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MSBT14/12

ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF BLOOD AND TISSUES FOR TRANSPLANTATION [MSBT]

MINUTES OF THE MEETING HELD ON 26 FEBRUARY 1998

Chairman:	Dr J S Metters
Members Present:	Dr A J Cant Dr D W Gorst Dr D B L McCelland Dr P Mortimer Dr E A Robinson Dr T J Snape Dr T Wyatt Dr R E Warren
Also Present:	Professor H Thomas Mr P Comer (agenda item 4.i) Dr L Williamson (agenda item 4.ii)
Observers:	Dr A Mairs (NI) Dr W Smith (WO) Dr A Keel (SO) Dr Doyle (DoH) Dr Nicholas (DoH) Dr Tsang (DoH) Dr Wingfield (DoH) Ms J Dhell (DoH)
Secretariat:	Dr M McGovern Ms G Skinner Mr T McHugh

1. CHAIRMAN'S INTRODUCTION & WELCOME

1.1 The Chairman welcomed members of MSBT, and Professor Thomas from the Hepatitis C Lookback Working Group. Also attending for the discussion on nvCJD were Mr P Comer from Det Norske Veritas and Dr Lorna Williamson from the National Blood Service. Dr Tsang was attending in place of Dr Rotblat. Mr McHugh was introduced as a new member of the Secretariat.

2. **APOLOGIES FOR ABSENCE**

2.1 Apologies for absence had been received from Professor Zuckerman, Professor McMaster, Dr Perry, Mr Forsythe, and Mr Hewlett from DoH.

3. **MINUTES OF THE THIRTEENTH MSBT MEETING HELD ON 27 OCTOBER (MSBT 13/4) & MATTERS ARISING**

MINUTES

3.1 The minutes were agreed. However, the Chairman emphasised the importance of the minutes accurately recording the decisions as well as the corporate conclusions reached by the Advisory Committee. This was particularly relevant to paragraphs 5.30 - 5.35 of the minutes where no conclusion had been noted. Members were asked to send any further comments to the secretariat.

MATTERS ARISING

Tissue banking

3.2 Dr Doyle advised that the submission was still under consideration by Ministers, who might be influenced by recent wider issues in relation to nvCJD. The Chairman advised that it might be necessary to revisit the MSBT guidance which is now almost 2 years old. In addition, there was also the problem that bone stored in freezers as ad-hoc tissue banks might need to be PCR tested. Dr Robinson had written to Dr Metters about the use of fresh frozen bone. A recent survey had shown that less than 20% of harvested hips were processed and accounted for. If advice was given not to use such materials, orthopaedic practice could be compromised. Members suggested that advice from SEAC might be requested with regard to CJD and nvCJD. In addition retrieval of tissues prompted concerns that the current guidance was not being followed.

Hepatitis C

3.3 Dr Robinson reported that no more cases had been registered. The information on the gap between identified components and recipients would soon be available. Dr Robinson advised that the NBA's advice had been to PCR test patients who were immunosuppressed as serology was insufficient in these cases. Where recipients were followed up by the transfusion service this would be done but it was far from certain where this follow up would be carried out in primary care.

Virally Inactivated Plasma

3.4 Dr Robinson had written to the Chairman about the prospect of NAT implementation in parallel with implementing leucodepletion. She reported that the introduction of virally inactivated plasma should be deferred until the outcome of the risk assessment in relation to leucodepletion became available. Leucodepletion would result in a major restructuring exercise and while users had been expecting virally inactivated fresh frozen plasma, they would understand the new priorities. It was also noted that availability of virally leucodepleted plasma practice in the other parts of the UK might

differ, and although it was preferable to avoid this, there were occasions when it was inevitable.

Informing patients who had received nvCJD implicated blood or blood products

3.5 Due to the large number of requests for advice on what to do in the case of recipients of nvCJD implicated blood products, advice had been issued by Dr Winyard. This was based on the unanimous opinion of a range of ethical committees, that recipients need not be informed [PL(CO)(98)1 issued on 6 February 1998]. However an individual clinician might decide to inform patients and there would be some situations which could not be avoided such as the recall of an implicated product.

Record Keeping for Patients who had received blood or blood products

3.6 Dr Robinson stated that the NBA already had a position statement to the effect that a permanent record should be maintained in the patient's notes. In the case of any patient treated with blood products, the batch number should be recorded in the patient's notes to allow for future "trackback". However it was recognised that the quality of medical record keeping might not be adequate to allow proper tracing. An alternative option might be for a sticky label which could transferred from the blood product to the patient record. However it was recognised that members needed to discuss further what information was required. It was agreed that this matter should be fully discussed at a future meeting.

Autologous Transfusion

3.7 The Chairman and Dr McGovern had met Col Thomas of the Autologous Transfusion Group and had had a useful discussion especially on the topic of intra-operative salvage of blood. CMO's initiative on blood would pick this up and it would feature as a future MSBT agenda item.

PROGRESS REPORT ON nvCJD

4.1 The Chairman informed members that a press release would be issued later that day, relating to advice from CPMP and CSM. The main issue was the use of UK sourced plasma in manufacture. CPMP had advised the recall of products made from plasma from donors in "strongly suspected" cases of having nvCJD. This would result in a greater number of recalls, a threat to supplies and more crises of confidence. CPMP was also advising against the use of albumin as an excipient from donors from an area where there were a cluster of cases of nvCJD eg UK sourced. As blood products were licensed medicines, the CSM was the relevant UK regulatory body advising Ministers. As the Licensing Authority, CPMP advised that national authorities should look at what should be done in their own countries.

4.2 Taking account of CPMP recommendations and concerns about UK plasma in relation to nvCJD, CSM's advice was to review all licensed products from UK plasma as well as those using albumin as an excipient. Licensed products would be reviewed on a case by case basis, and a decision would be taken about whether the licence should remain, be suspended, or revoked. Ministers had also agreed that BPL should be given

the go ahead to import plasma. In the case of imported non UK plasma, all proposed sources would need first to be inspected and licensed by MCA (taking donor screening arrangements into consideration) as is current practice.

4.3 The Chairman said that the announcement would stress that the measures taken were for purely precautionary reasons. There was no evidence of transmission of CJD via blood, but as nvCJD behaves differently from classic sporadic CJD, the precautionary approach was necessary.

4.4 Members agreed to await SEAC's decision on the introduction of leucodepletion of blood. However total leucodepletion would take many months to implement and reprovision of licensed blood products using imported plasma would also take time. The labile blood products could not to be imported as alternative supplies are not available.

4.5 While BPL geared up to process the alternative sourced plasma, UK plasma would still be in use in the interim during the MCA assessment. Abrupt cessation of production would lead to supply problems - indeed the US already had a shortage of certain products especially immunoglobulin. The CSM review would take account of clinical need, risk and product supplies. Dr Snape indicated that parallel fractionation of non-UK and UK sourced plasma would not be possible at BPL.

4.6 Dr Gorst informed members that his Trust had already decided to switch to Factor VIII made from US plasma for patients with haemophilia not currently receiving RTVIII. The chairman advised that SoS had decided that all patients under the age of 16 and new patients should receive recombinant Factor VIII. In response to concern about supplies of Anti D and certain niche products, Dr Snape confirmed that production would continue as now until such time as the licensing position changed.

4.7 Members were informed that the only vaccine made from UK plasma in current practice was rabies. None of the current childhood vaccines contain UK derived plasma and the last time was in 1994 when an MMR vaccine was used in a limited way in Scotland. The position of for instance a 6 year old child who would have been vaccinated post 1988/89 (when BSE controls started) and pre 1994 was discussed. Members agreed that 1994 was 2 years prior to nvCJD, and in addition the risk of human to human transmission through blood and blood products is, at the present time, a theoretical and unquantifiable risk.

4.8 Dr Mortimer raised the issue of use of the rabies vaccine by backpackers and individuals at risk of rabies. Members agreed that where the risk of rabies was high, vaccine should not be withheld and that specific immunoglobin and the vaccine should continue to be used in post exposure management.

Risk Assessment

5.1 Dr Wingfield reported on progress and stated that risk assessments were not static but evolving studies often involving a large number of unknown parameters. This study was particularly complicated and Det Norske Veritas (DNV) who had wide experience in risk assessments had been taking the work forward since early December. They had hoped to report by the end of February, but because of the complexities of the study only

an interim report would be available for discussion by SEAC at their meeting on 9 March. While a good framework had been achieved on the basis of the work so far, SEAC would be unlikely to reach conclusions at that meeting.

5.2 Mr Comer gave a slide presentation and underlined that the study involved a higher level of uncertainty than anything DNV had tackled previously. The risk assessment would provide useful insight, and while not clearly pointing in any one direction would help with understanding the potential benefit of the different options. The initial report would be available by the end of March. The secretariat agreed to send a copy of the slides used in the presentation to all MSBT members.

5.3 The objectives of the study were to

i. assess which blood components and products were risk factors for nvCJD transmission by analysing the processes involved in blood transfusion and the manufacture of blood products,

ii. identify groups of patients at risk from blood components and products and

iii. identify the benefits/disbenefits of measures to reduce the risks identified.

5.4 The general approach to the risk model involves looking at the number of potentially infected donors through exposure of the population to infectivity. This was difficult because of many uncertainties such as

i. infection from food relates to consumption of agent in beef products, the dose response model and the development of nvCJD cases,

ii. blood donation related to the number of infected donors and the infectivity of their blood,

iii. the effects of processing or infectivity of blood products and

iv. exposure of patients to blood and blood products and development of nvCJD

5.5 The incubation period for nvCJD was not known. For cases contracted through blood it might be between 12 and 15 years, but for food this is likely to be around 30 years because of species barrier. However, there are major certainties eg the potential for infection through blood to occur at all, the infectivity level in whole blood, the basis for splitting of infectivity between components and infectivity of licensed blood products.

5.6 Members agreed that the benefits of leucodepletion could not be ruled out on the basis of this initial report, and would need to be considered again with the benefits of the full report.

Scientific Aspects

6.1 Dr Williamson introduced paper MSBT 14/2. Attention was drawn to the implications of universal leucocyte depletion on page 3. It is not believed that infectivity will be solely confined to leucocytes. Furthermore it is not known what level of leucocyte reduction needs to be achieved. As such the possibility of filtration causing shedding or fragmentation of some cells cannot be excluded.

6.2 With regard to the percentage of blood already leucodepleted for certain patients, it is believe that it is possible to reduce consistently to a certain level. The technique for counting leucocytes is not easy. While total cell numbers can be determined, subsets are more difficult. In summarising the Chairman reminded members to keep in mind the question; on the basis of the evidence available should MSBT recommend leucodepletion now?

Operational Issues

7.1 Dr Robinson tabled paper MSBT 14/3 which concerned the operational side of introducing leucodepletion into the blood service. A number of options for introduction were outlined. The best option appeared to be option 3 which examined the potential of new pack configurations incorporating integral filters and thereby reducing sterile docking procedures. The scale of the project is highlighted by comparing the cost of introducing leucodeletion at £82m with the NBA's total budget of approximately £150m. The NBA would prefer option 3 which would allow for up to 20 months for implementation, however it could implement option 2 (a move to leucodeplete all components utilising a combination of integral blood pack/filter systems and sterile docked discrete filters) which would could be achieved within 12 months.

Blood Transfusion and Transplantation Implications of Proposed UK & European Preventative Measures

8.1 MSBT 14/4 was introduced by Dr McClelland. This concerned the exclusion of donors who had received implicated products (ie not accepting blood donors who had themselves been blood recipients). This would have an impact on between 15% and 17% of all donors. NBS centre staff to take an "if in doubt, don't take" approach. Another issue would be the impact of donor rejection and associated knock-on effects.

8.2 The Chairman queried the risk of reduction in donor numbers - which would be a critical question for MSBT - and if a 5% collapse in numbers could be tolerated. If the answer was no then the NHS would have to make do with less blood and provide red cells for only those really in need of them.

8.3 It was known that some public health doctors favoured deferral of all blood recipients. However Dr Robinson pointed out that the NBA is just about meeting demand now and could go into crisis mode if donor confidence were affected. Although this was a valid view, there would be a number of practical consequences.

8.4 MSBT agreed that there was insufficient data to show that the benefits of this

approach would outweigh the risks. Furthermore it was noted that in a number of months there should be more information for making decisions. Members therefore decided not to recommend deferral of previously transfused donors for the moment.

9. **UPDATE ON STUDY OF CJD SURVEILLANCE AND BLOOD SERVICES**

9.1 Dr Robinson presented paper MSBT 14/5 which gave an update on Transfusion Medicine Epidemiological Review. This was noted by MSBT members.

10. **CMO'S WORK ON BLOOD TRANSFUSION PRACTICE**

10.1 This paper was introduced by Dr McGovern. It highlighted the publicity around potential shortages of the supply of blood and blood components as well as the potential risk factors. Due to time constraints, members were invited to send any comments direct to Dr McGovern

11. **HTLV1**

11.1 Members were informed that this submission was with Ministers.

12 **HEPATITIS G PROPOSAL FROM THE PHLS**

12.1 Paper MSBT 14/8 outlined a proposed study from PHLS which would investigate hepatitis G virus in anti-hepatitis C virus positive samples. The paper was submitted to MSBT for its endorsement prior to it being submitted to the MRC for funding. Any comments should therefore be sent to Dr McGovern who would pass these to RDD.

13. **EXTENSION OF THE AGE FOR BLOOD DONORS - 17/70**

13.1 Attention was drawn to paper MSBT 14/9 which was a copy of the final report of the NBA's Working Group on the Age Limits for Blood Donors. This proposed changing both the lower and upper age limits for blood donation to 17 and 70 respectively. Members were invited to send any comments direct to Dr McGovern. A submission to Ministers was in preparation.

14 **TISSUE BANKING**

Update on the Council of Europe & European Activity

14.1 Dr Doyle submitted paper MSBT14/10 for consideration by MSBT members. Comments should be sent to Dr McGovern.

Update on Sir William Stuart Enquiry (CJD & Corneal Transplantation)

14.2 The review has now been completed, however the report has not yet been finalised. It is expected to be presented to the UK Health Departments in the near future.

15 **ANY OTHER BUSINESS**

15.1 There was none.

16. **DATE OF NEXT MEETING**

16.1 The next meeting will take place on Thursday 4 June in the Cathedral Room, in Richmond House.