Dr Allen 5

Mutli-Centre Study of ALT and anti-HBc Screening of Blood Donations

Minutes of meeting of steering committee, Manchester, 8th June 1988

In attendance:

Dr. Harold Gunson, Dr. Vanessa Mardlew, Dr. Kim Shwe } NBTS, Plymouth Grove, Manchester M13 9LL

Mr. Seneviratne — Department of Biochemistry, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL

Dr. Ian Fraser — SWRTC, Southmead Road, Bristol BS10 5ND

Dr. Marcela Contreras, Dr. John Barbara } NLBTC, Deansbrook Road, Edgware, Middx HA8 9BD

ACTION

1. Dr. Gunson proposed that Dr. Contreras chair the steering committee with Dr. Barbara as Secretary; both accepted since the proposal was unanimously backed.

2. North Western RHA is to be banker for the study; £72,000 credit has already arrived from DHSS. Dr. Gunson will monitor the budget as requested by DHSS. — Dr. Gunson

3. Centres participating in the study:
Manchester (not including Lancaster)
Bristol
Edgware
(Edinburgh has withdrawn from the study)

4. Comments from the Referees* reviewing the Grant application, requiring attention by the committee. (*summary distributed at the meeting).

4.1. Making the population sample representative of the donor population overall:

4.1.1. Gender ratio to be approx 1:1.

4.1.2 Age range varies around the country.

4.1.3. Centres to match the ratio of 'industrial to 'public' sessions in the sample to that of their population.

4.1.4. The total donor sample population will be checked to see that it conforms with the survey data collected by Janet Mortimer (CPHL).

4.1.5. A 'selection' bias in the donors involved in the study is unlikely as donors have to 'opt-out' rather than 'opt-in'.

4.1.6. The first 200 donors at each Centre are to be checked for consistency with the overall donor panel.

ACTION

4.2. ALT 'cut-off'?

4.2.1. To avoid waiting for completion of the study to obtain a percentile for cut-off estimation, a cut-off of 45 iu/l will be adopted, regardless of gender or of the possibility of regional differences in alcohol consumption. (45 iu/l is also the usual North American 'cut-off").

4.2.2. Dr. Contreras would arrange with Dr. Mijovic (NLBTC) and Dr. Barbara for collections of a panel of 20 serum samples with a range of ALT levels. These samples are to come from a roughly equal number of males and females. Samples would be coded by Dr. Contreras and held at 4°C. Dr. Contreras to arrange transport appropriately from BPL, so that simultaneous testing at the Centres would occur on Tuesday 28th June. (Testing at Southmead, Bristol, by David Goldie, Chemical Pathologist). — Dr. Contreras

4.2.3. The Biochemists from the 3 Centres will then arrange to meet, if necessary, in the light of the panel ALT results. — Biochemists

4.3. Will 'controls' in the study be matched to the 'positives'?

4.3.1. The committee felt this was impossible since age, gender, ethnic origin and socio-economic status would all be involved. Therefore the sample adjacent to a 'positive' would be chosen as a control.

4.4. Ultimate inferences from the study?

These will relate to follow-up test results (over and above ALT/anti-HBc) and donor's clinical status.

4.4.1. One referee advocated checking the recipients of ALT/anti-HBc "positive" donations. This had been the preference of Dr. Contreras and Dr. Barbara from the outset but ethical permission could not be obtained and the Referee's comment was not accepted by the DHSS.

4.5. Ethical problem with the issue of 'positive' donations

4.5.1. Manchester's Central District ethical committee has approved the study since mandated testing will have been carried out.

4.5.2. Bristol and Edgware will require ethical committee approval. Bristol normally approaches the ethical committee of each hospital individually. Dr. Fraser will use a copy of Manchester's ethical committee approval to try and obviate this. — Dr. Fraser, Dr. Contreras

ACTION

4.5.3. Permission from the donor for ALT and anti-HBc testing will not be sought since form NBTS 110 covers the requirements.

4.6. What is the size of the NANBH problem in transfusion recipients?

The committee felt this query was "begging the question".

5. Staffing approved in the Research Grant

5.1. Manchester: Clerical assistant; 8 months (clerk/typist grade).

5.2. Edgware: Senior Registrar; 8 months.
MLSO overtime to value of £1,000
Clerical Assistant; 8 months (clerk/typist grade)
Scientific Officer (Biochemistry); 3 months

5.3. Bristol: Medical Officer; 0.14 wte, 6 months
Clerical Assistant; 8 months (clerk/typist grade).

5.3. Bristol Southmead and Manchester Royal Infirmary: funding for ALT at rate of £1 per test.
i.e. £6,500 for ALT testing
Manchester: £3,000
Bristol : £3,000 (An RTC microplate method is in press. J. Clin. Path).
Edgware : £500 (performed on site, see Item 5.2.)

5.4. Anti-HBc: the original quotation of 85p per test from Welcome has been reduced to 50p + VAT + delivery. Dr Barbara will order 4000 tests to allow for 1,200 screen tests plus confirmations and follow-up etc. (1,200 tests rather than 900) will be done to compensate for the withdrawal of Edinburgh RTC from the trial). — Dr. Barbara

5.5. The following funding has been allocated for confirmatory testing on ALT 'positive donors:

5.5.1. £6,000 : Biochemistry and haematology
£12,000: PHLS (? and Dr. Tedder) for anti-CMV etc. (Dr. Contreras to approach Dr. Tedder and Dr. Mortimer to ascertain detailed breakdown of testing distribution and timing). — Dr. Contreras
2000
2000
£225 : Prof.Thomas (now at St. Mary's).

5.6. £6,000 was allocated for travelling, stationery and telephone charges.

6. Starting date:

6.1. Take on temporary staff for 1st August, 1988 for familiarisation/training: (see item 5). — Dr. Gunson, Dr. Fraser, Dr. Contreras

ACTION

6.2. Start screening on 1st September 1988.
(Ethical committees' approval and procurement of staff will be time consuming factors).

7. Management of funding

Likely to be on a 'recharge' basis with Centres paying their respective bills and then charging the study. Dr. Gunson will confirm this. — Dr. Gunson

8. Deliveries of samples to Edgware for anti-HBc testing

These are to be organised via BPL (Mr. Bailey is Transport Manager) with samples sent at a rate of 150-200 per week in phase with the ALT screening. Replicates of the samples from ALT testing will be sent for anti-HBc testing at NLBTC. They will be stored frozen and tested 'en bloc'. 1,200 samples will be chosen at Edgware at random for each Centre, using Random Number tables (Documenta Geigy). 400 samples will be chosen from each Centre's set of samples. — Dr. Gunson, Dr. Fraser, Dr. Barbara

9. Documentation of results

Dr. Barbara will prepare a form for recording of results, and will distribute copies to participants. Data to include: donation number, age, gender, date bled, OD vs ND, session name, public or industrial session, ALT and anti-HBc results. — Dr. Barbara

Dr. Barbara will arrange for production of address labels for distribution to each of the Centres to assist safe delivery to the Microbiology Dept., Edgware. — Dr. Barbara

10. Handling of Specimens

Serum will be separated and divided into two aliquots, one for ALT (1ml) and the rest for anti-HBc testing and any anti-HBc confirmatory tests.

11. If ALT is elevated:

further follow-up sample will be obtained at donor recall, for the special additional tests.

12. To obtain sufficient sample to ensure enough volume for testing and for storage of the remainder (for testing in parallel with follow-up samples) duplicate 'dry' sample tubes will have to be organised from donors entering the study. — Dr. Gunson, Dr. Fraser, Dr. Contreras

13. Investigating laboratories must endevour to store an aliquot of all "positive" samples for testing in parallel with follow-up samples.

14 'Special tests

Dr. Gunson will write to Prof. Zuckerman and Prof. Thomas to inform them that funding has been agreed for the study and to confirm what samples they require. — Dr. Gunson

ACTION

15. Sequence of testing.

The Senior Registrar will send weekly reports to participants so that anti-HBc positive donors can be recalled and re-tested with samples sent to PHLS/Dr. Tedder for confirmation. Anti-HBc positive samples which are negative for other HBV markers will be sent to Prof. Zuckerman and to Prof. Thomas — Senior Registrar

16. Other tests

Urinary neopterin and guanase will not be assayed. Dr. Gunson will approach Chiron to test for 'ALT-abnormal' and 150 or more control sera using the assay for the putative NANBH agent. — Dr. Gunson

17. Dr. Gunson will draft a letter to Dr. Kurtz (Oxford) for Dr. Fraser. — Dr. Gunson

18. Dr. Gunson will arrange printing of 10,000 donor information leaflets (incorporating the NBTS logo) via the 'anchester RHA printing department. Dr. Martlew suggested .hat these leaflets be amended to include: i) Centres telephone numbers in the logo; and ii) a note to the donors informing them of the delay in their receipt of results. These amendments were accepted by the committee. — Dr. Gunson

Dr. Contreras will ask the NW Thames RHA about printing, as a 'back-up' measure. — Dr. Contreras

19. Each Centre will inform its Medical Officers about the project. — Dr. Gunson, Dr. Fraser, Dr. Contreras

20. Medical examination of the ALT 'positive' donors will be by the Senior Registrar at Edgware and by Medical Staff at the other Centres. When the Edgware Senior Registrar is appointed a meeting to co-ordinate the details of the medical examination will be arranged.

21. The next meeting of the committee will be on Wednesday 4th August. Mr. Seneviratne will only attend if there are oblems with the ALT panel of 20 samples.

Dr. John Barbara
Secretary
15th June 1988
JB/rsb