To: CMO

From: Mark Noterman
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Cc: see list at end.

UPDATE ON CJD ISSUES

Issue

1. This note provides an update on current CJD issues.

Timing

2. Routine.

Recommendation

3. For information only. No action required.

CJD Prevalence Studies

National Anonymous Tonsil Archive

4. Over 70,000 tonsil samples have been analysed to date by the HPA, by enzyme immuno assay (EIA). None were positive. On SEAC's advice, HPA have stopped collecting and testing paediatric tonsils, making up the shortfall from higher risk birth cohorts. This will delay collection and testing of the full 100,000 until 2013.

5. For comparative purposes a subset of tonsils have been studied by immunohistochemistry (IHC), the method used in the original appendix study by Hilton *et al* in 2004. This work is being done by Professor Sebastian Brandner of the Institute of Neurology. He has reported on three samples that gave suspicious staining by IHC. These samples have also been examined by Professor James Ironside and Dr David Hilton, who report that they consider two of them to be due to non-specific background staining, but that the third had 'one strongly positive follicle with two antibodies'. Prof Brandner concurs with these conclusions. All three specimens have been extensively tested by the NATA algorithm: two EIAs, two Western Blots (WB) and repeated IHC and have been found negative.

6. Aliquots of the samples have been supplied to the National CJD Surveillance Unit and to the MRC Prion Unit for enhanced chemiluminescent WB tests, as a 'gold-standard'.

7. It is expected that the results will be completed in time for consideration at the next meeting of the Expert Advisory Group on the Laboratory Testing Strategy for Large Scale Abnormal Prion Prevalence Studies (EAG) – chaired by Dr Phil Minor - on 9 December 2009, after which a final version

of the IHC report will be sent to DH. Once we have EAG's report we will update SEAC of the findings.

Appendix Studies

8. An IHC study of 30,000 stored appendix samples, co-ordinated by the HPA, will start in December 2009, and is likely to be completed within three years. The aim is to enable the confidence limits of the 2004 Hilton study to be improved. The Hilton data, on which SEAC currently rely for prevalence estimates, are based on 12,000 samples and suggest a prevalence of 1:4,000, but with a very wide confidence interval of between 1:1,400 and 1:20,000.

Post mortem study

9. A pilot study to test four different tissue collection methodologies, will start in December 2009. The pilot will be a collaboration between HPA, NHSBT, NHS Trust bereavement services and two collaborative coroners. The results of the pilot are expected in June 2010, and will inform design and roll out of a wider study with co-operative coroners and Trusts. We will provide further advice on evaluation of the pilot in due course.

Prevalence estimates

10. The current vCJD prevalence estimate is based on the 2004 Hilton data (1:4,000). To date, SEAC have not been willing to revise the estimate to include the results from NATA. However, SEAC acknowledge the importance of interpretation of the results of all the past and in progress prevalence studies, along with the known incidence of vCJD, for determining future policy direction.

CJD and Blood

Diagnostic Blood Tests

11. A number of companies are developing vCJD assays. Tests developed by Amorfix and Microsens are currently being evaluated, but their performance to date has been poor and they remain under evaluation.

12. DH is working with colleagues in the MHRA to add vCJD blood tests to the In Vitro Diagnostic (IVD) Directive. This will ensure that any marketed test meets defined performance criteria.

13. If and when a test is shown to be effective, advice will be sought from SaBTO, SEAC and the ACDP on the appropriate use of the test by the blood services and in other settings, before any decisions are made to introduce it. Careful consideration will be required of the potential impact of the results (in terms of either false positives or false negatives) on both the individuals tested, potential recipients, and the blood services.

At Risk Patients

The Highly Transfused

14. In 2008, a joint working group of the Advisory Committee on Dangerous Pathogens (ACDP) and the CJD Incidents Panel (CJDIP) recommended that patients with over 80 donor exposures should, for public health protection purposes, be identified prior to undergoing high risk surgery, and that those with over 800 donor exposures should be prospectively notified of their "at risk" vCJD status.

15. DH had asked, (your letter to the working group Chair, David Pryer, in November 2008 refers), that these measures be implemented by April 2009 and October 2009 respectively. However, this has been delayed due to the HPA having to shift resources to Swine flu. The first recommendation was implemented in neuro and posterior eye surgery centres in July 2009. We expect an evaluation of the implementation of the proposal to identify those who have had over 80 donor exposures, from the HPA in January 2010. The prospective notification of those with 800+ donor exposures will start in early 2010.

Supporting compliance with risk reduction guidance.

16. There is some evidence that there is poor understanding and application of vCJD risk management guidance in the NHS, where vCJD transmission may be perceived as a very low risk.

17. The HPA is considering how to further strengthen awareness and implementation of guidance with the Royal Colleges and professional bodies. The ACDP, the Engineering and Science Advisory Group into the Decontamination of Surgical Instruments and the CJDIP are ensuring that their guidance is presented in a manner to increase awareness amongst Trust Medical Directors, RDsPH, Infection Control Teams and others. This has included the secretariats of the Committees promoting the guidance at infection control conferences.

Prion Reduction Filters

18. Prion Filters are being developed by at least three companies. The UK blood services have a Working Group considering this technology, and evidence of efficacy, quality and clinical safety that are required before considering introduction. The working group felt that one of the filters on the market met their criteria and they therefore passed it to SaBTO for their views.

19. SaBTO considered this technology when it met on 27 October 2009 and recommended that blood that has undergone filtration should be provided to those not exposed to BSE through their diet (ie. those born after 1 January 1996). Although there are as yet no clinical trials of filtered blood in paediatric patients, Ministers have been asked to agree to an

assessment being made of the potential impact of this advice, and we await their agreement.

Decontamination

20. We have not yet received the final report of the National Decontamination Survey but we understand that it will show that the NICE guidance on *Patient Safety and Reduction of Transmission of CJD via Interventional Procedures*, has not been fully implemented in the majority of centres. To try and redress this, Estates will be issuing an HTM, which will provide implementation guidance.

Current DH CJD surveillance and research programme.

21. DH's contract with the University of Edinburgh for the provision of the National CJD Surveillance Unit currently runs until March 2013, when it will be up for renewal. Even with a low incidence of clinical disease, continued surveillance is likely to be necessary.

22. CJD has the only ring-fenced budget in the DH Policy Research Programme - £5.5M per annum from a £32M budget, which is fully committed in 2009/10 and 2010/11. This has recently been supplemented by a recurrent transfer of over £2m to the HPA to provide on-going support for the prevalence studies.

CJD Advisory Committee Plenary

23. The Advisory Committees with an interest in CJD will be meet in plenary in Spring 2010. Possible issues for discussion are the impact of CJD risk minimisation upon direct patient care and the cost benefit analysis of precautionary measures. We will send further details of this event in due course.

The Future of SEAC

24. Following a steep decline in SEAC's business over the past few years, the SEAC Steering Group has agreed that it should conduct its business, for the most part, by correspondence, with occasional meetings when the need arises. This will enable the Committee to work more flexibly, by considering issues as and when they arise, rather than waiting for the next available meeting. The Chair, Professor Higgins, is content with the proposed new way of working. The matter is being discussed at the next SEAC meeting on 24 November 2009, after which Ministers and the FSA Board will be advised.

25. Professor Higgins is planning to meet Sir John Beddington soon, to explain the proposed changes. The SEAC Secretariat will also be writing to the Chief Scientists of DH, Defra and the FSA, in order to seek support for the proposed changes. We have asked that the proposals are also discussed and agreed by the four CMOs.

Conclusion

26. You are asked to note the position. We will be happy to respond to any queries you might have.

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