Prion diseases remain a mystery

In the 1980s and 1990s, the UK outbreak of bovine spongiform encephalopathy (BSE) in cattle, and the subsequent human cases of a then novel variant of Creutzfeldt-Jakob disease (vCJD) linked to the bovine disease, led to some of the defining political moments of the time and large-scale reassessment of agricultural practices and food safety. From the then Agriculture Minister, John Gummer, giving his daughter a hamburger to reassure the nation that British beef was safe in 1990, to the mass slaughter of over 4 million cattle to contain the BSE epidemic, images from the period still resonate in the country’s consciousness. Given the lingering shadow of the BSE and vCJD outbreaks, the news, as reported by David Holmes in this month’s Newsdesk, that so far in 2012 not a single case of the human disease has been reported in the UK is particularly welcome. 2012 looks like being the first year since 1995 without a reported case.

One could easily think that this news should be cause for celebration, a sign that the outbreak of this devastating, rapidly progressive, and invariably fatal disease is coming to an end. Indeed, since a peak in 2000 when 28 people died from vCJD, the number of deaths seemed to tail off, with no more than five deaths a year since 2005. But, as suggested several times since the start of the outbreak, serious concern exists that these early cases could be just the tip of the iceberg. All confirmed patients so far have had a particular prion-protein genotype (methionine homozygotes at codon 129), but people who are either homozygous for valine or heterozygous at this codon might have a longer incubation time, so a second wave of vCJD related to consumption of contaminated meat remains a possibility. Moreover, there is evidence that as many as one in 2000 people of all genotypes are asymptomatic carriers of the defective prions that cause the disease. Not only might these people go on to develop vCJD, but also they might pass on the infection to susceptible individuals through tissue donations and transplants.

These concerns highlight the real problem with vCJD and other prion diseases that affect human beings: the dearth of knowledge. So little is known about the role of normal prion proteins, how pathogenic prions replicate without genetic information, the pathogenic mechanisms, and why different prion diseases have different presentations. True of familial, sporadic, and iatrogenic CJD, fatal familial insomnia, and kuru, our limited understanding of these diseases prohibits attempts to develop sensitive diagnostic tests let alone effective treatments. As such, prion diseases remain a death sentence.

Thankfully, these diseases are rare. The total number of cases of vCJD in the UK in 1995–2011 was 176, with another 49 being recorded in 11 other countries. The UK has done detailed surveillance of CJD since the height of the BSE crisis in 1990. The latest report (published on Oct 8, 2012) from the National CJD Research and Surveillance Unit in Edinburgh shows that although the cases of vCJD have declined, the number of cases of sporadic CJD have remained fairly constant for the past 15 years, hovering around 70 per year, although in 2008, 2009, and 2011, the number of deaths was 85 or higher.

Alongside the detailed surveillance from the National Surveillance Unit, research done at the Medical Research Council Prion Unit (University College London Institute of Neurology, UK) has begun to elucidate possible mechanisms for human prion diseases and last year reported the first reliable blood assay to detect vCJD prions. This ongoing research and surveillance will be essential to further our understanding of these diseases in the hope of better assessing future risks and developing approaches to disease management.

In a research Article published online in The Lancet Infectious Diseases, Michael Head (University College London) and colleagues have estimated UK investments in global infectious diseases research from 1997 to 2010; they found that more than £30 million had been spent on research into prion disease, around £20 million of which came from the Department of Health. When compared with research investments in HIV (£461 million), hepatitis B (£12 million), hepatitis C (£60 million), and malaria (£346 million), the spending may seem disproportionate to the burden of disease. However, given the incurable nature of these diseases, the potential for prions to cross the species barrier, and the potential for future outbreaks among asymptomatic carriers of pathogenic prions, continued surveillance and research is essential to fill in the many gaps in our knowledge.

For the UK National CJD Research and Surveillance Unit and National figures see http://www.cjd.ed.ac.uk/
For the MRC Prion Unit see http://www.prion.ucl.ac.uk/
For the research on UK infectious disease funding see Articles Lancet Infect Dis 2012; published online Nov 8. http://dx.doi.org/10.1016/S1473-3099(12)70261-X

See Newsdesk page 914–15
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