MAD COW DISEASE

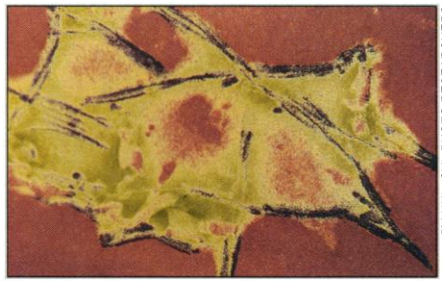
Scant Data Cause Widespread Concern

CAMBRIDGE, U.K.—Perhaps there was no way the British government could have avoided setting off a public panic last week, when it announced that 10 cases of a fatal human neurodegenerative disorder called Creutzfeldt-Jakob disease (CJD) may be linked to a similar disorder that has felled thousands of head of cattle in Britain. The government's press release contained scant detail of the scientific data behind the announcement—which are not yet published—but emphasizes that no link has been proven. To many of the British public, however, who had heard 10 years of official assurances, the news represented an abrupt about-face: "Can We Still Trust Them?" ran next morning's headline in the 21 March *Daily Express*.

The announcement, a five-page statement from the Ministry of Health, was based on the conclusions of an independent committee of scientists, known as the Spongiform Encephalopathy Advisory Committee. The committee examined 10 cases of CJD, diagnosed in Britain over the past 7 months, which involve several unusual but consistent features, the most striking being the young age of those afflicted. "The most likely explanation" for these infections, the committee concluded, was exposure to bovine spongiform encephalopathy (BSE), the disorder popularly known in Britain as "mad cow disease." While these cases do not provide direct evidence of a link, they are "cause for great concern," the committee stated.

The concern stems from research carried out by the government-funded CJD Surveillance Unit at the Western General Hospital in Edinburgh, the results of which are expected to be published in *The Lancet* within a few weeks. The unit was established in 1990 when an outbreak of BSE was at its height in Britain. The disease is believed to have been transmitted to cows in the early 1980s through feed that contained the remains of sheep infected with scrapie, another related neurodegenerative disease, and there were fears that it might cause CJD in humans who ate beef from infected animals. BSE has already spread into other species, such as mice, cats, and some zoo animals—presumably also via contaminated feedstuffs—and in laboratory experiments mice can be infected with BSE by injection of certain proteins from infected bovine brains. But until now there has been no sign that it has spread to humans.

Neuropathologist James Ironside of the CJD Unit says the 10 cases that are now raising concern—out of 40 or so cases of CJD reported in Britain in the past year—suggest that a new variant of CJD has arisen. "Firstly, they're in younger individuals," Ironside told *Science*, with an average age of 29, compared with age 63 for all CJD cases. They were first diagnosed because of psychiatric disorders, such as anxiety and depression, followed by movement disorders, he says; older patients first experience dementia. In addition, CJD typically causes a characteristic pattern of electrical activity in the brain, but this was absent in the 10 cases. Finally, says Ironside,



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Mad cow brain. Brain tissue from cow with BSE shows fibrils and spongy lesions.

pathology." The patients' brains showed a very widespread distribution of clumps of protein, called plaques. These do crop up in a classical CJD brain, but in nowhere near such densities. "There seems to be far more of the protein," says Ironside.

Some of the individuals affected were known to be keen consumers of beef burgers; another had regularly visited a relative's dairy farm. The scientists excluded other possible medical and genetic causes for the new variant of CJD, leaving open the possibility that it was triggered by ingestion of BSE-infected meat. They are, however, a long way from determining exactly how the 10 cases arose.

About 15% of all CJD cases are inherited, and geneticists have tracked down a specific gene that is mutated in such families, called *PRNP*. The genetic mutations can also occur sporadically, for unknown reasons. The gene codes for a "prion" protein, which is believed to be an infectious agent when in its mutant form. (Some researchers believe an additional, unknown element or virus is also required to effect transmission.) The normal form is a glycoprotein on the surface of neurons throughout the central nervous system.

Fred Cohen, a pharmacologist and biophysicist at the University of California, San Francisco, says that even if the BSE prion protein is responsible for the 10 anomalous cases of CJD, "I think what we're looking at is an extremely rare event." But "take 50 million people over 10 years," and the number of events is increased, Cohen says, referring to the population of the United Kingdom and the decade since BSE first appeared in British beef herds. Researchers and public alike await details of these, and perhaps more, cases.

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HUMAN GENOME PROJECT

Sequencers Split Over Data Release

HEIDELBERG, GERMANY—By the end of the session on sequencing at last week's Human Genome Organization (HUGO) meeting here, few attendees were unaware that the era of whole-genome sequencing has arrived—and with it some tough issues for the research community. After talks on the huge scale-up in sequencing capacity at two large genome centers, André Goffeau of the Catholic University of Louvain in Belgium announced that a multinational team has finished sequencing all 12 million bases of the baker's yeast genome, making it the first eukaryotic genome to be completely sequenced. The achievement drew a long round of spontaneous applause from a standing-room-only audience. But the reaction was less enthusiastic when Goffeau went on to say that the final portion of the sequence (up to 20%) would not be made public until 30 April.

Goffeau defended the delay on the grounds that the scientists who did the work deserve to be the first to reap some benefits. "We cannot just give this away," he said—a view shared by a few researchers, especially those from small labs, who spoke with *Science* later. But the practice contrasts strikingly with the immediate-release policies of the two sequencing powerhouses, Washington University in St. Louis and the Sanger Centre near Cambridge, U.K. And the issue of data release is so worrisome to some researchers that it occupied much of the agenda at a recent meeting in Bermuda, where scientists and funders involved in large-scale sequencing tried to hammer out principles aimed at increasing openness—such as releasing data quickly and refraining from applying for patents on raw sequence data with no known function. "There is lots of tension in the community over these issues," says genome researcher Michael Ashburner of the University of Cambridge and the European Bioinformatics Institute.

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Supports openness. John Sulston.

The issue is coming to a head