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Ref: ACVSB2a

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Date: 2 January 1991

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ACVSB PAPER: PRIONS & BLOOD

I invite comments on the first draft of a paper for the January meeting of the Advisory Committee on the Virological Safety of Blood. I think your deadline for the final version is the 10 January, so I had better have any comments by the 9th.

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NOT FOR PUBLICATION

ACVSB

JANUARY 1991

CJD AGENT/PRIONS AND BLOOD DONORS

1. In April 1989 at its first meeting the committee recommended that recipients of pituitary-derived human growth hormone (hGH) should not be acceptable as donors for blood or any other tissues because of the remote and theoretical risk of transfer of Creutzfeldt Jakob Disease (CJD). The NBTS now attempts to exclude such donors and all past recipients of hGH are being approached individually with this advice and for counselling.

2. Two related issues have been raised recently on which the ACVSB's advice is sought: (a) look-back on recipients of blood from donors subsequently confirmed with CJD and (b) exclusion as donors of those from families with Gerstmann Straussler Syndrome (GSS).

Background: Blood/blood products as risk factors for CJD

3. Case control studies in CJD have failed to demonstrate an excess risk of being either a blood donor or transfusion recipient (1,2). Although CJD has been transmitted iatrogenically with pituitary derived hGH and gonadotrophin, dura mater, cornea and contaminated surgical instruments, there

are no reported instances related to blood transfusion. CJD is not a recognised complication of treatment by blood products as in haemophilia, even though viral-inactivating procedures are unlikely to be adequate to deal with the CJD agent.

4. However, there are reports of successful transmission of infection from human blood by intracerebral injection into animals (3, 4). Some experts, however, are sceptical about this work. Nevertheless, the possibility remains that blood might be capable of transmitting infection and for that reason one obvious high-risk group, hGH recipients, are now excluded as donors.

Look-back?

5. The question of tracing the recipients of blood from hGH-recipients was raised at the ACVSB's first meeting. This type of research study might be able to shed light on whether blood has ever transmitted infection. The ACVSB rejected such a study as impracticable and unnecessary.

6. The same issue has been raised recently in a slightly different way by the Murray Committee, set up by the MRC to oversee coordination of research into spongiform encephalopathies in man. All CJD cases are now to be monitored in the UK in a study funded by DH and undertaken by Dr R G Will of Edinburgh. Relatives and records should enable those who had been donors to be identified and recipients of their

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products traced. The Murray Committee questioned whether this should be done.

7. The Murray Committee were informed this was being referred to the ACVSB but it was pointed out:

(i) numbers of CJD cases are so small the study would be unlikely to have sufficient power to be meaningful

(ii) NBTS records may not be available beyond 10 years and yet the CJD incubation period could be longer than this.

(iii) if the disease in blood recipients presents as CJD, any link between patients by this route would be detectable in the main study in any case.

(iv) there are ethical problems about what if anything can be said to those who received such blood.

(v) with the possibility of transmission through blood being so dubious, the NBTS may not be fully cooperative and without them the study would be impossible.

8. Presumably if such a study went ahead, it could include all hGH-recipients who had ever been donors (see 5 above).

9. This is being brought to the ACVSB at this stage in view

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of their earlier comments. If the response is different, a detailed protocol would have to be prepared and subjected to the usual review-process by the grant-giving body (presumably MRC). But perhaps the ACVSB still believes this sort of study to be impracticable and unnecessary.

Familial CJD and BSE

10. Apart from hGH-recipients, the only other clearly-identified high-risk group is those from families with GSS or familial CJD. These families are exceedingly rare but are now subject to intensive study since new techniques have been able to demonstrate deletions and/or insertions in PrP (prion protein/protease-resistant protein) genes (5, 6). If the association between these gene defects and dementia is confirmed, it should be possible to predict which of the currently asymptomatic family members will develop disease. Even these familial and clearly genetic forms of spongiform encephalopathy are transmissible to experimental animals, and hence possibly to humans in the right circumstances.

11. One of the researchers involved, having identified one family member who was a blood donor, referred this matter to the department pointing out the prion protein is expressed in lymphocytes and thus such individuals perhaps should not be donors. Others may argue that everyone with prion gene abnormalities should not be donors, whether or not they or their families have recognised neurological disease.

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12. The ACVSB is asked what action might be appropriate:

a. Further research to see if recipients of blood from these family members have been adversely affected (as in 5-9 above), or

b. If we decide this is not realistically testable then we could attempt to exclude such people from being donors by:

(i) individual approach to the handful in known CJD/GSS families [and anyone else with known prion protein gene defects] and/or

(ii) excluding anyone with a family history of dementia, which risks excluding the high proportion (30%?) with family members with Alzheimers (AHD) as well as the smaller but still substantial numbers with familial AHD, or

c. On the basis GSS/familial CJD is so rare, and most transfusion recipients do not live long enough to develop a slow viral infection, decide no action is necessary.

13. If action is thought appropriate, it would have to be handled very carefully. Some still believe the alarmists who stated that "prion dementias" are widely underdiagnosed (7),

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and would read any new action as confirming these fears. The consensus expert view is that all CJD is very rare, and familial cases less than 10% of these (8). But the extent of prion gene "abnormalities" is not known, with only a few hundred controls and cases examined worldwide to date. It is not clear what if anything is being said at present to those who have prion gene analysis.

14. If the ACVSB wishes to explore option 12 b(ii), then further work would be needed on the validity and expected dropout rate from the questioning of donors about family history of dementia.

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