NQH/23/3

A0994165.

20 SEPT 94

NATIONAL BLOOD AUTHORITY

REVISED REPORT OF THE NBS WORKING GROUP ON ALT TESTING OF PLASMA

1. **Background.**

1.1 Despite the fact that the EC have no requirement for the ALT Testing of Plasma for fractionation, the National Authorities in several European Countries demand ALT tests on such plasma prior to the importation of products.

1.2 France has had a formal requirement for ALT testing (as well as Anti Hbc) for several years; Germany, the largest single market, requires ALT testing. The actual wording of the German Regulations is not entirely clear, but to import plasma products into Germany any plasma donations with abnormal ALT results must be withdrawn. ALT testing of Plasma is also required in Austria, Italy, Spain and Switzerland, and is preferred in several other countries, e.g. Belgium. In countries requiring ALT testing, it is possible that products from non-ALT tested plasma may occasionally be given exemption to permit import under special licence for a limited period to alleviate a local shortage, but product registration and long-term import is not possible. Is this true? Perhaps MCA could confirm.

1.3 Testing of Blood Donations for ALT is not required in the UK. The Advisory Committee for the Virological Safety of Blood has considered the introduction of routine ALT tests on several occasions. On the final occasion, on 21 February 1922, they concluded that "... there was insufficient reason to justify a recommendation to Ministers that ALT screening of donated blood should be introduced in this country".

1.4 In order to supply the clinical demand for Factor V111 in the NHS, BPL has to fractionate a quantity of plasma which realises surpluses of albumin and immunoglobulin above the NHS requirements. With respect to albumin the potential surplus is 12,650 kg (which could rise to 14,000 kg with improved yields) and by 1996 the potential surplus of immunoglobulin could be as great as 900 kg.

1.5 Europe has not yet achieved self-sufficiency in blood products from voluntary unpaid donations as envisaged in the Directive 89/381 EEC. An export market is available, therefore, for surplus albumin and immunoglobulin which would benefit the NHS by an estimated £14 million.
Such exportation is dependent upon ALT testing of the plasma donations. Failure to export means that the surplus products (or the fractions in which they are contained) would have to be destroyed.

2. **Proposal.**

2.1 A sample of serum/plasma from ALL donations should be dispensed into an appropriate microplate under controlled conditions to a prescribed specification which is encoded to ensure positive identification of each sample and sent to BPL for testing.

2.2 The microplates should be placed in a freezer at -30° C or below and despatched to BPL with the corresponding plasma donations with an accompanying data disc to link the donor samples in the microplates to specific donations. BPL will determine the sample numbers which correspond to the plasma donations. The remaining sample numbers will not be linked to plasma donations.

2.3 **BPL will:**

(i) ALT test the samples at 37° C approximately 10-14 days prior to the pooling of the corresponding donations. (On average this will be four weeks after receipt of the samples). At the same time those samples without a corresponding plasma donation will be tested.

(ii) The cut-off value in the European Countries concerned is usually twice the upper limit of normal. After testing blood samples from 9,215 donors at three English RTC's the upper limit of normal was 50 iu per litre as determined at the 98th percentile. (Anderson et al. Transfusion Medicine [1992] 2, 301-310). Thus, twice the upper limit will be 100 iu per litre.

(iii) Carry out the following policy.
- Plasma ALT <100 iu per litre — full fractionation procedure.
- Plasma ALT > 100 iu per litre — withdraw the plasma donation and destroy

(iv) Notify the appropriate BTC who supplied the plasma of the actual result of any donations where the ALT is > 100 iu per litre.

2.4 **Blood Transfusion Centres will:**

(i) Adopt a donor deferral policy based on that proposed by the AABB on 27 August 1993. As there is evidence from the USA that many donors with high ALT retain abnormal levels, re-calling such donors is counter-productive. An ALT > 160 iu per litre may indicate hepatic dysfunction and donors with this level should be referred to their GP. The same applies to donors with two results > 100 < 160 iu per litre.

(ii) For the donors detailed in (i) above, write a letter to the donor informing them that one of the many screening tests routinely performed has fallen outside normal limits; that this result may indicate that they may have a liver upset and ask their permission of the donor for this information to be given to his G.P.
Specimen letters to the donors of whole blood and to the G.P. are attached (Appendices 1 to 4).

(iii) The donor's record will be flagged if the ALT is > 100 < 160 iu per litre. If the donor has a normal ALT 12 months after the date of the second ALT result at this level,

he/she may be re-entered as an eligible donor providing the current donor criteria are met. When the ALT is > 160 iu per litre, the donor is withdrawn.

(iv) There may be occasions when the donor has given a subsequent donation prior to receipt of the result of the ALT test (e.g. plateletpheresis). Under these circumstances, if there is an isolated abnormal ALT, subsequent donations may be fractionated, according to 2.3 (iii) above. The policy undertaken with respect to the donor will be in accordance with paragraphs 2.4 (i) to (iii) above.
There is no evidence that transfusion of blood from a donor with high ALT levels is harmful in the absence of hepatropic viral infection. The action taken is a public health measure on behalf of the donor.

3. Costs Involved

3.1 Blood Transfusion Centres.

(i) The costs are based on tests at 10 BTC's, they have been averaged and are for guidance only. They include London Weighting where appropriate but do not include overheads or provision for possible changes in computer software.

(ii)

		£
Staff. 0.5MLA	£4,500 + on costs + (London Weighting)	54,000
Microplates and lids	£3222 per 100,000	80,550
Freezer.	£2000 (devalued over 5 years)	4,000
Total:	per year	138,550

(iii) On average there will be 0.09% donors found to have ALT levels >160 iu per litre and 0.24% > 100 < 160 iu per litre. (See Appendix 5 - Anonymous study to determine ALT levels in approximately 10,000 donors at North London BTC).
The cost of the loss of approximately 8000 plasma donations and recruitment of replacement donors correspondence and documentation, has been estimated at £250,000 per year. There will be an additional cost for loss of FFP donations, possibly bringing this total to £300,000.
Total annual costs for BTC's is approximately £440,000.
Each RTC will agree a standard national price for this service.

3.2 **BPL**

(i)

		£
Capital	£200,000 (devalued over 5 years)	40,000
Staff	£60,000 per year	60,000
Consumables	£0.20 per test	500,000
Maintenance	£20,000 per year	20,000
	per year	620,000

Total Annual cost is in the order of £1.06 million.

(ii) An estimate for contracting out the ALT testing was £1.50 per test. In-house testing is fully justified at £0.62 per test.

4. **Implementation**

4.1 BPL will familiarise themselves with the various high through-put systems for ALT tests.

4.2 When the identification and linkage programme and ALT testing is available at BPL, North London BTC will carry out a pilot trial to an agreed protocol. BPL will agree the costs involved in this trial with North London BTC.

4.3 When the trial has been satisfactorily completed and a definitive procedure has been identified BPL will create a Working Group with representation from the 10 testing BTC's to develop and implement an operational plan.

Distribution:

Dr M Contreras
Dr H H Gunson
Dr A Robinson
Dr W Wagstaff
Mr R C D Walker

September 1994

NATIONAL BLOOD AUTHORITY

Oak House
Reeds Crescent
Watford
Herts WD1 1QH
Telephone: 0923 212121 (8 lines)
Fax 0923 211031

APPENDIX 1

Specimen letter to donor of whole blood with ALT > 160 iu per litre

Date

Address

Dear .....

One of the tests we carried out on the blood donation you gave on (date) was found to be abnormal. The test measures a liver enzyme called alanine aminotransferase (ALT). Higher than normal levels may be found in persons who drink a large amount of alcohol, who are overweight or who take strenuous exercise. It could indicate, however, that you have a liver upset.

For this reason I ask you not to give blood again at present and I recommend that you visit your General Practitioner so that he/she can advise you if you need further investigation or treatment. Could you please complete the form at the foot of this letter so that I have your agreement to send the results to your doctor. I stress that the remainder of the tests we carried out including the test for HIV ("the AIDS Virus") were entirely normal.

It may be possible to reinstate you as a blood donor in 12 months time if your ALT level is within normal limits. I should like to thank you for your support to the Blood Transfusion Service.

Name of Donor ..... (completed at RTC)
Address of Donor .....

I agree that you can send the results of the ALT test carried out on my blood donation to my General Practitioner who is Dr: .....
.....
.....

Signature ..... Date .....

NATIONAL BLOOD AUTHORITY

Oak House
Reeds Crescent
Watford
Herts WD1 1QH
Telephone: 0923 212121 (8 lines)
Fax : 0923 211031

APPENDIX 2

Specimen letter to donor of whole blood with 2 ALT results > 100 < 160 iu per litre

Date

Address

Dear .....

One of the tests we carried out on the blood donations you gave on (date) and (date) was found to be abnormal on both occasions. The test measures a liver enzyme called alanine aminotransferase (ALT). Higher than normal levels may be found in persons who drink a large amount of alcohol, who are overweight or who take strenuous exercise. It could indicate, however, that you have a liver upset.

For this reason I ask you not to give blood again at present and I recommend that you visit your General Practitioner so that he/she can advise you if you need further investigation or treatment. Could you please complete the form at the foot of this letter so that I have your agreement to send the results to your doctor. I stress that the remainder of the tests we carried out including the test for HIV ("the AIDS Virus") were entirely normal.

It may be possible to reinstate you as a blood donor in 12 months time if your ALT level is within normal limits. I should like to thank you for your support to the Blood Transfusion Service.

Name of Donor ..... (completed at RTC)
Address of Donor .....

I agree that you can send the results of the ALT test carried out on my blood donation to my General Practitioner who is Dr: .....

.....

.....

Signature ..... Date .....

NATIONAL BLOOD AUTHORITY

Oak House
Reeds Crescent
Watford
Herts WD1 1QH
Telephone: 0923 212121 (8 lines)
Fax 0923 211031

APPENDIX 3

Specimen letter to GP when donor ALT is > 160 iu per litre

Date

Address

Dear Dr .....

Name of donor .....
Address of donor .....

Your patient attended to donate blood on (date). We have found that a blood sample taken at this time showed an elevated alanine aminotransferase (ALT) result. The most common reasons for abnormal ALT levels are excessive intake of alcohol, regular strenuous exercise, obesity and liver disease.

The ALT value for your patient was .....iu per litre (the upper limit of normal is usually 50 iu per litre). I have withdrawn your patient's name from the donor panel and have recommended that he/she consults you, since with this ALT level I advise that he/she is referred to a hepatologist.

If the ALT level falls below 100 iu per litre and remains consistently so, and no abnormal liver pathology is found, it may be possible for your patient to be eligible to resume blood donations in 12 months time.

Thank you for your assistance.

Yours sincerely

Consultant

NATIONAL BLOOD AUTHORITY

Oak House
Reeds Crescent
Watford
Herts WD1 1QH
Telephone: 0923 212121 (8 lines)
Fax : 0923 211031

APPENDIX 4

Specimen letter to GP when donor ALT is > 100 < 160 iu per litre

Date

Address

Dear Dr .....

Name of donor .....
Address of donor .....

Your patient donated blood on (date) and (date) On both occasions we found that there was an elevated alanine aminotransferase (ALT) result. The most common reasons for abnormal ALT levels are excessive intake of alcohol, regular strenuous exercise, obesity and liver disease.

The two ALT values for your patient were .....iu per litre and ..... iu per litre. The upper limit of normal is usually 50 iu per litre. I have asked your patient not to domate again at present and recommended that he/she makes a visit youwithdrawn your patient's name from the donor panel and have recommended that he/she consults you. so that you can arrange for further investigations if your consider them necessary or advise him/her on corrective measures.

If the ALT level falls below 100 iu per litre and remains consistently so, and no abnormal liver pathology is found, it may be possible for your patient to be eligible to resume blood donations in 12 months time.

Thank you for your assistance.

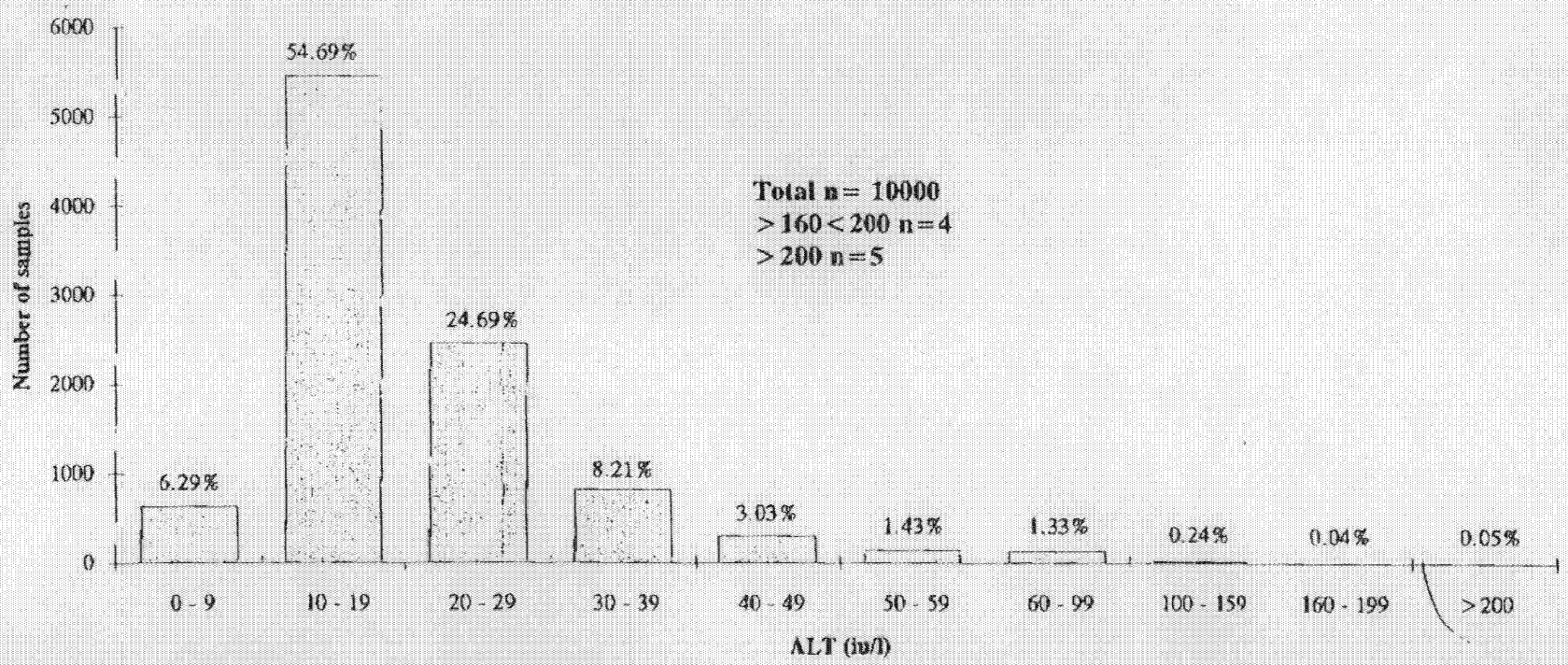
Yours sincerely

Consultant

North London Blood Transfusion Centre
Colindale

QUALITY DEPARTMENT

Cumulative Distribution of ALT Values of Routine Donations from August to September 1994



APPENDIX 5

Bharti Chandegra, Martin Beard, Dr Je[illegible]rd Seghatchian (NLBTC, September 1994)