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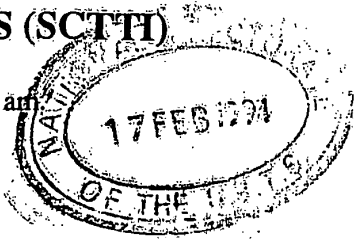
NBA/E 6/94

UK BTS/NIBSC STANDING ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED INFECTIONS (SCITH)



Minutes of the meeting held at NLBTC, Colindale, on 18th January 1994 at 10.30 am.

Present:	Dr. F. Ala	(Chairman)	Dr. E. Follett	
	Dr. J. Barbara	(Secretary)	Dr. R. Mitchell	
	Prof. J. Cash		Dr. P. Mortimer	
	Dr. H. Gunson		Prof. R. Tedder	
	Dr. M. Ferguson	(for Dr. P. Minor)	Dr. L. Williamson	
	Dr. P. Flanagan			

Action

1. **The minutes of the previous meeting were approved.**

2. **Matters arising**

2.1. Letter from Dr. Contreras to Dr. Gunson re reappraisal of decision not to screen for anti-HBc.

This letter, with two others (one from a haematologist in the North of England asking about the position with the Medical Defence Union and liability, and a second from a Liverpool solicitor advising the Department against their decision because of the projected value of screening) were forwarded to DoH to be raised at the next meeting of MSBT.

Mr. Sackville will be arranging a meeting with Dr. Gunson.

In the discussion that followed, these points were made:

2.1.1. Prof. Tedder cited a joint analysis of the past 10 years reported PTH cases at NLBTC. Of 22 cases of PTH-B, 18 involved donors with anti-HBc as sole HBV marker (usually at the 'tail-end' of carriage) and 4 were due to donors in the early stage of acute HBV infection. He understands that Dr. [redacted] feels there is gross under-reporting of PTH-B and UCH has been investigating between 4 and 5 possible PTH-B cases in the past 18 months. 1 case of classical PTH-B took 9 months to be 'discovered' by the patient's GP.

He, like others, recommended testing the donor panel for anti-HBc and then testing only new donors.

The importance of testing archived 'index' sera, as well as follow-up sera, from implicated donations was re-iterated.

2.1.2. Dr. Mitchell commented that Dr. Metters suggested that GPs might be asked to improve their reporting, but the committee felt that this would probably not be successful.

Dr. Mitchell has had approximately 1 PTH-B case reported per year up to 1989 and no other cases subsequently. [redacted]hough this might reflect a decline in the intravenous drug use risk-factor in Scotland, whereas 'tail-end' HBsAg carriers from HBV endemic countries may be more preponderant elsewhere.

2.1.3. Dr. Barbara provided a preliminary analysis of the returns from RTD's relating to PTH-B cases. Returns are awaited from 8 centres (Dr. Ala to send a reminder). From the returns it appears that approximately 10 cases are reported per annum in the UK, which was [redacted] estimate in his original analysis when the question of anti-HBc screening was first raised. This would obviously be a considerable underestimate of the actual number of cases. **Dr. Ala**

Action

2.1.4. It was decided that when all the returns were received, Dr. Barbara would analyse them in detail and prepare a further paper for MSBT formally suggesting that only 'new' donors be screened for anti-HBc once the existing donor panel has been tested. **Dr. Barbara**

2.1.5. Prof. Cash questioned the cost-benefit of anti-HBc testing, but members felt a similar question pertained with anti-HIV, anti-HCV and anti-HBV testing of previously-tested donors because of the low seroconversion rates involved.

2.1.6. Dr. Barbara's analysis of returns from RTDs indicated 4 instances of litigation concerning 'anti-HBc positive' transmission of PTH-B. Prof. Tedder is aware of others including one where transmission to the recipient was only discovered because of icteric secondary 'house-hold' transmission to his daughter. Prof. Cash felt we would not be liable to charges of negligence but Dr. Ala and Prof. Tedder felt we could be liable under product liability. Dr. Gunson knew of no test case involving anti-HBc. Prof. Cash felt that a 'no resource' plea could apply in Europe.

2.1.7. Dr. Ala will write to [redacted] to ask how PTH-B reports that she receives might be integrated with individual reports to Centres, and her opinion about the extent of under-reporting. **Dr Ala**

2.2. **Dr. Ala's pre-prints of follow-up studies on anti-HCV positive donors** (previously circulated)

These were noted, as was the likely lack of consistency regarding management of individuals infected with HCV.

Dr. Mortimer suggested that a symposium might be held to discuss this topic. Dr. Ala will write to Dr. Flanagan formally suggesting that the matter be raised with the standing committee on care and selection of donors. Dr. Flanagan (who, as a member of that committee and the SCTTI, can act as a link between the two) pointed out that, although only pre-donation selection had been addressed to date, post-donation care should be within the former committee's remit. **Dr. Ala**

Because of the variability of the results of published work, the committee welcomed the idea of such a meeting.

2.3. Dr. [redacted] response re CPHL charges for virology reference work.
Dr. Ala has written to Dr. [redacted] and, in October 1993, was informed by [redacted] personal assistant that he would receive a 'substantial reply within 10 days'. Since this has not been forthcoming, Dr. Ala will give a copy of his letter to Dr. Mortimer, who will take the matter up with [redacted] **Dr. Ala** **Dr. Mortimer**

Prof. Tedder noted that the relevant Health Service circular stated unambiguously that contracts for reference work should be in place by April 1994.

Dr. Flanagan understood that CPHL would make no charge for reference work for syphilis, nor for HIV (which is centrally funded) but would charge for HBV and HCV confirmation. Dr. Mortimer thought that this was essentially the case.

[redacted]

Action

2.4. Dr. [redacted] letter regarding donor re-admission protocols.
Dr. [redacted] asked if it was really necessary to refer for confirmation a sample which is screen test negative by a current assay (for any of the mandatory tests) although a previous donation (possibly tested with a different generation or manufacturer's test) was repeatably reactive but confirmed as false-positive. Could not the latest donation be issued regardless? The committee, while appreciating the low risk of infectivity in such a situation, felt it safest if the recent protocol for false-positive donor readmission was adhered to.

Dr. Ala will write to [redacted] to this effect. — Dr. Ala

2.5. **Lyme disease *(Borrelia burgdorferi)***
Dr. Barbara had been asked to respond to a question for BMJ regarding when it was acceptable for an individual to donate blood after suffering Lyme disease. The committee agreed with the response 'when fully recovered' and Dr. James has endorsed this as consistent with current BTS guidelines.

Dr. Ala commented that policy varies with, for example, Sweden readmitting while France has a permanent exclusion even though the infection can be successfully treated (usually with penicillin).

2.6. **Dual anti-HCV ELISA to predict infectivity**
Dr. Williamson reported that all RIBA-positive sera reacted on each of the pairs of anti-HCV ELISAs; some RIBA indeterminates did not, and reactives in the study will be tested by PCR at Cambridge, this to be jointly funded by the 3 centres involved (Cambridge, Brentwood and Colindale).

2.7. **Letter to kit manufacturers re QC of plate coating and sample addition**
This letter has now been sent out by Dr. Barbara and Dr. Mortimer. The outcome will be reported when replies have been received. — Dr. Barbara, Dr. Mortimer

2.8. **Submission of results of national evaluation of anti-HBc kits for publication.**
A draft manuscript is almost complete. The committee agreed that manufacturers should be identified with their results as they all appear to know their comparative performance anyway! They will each be sent a pre-print copy on acceptance of the paper. — Dr. Follett

Dr. Gunson has sent details of their own results to those manufacturers who asked for it. He will send this information to Dr. Follett so that data on the outcome of any revisions to 'cut-off' calculations can be included in the manuscript. — Dr. Gunson

Dr. Mortimer's suggestion to comment in the Discussion section that 'hard and fast conclusions should not be drawn from this comparatively small study' was accepted.

3. **Mr. Slopecki to join SCTTI sub-committee chaired by Dr. Barbara.**
The committee welcomed the announcement that Mr. Slopecki had accepted the invitation to serve on the subcommittee. This will provide enhanced liaison and consistency between ACTTI and NBA initiatives.

4. **Abbott anti-HCV ELISA-3 and other kit evaluations.**
The Abbott anti-HCV ELISA-3 was not cited in the BPL license. However, Dr. Gunson informed the committee that the MCA might be satisfied (in the short term) with a generic list of microbial screening assays. New modifications can then be introduced *without delay* if suitably validated, with NBA maintaining a register of the various tests in use, and where they are being used. The definition of 'minor variation' will need to be agreed with MCA. Longer term, the question of kit validation will need to be resolved.

Action

England is in need of a validation/approval system similar to that in Scotland, preferably avoiding duplication of effort. While VRL (CPHL) can assess sensitivity, the BTS will need to assess specificity because of the large number of samples required. Dr. Mortimer raised the question of funding the increasing number of kit evaluations; Dr. Ala will write to the Medical Devices Directorate (MDD) to question the need for full validation of sensitivity for each minor variation of an assay. Where it is considered necessary, the service would presume that VRL will be appropriately funded by MDD to cater for the increased rate of kit development. To date, MDD only fund VRL for evaluations of new kits with 'major' differences from existing ones. — Dr. Ala

In 1997 kit licensing will be Europe-wide and the UK's position (including that in relation to BPL's requirements) will have to be consistent.

5. **Murex HBsAg GE16 kit vs VK21 kit**

Dr. [redacted] has asked if the new GE16 HBsAg kit is approved for routine use. This kit was not available in time for Dr. Mortimer's current evaluation of HBsAg kits. However, Scotland has approved the kit and experience to date is favourable, especially as sample addition monitor and colour changes for other key assay steps are incorporated.

Discussion about the general principles of kit approval resumed. A rapid, simple and reliable approval system, (consistent with the Scottish procedures), was required. Dr. Gunson will liaise with Mr. Slopecki regarding consistency of NBA and SCTTI endeavours in this field. Definition of specifications for kit validation will also simplify matters for the NBA working party on the separate topic of kit *batch* validation, which Dr. Barbara will be chairing. — Dr. Gunson

In the meantime Dr. Gunson will inform transfusion centres that the final responsibility regarding adoption of a test rests with the medical director. He will also point out that both the Murex GE16 HBsAg assay and the Abbott anti-HCV ELISA-3 are acceptable on the basis of Scottish data, subject to his having sight of the Scottish evaluation report. — Dr. Gunson

6. **Syphilis testing**

The question of whether we need to retain syphilis screening will be referred to Dr. Barbara's sub-committee which will seek evidence from appropriate experts.

Dr. Gunson felt that cessation of syphilis screening would adversely affect public relations; Prof. Cash felt that ultimately this may turn out to the most important aspect of the question.

7. **Testing pools of samples.**

Despite the current political overtones associated with fears of 'sub-optimal' screening of blood following recent German problems, the committee felt that the feasibility of testing of pools should at least be assessed. Financial constraints in the NHS were increasing and cost savings vs the likely 'miss' rates from pool screening should be examined. Even with anti-HCV assays (where end-point dilutions are lower than for other assays) only very early seroconverting individuals would be likely to present difficulties when tested in a pool. Would these be more frequent than the 'misses' due to inherent variations of different assays at the margin of marker detectability?

One practical problem of pool-testing is that sample identity and information transfer integrity will require provision of special computer programmes. However, specificity increases when pools are tested. Dr. Williamson suggested that pool-testing might be restricted to previously-tested donors, retaining 'full sensitivity' by individual sample testing for new donors.

Dr. Ala and [redacted] have prepared a preliminary draft protocol on pool testing which they will circulate to members. Dr. Follett has also been preparing a draft assessment protocol. A three centre evaluation may be sensible. Dr. Ala identified NE Thames and Birmingham as willing to participate and asked if any third centre would be interested. — Dr. Ala

Action

The committee expressed a strong feeling that pragmatic approaches to enhancing cost-effectiveness *should* be explored in view of current financial constraints, and the topic should not necessarily be considered as 'just for developing countries'!

Prof. Tedder commented that if pragmatism was on the agenda, why not consider economical kit modifications such as the well validated 'dilution-centrifugation' agglutination assays, especially if image analysis can be incorporated? The anti-HIV modification was particularly successful, an observation endorsed by Dr. Follett.

8. **Bacterial studies and 'Bac T Alert'.**

8.1. The Bac T Alert (Organon) system for bacterial detection was discussed.

8.2. Dr. Ala suggested its use in a study of 4° storage vs 20° for 24 h holding of blood.

Statistically, examination of 5,000 blood units for bacterial contamination in each arm of the study (i.e. 4° vs 20°) would suffice. Aseptic sampling might require a special docking device (e.g. a 'Y' piece). Access to Bac T Alert systems would need to be identified.

9. **Protocol for reporting bacterial transmission.**

Dr. Mitchell has written to Dr. Napier (BCSH) about reporting of bacterial transmissions by hospitals. The problem is the definition of criteria for initiating a report. Dr. Barbara suggested that even if the definition was 'loose' (i.e. each case judged on its merits), once standardised guidelines and report forms were available, comprehensive reporting might be more likely. Prof. Cash and Dr. Mitchell will send a draft proposal to Dr. Gunson, to consider in conjunction with Dr. Uttley's initial draft. Transfusion Centres will then be sent copies of the guidelines and reporting forms following liaison with Dr. Napier.

Prof. Cash
Dr. Mitchell
Dr. Gunson

10. **Working standards for anti-HCV and anti-HIV.**

Dr. Ferguson reported on the NIBSC/BTS collaborative studies. With Dr. Garrett (for anti-HIV), preliminary distributions of candidate standard preparations are planned for 1994. Potential assay discrepancies (especially with type 3 capture assays) were noted. For type 3 tests, the standard may have to be prepared in different diluents.

For anti-HCV, 4 pools (each made from at least 11 RIBA-2 positive units) have been prepared and assessed at Centres. The UBI kit consistently 'misses' the 1 in 20 dilution of these pools and NIBSC is awaiting a response from Organon in relation to this observation.

11. **'Look-back' on recipients of blood from donors subsequently shown to be anti-HCV positive.**

Prof. Cash noted that Dr. Dusheiko advocates such a look-back because of the potential benefits of interferon + ribavirin treatment, especially if initiated early in the course of infection. Initially this might be restricted to notification to hospitals of such cases; even so, funding would be required, probably involving a research grant application.

Prof. Cash and Dr. Ala will seek their local hepatologists' opinions on the value of treatment (a 60% HCV clearance rate has been suggested) and report back to the committee.

Prof. Cash
Dr. Ala

Prof. Tedder and Dr. Barbara will examine protocol options for such studies.

Prof. Tedder
Dr. Barbara

The committee supports the concept and encourages grant seeking for this potentially clinically beneficial undertaking.

Action

12. Any other business.

12.1. Anti-HIV/anti-HTLV combined assay.

Dr. Flanagan reported that this assay was formally introduced at Leeds at the end of November 1993. With the first batch of reagents, the IR rate was 0.36% and the RR rate 0.16% in 20,000 samples. The next batch appears to have similarly specificity. Of the 36 RR samples, none confirmed positive for any of the 4 agents involved.

12.2. Requirement for permission to run trials?

Prof. Tedder asked if it was necessary to obtain SCTTI permission for running trials of assays or for market prevalence studies at Centres. The chairman felt it was not compulsory, but notification of such trials would be a courtesy. The question might require special attention if the trial involved replacing an existing assay, especially if an additional marker (e.g. anti-HTLV), was involved in combined tests.

Prof. Tedder felt that additional local studies of anti-HBc prevalence were warranted and had a specific concern about residual PTH-B in his own hospital. The committee felt that provided a defined study period was stated such studies may well be useful, possibly extended to more than one Centre.

A further question of whether screening policies might require 'tailoring' to local donor epidemiological conditions was not resolved but was considered likely to be unworkable.

12.3. CJD and donor selection

Prof. Cash asked whether human pituitary hormone treatment as an exclusion for blood donors only related to fertility hormones. Dr. Flanagan will ask Dr. James of the donor selection committee and will then inform SCTTI. Dr. Flanagan

12.4. Reference Laboratories

Prof. Cash felt that minute 9 of the previous meeting did not go far enough in stating the need for definition of the specifications for a confirmatory laboratory. Would an RTC comply? Dr. Barbara asked whether all existing external Reference Laboratories comply? Prof. Cash considered that once specifications had been set, the quality and consistency can then be audited (as with screening laboratories).

Dr. Mortimer stated that, in future, Reference Laboratories will require accreditation. In the interim he will provide a draft list of requirements for effective confirmatory testing in Reference Laboratories.

12.5. Trial of SD treated FFP

Dr. Gunson reported that MCA will be issuing a CTX for a trial of solvent-detergent treatment of FFP prepared from a pool of 1000 donations. Birmingham, Cambridge and Leeds RTCs will participate in the trial. Edinburgh will not take part because of concerns raised by HAV transmission associated with Octapharma factor VIII. Dr. Mortimer and Prof. Cash felt that parvovirus testing was required.

Dr. Williamson will send samples to laboratories involved. Dr. Williamson

12.6. Retirement of Vi Rawlinson

Dr. Gunson informed the committee that Vi Rawlinson will be retiring at the end of March 1994. She will prepare her remaining returns in conjunction with Mr. Slopecki who will then take over the compilations in conjunction with Dr. Barbara. Collation of HBsAg testing data will also be undertaken, although the register of HBsAg positive donors will continue to be updated by Dr. Barbara and Dr. Howell. Eventually it is also intended to provide central collation of reports of post-transfusion infections.

Action

12.7. SCTTI and Tissue Banks

Prof. Cash enquired about the role of SCTTI in Tissue Banking.

Dr. Williamson will write to David Pegg, Chairman of the British Association of Tissue Banks to obtain a draft copy of their guidelines for microbial testing of tissues. **Dr. Williamson**

Dr. Ala and Prof. Cash will bring this item to the attention of English and Scottish Directors, respectively. **Dr. Ala** **Prof. Cash**

12.8. Priorities for the SACTTI subcommittee on testing

Dr. Ala will discuss with Dr. Barbara the subcommittee brief regarding kit evaluations and syphilis screening. **Dr. Ala**

13. Next meeting of SCTTI

This will be held at Birmingham RTC on 19th April 1994.

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