

Human BSE, nvCJD

Statistics point to increased incidence of brain-wasting disease in Britain

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A research letter published in the *Lancet* medical journal points to a possible increase in the rate of people dying from new variant Creutzfeldt-Jakob disease (nvCJD), a fatal brain-wasting disease also called Human BSE.

BSE in cattle, or "Mad Cow Disease", was first officially noted in Britain in 1986. The number of cases then accelerated dramatically, rising from 60 in 1986 to over 600 in 1987 and more than 3,000 in 1998. The crossover from cattle BSE into the human population was finally admitted in March 1996, when then Conservative Health Secretary Stephen Dorrell admitted that scientific evidence showed the most likely cause of nvCJD was through consumption of meat or meat products from BSE infected animals.

The CJD Surveillance Unit had been set up in Edinburgh, Scotland to monitor the numbers of mainly young people dying from this new and frightening disease. The letter in the *Lancet* is from a group of research workers at the unit headed by Dr. R.G. Will. The unit monitors those suspected of having the disease and carries out postmortem tests to determine if nvCJD was the cause of death. The unit has compiled figures on the numbers dying from the disease from 1995 onwards, and publishes them quarterly.

Up to March 2, 1999 the unit reports 39 deaths from nvCJD. Subjecting the quarterly figures to statistical analysis it concludes that, up to and including the third quarter of 1998, the number of deaths from the disease was fairly constant over time. However, the nine deaths in the last quarter of 1998 mark a departure from this and could signify an increase in the mortality rate.

This has led scientists to express concern that the country may be witnessing the start of an nvCJD

epidemic. Professor John Collinge, the director of the Medical Research Council's Prion Unit who sits on the government appointed committee to advise on CJD, told the *Independent* newspaper of March 18, "I am personally concerned the country may face a serious epidemic of this disease--it is entirely possible." A report in the *Daily Express* on March 17 quoted a Department of Health representative saying, "If there is bad news, it could be that we will get the bad news within six months, certainly within 12 months."

Tests are being conducted by the Medical Research Council to try to determine the level of the disease's incubation in the British population. Tissue samples from tonsillectomies and appendectomies are routinely collected. These are being examined to see if they are infected. The prion protein believed to be responsible for the disease is present in these organs, as well as the brains of infected individuals. Tony Barrett, a coastguard from Torbay, died of nvCJD in 1998. He had undergone an appendectomy in September 1995 before displaying symptoms. Tissue analysis of the removed appendix showed traces of the prion protein.

A separate development is reported in the journal *Science*. It notes that a team led by Professor Collinge has made a breakthrough in understanding the cause of nvCJD. BSE and CJD are part of a family known as Transmissible Spongiform Encephalopathies (TSEs). They are unique in that the disease agent is not a bacteria or virus as in other infectious diseases, but the prion protein which occurs naturally in the body tissues. The disease mechanism occurs when the prion becomes deformed and changes shape.

The change of shape is initiated by a rogue misshapen prion. This will go on to corrupt other prion protein

molecules in a domino effect. These prion proteins are present in the brain. Whereas the normally shaped prion protein molecule can be dissolved, the misshapen form cannot. The deformed prion molecules build up on the surface of brain cells and form plaques or clumps. The brain cells die off and leave the characteristic holes when brain tissue samples of CJD infected victims are examined under the microscope.

Professor Collinge's team has been able to capture the transformation of the normal type of prion into the abnormal type in a test tube. They were able to show that the conversion is as a result of the breaking of a single bond within the prion protein molecule. (A bond is a joining of two atoms within the molecule--protein molecules are made up of chains of carbon, hydrogen, oxygen and nitrogen atoms joined in long convoluted chains). It seems that the prion protein is unique in being able to exist in two entirely unrelated shapes.

This development opens up the possibility of creating antibodies, which could be used to detect the rogue prion protein. It could lead to new tests to detect the disease in humans and animals and may eventually produce an effective treatment for the disease. Professor Collinge cautions against expecting an early result, saying, "While it leads to the possibility of developing much better diagnostic tests, our eventual goal of an effective treatment for these devastating brain diseases still remains an enormous challenge."

Solicitors acting for the families of victims of nvCJD have started legal action against the government. Their writ seeks damages for loss, pain and suffering by the victims and their families. It alleges that the Ministry of Agriculture, Fisheries and Food (MAFF) and the Department of Health demonstrated a failure of "due care" by exposing people to the danger of contracting the disease.

Solicitors had to act by March 20, three years since the previous Conservative government accepted the link between nvCJD and BSE in cattle. Under English law there is a three-year limit on claims for damages. It is expected that the legal process will be protracted and will not commence until the current government inquiry into BSE concludes. The inquiry is due to move into its second stage after Easter, when prominent witnesses could face cross-examination.

The *Lancet* report on the CJD Surveillance Unit's findings carries an editorial giving a brief historical

outline of the course of the BSE and subsequent CJD infections in Britain. It warns against any complacency about the future course of the disease and is very critical of the actions taken by government throughout the epidemic. It concludes: "The outlook, from many aspects, is grim. In the UK the BSE inquiry will almost certainly publish an anodyne report replete with hand wringing, but conclude that no one is to blame. Worldwide, animal-feeding practices will continue to be driven by the prospect of a quick profit and not by considerations of sound animal husbandry."



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