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

MINUTES OF THE FIFTH MEETING HELD ON 25 MAY 1995 IN ROOM 149 RICHMOND HOUSE

Chairman: Dr J S Metters

Members:
Dr D W Gorst
Miss R H H Lord
Dr P Mortimer
Dr R J Perry
Dr A Robinson
Dr T Snape
Dr R E W Warren
Professor A Zuckerman

Observers:
Dr P Doyle
Dr A M George
Dr A Keel
Dr G Mock
Dr I H Nicholas
Mr J S Sloggem

Secretariat:
Dr A Rejman
Mr P Pudlo
Mr D Burrage
Mr L Levy

Dr A Wight and Mr C Lister were present for Item 6 only.

1. Chairman's Introduction and Welcome

The Chairman informed the Committee of Dr Ruthven Mitchell's resignation from the Committee following his retirement as Director of Glasgow and West of Scotland BTS, and recorded the Committee's thanks for Dr Mitchell's valuable contribution to this Committee and its predecessor Committee ACVSB. Dr Peter Doyle joined the Committee as DH observer with responsibility for organ transplantation and tissue banking.

The Chairman introduced two new members of the Secretariat, Paul Pudlo, who replaced Tom Kelly, and Leonard Levy, who replaced Mary Sandillon.

2. Apologies for Absence

Apologies for absence were received from Dr Cant, Mr McMaster, Mr Scofield, Professor Williams and Dr Purves, for whom Mr Sloggem deputised.

3. Minutes of the fourth MSBT meeting - 15 December 1994 (paper MSBT 4/4)

The minutes were agreed. The minutes of the third meeting on 29 September (Paper MSBT 3/12) were also agreed. (These were circulated too late for members to comment substantively at the last meeting.)

4. Matters arising from these minutes, not dealt with as separate items:-

- minute 4.2: guidelines for reporting the transmission of microbiological agents by blood

4.1 Members noted paper MSBT 5/1 - Yersinia Report from CDSC.

Dr Robinson tabled a paper (MSBT 5/9) on the Investigation of Transfusion Reactions suspected to be due to Bacterial Contamination. The aim was to set up a reporting system for all hazards, starting with bacterial contamination. It was intended that the information would be included in the Handbook of Transfusion Medicine, with the production of a card for use on wards. Details of a possible public launch for the initiative, degree of anonymisation of patient details, etc, would need to be considered. It was agreed that Members would comment to Dr Robinson on the paper by the end of June and that Dr Keel and Dr Mock would obtain comments from Transfusion Directors in Scotland and Northern Ireland.

ACTION - Dr Robinson, Dr Keel, Dr Mock and all members for comment.

- minute 4.5: ALT testing of blood donations - update

4.2 Mr Pudlo reported that Ministers had endorsed the Committee's decision that ALT testing should not be introduced.

Paper MSBT 5/2: NIH Consensus Development Conference: "Infectious Disease Testing for Blood Transfusions" was tabled for Members' information.

- minute 5.8: HIV O - update

4.3 Dr Mortimer said that there was nothing new to report. The French had not released sera, but PHLS had obtained some through the good offices of Dr Robinson.

4.4 Mr Sloggem said that a meeting had been held of representatives of MCA, MDA and DH policy [HC(M)] to discuss kit validation. He added that viral marker test kits would be included in an EC Directive on in vitro Medical Devices, which will come into effect in 1997 or later, and that the World Health Organisation is taking an interest in their development. Dr Rejman said that UK was trying to stimulate international co-operation, particularly with France and Germany on using the same sera panels for testing. Dr Mortimer welcomed this initiative and added that Denmark and the Netherlands were also active in this field. There was some discussion about whether UK efforts should be restricted to the EC, but Dr Metters supported Mr Sloggem's view that it was preferable to have global co-operation, without detracting from European work.

4.5 Dr Perry thought there should be UK standardisation before we proceed with international standards. A meeting of various UK interested parties should be arranged. Dr Metters said that colleagues in the territorial Departments would be kept up to date on progress.

- minute 6.1: EC activities relevant to the Committee

4.6 Mr Sloggem reported that the CPMP took the view that *intra-muscular* immunoglobulins, which did not have a defined virus inactivation step in their production method, should be tested by a PCR method to determine whether hepatitis C RNA could be detected in final product or preferably plasma pools used to make the product. Positive material would normally not be used, but the use of the product and the supply position may need to be taken into account, when making a risk/benefit decision on whether to use a particular material.

4.7 Dr Snape thought a blinded study would be helpful, so that the percentage positivity could be found.

4.8 The Chairman agreed that the Committee's view should be noted, but it was up to the MCA as regulators (with NIBSC) to take this forward, in line with the CPMP decision.

- minute 8.1: revision of AIDS leaflet for donors (paper MSBT 5/3)

4.9 Dr Robinson said the new leaflet would be called the "Blood Safety Leaflet", and would include other viruses such as hepatitis B and C, as well as AIDS. She said that the leaflet would contain information expressed in ways which would be easily understood, and based on epidemiological evidence about the spread of viruses. At present, the heterosexual spread of AIDS was most prevalent in sub-Sahara Africa. The Chairman was concerned about use of the word "race", which Dr Robinson assured the Committee would not appear in the leaflet.

4.10 Dr Keel said that the precise wording of the "Africa exclusion" would require careful consideration, if the aim of

excluding non-regular partners is to be achieved without causing grave offence to those who are in a stable monogamous relationship with partners who have lived in African countries. It would be unfortunate if the revised version of the leaflet was seen to conflict with the aim of encouraging donations from the Afro-Caribbean population to meet the specific needs of the sickle cell community.

4.11 On (xi) Heterosexual partners of Individuals believed to be HIV positive, Dr Keel commented that this presumably referred to **non-regular** partners of such individuals, and that it would be difficult to see how this could safely be made a temporary exclusion in the case of regular partners, as cohort studies of heterosexual couples had shown that partners of HIV positive individuals seroconvert as the HIV infected individual becomes increasingly immunocompromised.

4.12 It was agreed that the leaflet would need to take account of these points and that a draft would be circulated to the Committee for comment before submission to EAGA.

ACTION - Dr Robinson, Secretariat

5. Hepatitis C Look Back Programme

5.1 The Chairman reported to the Committee that the procedures for the look back exercise were circulated to all doctors under cover of letters from the Health Departments' Chief Medical Officers on 3 April and that an HSG was issued concurrently on the management network.

5.2 The Chairman reported from the adhoc working party in the morning, where it had been confirmed that some 7,500 components had been identified for follow up and that the estimate of some 3,000 recipients to follow up was thought to be about right. Some reluctance among hospitals and GPs to undertake counselling had been reported and the burden of counselling had therefore fallen to the blood service.

5.3 The main points of discussion at the ad hoc working party concerned research and stored samples. On research it had been agreed:

- that a central register would be created together with archives of sera and of cells contained in clots. The PHLS and the NBA would consider proposals;

- there should be follow up of spouses and partners of HCV infected persons to give data on the rate of sexual transmission;

- investigation was needed of genotypes which were likely to progress to cirrhosis and those which were not.

Proposals would be prepared and submitted to Ministers and the Director of Research and Development.

The Chairman informed the Committee that checking pre-1989 archived samples held in North London and Scotland would cost about £2 million and only find about 100 patients. If checking was not undertaken the NHS could be said to be failing in its duty of care. The alternative, favoured by the ad hoc working party, was a public campaign to encourage people to have a hepatitis C test. More work needed to be done in the working party on this option. The Chairman said that 6 months had elapsed since the look back was conceived and 2 months since the exercise went live.

ACTION - A report to Health Ministers was needed when more information was available after the next meeting.

6. CJD and blood transfusion

6.1 Dr Rejman introduced Paper MSBT 5/4, concerning the SACTTI proposal that an attempt should be made to perform a "lookback" exercise in respect of CJD and blood transfusion. The exercise would involve the National CJD Surveillance Unit at Edinburgh making its records available to the Blood Transfusion Service, which would check if any of the individuals had been blood donors. There was no evidence of transmission of CJD through blood. However there were a number of points to consider as set out in 1. to 7. of paper MSBT 5/4 and the matter had been referred to MSBT. Dr Wight commented that it was important to identify the purpose of a look back, what information would be obtained and what would be done with that information. Blood transfusion was not thought to be a transmission route, although it might be theoretically possible. Epidemiological information may be the only way of checking this, and the views of the Committee were sought on what would be gained.

6.2 Dr Mortimer said that it was not known what agent transmitted CJD, and that there was no basis for suggesting that it was transmitted by blood transfusion. There was insufficient information and no scientific basis for the decision which the Committee was being asked to make. Dr Gorst said that the information would take a long time to produce. Professor Zuckerman said that as the agent was unknown, there was no test and no treatment available, it was difficult to see what could be said to or done for recipients of blood or blood products if the look back identified the blood received was from donors who subsequently developed CJD. Members thought that worry might be caused to blood transfusion recipients for no good reason. Miss Lord said that it would be useful to look at the numbers proven to have CJD who had received blood transfusions, then look at the donors and what had happened to them. Dr Doyle said that there did not appear to be any scientific justification for the lookback.

6.3 The Chairman said that the incidence of CJD was similar to other European countries, between 0.5 and 1.0 per million;

it was not known how many of the 550 patients with CJD had given blood, but the numbers were too small to make quantitative assessments.

6.4 Mr Sloggem reported that plasma products have been withdrawn from the French and USA markets because the donor or a near relative was later diagnosed as suffering from CJD. The CPMP had considered the problem. Familial CJD was a donor exclusion criterion. However, where a batch of plasma derived product was found to include material from a donor later diagnosed as suffering from CJD, the material would not be withdrawn.

6.5 The Chairman said that it would be interesting to see if BSE is transmitted from cows with the disease, through blood transfusions, to calves. Dr Perry said that if CJD were transmitted by blood products, a higher incidence of CJD in haemophilia patients would be expected. The CJD Surveillance Unit could check for this.

6.6 The Chairman summed up the views expressed by Members that the Committee was not in favour of the SACTTI proposal, the Committee suggested experimentation to see if CJD was transmissible through blood transfusion in cattle, and considered that National CJD Surveillance Unit should continue to keep records on the numbers of people with CJD who had received donated blood.

7. HIV 1 and 2 and HTLV1 and 2 Combi test (Paper MSBT 5/5)

7.1 The Committee noted that the Yorkshire BTS paper "Evaluation of a Combined HIV - 1/2, HTLV I/II - Assay for Screening Blood Donors" paper MSBT 5/5 reported problems with too many repeat reactives and specificity not as high as that of HIV1 and 2 kits already in use in the blood transfusion service. The Committee agreed to defer discussion of paper MSBT 5/5 in view of the paper put forward by Dr Mortimer "Report of an Ad Hoc Group on Possible Additions to Virological Screening of UK Blood" - paper MSBT 5/8.

8. Quarantining of FFP for clinical use (Paper MSBT 5/6)

and

9. Viral inactivation of plasma (Paper MSBT 5/7)

were discussed together.

8.1 Dr Robinson tabled and introduced papers MSBT 5/6 and MSBT 5/7. The first paper commented on the SACTTI recommendation for a quarantine period of 90 days, to ensure exclusion of any window period infection. All FFP and Cryoprecipitate was prepared from regular donors, who on average donated just over 1.2 times per year. The proposal would require donor call up at least six times a year, a sophisticated IT system to manage the inventory, a four or fivefold storage capacity increase and significant increases in capital and revenue costs totalling some £4.2M. Dr Robinson highlighted a number of concerns raised in the paper: whether the current risk assessment justified a quarantining policy; the majority of transfused patients received red cell and platelet transfusions as well as FFP/cryoprecipitate; the persistence of inappropriate use of FFP and cryoprecipitate; whether other measures eg HTLV and anti-HBc testing of first time donors should be given priority. Dr Robinson concluded that given the practical and resource implications an FFP/Cryoprecipitate quarantining policy would take over 2 years to introduce.

8.2 On paper MSBT 5/7 Dr Robinson commented that more time would be needed to look at the implications of viral inactivation of plasma in more depth. Although there was concern that UK should not be left behind by other European countries, a much more accurate risk assessment was needed. Mr Sloggem stated that he thought the virus inactivation process would be seen as a manufacturing step, which meant it would be subject to a licensing authority decision. Dr Perry said that in Scotland it was policy to replace the use of cryoprecipitate by a safe pharmaceutical fibrinogen product. He confirmed that virally inactivated plasma in Europe was very expensive.

8.3 After discussion the Committee concluded that there was insufficient scientific data available to recommend quarantining of FFP or viral inactivation of plasma at present, but that there was a need for increased education in the use of FFP. Dr Keel said that a report was being prepared by the Scottish Clinical Resource and Audit Group on optimal use of blood and blood products which quoted large parts of the relevant guidelines. It was agreed that attention needed to be drawn to the existing guidelines, which were circulated to all haematologists, by

a) a message from the Departments' Chief Medical Officers, for instance an entry in CMO's Update and

b) letters from the Health Departments to the Royal Colleges seeking inclusion of the guidelines as part of clinical audit educational sessions for those prescribing as well as those issuing FFP.

The Committee agreed to keep these items under review, in the light of developments in other countries, in particular in relation to Methyline Blue and Light (paper MSBT 5/7) and other viral inactivation and would discuss again at a subsequent meeting.

In the meantime a report would go to Ministers not advising quarantining or viral inactivation of FFP at the present time for scientific and cost reasons, and that guidelines on optimal use would be brought to the attention of clinicians by the BTS and CMO Update.

ACTION - Dr Robinson, Secretariat

10. Promoting the safety of transplantation of human tissues and organs.

10.1 Dr Rejman reported that the Committee's paper has been cleared with Ministers and had been widely circulated for consultation with the professional bodies concerned. A consultation period of 6 weeks had been allowed with a closing date for comments of 12 June. The paper contained some new concepts and methods, but the fundamental test requirements were not new. The Committee would be asked to comment further if any major concerns came out of the consultation.

10.2 Miss Lord said that the feedback from transplanters was that the paper was very much needed. It was generally accepted that hepatitis C positive donors would not be used for transplantation although Miss Lord was not sure of the liver transplanters' position.

10.3 Dr Perry thought that the guidelines should be different for tissues and organs which were to be used immediately as opposed to those which were to be stored in tissue banks. Dr Warren stated that the Association of Medical Microbiologists felt that specific advice was needed for each type of tissue, and details would be provided in their response.

ACTION - Secretariat

Advice donation tissues Regulation

11. Tissue Banking Review

Dr Doyle, HCD SCS, said that the report of the tissue banking review team had only just been received by the Department. The recommendations would need to be considered and Ministers' views sought on handling the report. A timetable would be drawn up when Ministers had given a steer.

12. Virological Screening of UK blood donations (Paper MSBT 5/8)

12.1 Dr Mortimer summarised paper MSBT 5/8, which reviewed possible gaps in the viral screening programme for UK blood donations, in particular Anti HBc and anti-HTLV1/II. Dr Mortimer said that the paper emphasised that more economically attractive options were available which fell short of universal screening, for example screening of first time donors only and cheaper particle based assays. The purpose of the paper was to ensure that these options were more widely known.

12.2 Dr Gorst was concerned to see the Committee's earlier deliberations on anti-HBc and HTLV testing reported in the Times and said that it had to be recognised there was still

strong feeling on these issues.

12.3 Dr Snape warned against introducing tests which could be modified locally, only properly validated test procedures should be used.

12.4 Dr Snape confirmed that at present there was no way in which manufacturers could deal with inactivation of parvovirus B19.

12.5 The Chairman said that the value for money issues and epidemiological arguments needed full exploration. He wanted to use discussion of the paper to question the position of the transfusion service and the Health Departments when the Committee recommended against a test which has undergone validation and been found to work, but only picked up a handful of cases a year. He recognised that in a legal sense there could be a duty of care which suggested the test should be introduced. However, MSBT might be reluctant to recommend the introduction of a test if the outcome would mean a small margin of benefit for a disproportionately high cost. The Chairman asked the question whether the Committee would be more prepared to recommend against the introduction of a test if an appropriate mechanism existed to recompense any recipients who might be harmed as a result of the non-availability of the test.

12.6 Miss Lord said it put hospitals in a difficult position if they were prevented from screening individual donors because a particular screening test had not been officially sanctioned. Dr Rejman reminded the Committee of the study carried out in 1991 by the North London Regional Transfusion Centre to determine the incidence of HTLV among their blood donor population and the small incidence which was found.

12.7 The Chairman said that a submission would be put to Ministers to inform them of the need to reconcile the scientific and public policy dimensions. These could be more easily reconciled by a mechanism that provided an alternative to the introduction of testing that would identify only very small numbers of donors who would need to be deferred. It was agreed to continue discussion at MSBT's next meeting.

13. Any Other Business

Dr Rejman informed the Committee that guidance notes on collection, storage and infusion of bone marrow and stem cells will be sent to Members in the next few weeks for written comments prior to submission to Ministers, limited external consultations and finally issued as guidance.

ACTION - Secretariat

14. Date of next meeting

The Committee agreed to Dr Metters' proposal that the next meeting would be held in September, date to be arranged.
ACTION - Secretariat