NATIONAL STUDY ON SURROGATE NANBH MARKERS IN BLOOD DONORS

Minutes of the meeting on 9th June 1989.

Present: Dr Gunson, Dr Anderson, Dr Shwe, Dr Contreras (Chair), Dr Mijovic, Dr Paver, Dr Raafat, Dr Barbara (Sec.), (for Dr Craske)
(Copies of tabled reports were available at the meeting).

Apologies: Dr Martlew, Dr Lee, Dr Fraser
(to be circulated with tabled papers, in addition to these minutes)

1. Matters Arising

1.1 The freezer from Manchester will be delivered to NLBTC soon.

1.2 Dr Raafat reported that Prof. Thomas will perform PCR for HBV DNA on "anti-HBc-only" samples. ACTION

1.3 Anti-mitochondrial antibody tests (but not anti-smooth muscle) will be available for donors with persistently elevated LFTs of unknown aetiology.

2. Progress Reports

2.1 Dr Gunson tabled a report (Report A) from the Army Blood Supply Depot which showed ALT distributions in 1650 donors which closely resembled the data from Bristol and NLBTC. This data is confidential.

2.2 Manchester; Dr Shwe (Report B). Manchester Royal Infirmary (MRI) results for ALT continued to show significant discrepancies from Bristol and NLBTC results. MRI used a 'parallel analyser' designed for patient samples likely to show very elevated LFTs. This analyser was not appropriate in the donor context. This in itself proves to be a significant finding in relation to standardisation of methodology if routine screening was ever to become mandatory.

2.2.1 Review of the data showed that the history taking category 'occupational hazard' required sub-division into 'hepatitis exposure' eg with nurses and 'other hazard' eg solvent exposure.

2.2.2 A discrepancy in anti-HBc results from Manchester and NLBTC for one donation was due to the low level of reactivity and assay

variability.

2.2.3 Donors with elevated ALT showed no significant difference in anti-CMV positivity rate from donors with normal ALT. There was no correlation between elevated ALT and high anti-EBV titres.

2.3 Bristol Dr Anderson (Report C). Obesity and high alcohol intake appeared to relate to elevated ALT. Fewer control donors admitted high alcohol intake than at Manchester. There were significant changes in ALT levels on follow-up (control donors showing elevations and, even more so, 'elevated' donors showing reductions) and some of these changes were considerable.

2.4 NLBTC

2.4.1 Dr Mijovic (Report D). Bristol and NLBTC ALT results continued to show close agreement. Manchester results will require separate analysis.

2.4.2 Dr Barbara (Report F). 1 in 150 anti-HBc negative donors were repeatably anti-HCV positive. 2.2% of 64 NLBTC donors with elevated ALT were anti-HCV positive. Dr Barbara received additional data from NLBTC during the meeting for anti-HCV rates in anti-HBc positive donors; the revised figures for this data (following repeat testing) is 4.4% of anti-HBc positive donors have given positive results for anti-HCV (1 in 23).

To date, the anti-HCV test provided consistent results and was convenient to perform. In a typical run the cut-off OD value would be approx 0.5; the kit positive control = 1.2 and most negative samples have an OD approx = 0.02. However 2% of samples have ODs of 0.2 to 0.3 and their significance at this time is unclear; we assume that the cut-off has been selected to provide specificity rather than sensitivity since confirmation methods as yet, have not been finally settled.

3. Any Other Business

3.1 Dr Gunson asked Dr Barbara to provide a summary of anti-HCV testing progress for a meeting of the Committee of the Virological Safety of Blood on 3rd July 1989. — Dr Barbara

3.2 Dr Barbara brought the paper by Lai et al (Blood 73 (1989) 17-19) to the attention of the committee. This relates to HBV DNA detection in Sardinian blood donors with or without anti-HBc. The data suggested the existence of genetic variants of HBV that might be responsible for some NANBH.

3.3 It was agreed that results from this multicentre study could be reported verbally at local meetings or seminars but not provided in a written form or as posters, at this stage. We would aim to submit abstracts for presentation at the ISBT/AABB meeting at Los Angeles in October 1990.

3.4 Funding for anti-HCV testing

Since sample retrieval and assay was very labour intensive, Dr Gunson would check whether any DoH study funding was still available and if not, would approach the Dept. of Health for financial help for NLBTC's anti-HCV testing. — Dr Gunson

3.5 If donors in the study did not respond to requests for follow-up after 3 letters, no further attempts to contact them would be made.

3.6 'Look back'

Because of the enormous effort involved and the lack of cost effectiveness, we would not attempt to follow-up the recipients of surrogate marker-positive donations, even though the ethical committees had only witheld permission for checking the recipients of the donations tested during the study, and not the recipients of previous donations from 'surrogate-positive' donors. Although valuable scientific information might be derived from 'look-back', this might constitute the basis of a separate study for which ethical permission and funding would be needed.

3.7 Management of 'surrogate marker-positive' donors — RTC

3.7.1 Anti-HBc positive donors with <100 miu/ml of anti-HBs should be offered one dose of hepatitis B vaccine. Long-standing donors with anti-HBc as their only marker might also be offered one dose of vaccine. If such donors refuse the vaccine or do not produce a response >100 miu/ml of anti-HBs they should be withdrawn. If they produce >100 miu/ml anti-HBs they should be safe as donors.

3.7.2 Donors with elevated ALT (> 1.5 x ULN) — RTC

If the ALT is >70 iu/l on two occasions they should be counselled and deferred with the option of flagging the records for review in 3 months for checking whether weight loss and/or reduction in alcohol intake, where appropriate, have resulted in reduction in ALT level. They would only be finally withdrawn, if ALT is still >70 iu/l, at this stage.

3.7.3 Donors with confirmed anti-HBc and ALT >70 iu/l should be withdrawn.

3.7.4 Donors positive for anti-HCV

Repeatable anti-HCV positive or "grey-zone" donors should be flagged, without counselling* or notification. Plasma to be stored frozen. Future donations to be treated similarly pending decision on the significance of the anti-HCV assay. — RTC

3.8 Analysis of data and statistical assistance

Dr Barbara to contact Janet Mortimer and introduce her to Dr Raafat who will convene a meeting at WEDC for: Mrs Mortimer
Dr Raafat
Dr Mijovic
Dr Shwe
Dr Anderson
Dr Paver
Dr Howell
and Dr Barbara to explore the best ways of analysing the scientific and clinical data from the study. — Dr Barbara Dr Raafat

4. Date of next meeting

To be decided when further anti-HCV data are available. — Dr Contreras Dr Raafat

*See attached comment

Dr John Barbara
Secretary
9th June 1989
jb/uhm

*Anti-HCV reactions and donor counselling

On reflection and after discussion with Dr. Hewitt, consultant in medical charge of Microbiology, and Dr. Christine Moore we feel that the anti-HCV results should not be witheld from the donor at counselling, especially if they corroborate one or both surrogate marker findings. Notification would include emphasis that the test is still in the research phase, as they were informed at the beginning of the trial. Findings may not be 'absolute' but are extra evidence suggesting that the donation is unsuitable for transfusion. We think this will reduce rather than increase doubt and worry on the part of the donor. Provided Ortho Diagnostics allow us to do so, we think that the GP should also be informed of these results, as research findings.

Dr. J. Barbara; Dr. A. Raafat