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NOT FOR PUBLICATION

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

MINUTES OF THE MEETING HELD ON 2 MAY 1996

Chairman : Dr J S Metters (Items 1-5, and 6 : minutes 6.7-6.8 and 7.1-7.8 only) *

Members present :
Dr A J Cant
Dr D W Gorst
Dr D B L McClelland
Professor P McMaster (Items 1-8 only)
Dr P Mortimer
Dr R J Perry
Dr E A Robinson
Dr T J Snape
Dr R E Warren
Professor J D Williams
Professor Zuckerman

Also present : Professor H Thomas (Items 1-4 only)

Observers :
Dr P Doyle *
Mr M Harvey *
Dr A Keel
Dr J Ludlow
Dr I H Nicholas
Dr J Purves
Mr J S Sloggem
Dr J Toy *

Secretariat :
Dr A S M Rejman
Mr P Pudlo
Miss A Towner
Mr L Levy

* Present only for part of the meeting.

1. Chairman's Introduction and Welcome

1.1 The Chairman welcomed Professor Thomas and Dr Toy, who had been invited

for the discussion of matters which related to the Working Party on the Hepatitis C Look-back. He introduced Mr Harvey, who was likely to serve on the Secretariat at future meetings.

1.2 Dr Metters explained that he needed to leave early. Professor Zuckerman had agreed to chair the remainder of the meeting.

2. Apologies for absence

Apologies were received from Dr Mock.

3. Hepatitis C look-back

3.1 A table showing updated progress figures for individual countries, and including data from the NBA which was also presented separately, was made available at the meeting. Contrary to earlier expectations, more negative than positive results were being reported (for England). It was suggested that a revised table might be circulated giving up to date figures for all 4 countries.

3.2 Dr Mock had advised it was now clear that delays in Northern Ireland were occurring at the hospital records stage. Counselling by the deputy director was not a problem, as had been suggested at the last meeting (paragraph 4.3 of minutes). Dr Mock had also advised that checks of Northern Ireland's figures indicating a high number of donations per donor (paragraph 4.3 of minutes of last meeting) indicated they had been correct.

3.3 The Chairman advised that Ministers had been content with how things were going and that planned structured approach be maintained. But action should be taken to identify those hospitals where delays were occurring.

3.4 The committee agreed that a further general communication from DH would not be helpful when many hospitals had already made good progress. Instead each national transfusion service should identify particular problem hospitals and refer details to the relevant health Department for action, eg in the case of England via the NHS Executive.

3.5 Dr Robinson showed tables of information extracted from the lookback exercise so far. It was recognised that this would represent a very valuable data base for future use. An opportunity would be provided for updated information to be presented at future MSBT meetings.

3.6 Although the NBA figures suggested that 3% were already suffering from symptomatic liver disease, precise details were not available. However the committee still did not envisage any great disadvantage to patients if the exercise continued as planned, to be completed at the end of 1996.

3.7 Dr Robinson asked if information from the lookback could be given at a meeting in September for the 50th anniversary of the transfusion service. The Chairman thought there should be no restrictions, as this was part of a nationally co-ordinated exercise. But Health Departments would need to be alerted to the media attention that could result, including questions about people traced but not yet followed up. The provisional nature of the figures, and any other limitations, would need to be made clear. Figures would be best presented for the UK as a whole.

Action :

(a) Secretariat to circulate updated progress figures for all countries currently, and in advance of future meetings.

(b) Each blood service to identify hospitals where delays occurring. Health Departments to be informed and arrange action.

JG

(c) Dr Robinson to warn Health Departments if plans to give lookback information at meeting in September.

JG

BBS

(d) Dr Robinson to present updated findings from the exercise at future meetings.

4. New Hepatitis virus

4.1 The Chairman referred to the recent meeting in Rome and asked for matters arising that were not covered by Paper MSBT 8/4. He drew attention to advice sought from the Committee at the last paragraph of the paper.

4.2 Professor Zuckerman stated that a few points emerged from the Rome meeting. Firstly the evidence suggested that Hepatitis G was associated with a low disease rate - 73% with no evidence of liver damage and that 16 % had low ALT. It was comparable in this respect with CMV. The US blood banker Paul Holland had presented similar findings, concluding with the hope that screening would not needed. Acute hepatitis was caused by the different hepatitis viruses in the following proportions :-

Hepatitis A - 47%
Hepatitis B - 34%
Hepatitis C - 17%
Hepatitis G - 0.3%
Others - 1.7%

There was now experimental evidence that Hepatitis G can be transmitted from Factor VIII concentrates and 10% of haemophiliacs had been shown to be positive. This result was surprising but it was likely to provoke lobbying from the Haemophilia Society. There was no serological test available but it was likely that PCR assays currently being developed by commercial firms would be routine for blood by the turn of the century.

4.3 Professor Thomas said that there was evidence of neonatal transmission (50-75%

PCR positive). Also there was evidence that the virus, which is present in lymphoid cells, causes signs of liver disease, a proportion of which have abnormal transaminase and 10-40% who are viraemic have been shown to have elevated ALT. A paper in the Lancet indicated that 1 in 17 fulminant hepatitis cases were HepG positive. Blood was not evidently a major cause of problems. There was no evidence that viral inactivation works but it is reasonable to assume that it does. The HepG virus has some structural similarities to HCV.

4.4 It was pointed out that although there was no readily available screening test current donor exclusion criteria will reduce the potential risk associated with some groups eg IV drug abusers.

4.5 The Chairman summarised the discussion as indicating the Committee's need for a structured set of questions about the epidemiology, transmission and natural history of Hepatitis G, and a strategy to answer those questions . In order to take this forward it was agreed that Dr Rejman should get a subgroup together to look at what research needs to be done in the light of the discussion. BOB PERRY IS ON. PLY

Action : Dr Rejman to convene a subgroup to look at research into hepatitis G. Members were identified during the late stages of the meeting.

5. Minutes of the Seventh MSBT Meeting

The minutes were agreed, subject to the substitution of "feasibility " for "viability" in the second sentence of paragraph 8.8.

6. Matters arising from the minutes not dealt with as separate items :

- minute 6.1-6.5 : arrangements for reporting transfusion events.

6.1 It had not been possible to introduce the new system in April, as planned. But it was expected that it would start shortly, following a meeting with an interested group.

- minute 6.7-6.8: Fresh Frozen Plasma

6.2 Paper MSBT 8/5 was produced in response to concerns raised by Dr Robinson. SD trials were unlikely to be completed until October/November 1996, and Methalene Blue trials seemed likely to be further put back. Octapharma might obtain a licence for their SD-plasma (Octaplas) by October. This posed the question of the comparative

safety of pooled plasma treated in this way and FFP from individual UK blood donors.

6.3 In several other parts of Europe, inactivation or quarantining of FFP was mandatory. There had been no discussion on this topic in the Bio-Technology Working Party, therefore there was no formal European position.

6.4 Dr Robinson reported that clinicians liked the product produced from pools from 200 UK donors, and there appeared to have been no adverse reactions. This was thought far safer than the Octapharma pooled product. The NBA hoped to have a model for residual risks by July, and also by then more clinical information about current trials.

6.5 The committee concluded that FFP was capable of transmiting viruses, despite exclusion of at risk donors and serological testing of donations. Pooling donations significantly increased risks, and inactivation processes only destroyed some viruses. Clinicians were currently being left to decide the balance of risk/advantage to individual patients. Rather than make an immediate decision, eg to introduce quarantining or await effective viral inactivation processes, it was agreed to defer a decision until the July meeting, when further data on action currently in progress would be available. RSA/CVP

ACTION - Dr Robinson to provide further information for next meeting

- minute 6.9 : tissue banking review

6.6 Following a submission to Ministers, options for the establishment of a national regulatory authority were being examined. There should be a limited consultation exercise later in the year.

- minute 6.10 - 6.12 : Guidance on the Safety of Transplantation of Human Tissues and Organs

6.7 The Committee welcomed the Guidance as a very helpful clarification of earlier safety recommendations. The only caveat was that Annex 2 included criteria for HIV exclusion which were in operation when the document was being prepared but which had now been superseded. This would be corrected when the document was reprinted.

- minute 6.13 : Guidance on the Collection, Storage, and Infusion of Bone Marrow and Stem Cells

6.8 The draft guidance had been amended since the last MSBT meeting and submitted to Ministers, who had agreed to a limited consultation. The draft would therefore be sent to bodies such as the Royal Colleges, professional bodies and the blood transfusion services at the end of May, requesting comments by July. A report would be

made to MSBT.

- minute 7.1-7.8 : CJD

6.9 The Chairman introduced the topic by saying that there was a need to be clear about whether there was a relationship between CJD and blood transfusion. There were two issues to be considered. First, whether there should be a "lookback" study and secondly, the deferral from blood donation of relatives of patients dying of CJD.

6.10 On the first question of whether a "lookback" study should be instigated, the Chairman referred to a letter from Dr Will who reported that the Edinburgh Surveillance Unit had identified 50 patients with CJD who are understood to have previously given blood. It might therefore be possible to determine where those units went and through the NHSCR, identify whether recipients were alive, what they died of and then cross check them with the Edinburgh register to see if there were any matches. There would be no question of contact with any patients or GPs. The first step would be to develop Bob Will's proposal into a research paper. Ethical clearance would be essential given the implications.

6.11 Dr Robinson supported the proposal saying that it was crucial that it should be anonymised. Of the 10 new cases of CJD variant, one was known to have been a blood donor. There was lack of information on transmissibility through transfusion in other animal species, including cattle. On current evidence however it appeared that buffy coats played a role and if the human agent was related to the bovine agent then the possibility of removing buffy coats from blood could be explored.

6.12 It was suggested that further specific experiments relating to transfusion needed to be done using cattle including on whether buffy coats were relevant, since removal of these from blood for transfusion was a viable option. SEAC had previously been asked for advice and it might be appropriate to ask them again.

6.13 It was agreed that the CJD surveillance unit and the Blood Transfusion Services would prepare a protocol to be submitted to the Health Departments.

6.14 The second issue concerned how wide the deferral of relatives of patients dying of CJD should operate. It was suggested that the BTS considered that the current COE requirement of "those have a family history of CJD" was unclear and probably too wide. After general discussion it was proposed that exclusion should be confined to parents, siblings and children of sufferers. However it was pointed out that exclusion criteria must follow the COE requirements.

6.15 The Chairman concluded that this was a matter that needed to be clarified but the consensus of the committee was that the exclusion should apply to children, parents and siblings. At this point the Chair was taken over by Professor Zuckerman.

6.16 Dr Purves stated that paper 8/3 gave the details of the CPMP Biotechnology Working Party deliberations which he had reported to the MSBT in January. He

informed the Committee the Working Party may raise this matter again in the week commencing 6 May and that he would report the results to the next meeting of MSBT.

6.17 Dr Robinson reported on the recent meeting in Edinburgh following the announcement of the new CJD variant.

Action : Dr Robinson and colleagues from the UK Blood Transfusion Service to prepare a protocol together with Dr Will.

7. Virological screening of UK blood donations (including HTLV-1)

7.1 There was current media and Ministerial interest in HTLV-1 testing.

7.2 Dr McClelland and Dr Robinson had thought it sensible to defer production of their promised paper (paragraph 8.7 of minutes of last meeting) until they could take account of the view taken by SAACTI at a meeting now being held on 14 May. They intended to present options and outline their implications, as well as indicating what might be feasible if a decision were taken to introduce testing. The Chairman stressed that it was important that the paper be available prior to MSBT's meeting in July.

7.3 Recent interest in Abbott IMX testing was also mentioned. At earlier MSBT meetings their had been concerns that the IVD directive might not be stringent enough. A meeting representing the relevant interests set up by the Department had nominated a steering group to look at validation of test kits and at practice in the field. The group's report should be completed by the end of the year. MSBT's views would be sought before the document went forward to Ministers.

ACTION : Drs McClelland and Robinson to produce the paper for next meeting (para 7.2).

8. Parvovirus B19

8.1 Members were not aware of any country currently screening blood donors routinely for Parvovirus B19.

8.2 It was agreed that a combination of selective screening and gamma irradiation - which inactivates B19 - would be the best way of protecting vulnerable people, such as non immune patients with sickle cell disorder and haemophilia patients who are HIV positive, from the virus.

ACTION - Dr Robinson to investigate the logistics of selectively testing for, and inactivating, B19

9. Anti-HBc study

9.1 Dr Robinson provided members with a copy of a progress report on the study by Cambridge and South Thames into the significance of HB, Ag negative donors with isolated anti-HBc or anti-HBc with low and high levels of anti-HBs. Donors had been identified and the lookback stage was under way, with ethical committees approval.

9.2 The committee recognised this as an important study and looked forward to receiving further reports.

ACTION : Dr Robinson to keep committee advised of developments and to double check some of the details

10. Other EU Activities relevant to the Committee

A meeting with the two European plasma fractionator associations has been organised for the May meeting of the Biotechnology Working Party, and PCR testing is one of the topics to be discussed.

ACTION - Dr Purves to report the outcome of the meeting with the European plasma fractionator associations to MSBT

11. Any other business

No other business was raised.

12. Date of next meeting

The next meeting would be held in July, on a date to be arranged.

ACTION - Secretariat to arrange next meeting