against bacteria. He said he believes that the United States Food and Drug Administration should regulate the distribution of triclosan just as it regulates other antibacterial drugs.

# BSE Risk Assessment by EU Scientists Leaves Questions



The EU's Scientific Steering Committee (SSC) Does not believe that bovine spongiform encephalopathy (BSE) can be transmitted through milk, but it recommended as a precautionary measure that all milk from BSE-infected cows should be destroyed.

In an "opinion" released last week, the committee warned that, "in the absence of any infectivity studies on semen, embryos, fetal tissue, milk and colostrum, and in the absence of all the necessary experimental and epidemiological data, precise estimates of the risks of vertical transmission of the disease cannot be made."

The 16 independent scientists said there is no evidence that milk is a source of infection. But their investigation showed other possible routes of infection through maternal transmission. The opinion contains a risk assessment for the routes, and recommendations for options to mitigate the risk.

The scientists considered the question: "What is the nature and extent of the risks of vertical transmission, including semen, embryos or other ways of maternal transmission of the BSE agent between cattle or between small ruminants of the same species, based on current data?" Working from that base, they found that there are very few studies, particularly on the use of semen and embryos traded between countries. They called on the European Commission to initiate epidemiological analyses to investigate traded semen and embryos and to take the findings into account.

Where there has been a high incidence of infection through feed, the scientists found, there is a risk of transmission from the dam to offspring. But the mechanism is not understood. There may be a higher risk from maternal derived from the female rather than the male animal, they suggested. All epidemiological studies to date show the rate of maternal risk is approximately 10% in the offspring of dams within 12 months of the onset of clinical signs of BSE. If there is a shorter time lapse between parturition and onset of clinical symptoms of longer than 12 months, the rate of

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maternal transmission is reduced. The scientists are uncertain whether infection is transferred before or after birth.

There are no scientific data to show that infected calves are unduly sensitive to infection on a genetic basis, the SSC said. It is unlikely that semen constitutes a risk factor for BSE transmission because there is no particular risk of calves developing BSE from sires that develop BSE. There is a very low risk of transmission from embryo transfer, showing that maternal transmission appears to happen either later in the gestation period or following the birth of the animal.

When they looked at the risks from bovine milk, the SSC took account of the continuous review of the safety of milk by the U.K. Spongiform Encephalopathy Advisory Committee (SEAC). U.K. law currently states that milk derived from BSE-affected cattle or cattle suspected to have BSE shall not be sold, supplied, or used for human or animal consumption, with the exception that it may be fed to the cow's own calf. SEAC concluded in April 1997 that no evidence had been found to suggest that milk from any species affected by transmissible spongiform encephalopathies was infectious. But the SSC questions this certainty in light of the lack of scientific evidence on possible vertical transmission routes.

Scrapie, they noted, is not reported as a natural disease of cattle. There is a lack of data and for now there is no evidence to suggest that semen presents a high risk of transmission to small ruminants. However, maternal transmission via contact with, or consumption of, placentas from infected sheep can result in exposure of the offspring to infection. The SSC warns that infection by means of the placenta of infected sheep is probably the most important means of spreading infection within a flock.

The SSC recommended a series of measures that could apply EU-wide to reduce the risk of vertical transmission of BSE and further protect animal health:

- Ensure that semen and embryos are derived from clinically healthy animals.
- For embryos, the SSC cites the measures listed in the January 1999 version of the draft OIE Code on BSE. In addition, it is recommended that embryos from healthy females, not the offspring of BSE-affected females but conceived by mating with semen from bulls suspected to have BSE, should not be used unless and until the bull either recovers to normality or, if slaughtered, BSE is eliminated by pathological examination of brain tissue using an approved method.
- Although the OIE considers that bovine semen can be traded or imported without restriction, the SSC also recommends that semen from bulls suspected clinically to have BSE should not be used for artificial insemination unless and until the bull either recovers to normality or, if slaughtered, BSE is eliminated following pathology studies of brain tissue by an approved method.
- A bull suspected to have BSE should not be used for natural service until the suspicion is removed.
- Milk and colostrum from cattle suspected to have BSE should be destroyed so that they can not enter the food or feed chain except to feed the cow's own calf for research under the control of a competent veterinary authority.
- Calves suspected to have BSE should be isolated under the control of the veterinary authority until at least 72 hours after parturition. All fetal membranes, bedding and other contaminated waste material should be incinerated. The premises should be cleaned and disinfected using an approved disinfectant capable of inactivating the BSE agent.

# AIP Breakthrough Could Lead to Prevention of Cattle Killer

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Lethbridge, Alta., June 18: The Lethbridge Research Centre has identified a possible cause of Acute Interstitial Pneumonia (AIP), the costly cattle disease with a fatality rate of 30–50 percent. In a two-year field study of southern Alberta feedlots, researchers found high levels of toxic metabolites in the blood plasma of cattle killed by AIP. Those metabolites, which damage lung tissue, are derived from a compound called 3-methylindole (3MI).

"The results are the first that point to 3MI as a possible cause of AIP in feedlot cattle," says researcher Dr. Tim McAllister. "By establishing that link, we have a much clearer target for finding ways of preventing the disease."

Though AIP causes less than 5 percent of feedlot deaths, the disease is costly because it almost exclusively infects heavyweight cattle which are close to slaughter. The disease is not contagious, but appears sporadically from year to year, and over 90 percent of cases are in heifers. It seems largely confined to southern Alberta, where the majority of Canada's cattle feeding industry is concentrated. AIP makes it difficult for cattle to breathe and often causes other complications related to stress. Symptoms include panting, frothing at the mouth, lowering of the head, increased respiration rate and grunting. Many diseases have similar symptoms, so scientists have to diagnose AIP at a histological level.

To conduct the study, researchers worked with several commercial feedlots with over 5,000 head in southern Alberta's "feedlot alley," which roughly includes the 50 km radius around Lethbridge, especially the areas north of the city. They collected eight AIP cases for study in 1995 and 42 cases in 1996.

Of the animals studied, the plasma of those killed by AIP contained almost double the level of 3MI metabolites in comparison to that of cattle killed by other respiratory diseases. Before this research, others had proposed that Bovine Respiratory Syncytial Virus (BRSV) plays a role in the development of AIP, but the study found no evidence of this virus in AIP-infected cattle.

Since indications are the disease is not viral, a range of factors may come into play, says McAllister. Though the results suggest 3MI metabolites cause AIP, researchers don't know what contributes to the level of 3MI metabolite production and susceptibility. "It is becoming more apparent that AIP may arise from a complex interaction of feed intake, feed composition, individual animal physiology and possible environmental triggers," he explains. Since AIP is mainly a problem in heifers, fluctuations in sex hormones may play a significant role.

Researchers will explore potential contributing factors and examine the disease further in a new three-year study, supported by the Canada Alberta Beef Industry Development Fund. Initially, they will use samples collected from 125 cattle that developed AIP last year. One aspect of the new study will be to explore the potential of management practices to control AIP, says McAllister. For example, increasing the level of cysteine in the diet has been shown to reduce the severity of lung lesions in

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goats infused with 3MI. Feathermeal is high in cysteine and, as a result, may indirectly reduce the damage of 3MI metabolites on lung tissue in heifers. If AIP results from a greater sensitivity of lung tissue to 3MI metabolites due to dustborne allergens, dust control measures such as sprinkling of the feedlot may also reduce the incidence of the disease. Additionally, there are additives that have been identified that are capable of inhibiting the biochemical pathway responsible for 3MI metabolism.

"A key remaining question is whether AIP is linked to higher 3MI metabolite production or greater susceptibility to those metabolites," says McAllister. "With further study, we can narrow down the contributing factors and that may lead to the development of preventative strategies."

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