Tissue survey raises spectre of 'second wave' of vCJD

Jim Giles, London

Britain's epidemic of variant Creutzfeldt–Jakob disease (vCJD) could be worse than current death rates predict, a survey of a marker for the condition in body tissue suggests.

The disease, thought to be contracted by eating beef from cattle infected with mad cow disease, was first seen in Britain in 1995. Since then, 141 people have died, and government scientists have struggled to estimate the likely scale of the epidemic. vCJD can only be diagnosed after death, so previous estimates of its prevalence have been confined to projections from the known death statistics.

Now a study of around 13,000 tissue samples taken from hospital patients has found that three of them contained traces of a prion that is associated with vCJD (D. A. Hilton *et al. J. Path.* doi:10.1002/path.1580;2004). The figure is surprisingly high: "Finding three cases in a sample this size is sobering stuff," says John Collinge, a prion-disease researcher at University College London.

The study, led by pathologist David Hilton of Derriford Hospital in Plymouth, looked at tissues from tonsils and appendices removed in hospitals across Britain. vCJD is believed to be caused by the build-up in the brain of an abnormal form of a normally benign but little-understood type of protein called a prion. Abnormal prions are known to accumulate in tonsil and appendix tissue in vCJD sufferers. Hilton's team first removed the normal form of the prion and then used an antibody that binds to either form to search for the abnormal version.

James Ironside, an author on the paper and director of the National CJD Surveillance Unit at the Western General Hospital in Edinburgh, says that current estimates of the disease's prevalence would predict that none — or perhaps one — of the samples would test positive. But he cautions that the numbers involved are too small to allow new estimates of overall vCJD prevalence. There is also an unexpected feature of the results: the distribution of the abnormal prion in two of the three positive samples was different from that previously observed in vCJD patients.

One explanation for the result is that more people are carrying the disease than the death rates suggest. All known individuals with vCJD have a particular genotype, called *MM*. People with other genotypes may incubate the disease for even longer, and so haven't yet shown up in the death rates. "There could be a second wave of cases," says Ironside. He would like to retest the two positive samples that show odd distributions to see if they are from people with different genotypes, but isn't sure if there is enough tissue to do so.

PCL

The prevalence of vCJD in Britain remains a subject of contention.

Another possibility is that the survey has unearthed a group of people who are infected with abnormal prion proteins, but who will not go on to develop vCJD.

One prion-disease expert, who declined to be named, questioned whether Hilton's team should have gone public with their potentially alarming results on the basis of so few data. This researcher noted that false positives have emerged in similar surveys and says Hilton should have run western blot tests, which are more sensitive than the antibody staining method used by Hilton's group. Ironside says the method used by hospitals to preserve tissue samples — immersion in paraffin — precluded the use of western blot tests.

The pattern of vJCD infection in Britain should become clearer in late 2006, when the Health Protection Agency is due to complete a study of 100,000 tonsil tissue samples. These are frozen, and therefore suitable for western blot analysis. ■

Biodefence project accused of violating weapons treaty

Erika Check, Washington

Three prominent US arms-control experts have hit out at the Department of Homeland Security's plans to start a new programme in biodefence research.

In an article published online on 17 May, the specialists say that activities planned at a National Biodefense Analysis and Countermeasures Center, scheduled to be built at Fort Detrick in Maryland, could breach the Biological Weapons Convention. The convention, which the United States has signed, prohibits offensive bioweapons programmes.

According to a presentation made by a US Army official at a Department of Defense meeting on 9 February, the centre would carry out studies to anticipate how bioterrorists might develop and deploy new biological threats. But the authors of the article, published in *Politics and the Life Sciences* (www.politicsandthelifesciences.org), say that these studies may cross the line from defensive into offensive territory. Taken together, they write, many of the activities "may constitute development in the guise of threat assessment, and they will certainly be interpreted that way".

The authors are Milton Leitenberg, an arms-control analyst at the University of Maryland; James Leonard, who led US negotiations to the Biological Weapons Convention; and Richard Spertzel, a scientist who worked with the United National Special Commission investigating bioweapons in Iraq.

Leitenberg says he is also troubled by the fact that no independent group is reviewing all of the US government's planned biodefence research to decide whether it complies with the convention. He adds that a new body announced on 4 March, the National Science Advisory Board for Biosecurity, will not solve the problem because it is not permanent and will not review classified projects.

Most of the terrorist groups about which the United States is concerned, including al-Qaeda, have not developed effective bioterrorism programmes, Leitenberg adds. The United States risks accelerating their progress, he argues, by investigating new horizons in bioweapons. "We will become the Johnny Appleseed, providing sophisticated technical know-how related to bioweapons to the rest of the world," he says.

The Department of Homeland Security did not return calls seeking a response to the critique. ■