Mad Cow disease: Dealing sensibly with a new concern

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After a period out of the spotlight, Mad Cow disease is again causing a stir. Following the first documented case in this country on December 23, 2003,[1] the US government is instituting new preventive measures, and patients may be asking for assurances of safety (see "What to advise patients," page 565).

Mad Cow's connection to humans: vCJD

Mad Cow disease is the bovine form of transmissible spongiform encephalopathy (TSE), a disease that can also affect sheep, deer, goats, and humans (**Table 1**). The causative agent is thought to be an infective protein called a prion, discovered in 1997.

Bovine spongiform encephalopathy (BSE) was first identified in the United Kingdom in 1986 and caused a large outbreak in cattle, which peaked in 1993. Subsequently, it was discovered that BSE could rarely spread to humans, causing a variant of Creutzfeldt-Jakob disease (vCJD) that is universally fatal. As of December 2003, 153 cases of vCJD had been reported worldwide, most in the UK. Confirmation of either the classic or variant form requires pathology examination of brain tissue collected by biopsy or, if a patient has died, at autopsy.[2]

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Uniqueness of vCJD

In medical school, family physicians learned about classic CJD, which is endemic throughout the world and, in the US, causes an average of 1 death per million people per year. The epidemiology of vCJD and CJD are quite different (**Table 2**). Because vCJD is a new disease, its incubation period is unknown, but it is likely to be years or decades. In the UK it is thought that exposure to BSE-contaminated food from 1984–86 and the onset of vCJD cases in 1994–96 is consistent with such a long incubation period.

Since 1986, BSE has been identified in 20 European countries, Japan, Israel, Canada, and now the US. The main method of its spread through herds is believed to be the former practice of feeding cattle the meat and bone meal products that, at some point, were contaminated with BSE. In 1997, the US and Canada prohibited the feeding of ruminant meat and bone

TABLE 1

Transmissible spongiform encephalopathies

Species affected	Prion disease	Transmissible to humans?
Mink	Transmissible mink encephalopathy	No
Sheep and goats	Scrapie	Historically no; questionable in newly discovered atypical cases
Deer and elk	Chronic wasting disease	Possible (under investigation)
Cattle and bison	Bovine spongiform encephalopathy	Yes (variant CJD)
Humans	Creutzfeldt-Jakob disease; variant CJD, Gerstmann-Straussler-Scheinker disease, Kuru, fatal familial insomnia	Through contaminated medical products, instruments, possibly blood

meal to other ruminants. It is thought that most cases of vCJD are transmitted to people when they eat beef products containing brain or spinal cord material contaminated with BSE.

Neuropathology. Variant CJD deposits plaques, vacuoles, and prion protein in the brain. To date, all persons with vCJD have had methionine homozygosity at the polymorphic codon 129 of the prion protein gene, suggesting that persons not carrying this genotype (who make 60% of the population) have increased resistance to the disease. In addition, vCJD and BSE are both dose-dependent infections, so both genetics and exposure may explain why so few human cases have occurred despite the widespread outbreak of BSE in the UK.

Prevention measures have been updated

Before December 30, 2003, prevention measures in place to prevent BSE in this country were the following:

1. Import restrictions on bovine-derived consumer products from high-risk BSE countries (initiated in 1989).

2. Prohibition of the use of ruminant derived meat and bone meal in cattle feed (initiated in 1997).

3. A surveillance system for BSE that involved annual testing of between 5000 and 20,000 cattle slaughtered for human consumption (out of about 35 million cattle slaughtered per year).

Since December 30, 2003, the US Department of Agriculture (USDA) and Food and Drug Administration (FDA) have added or proposed a number of additional provisions to prevent BSE:

1. Defining high-risk materials banned for human consumption, including the entire vertebral column.

2. Banning the use of advanced meat recovery systems on vertebral columns. These systems use brushes and air to blast soft tissue off of bone and led to up to 30% of hamburger sampled to be contaminated with central nervous system tissue.

3. Proposing an expanded annual surveillance to include about 200,000 high-risk cattle (sick, suspect, dead) and a random sample of 20,000 normal cattle over 30 months old.

But are these measures enough?

Concerns about these new measures center on the surveillance program. First, how long will it take the USDA to expand its testing? Second, will even this expanded testing be sufficient? Some scientists and consumer advocates propose adopting the policy of the European Union, which is to test all cattle over 30 months of age, since

TABLE 2

Characteristics distinguishing vCJD from CJD

Characteristic	UK vCJD	US classic CJD
Median age at death	28 (range, 14–74)	68 (range, 23–97)*
Median illness duration (mo)	13–14	4–5
Clinical presentation	Prominent psychiatric/ behavioral symptoms; delayed neurologic signs	Dementia; early neurologic signs
Periodic sharp waves on EEG	Absent	Often present
"Pulvinar sign" on MRI†	Present in >75% of cases	Not reported
Presense of "florid plaques" on neuropathology	Present in great numbers	Rare or absent
Immunohistochemical analysis of brain tissue	Marked accumulation of PrP^{res}	Variable accumulation
Presense of agent in lymphoid tissue	Readily detected	Not readily detected
Increased glycoform ratio on immunoblot analysis of PrP^{res}	Present	Not present
Genotype at codon 129 of prion protein	Methionine/Methionine	Polymorphic

*Surveillance data 1997–2001.
† High signal in the posterior thalmus.
CJD; Creutzfeldt-Jakob disease; vCJD, variant CJD; EEG, electoencephalogram; MRI, magnetic resonance imaging; PrP^{res}, protease-resistant prion protein.
Source: Centers for Disease Control and Prevention, *MMWR Morb Mortal Wkly Rep* 2004; 52:1280–1285.[1]

this age group can harbor BSE without being ill.

Other congressional proposals include banning all high-risk meat products from all animal feeds and cosmetics, and creating a prion disease task force to coordinate surveillance and research for all prion diseases. Unfortunately, because we have been testing so few cattle for BSE, we don't really know if there are more infected cattle in our food system. Interestingly, in Japan, where all cattle are tested for BSE after slaughter, 10 more infected animals were discovered, most of which lacked the characteristics that would put them at high risk.[3]

To date, the beef industry has supported the changes already put into effect, but not the additional ones noted above. Ironically, a number of small, upscale slaughterhouses have proposed testing all cattle they slaughter (mostly under 30 months old) so they may resume sales to Japan. The USDA has turned down their requests for the chemical reagents to run the BSE tests (the agency controls the sale of these kits), citing its concern that testing all cattle would give the impression it is necessary for the entire US herd—a proposition the USDA and many scientists believe is unnecessary. Thus, the

controversy over BSE surveillance has now become an economic, political, and scientific issue.

What to advise patients

The risk of contracting vCJD from eating contaminated beef is extremely small.[4]

There has yet to be a case of BSE found in any native-born US cattle.

There is no association between BSE and milk or milk products.

If traveling to countries where BSE is endemic—ie, UK and Portugal—patients may avoid beef altogether or limit consumption to whole cuts, not ground beef or sausage.[5]

Avoid bovine-derived nutritional supplements, especially those containing bovine pituitary, thyroid, adrenal, thymus, or other organ tissue.

Avoid products containing bovine meat or bone meal, such as some types of garden fertilizers.

Deer and elk can develop chronic wasting disease (CWD), another form of TSE. States that have recorded CWD cases include Colorado, Illinois, Wisconsin, and Wyoming. CWD is not known to cause disease in humans, but the risk to hunters and those who eat the meat is unknown. Physicians may want to advise hunters to have deer and elk hunted in CWD areas tested and only CWD negative animals processed for meat. Guidelines for field dressing deer and elk to prevent possible contamination of meat are available at state Departments of Natural Resources.

Investigating suspected disease

Physicians who suspect a patient may have vCJD or CJD, or that a patient has died of such disease, should advocate for brain biopsy or autopsy. The National Prion Disease Pathology Surveillance Center at Case Western University (funded by the Centers for Disease Control and Prevention) provides diagnostic services free of charge to physicians and health departments (available at www.cjdsurveillance.com).

The first US case

Federal agencies, Congress, and the public became more aware of BSE on December 23, 2003, when the US Department of Agriculture (USDA) diagnosed the disease in a dairy cow in Washington state.[1] The cow, traced to a herd originating in Canada, was 6.5 years old and had been slaughtered on December 9. Whether the cow was a "downer" (nonambulatory) is still under investigation. Downer cows are automatically tested; however, it is possible this cow was tested as part of a routine surveillance system rather than because it was at high risk of disease. Regardless, the carcass was released for use as food while tissues considered more risky for BSE transmission (brain, spinal cord, and small intestine) were kept from the human food supply.

After the case was diagnosed, the USDA recalled all meat from cattle slaughtered at that plant the same day. Unfortunately about 30,000 pounds of potentially contaminated meat was never recovered and ended up on consumers' plates.

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