Left, **a Canadian rancher herded healthy calves in southwestern Alberta; Canadian authorities have reported three cases of mad cow disease since 2003. *Above,* on Dec. 30, 2003, protesters met a U.S. delegation arriving in Seoul to discuss mad cow disease with South Korean officials; South Korea banned U.S. beef imports following the discovery of the first confirmed U.S. case.**

New BSE cases limit U.S. beef exports, change cattle testing

The second case of mad cow disease (bovine spongiform encephalopathy, or BSE) in the United States has led to heightened scrutiny by critics and fine-tuning of the testing process, but has had little impact on domestic economics or consumer confidence. "The U.S. has gotten off more lightly than other countries such as Germany, which had only seven cases in 2001 but had a huge public outcry," says Kate O'Neill, associate professor in the UC Berkeley Department of Environmental Science, Policy and Management.

BSE was first found in the United States in December 2003 in a Washington state cow that originally came from Canada. This case led to the collapse of the U.S. beef export market, which used to account for one-tenth of U.S. beef production. While some countries have since lifted their bans on U.S. beef, others have not and the export market is far from recovered.

In contrast, there has been little economic reaction to the second U.S. BSE case, which was confirmed in June 2005 in a Texas cow. "The impact of the second case has been pretty negligible," says Donald Klingborg of the UC Davis School of Veterinary Medicine. For example, while Taiwan and the Philippines banned U.S. beef immediately after the second case was confirmed, these bans were short-lived. "However, the second case might still have a long-term economic impact if it keeps other countries from lifting bans that have been in place since the first case," Klingborg adds. The most significant of these countries is Japan, which had been the most lucrative beef export market and accounted for $60 million in California and $1.5 billion nationwide. In 2004, Japan said it would reopen its market to U.S. beef in 2005. While this has yet to occur, Japan has said that the second U.S. BSE case will not affect the planned resumption of trade.

For more information:

Commonly Asked Questions About BSE in Products Regulated by FDA's Center for Food Safety and Applied Nutrition (CFSAN):
www.cfsan.fda.gov/~comm/bsefaq.html

USDA BSE Testing Program:
www.aphis.usda.gov/lpa/issues/bse_testing/plan.html

USDA BSE Surveillance Plan:
www.aphis.usda.gov/lpa/issues/bse_testing/plan.html

Food and Safety Inspection Service fact sheet,
Bovine Spongiform Encephalopathy — "Mad Cow Disease":
www.fsis.usda.gov/Fact_Sheets/Bovine_Spongiform_Encephalopathy_Mad_Cow_Disease/index.asp

Debate over testing policy

Perhaps the biggest impact of the second case has been on the debate over U.S. policy on BSE testing (see page 203). "It has given strength to consumer group arguments that we're going about testing all wrong," O'Neill says. In 2004, the United States vastly expanded its testing program to assess the incidence of BSE nationwide. Called a surveillance plan, the expanded program was designed by an international group of experts to be able to detect one case of BSE in a million cows. This entails testing all identified cows from the highest-risk populations: downers, which can no longer walk, and cows older than 30 months with BSE symptoms such as emaciation and unusual behaviors, from agitation to kicking. Focusing on high-risk populations "is like using a canary in a coal mine," Klingborg says.

To date, the United States has tested more than 470,000 cattle for BSE. Critics such as the Organic Consumers Association say this is far too few, given

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Feed tests, models helping to control BSE

Over the course of 2 decades, UC San Francisco neurologist and Nobel laureate Stanley Prusiner proved that the infectious agent in mad cow disease and related brain-wasting syndromes was a misfolded protein called a prion. Today, UC scientists in several disciplines continue to combat prion-caused diseases (or transmissible spongiform encephalopathies), working to control them through both prevention and treatment.

Prusiner, who won the 1997 Nobel Prize for his discovery of "proteinaceous infectious particles" (prions), demonstrated that these agents engender fatal brain diseases that occur in humans, cattle, sheep, elk, deer and other animals. "By showing that these misfolded proteins could be infectious agents, he redefined the long-accepted principles of infectious disease, creating the need for a new paradigm addressing its prevention and treatment," says Donald Klingborg, associate dean of the UC Davis School of Veterinary Medicine.

Among UC scientists focusing on mad cow disease is a team at UC Davis that has developed a new cattle-feed test to help keep the disease from spreading, and another team doing molecular-level modeling that could eventually yield treatments for the disease.

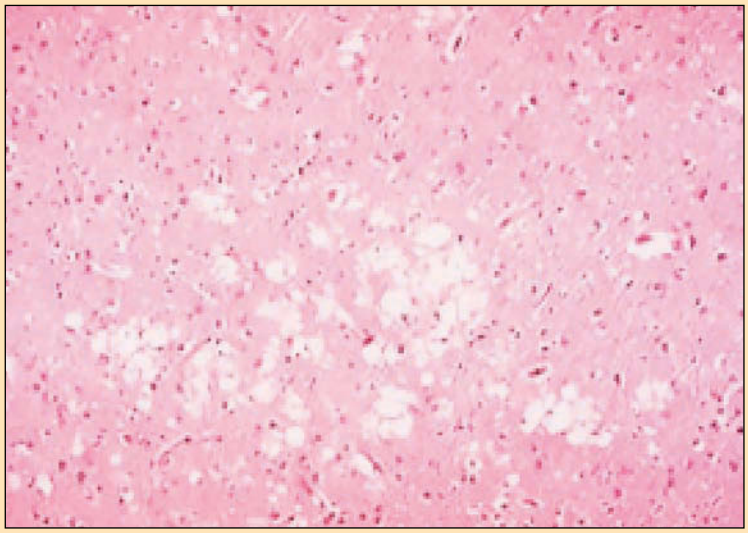
Feed test. Cattle can catch BSE from feed that contains byproducts from infected cows. While banned from cattle feed, byproducts from cows and other ruminants are allowed in poultry and swine feed. That means cattle feed can be contaminated accidentally if, for example, a feed mill is not cleaned properly between producing different types of feed.

The new test is DNA-based and can detect smaller amounts of ruminant contaminants than the current antibody-based test (see page 212). "The DNA test is 10 to 100 times more sensitive," says James Cullor of the UC Davis School of Veterinary Medicine (based in Tulare), who led the team that developed the new test. However, the antibody test is faster than the DNA test: the former takes only 25 minutes while the latter can take up to 6 hours for complicated feeds, which can contain grain, fruit, silage and even rejected M&Ms.

Now Cullor and his team are fine-tuning the DNA test, in part because the federal government wants it to work on European feed, which has smaller pieces of DNA due to processing differences. "We will keep refining the test to make it faster, better and less expensive," he says.

Prion models. Having a sensitive test for ruminant byproducts is critical because it does not take much to infect cows. BSE is caused by prions, an abnormal form of a protein found mostly on the surfaces of neurons and lymph system cells. Prions are folded incorrectly and can convert the normal proteins into more prions, which then stick together in aggregates called plaques. Much is still unknown about BSE, including why the incubation period is so long — up to 10 years in cattle and up to 30 years in people. It is also unknown how BSE crossed the species barrier to infect humans, an event first documented in the United Kingdom in 1996. While the human disease, named "variant Creutzfeldt-Jakob disease" is infectious, other diseases characterized by abnormal plaque accumulation are not. (These include Alzheimer's, Parkinson's and type II diabetes.)

UC Davis biophysicist Daniel Cox and his colleagues have developed models of prions, because these misfolded proteins are hard to study directly. Their prion aggregation model fits the actual incubation times for BSE derived from epidemiological data on about a million cattle from the United Kingdom. This model also fits the actual incubation times of laboratory animals experimentally dosed with prions.



Human brain tissue afflicted with Creutzfeldt-Jakob disease becomes riddled with holes (white areas). UC scientists have developed models of the abnormal prion that causes the fatal disease to aid in the search for treatments.

Another model supports work by other researchers, which suggests that it only takes three prions bound together (a trimer) to spread BSE. While the previous work did not explain what held the prion trimer together, the model by Cox and his colleagues shows that hydrogen bonding can do it. The fact that such a tiny prion dose can spread BSE argues against a proposed treatment. "Cutting up [plaques] has been suggested as a treatment but this would just provide more 'seeds' of the disease," Cox says.

Most recently, Cox and his colleagues have developed a model of how prions change shape when they bind to copper and other metal ions. "This could lead to a treatment that blocks other proteins from misfolding," he says.

— Robin Meadows

New BSE cases — *continued from page 198*

that there are about 96 million cattle nationwide, of which about 36 million are slaughtered each year. In comparison, Japan tests every cow slaughtered and the United Kingdom tests a quarter of them. However, Japanese testing is driven by consumer demand and the United Kingdom has had more than 180,000 BSE cases altogether, neither of which applies to the United States. "BSE is at such a low level here that it doesn't make sense economically to test all cows," says Alex Ardans, director of the California Animal Health and Food Safety Laboratory System (CAHFS) at UC Davis, one of seven nationwide that screen cows for BSE.

Critics also call for testing cows before the 30-month cutoff because Japan has found BSE in two cows that were younger (21 and 23 months). However, the overwhelming majority of positive BSE cases are in cows older than 30 months, and there is a key distinction between the Japanese and U.S. testing programs. "The U.S. program is not food safety testing," Ardans says. Rather than determining whether cows slaughtered for human consumption are BSE-free, the goal is to assess whether the disease is present in the U.S. cow population and, if so, where and how widespread it is.

Changes in testing program

The second U.S. BSE case prompted important changes in the U.S. cattle-testing program for BSE. All along, the first step in this program has been a rapid screening test called an enzyme-linked immunosorbent assay (ELISA). This antibody-based test costs about $25 per sample, and the CAHFS lab at UC Davis can process up to 550 per day. If the ELISA result suggests that a sample may be BSE-positive, the next step is confirmatory testing at the National Veterinary Services Laboratory in Ames, Iowa. Between June 2004 and Sept. 18, 2005, only two of the more than 470,000 samples screened had gone on for confirmatory testing.

Originally, that meant doing an immunohistochemistry (IHC) test, which takes 4 to 7 days and has two components: examining brain tissue for the spongy-looking areas characteristic of BSE, and testing the tissue with antibodies. However, the IHC test failed to catch the second U.S. BSE case, which was ultimately confirmed by another, more sensitive antibody-based test called a Western blot. As a result, future confirmatory testing will include both the IHC and Western blot tests. The latter costs about $500 and takes about 2 days.

The second U.S. BSE case may also hasten parts of the testing program that are planned but have not yet been implemented. For example, in addition to testing downers and cows with BSE symptoms, the program is supposed to test 20,000 healthy-looking cows brought to slaughterhouses.

Eriko Sugita/Reuters/Corbis

Japan, the world's top buyer of U.S. beef, suspended imports in late December 2003, after the U.S. confirmed its first case of mad cow disease. On Dec. 24, 2003, a Japanese chef sliced imported U.S. beef at a Tokyo restaurant.

Livestock tracking several years away

The second U.S. BSE case also underscored the importance of being able to track individual cows. Federal investigators were unable to trace all the herd mates and offspring over the lifetime of this 12-year-old Texas cow, so the question of whether any of them also had BSE remains unresolved.

Livestock tracking is already required in countries such as Canada, the United Kingdom and Japan. Effective January 2009, the U.S. National Animal Identification System will also require U.S. producers to track all cows and other meat-producing livestock. For cows, tracking will likely be via radio-identification ear tags that send information automatically to a national database.

O'Neill says that while the risk of BSE may be small in the United States, the significance of the second case should not be downplayed. "BSE is indicative of larger problems in industrialized agriculture," says O'Neill, noting that avian flu and other diseases that spread among species could pose a larger health threat to people. "Economic integration brings other kinds of integration," she says. "Food and animals are shipped around the world, and countries need to work together better."

— *Robin Meadows*