Summary results of the third national survey of abnormal prion prevalence in archived appendix specimens

In July 2012, the Transmissible Spongiform Encephalopathies (TSE) Risk Assessment Sub-Group of the Advisory Committee on Dangerous Pathogens (the successor national advisory committee to the Spongiform Encephalopathy Advisory Committee (SEAC)), considered the results of the second unlinked anonymous national survey of the prevalence of abnormal prion protein in human appendix samples (Appendix-II [1]), and concluded that a further similar survey should be conducted on tissues from population groups considered unexposed to BSE [2]. This third national survey (Appendix-III) of appendix specimens removed at operations prior to the BSE epizootic and appendix specimens from those born in 1996 or later, by which time measures had been put in place to protect the food chain, has now been concluded. This report provides a summary of the results of the Appendix-III survey prior to publication in due course of the complete data.

The Appendix-III survey examined by immunohistochemistry (IHC) appendices removed at operation and collected from 44 hospitals throughout England. Abnormal prion accumulation was detected within the follicular dendritic cells of seven appendices out of 29,516 suitable samples examined. Indirect comparison of available data showed that none of the positive appendices could have come from the 178 known vCJD cases in the UK.

Two of the seven positive samples were from the 14,692 appendices removed at operations conducted in 1962 through 1979: both these positive samples were from the 5,865 appendices removed in 1977 through 1979. The other five positive samples were found in the 14,824 appendices from subjects born in 1996 or later and removed at operation in 2000 through 2014: all five were in the sub-group of 10,074 born in 1996 through 2000. Therefore, none of the seven positive appendices were in specimens removed before 1977 or in patients born in 2001 or later.

The planned statistical analysis found no difference between the prevalence observed in the Appendix-II survey of 493 per million (95% Confidence Interval (CI): 282 to 801 per million) and the Appendix-III prevalence in appendices removed between 1962 through 1979 of 136 per
million (95%CI: 16 to 492 per million; exact p=0.08), nor with the Appendix-III prevalence in appendices from those born in 1996 through 2000 of 337 per million (95%CI: 110 to 787 per million; exact p=0.64). Test accuracy calculations using the Appendix-III data suggest the IHC technique specificity is in the range of 99.975% to over 99.99%. Although specificity of this magnitude (99.99%) implies few false positives, if the true prevalence is very low, then the positive predictive value of the IHC technique will diminish. At the one in 7,000 prevalence observed in the Appendix-III survey of specimens removed in 1979 or earlier, the positive predictive value (PPV) will be 56%, for a specificity of 99.99% and a sensitivity of 90%, compared to a PPV of 82% at the one in 2,000 prevalence observed in the Appendix-II survey.

The Appendix-II and -III surveys were conducted by a collaboration of PHE, the Department of Neurodegenerative Diseases at the UCL Institute of Neurology, the Animal and Plant Health Agency, the National Creutzfeldt-Jakob Disease Research and Surveillance Unit, the Histopathology Department of Derriford Hospital in Plymouth, and the MRC Prion Unit.

In summary, the Appendix-III survey data have not produced a clear answer to the question of whether abnormal prions detected by IHC in the British population is limited to those exposed to the BSE epizootic, and various interpretations are possible. The survey results have been considered by the ACDP TSE Sub-Group and a position paper detailing the conclusions of the committee has been published online, simultaneously with this summary report [3].

References

