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Clues to Mad Cow Disease Emerge in Study of Mutant Proteins

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Now, six years after young people in Britain started dying from a human strain of mad cow disease, scientists are still struggling to understand how the disease spreads to humans, how many more will die from it and if a similar epidemic could start in the United States spread by infected deer and elk.

While there are no firm answers, clues are being discovered on an almost weekly basis as scientists explore the nature of a mysterious infectious agent the prion. Unlike disease-causing viruses or bacteria, prions are normal proteins found throughout the body tissues of humans and other animals. But for reasons that are not at all understood, normal prions sometimes transform themselves into tiny particles that cannot be killed with boiling water, chemical disinfectants or strong radiation.

These prions, almost impossible to destroy, accumulate in the brains of infected animals and people, destroying cells and leaving spongy holes in the tissue. The most common human form of this malady, called sporadic Creutzfeldt-Jakob disease or C.J.D., seems to arise spontaneously in the brains of about one per one million people. An estimated 300 Americans, mostly over age 50, die from it each year.

But a new variant of C.J.D. now is killing young Britons who acquired the disease from eating cattle infected with abnormal prions of their own. The cattle malady, called bovine spongiform encephalopathy or mad cow disease, has infected hundreds of thousands of animals since the mid-1980's.

Two weeks ago many of the world's leading prion researchers went to Miami to meet with the families of American victims of sporadic C.J.D. and to tell them everything that was known about prion diseases.

"It was a unique medical conference," said Cecile Sardo, secretary of the Creutzfeldt-Jakob Disease Foundation in Miami, which organized the meeting, held May 7 and 8. "When scientists get together they talk technically," she said. "They rarely talk in person to families."

Of the 125 people attending, half were family members and half were medical professionals. Dr. Stephen DeArmond, a pathologist at the University of California School of Medicine at San Francisco, explained that the normal prion protein was folded in a loopy pattern resembling

corkscrews. But when it misfolds and acquires ribbon-like sheets, the prion becomes deadly. When a misfolded prion comes into contact with a healthy prion, he said, it can sometimes force the normal prion to change shape. The process continues, like a nuclear chain reaction, until the brain is destroyed.

It was recently proved beyond doubt that new variant C.J.D. was a human form of mad cow disease, said Dr. Robert Will, a neurologist and director of Britain's National C.J.D. Surveillance Unit in Edinburgh. This new disease could eventually kill tens of thousands of people in Britain or, given the many uncertainties about prion diseases and long incubation periods, it may eventually die out, he said.

Thus far 56 people in Britain, 2 in France and 1 from Ireland have died of new variant C.J.D. British health officials recently found a method that might assess the scope of the epidemic, Dr. Will said. Unlike the misfolded prions in sporadic C.J.D., which are found exclusively in brain tissue, new variant prions are found in the brain, tonsils, appendix, spleen and lymph nodes. Pathologists are examining 18,000 specimens from tonsil removed in the last two decades; 3,000 tonsils have been tested but the results have not been made public, Dr. Will said.

One of the biggest mysteries is why the new variant form of the disease attacks young people, Dr. Will said. The British victims were 13 to 43 years old, whereas sporadic C.J.D. affects much older people. Dr. Will said that one possible explanation was the widespread use of "mechanically extracted meat." After meat is removed from the carcass, he said, it is compressed with a machine not unlike an automobile crusher used in wrecking yards. Bone comes out one end and a meat-like goo at the other end.

This "meat" was once widely used in baby food and institutional school meals, Dr. Will said. It was fed to children all over the country, but the link between eating the food and getting the disease has not been proved.

No cases of new variant C.J.D. have been found in the United States, said Dr. Lawrence Schonberger of the Centers for Disease Control and Prevention. There have been a few instances of deaths of younger Americans from C.J.D., but tests of their brain tissue showed that they had sporadic forms of the disease, he said.

But according to Dr. Michael Hansen, a researcher at Consumers Union in Yonkers, deer and elk in several western states are experiencing a growing epidemic of a prion disease called chronic wasting disease.

In Larimer County, Colo., 15 percent of deer are infected, Dr. Hansen said. Some experts fear that many hunters and their families have almost certainly been exposed to the misfolded proteins from eating infected deer and elk meat, Dr. Hansen said. But it is not known if the deer version of the disease has been transmitted to humans.

Such transmission is possible, said Dr. Byron Caughey, a senior investigator at the Laboratory of Persistent Viral Diseases of the Rocky Mountain Laboratories in Hamilton, Mont. Results of experiments, to be published soon, show that the misfolded deer prion can, in a test tube, convert normal human, sheep and cattle prions into deadly prions. The rates are very low, he said, but conversions can occur.

At the end of the meeting, family members told researchers horror stories about how their loved ones had been told, wrongly, that they had Alzheimer's disease or got no satisfactory diagnoses at all. Many said that local pathologists, fearing prions, would not carry out brain biopsies and that some morticians had refused to embalm the bodies of C.J.D. victims.

Families are confused and angry, said Mel Steiger, an engineer from Salt Lake City, whose wife died of sporadic C.J.D. They want to know if there is an environmental factor, and, he said, they worry that officials in the United States are not doing enough to monitor the situation.