

The UK Times (March 27, 2006)  
Hidden CJD is new threat to thousands  
By Nigel Hawkes, Health Editor

THOUSANDS of people in Britain may be infected with variant CJD, the human equivalent of mad cow disease, without knowing it, research suggests.

Experiments have confirmed that it is possible for a much wider group of people than had been assumed to be infected with the incurable brain condition. The presence in the population of undetected carriers of the infection has serious implications for the safety of the blood supply, and it increases the risk of passing on vCJD to others through infected surgical instruments.

It could make it much harder to eliminate the human infection, even though cattle no longer carry it. Potentially it could linger for generations, or for ever. The team behind the research suggested that their finding represented a “significant public health issue”.

Independent experts said that the work highlighted the need for a national autopsy programme for people who died of causes other than vCJD, to determine the extent of latent infection among those with no symptoms. So far, 161 cases of vCJD have been reported in Britain, 18 in France, and 12 in other parts of the world. These figures are much lower than some early estimates suggested, but the new data indicate that complacency is unjustified.

Up to 14,000 people may be carrying the rogue prion proteins that cause the disease without symptoms, the study indicates. Many scientists believe most of these will die of other causes before developing vCJD, but the length of the incubation period remains uncertain and it is possible they could account for a “second wave” of deaths from the disease.

In the study, published in *The Lancet Neurology*, a team led by Jean Manson, of the Institute for Animal Health, used genetically engineered mice to investigate the transmission of vCJD.

The disease — known as BSE in cattle and vCJD in humans — is caused by a rogue version of the prion protein that curls itself up into the wrong shape. In the brain this leads to extensive damage, producing spongy voids that cause progressive symptoms and lead to an early death. There are no proven treatments.

Prions vary slightly from person to person according to genetic make-up, which influences how susceptible an individual is to catching the disease from meat.

Like all proteins, prions consist of a chain of amino acids. At a certain point on the chain there is a variation that occurs according to your genes.

Some people have two copies of the amino acid valine at this position, some have one copy of valine and another copy of a different acid, methionine, while others have two copies of methionine. This creates three potential genetic types, known as VV, MV and MM.

So far, every single case of vCJD caught from beef has been in MM individuals, who make up about 40 per cent of the population. It has appeared that VV and MV individuals are protected from catching it, at least in this way, by genetic chance.

To check this, the Edinburgh team made three versions of the genetically modified mice, giving them the human genes to produce MM, VV, and MV prions. They also made mice with prion genes from a cow. They then injected BSE or vCJD into the mice's brains and waited for the results.

They found that BSE transmitted to the mice with cow prions, but not to mice with human prions — confirming what experience has taught us: that there is a fairly stiff “species barrier” preventing humans getting BSE. If this barrier had been lower the vCJD toll might have been as high as some early estimates suggested, and it is largely luck that it was not.

But they also found that vCJD transmitted to all three of the human lines: MM, as expected, but also MV and, to a lesser extent, VV.

The implications are that when it comes to horizontal transmission of vCJD, all human beings — not just 40 per cent — are vulnerable. While the species barrier makes it hard to get BSE, it comes down for vCJD. Nobody is immune.

Interestingly, however, while brain tests of prions showed that MM and MV mice were equally easily infected, the MV mice did not develop any clinical signs of the disease within their lifetimes.

They died of something else, such as old age, before the brain disease could kill them.

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## Med India (March 27, 2006) Mad Cow - Worst Yet to Come

With new studies, researchers claim that more people could be at risk of contracting the human form of mad cow disease than previously thought after new evidence emerged that the condition could lie dormant for years before developing.

According to the scientists from Edinburgh a long incubation period for the disease, and an ability to pass through blood transfusions and surgical instruments, can become a significant public health issue. Already the link between Mad cow disease and the vCJD (variant Creutzfeldt Jakob Disease) had been established by the scientists. Now with studies on mice they have concluded that the vCJD could lie in the body for many years without showing any symptoms.

With the long incubations period, they believe that many people are already infected by it, and are yet to know. When the number of deaths rose steadily from a few to 28 in 2000 many believed that the worst had passed and that they had the disease in control. But now with the new research, they are leading to believe that the worst is yet to come, and a lot more lives could be lost.

The disease is believed pass from cattle to humans through eating meat infected with BSE. During the 1980s and 90s, it has killed 154 people in Britain to date, according to the vCJD Surveillance Unit at the Western General Hospital. Six people are still fighting the disease. Till now all those affected seem to have a particular gene type MM. But now with studies done at the Institute for Animal Health in Edinburgh it is found that the variant vCJD could also be found in other genotypes but lie in the body for many years without showing any symptoms.

The studies claim that a significant level of underlying vCJD may already be present in the population without knowledge. Experts feel that that vCJD could be passed from human to human through secondary transmission such as blood transfusions and contaminated surgical equipment in all genotypes. The Lancet Neurology published these studies in on-line today said that the fact people may not know they are carrying the disease in its dormant form meant it could be spread through blood transfusion to which all genotypes are susceptible. This could make the number of individuals susceptible to this secondary transmission much larger.

Professor Hugh Pennington, the president of the Society of General Microbiology, said there could be a second wave of fatalities if more genotypes are affected but not yet coming down with symptoms. He said that the possibility that there may be some effect of BSE on people who have so far shown no effect cannot be ruled out.. With the increase risk of unknowingly transmitting the infection, there would increase the risk to the population as a whole, but it is impossible to say how many people would die as a result. Stating that this was just a warning sign, he stressed that things should be taken with utmost priority.

Marc Leighton Turner, a clinical director for the Scottish National Blood Transfusion Service, said the findings were of concern, especially for people in the in the blood transfusion service and surgeons as they may be a source of secondary transmission.

The UK Independent (March 27, 2006)  
'Silent killer vCJD is more widespread than thought'  
By Jeremy Laurance, Health Editor

The incurable brain disease vCJD, the human form of BSE (mad cow disease), may be widespread and advancing undetected, scientists say.

Concerns over the safety of blood transfusion and the use of surgical instruments were raised by the stark warning from researchers at the Institute for Animal Health in Edinburgh today.

So far, 161 people in the UK have succumbed to the fatal infection which slowly destroys the brain. Two cases have been linked to transfusions.

Estimates of the eventual size of the epidemic have ranged up to hundreds of thousands of people, but most scientists hoped that, 10 years after the first cases were identified, we were over the worst.

The new warning will raise pressure on the Government to change the rules on post mortem examinations to include tests for vCJD - which cannot be detected until after death- to determine the extent of the epidemic. A scientific review is under way.

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