NOTES OF MEETING HELD FRIDAY 16TH JANUARY 1998 TO DISCUSS THE SAFETY OF THE PRODUCTS FOR HAEMOPHILIA PATIENTS

Working group: Dr Caron Grainger
Dr Brian McCluskey ✓
Dr Steven Munday
Dr Jeremy Hawker
Dr Chris Hyde ✓
Mr Simon Hairsnape ✓
Mr Mick O'Donnell ✓

Apologies: Dr Chris Heath ✓

Invited Experts:
Dr Bob Wills, Consultant Neurologist CJD Surveillance Centre,
Dr Warren, PHLS Shrewsbury
Dr Tim Wallington, Zonal Clinical Director, NBS West and South West Region

BACKGROUND

All were aware of the 1997 advice from the UK Haemophilia Centre's Directors Organisation (UKHCDO) which was issued following new advice from the Spongiform Encephalopathies Advisory Committee (SEAC). The difference between the 1996 UKHCDO statement and the 1997 statement is as follows:

- **1996:** Creutzfeldt - Jacob disease (CJD). "The theoretical possibility of CJD by transfusion has been extensively examined. There is no evidence that the causative agent is transmitted by plasma products. There have been no links between CJD and haemophilia"
- **1997:** "There is concern about the possibility that blood and blood products might transmit the agent responsible for nvCJD. As a result of the recent directive from the Committee for Proprietary Medicinal Products (CPMP) two batches of FVIII concentrate have been withdrawn in the UK by the manufacturer because they were produced from plasma containing donations from individuals who subsequently developed nvCJD.

Directors of Public Health have asked the working group to reconvene to examine the new evidence around nvCJD, in relation to purchasing blood products for haemophilia, in particular:

- Should recombinant factor VIII be the product of choice
- In the absence of a change to rFVIII, should US blood products be the preferred choice.

ADVICE FROM EXPERTS

The following points were made:

- There is no major risk of transmission of sporadic CJD in blood and blood products, and there has been no case in which a haemophiliac patient has developed sporadic CJD (evidence from lookback exercises where haemophiliacs have received factor VIII from donors who subsequently developed following CJD).
- NvCJD is due to a different agent to sporadic CJD, and it is not therefore possible to assume a similar risk assessment for nvCJD as for sporadic CJD.
- To date, lymphoreticular tissue has found to be infected with the prion protein responsible for nvCJD. This phase is enhanced to that seen in sporadic CJD.
- There is a prolonged viraemia (sic) associated with nvCJD, prior to diagnosis. There is therefore a possible risk that infective agents are present in blood donated many months/years earlier by an individual who subsequently develops nvCJD.
- It would be reasonable to assume that any infective agent associated with nvCJD is likely to concentrate in the Buffy coat
- There is no *direct* evidence relating to transmission of nvCJD via blood at present. All experimental and epidemiological studies will take years to reach fruition. However, various laboratory experimental models suggest that it is possible to transmit TSEs (other than nvCJD) by direct inoculation of infected blood into cerebral tissue. Chimpanzee experiments show no evidence of blood to blood transmission of TSEs.
- With the exception of nvCJD, the UK donor pool is considered to have the lowest risk of infectivity of all world wide donor pools. However, appropriate selection of donors, quarantining of supplies, virucidal measures etc render all donor pools of comparable risk. In general, it takes the process to fail for infection to be transmitted through blood products.
- According to various mathematical models for nvCJD, there are an estimated 300 to 80,000 cases likely over the next 25 to 30 years. Accordingly it is impossible to know how many donors are incubating the disease. Each unit of Factor VIII concentrate is produced from about 20,000 pooled donations.
- Although human albumin is considered to be an extremely safe blood product, the risk of transmission of an agent cannot be excluded, although any risk is likely to be minimal.
- Laboratory experiments suggest that there is probably a threshold level above which infection with TSEs is possible. There is currently no evidence as to whether or not cumulative risk affect is also in operation, although this is clearly a possibility.
- There is currently a risk assessment being undertaken looking at the risk of human to human transmission via blood, for which leucodepletion may be an answer. The NBA is undertaking a feasibility exercise for leucodepletion. The report of the assessment and feasibility exercises are likely to be available in mid February. Any leucodepletion will not reduce the risk of infectivity completely as only 2 to 5 logs of cells are removed (i.e. leaving about 5 million leukocytes per dose of product.
- Looking across the regions, funding of recombinant Factor VIII in the summer of 1997 was extremely variable, with the West Midlands, most of the North West,

South West and Northern and Yorkshire regions not supporting its use. The situation is likely to have changed following the nvCJD problem, eg Avon HA is looking to switch to recombinant products for children in the near future.

- Little primary/secondary research literature is available which relates specifically to the transmission of nvCJD in blood products. Best evidence in this area comes from expert opinion and the grey literature.

POSITION AGREED BY THE WORKING GROUP

Pending the current risk assessment exercise and leucodepletion feasibility study, there is no change in the evidence such that one would recommend a change in current policy. There is no justification at present to switch to non UK/European products at this time.

ACTIONS

- Mr Mick O'Donnell to seek current positions with regard to recombinant Factor VIII from other regions.
- Dr Caron Grainger, Dr Steven Munday and Mr Mick O'Donnell to meet with Dr Frank Hill, Dr Mike Williams and Dr Jonathan Wilde to obtain their views.
- Report to DsPH in February should detail the evidence presented by the experts, the clinicians comments, and the working groups recommendations.
- Any decision by DsPH should be ratified by Purchaser Chief Executives and then by Health Authorities
- Any decision should be considered an interim solution subject to review once the national exercises have reported.
- CG to obtain a health economics view from Prof Rafftery.