1. Are the tests and results published by Collinge's group on over 8000 appendices in the BMJ robust enough?

This question is very relevant since a number of authoritative groups are extrapolating risk analyses and calculations on the future of the epidemic from Collinge's estimates.

Markus Glatzel and A. Agguzzi are using a protocol adapted from Collinge's group routinely. The Swiss vCJD prevalence study is also being performed using the same method. The Swiss have found the method to be relatively stable. However, the spiked controls are crucial.

The article by Hilton et al in BMJ which showed that one of 8218 tonsils were positive for abnormal prion is not robust enough. This is why John Collinge is planning a prospective assessment now.

Recent presentations by experts such as R Will and Paul Brown seem to state that the results reported by Hilton et al have very limited significance, considering the very large confidence interval. These data should be considered as soft. In addition, the preliminary study by Collinge's group on 2000 samples was negative.

2. Do you have any data on tests for abnormal prions performed on:

* Bone marrow samples
* Retinal/Optic nerve
* Other tissues?

The available data is best summarised in the latest annual report on the CJD Surveillance Unit website.

Dr Head, in the CJD Surveillance Unit in Edinburgh, has studied optic tissues (including optic nerve) in sporadic and variant CJD cases, and found PrPres in both types of disease.

3. Are there any new developments on screening assays that could be used on blood donor samples?

Nobody in the group knows of any assays so far. However, the CDI revised assay from the Aventis group has just been published in J gen Virol. The German Fourier transform spectroscopy approach is said to be looking hopeful but this has not been published yet. The Baxter group have looked at EDRF levels in normals and see a 1 log range. The Roslin group now have EDRF data on about six vCJD cases (unpublished).

Cashman's group in Toronto will be publishing an important paper in Nature Medicine describing a prion protein epitope selective for the pathologically misfolded conformational conversion of the prion protein in disease is likely to be accompanied by molecular surface exposure of previously sequestered amino-acids side chains. The misfolded conformation of the abnormal protein is associated with increased solvent accessibility of tyrosine. Hence, antibodies directed against the abnormal prion protein repeat motif, tyr-tyr-arg, recognise the pathological isoform of the prion protein but not the normal form. Antibody binding to the pathological epitope is specific. Conformation-selective exposure of tyr-tyr-arg provides a probe for the distribution and structure of

pathologically misfolded prion protein, and may lead to new diagnostics and therapeutics for prion diseases.

4. What tissues, other than blood, should we be archiving to screen, should a screening assay for vCJD become available in the future?

Members of the sub-group would not commit on this issue. They realise that there are several options that may be possible for cadaveric donors. Urine would not be realistic. Some members consider that a flushback of the LD filters would be very useful, since they contain lymphocytes and platelets and this might be the best way to concentrate prions. Some members state that the NBS is interested mainly in the infectivity of blood components and therefore should concentrate on these as a start point for screening assays. To try and second guess which tissues/samples may be used for surrogate assays is not only counter productive but may involve us in the expenditure of significant monies on the collection and storage of material which may never be used. The outcome of MSBT's deliberations gives the NBS a clear direction for its Test Assessment Panel and this is the most significant step we can make in preparation of PrPsc specific assay testing.

Useful references:

* *Lancet Infectious Diseases, (03), 4: 214-22 Organ distribution of prion proteins in variant Creutzfeldt Jakob Disease*

I Ramasamy, M Law, S Collins, F Brooke

* *Eur J Haematol (03) 70: 11 - 16*

* *Wilson K, Wilson M, Hebert PC, Graham I Transfusion Medicine Review this May, article on Canadian approach to vCJD (April 2003) Vol. 17: pp89-98. See Application of the Precautionary Principle to the Blood System: the Canadian Blood System's vCJD Donor Referral Policy*