Unique Number
10118

? late 1986 / early 1987

FINAL

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Note: App I is largely the same as HG's working paper for 24/11/86 mtg of RTD WP TAH. GRO-C 20.10.2010

ALANINE AMINO-TRANSFERASE (ALT) AND

ANTI-HEPATITIS B CORE (ANTI-HBc)

SCREENING OF BLOOD DONATIONS

PROPOSALS FOR A MULTI-CENTRE STUDY

U.K. WORKING PARTY ON

TRANSFUSION ASSOCIATED HEPATITIS

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INTRODUCTION

Transfusion associated hepatitis still occurs despite the routine screening of blood donations for the hepatitis B surface antigen (HBsAg). It has been estimated in the USA that approximately 90 per cent of such infections are caused by the non-A, non-B (NANB) hepatitis viruses, the remaining 10 per cent being due to EB virus, cytomegalovirus and less commonly hepatitis B. (1)

Transfusion associated NANB hepatitis usually runs a milder acute course than hepatitis B and many patients are anicteric; currently it is diagnosed by at least two consecutive two-fold elevations of ALT levels occurring between 2 and 26 weeks after transfusion (2). Exclusion of specific markers for other types of hepatitis, hepatotropic drugs and underlying clinical disease are implicit in making the diagnosis. Although the disease is mild there is a tendency for chronic liver damage to result in up to 50 per cent of patients; this may vary from mild but persistent abnormality of liver function tests through various degrees of chronic persistent and chronic active hepatitis to cirrhosis (3).

There is no specific test available for the detection of the viral agents which cause NANB hepatitis. Independent studies have suggested a relationship between the development of transfusion associated NANB hepatitis and both raised ALT levels and the presence of anti-HBc in blood donors (3,4,5)

The association with raised ALT levels was reported in the Transfusion Transmitted Virus (TTV) study in the USA (4) when it was shown that in approximately 40 per cent of the cases of NANB hepatitis associated with transfusion the donors had an ALT level greater than 45 IU/1, which corresponded to the upper 3 per cent of the distribution. It was estimated that there might be a decrease in the incidence of NANB hepatitis as high as 31 per cent if blood with an ALT value of less than 45 IU/1 was administered. These findings were confirmed by Alter et al (5) who estimated that by excluding donors with an ALT higher than 2.25 standard deviations of the log mean, the reduction of NANB hepatitis would be 29 per cent with a loss of 1.6 per cent of donors.

That the presence of anti-HBc in blood donors may act as a non-specific marker for the transmission of NANB hepatitis by transfusion has been suspected for some time (6) and was an unexpected finding in the TTV study (4). Using similar retrospective methods, Koziol et al (3) also showed an apparent relationship.

These workers found that 11.9 per cent of recipients developed NANB hepatitis when at least one donor was positive for anti-HBc compared with 4.2 per cent of recipients receiving blood negative for anti-HBc ($p>0.001$). However, these authors point out that both ALT and anti-HBc are surrogate tests for NANB hepatitis and the use of either to screen blood donations will still lead to the continuance of 60-70% of transfusion-associated NANB hepatitis.

Allowing for the fact that the data from the above studies was derived from transfusions performed during the 1970's and that the incidence of sporadic NANB hepatitis varies from country to country (25 per cent of all sporadic hepatitis in the USA and 4.3 per cent in the U.K. (7)), the results of the above studies may neither reflect the current situation nor apply in all countries.

The introduction of ALT screening and its economic implications have been widely debated (8,9,10) and, until recently, only the Federal Republic of Germany and Italy have routinely screened donations for ALT. During 1986, however, the American Association of Blood Banks (AABB) announced its intention to screen donations for both ALT and anti-HBc, with an implementation date of

November 1986. Donations taken by the American Red Cross will be screened for ALT. The AABB have subsequently deferred anti-HBc screening in order to resolve the problem of false positive reactions.

The use of non-specific markers will inevitably lead to the identification of donors who will not be carriers of NANB hepatitis. At present, little is known about donors who are anti-HBc positive, or have raised ALT levels, and guidelines are not available for counselling them and deciding on the need for further medical care. In the only study reported to-date, 60 per cent of abnormal levels were due to identifiable causes other than NANB hepatitis, of which the commonest were obesity and excessive alcohol consumption (11).

Before deciding whether or not to introduce routine ALT and anti-HBc screening in the U.K. an important step is to examine a sample of the current donor population to determine the distribution of abnormal ALT levels and the presence of anti-HBc, and to study such donors in order to try to establish the presence or absence of disease. If it is subsequently decided to introduce these tests the study will be of great value in deciding the appropriate cut-off value for the ALT appropriate for the donor population and will be helpful in the development of strategies for counselling and investigating donors identified as abnormal.

AIMS OF THE STUDY

1) To determine the distribution of ALT levels and the rate of positivity for anti-HBc in a cohort of blood donors during 1987.

2) To investigate the possibility, by examining the donor and carrying out further tests, of determining whether the presence of an abnormal ALT value and/or a positive anti-HBc result could be regarded as significant in terms of risk of hepatitis transmission.

3) To evaluate the economics/two aspects of routine ALT and anti-HBc screening of blood donations, viz: the cost of performing the tests and the effect on donor management.

4) To determine the effects that routine ALT and anti-HBc screening would have on blood donor panels.

PROPOSALS

1) To collect 3000 donor samples from each of four Regional Transfusion Centres (RTC's), North West Thames, South Western, North Western and Edinburgh, i.e. 12,000 samples.

2) Each sample will be ALT tested either at the RTC or by arrangement with a local D.G.H. Nine hundred donor samples, selected at random from the 3000, will be sent to N.W. Thames RTC who will perform 3600 anti-HBc tests.

3) The upper 3 per cent of ALT values will be regarded as abnormal and donors in this group, together with those who are anti-HBc positive, will be recalled and interviewed and with their consent medically examined. An equal number of controls with normal ALT values and anti-HBc negative will be treated similarly. Further investigations of liver function, as indicated and additional markers for hepatitis B will be performed.

4) N.W. Thames RTC will act as the co-ordinating Centre for the study.

PROTOCOL

1. General Remarks

1.1 3000 donations will be screened for ALT at the rate of 150-200 per week, and from these donations 45-60 will be randomly selected for anti-HBc tests at N.W. Thames RTC. These serum samples should be frozen and despatched in the frozen state to Edgware at agreed intervals.

1.2 This allows 15-20 weeks for the screening tests, and after allowing for follow-up of the donors it is anticipated that the study will last for 6 months.

1.3 It is important that donors are identified as those who have donated previously and new donors, defined as those donating for the first time. The sex and age of all donors entering the study will be recorded.

1.4 Donors who are HBsAg positive will be excluded from the study.

1.5 It is essential that for donors who give blood twice during the period of the study, the second sample from a donor is NOT included in the study.

1.6 The selections of sessions for inclusion in the study should be such that as wide a geographical spread as possible within the region is achieved.

1.7 Donors will be invited to join the study by asking them to read a notice whilst donating blood (copy attached). The results of the ALT and anti-HBc tests will not be used to determine the fate of the donation.

1.8 All donations subject to the screening would be available for issue to hospitals or for the preparation of products, providing that all the usual criteria for issue are fulfilled.

1.9 Ethical permission will be obtained by each of the participating RTC's prior to commencement of the study.

2. ALT testing

2.1 It is important that the variables involved in performing the ALT test should be kept to a minimum in the four centres. These have been identified as temperature, pH, the concentration of alanine in the substrate and the addition of pyridoxal phosphate.

2.2 It is proposed that, prior to the commencement of the study, the biochemists in the four centres performing the tests should meet to define a common protocol, and monthly during the study, the co-ordinating centre will send to the other three centres samples for testing, which should be assayed on the same day.

2.3 A decision must be made on the exclusion level for the definition of a normal value. In the study this will be arbitrarily fixed at the top 3.0 per cent of the range of values. Closer definition may become apparent after further examination of the donors.

3. Anti-HBc testing at N.W. Thames RTC

3.1 Each donation giving a positive reaction will be tested again twice.

3.2 The Wellcome test will be used to test the samples.

Positive results will be referred to Dr. R. Tedder, Middlesex Hospital, for confirmation,

When a confirmed positive result has been obtained a report will be sent to the referring RTC.

4. Donor Recall

4.1 Donors identified as having an abnormal ALT level and/or positive for anti-HBc by the Wellcome assay will be asked to return to the RTC.

4.2 As controls the donor immediately preceding the one with an abnormal ALT or positive anti-HBc result will be recalled.

4.3 The reason for the study will be fully explained to the donors and they will be asked to give a full medical history and have a clinical examination.

4.4 With the donor's agreement blood will be taken for:-

(i) Tests performed at the Local D.G.H.

ALT, GST, bilirubin, alkaline phosphatase
AST and GT
Albumin
Prothrombin time
Full blood count and ESR

(ii) Tests carried out at viral reference laboratories

N.W. Thames, Middlesex Hospital - Dr. R. Tedder
S. Western, Oxford PHLS - Dr. J. Kurtz
N. Western, Manchester PHLS - Dr. J. Craske
Scotland, Edinburgh University - Dr. J. Peutherer

anti-HBc+ IgM
anti-HBs + titre on positives
anti-HAV + IgM on positives
CMV (IgG and IgM)
EBV

(iii) For those donors who are anti-HBc positive only.

(a) Tests to be performed at the London School of Hygiene and Tropical Medicine (Professor A. Zuckerman)

HBV DNA
DNA polymerase
Concentration of serum and examination for HBsAg
Reverse transcriptase

(b) Tests to be performed at The Royal Free Hospital (Dr. H.C. Thomas)

Monoclonal based HBs assay.

4.4 Donors showing evidence of clinically significant disease will be offered further investigations and specialist referral.

MATERIALS		£	£
SCREENING TESTS			
ALT tests 12,000 at £1.00*		12,000	
Anti-HBc (Wellcome) 4,000 at £0.85 + VAT		3,910	
CONFIRMATORY TESTS			
800 tests (biochemistry and haematology) at £10.00		8,000	
800 tests at PHLS at £20.00		16,000	
80 tests (AZ) at £60.00		4,800	
80 tests (HT) at £3.75		300	
COST OF PRINTING LEAFLETS		65	
			45,075

STAFF			
N.W. Thames RTC	Senior Registrar (8 mths).....	9,300	
	Overtime MLSO	1,000	
	Clerk/Typist (8 mths).....	3,250	
S.W. RTC	Clinical Assistant (0.14 wte,6 mths)	3,600	
	Clerk Typist (8 mths).....	3,250	
N.W. RTC	Clerk Typist (8 mths).....	3,250	
Scotland	Medical Officer (0.46 wte, 6 mths)..	5,178	
	Audio Typist (8 mths).....	3,711	
			32,539

OTHER EXPENSES			
Travelling:	M.O's within region to interview donors, meetings of biochemists, co-ordinators. Estimated £2,000 per RTC.....	8,000	
Stationery, telephone calls, etc. Estimated £250 per RTC.....		1,000	
			9,000

TOTAL £86,614

* At S.W. RTC, N.W. RTC, and in Scotland these tests will be contracted out to District General Hospitals. At N.W. Thames RTC the tests will be done 'in house' with a temporary scientific officer for three months (cost £2500) plus £500 for materials, i.e. 3000 tests at £1.00 each.

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APPENDIX

WILL YOU HELP US WITH SOME RESEARCH?

Please read this and let us know before you leave.

A liver function test has been developed which may improve the Blood Transfusion Service test for hepatitis (jaundice). Before the test goes into routine use, it is important to know the range of liver functions in healthy people. This is where we need your help.

We would like to try out this test on your blood today. In the unlikely event of anything unusual showing up, or even if this test proves normal, we may wish to contact you and ask you to attend for an interview and, if you agreed, further samples. This would help us to interpret the usefulness of the test.

This is purely a research project and your blood donation will be used in the normal way. If you would like to have more information, please ask to speak to the doctor.

If you do <u>not</u> wish us to test your blood in this way, please hand this back to a member of staff.

THANK YOU!

APPENDIX I

ALANINE AMINO-TRANSFERASE (ALT) AND HEPATITIS B-CORE (ANTI-HBc) SCREENING OF BLOOD DONATIONS

MG 1986

INTRODUCTION

Recent proposals by the American Association of Blood Banks (AABB) and the American Red Cross concerning the introduction of ALT and anti-HBc screening of blood donations as a means of reducing the incidence of transfusion associated non-A, non-B (NANB) hepatitis have brought attention to the consideration of implementing such a policy in the U.K.

The purpose of this paper is to summarize the investigations which have led to the proposals from the U.S.A. blood collection agencies and to use the paper as a discussion document for recommendations to the D.H.S.S. with respect to the possible introduction of such tests in the U.K.

INCIDENCE OF TRANSFUSION ASSOCIATED NANB HEPATITIS

Several hepatotropic viruses have specific markers, i.e. hepatitis A and B, EB virus and cytomegalovirus. After the exclusion of these causes of hepatitis, and those drugs which may affect liver function, there remains a group of patients who develop transfusion associated hepatitis and these have been attributed to NANB agents. It is thought that there may be at least two distinct infectious agents and that these are almost certainly of virus origin. Despite considerable investigation a specific marker test for NANB hepatitis has not been found.

Clinically, transfusion associated NANB hepatitis runs a milder acute course than hepatitis B and many patients are anicteric; currently it is diagnosed by at least two consecutive two fold elevations of ALT levels occurring in patients with or without jaundice during a time interval of 2 to 26 weeks after transfusion (1). Exclusion of specific markers for other types of hepatitis, drugs and underlying clinical disease are implicit in making the diagnosis.

The incidence of transfusion associated hepatitis in the U.S.A. has been stated as 5.4% to 27.1% (2, quoted by Deloris et al (3)) and of these cases it is estimated that greater than 90% are due to NANB (4). From this it may be deduced that of the three million blood recipients, 150,000 may develop NANB hepatitis. Although the disease is mild there is a tendency towards chronic liver damage and it has been estimated that there may be as many as 7500 cases of cirrhosis induced per year by transfusion (3).

BACK CENTRAL COMMENT!

The incidence of transfusion associated NANB hepatitis varies widely from Country to Country. It has been reported to be 13.8% in Italy, 18.9% in Sweden, 30.4% in Japan and 3.4% in the Netherlands (quoted by Collins et al (5)).

REFERENCES!

It is more difficult to estimate the incidence of transfusion associated NANB hepatitis in the U.K. In the MRC study (5), 768 patients were prospectively studied between 1969 and 1971. Eight patients were judged to have developed icteric or anicteric jaundice, four of whom remained HBsAg negative (0.5%). In addition 35 patients had significant or sustained rises of ALT although in 19 a possible cause for this was put forward (HB, CMV, EBV). Thus, it is possible that the remaining 16 (2%) may have suffered NANB hepatitis, giving an overall incidence of 2.5%. This figure agrees well with the conclusions of Collins et al (6) who found an incidence of 3.2% presumed NANB hepatitis in a prospective study of 248 patients undergoing cardiac surgery who received an average of just over six units of blood each.

Perhaps Hesling !!!

Is this the Newcastle study

get the paper

From this data, the incidence of NANB hepatitis in the U.K. could be half that of the lowest estimate for the U.S.A. Before HIV testing OK

ALT SCREENING

The first indication that a relationship existed between raised ALT in blood donors and the risk of transmitting NANB hepatitis was reported in the Transfusion Transmitted Viruses Study (TTV) (7). The study comprised a prospective investigation of 1513 recipients of 5564 units of blood. In approximately 40% of the cases of NANB hepatitis asociated with the transfusions there was an association with an ALT value over 45 iu/l which corresponded to the upper 3% of the distribution. If a correction is made for the substitution of units with ALT values less than 45 iu/l with respect to the NANB hepatitis risk, it could be calculated that one might expect a 31% decrease in the incidence of NANB hepatitis in recipients receiving more than one donation of blood if blood with ALT values less than 45 iu/l were used.

These findings were confirmed in a second study by Alter et al (8) in which 283 transfused cardiac surgery patients were followed; 12.7% developed hepatitis of which 97% was assessed to be NANB. Using an ALT exclusion value of 53 iu/l (2.25 standard deviations of the mean log of the donor population) it was estimated that 29% of transfusion associated NANB could be prevented with a loss of 1.6% donor units. In a more extensive study by the same group of workers (3) a correlation was again found between ALT values and the incidence of transfusion associated NANB hepatitis ($p = \sim 0.01$).

I am not aware of any study in the U.K. which links ALT levels in donors to the development of NANB hepatitis in recipients. However, screening of donor bloods for ALT has been carried out in various countries and the results are reported below.

(a) Mijovic V, Patapion H and Barbara J.A.J. (1982) Hopkins book

Study carried out in 1973

1004 donors in North London
Mean ALT (35°) 16.5 iu/l S.D. 8.4
(Male donors had a wider spread of ALT values than females and were more likely to have elevated ALT values).

At cut-off value	35 iu/l	3.1% donations lost
	40 iu/l	1.8% donations lost
	45 iu/l	0.9% donations lost
	50 iu/l	0.7% donations lost

It is not possible to accurately determine 2.25 x SD log values from the data available but I calculate that it will be in the region of 47.5. Therefore, the donation rejection rate will be in the order of 0.7-0.9%.

(b) Dow B.C., (1986)

5464 donors in West of Scotland
No. 2.25 x SD log values over log mean: 41 (0.75%)
(484 donors had a history of previous jaundice and 6 (1.2%) were above 2.25 x SD over log mean).

ANTI-HBc

There have been suggestions for several years that anti-HBc might act as a non-specific marker for NANB hepatitis transmission (9). However, the definitive study has been recently performed by Deloris et al (3), in which the relationship between the presence of anti-HBc in 6293 donors and the development of transfusion associated hepatitis in 481 recipients between 1973 and 1980.

Their results can be summarized as follows:

1. Of 193 recipients receiving at least one unit of blood positive for anti-HBc, 23 (11.9%) developed NANB hepatitis compared with 12 (4.2%) of 288 recipients of only anti-HBc negative blood ($p < 0.001$).

2. There was no statistically significant difference in the incidence of hepatitis B or serological markers for hepatitis B among recipients having anti-HBc positive or negative blood.

3. Within the anti-HBc categories the presence or absence of anti-HBs was not significantly associated with transfusion associated hepatitis.

4. Eighty-eight per cent of recipients of blood positive for anti-HBc did not develop NANB hepatitis; the predictive value of the test is, therefore, 11.9%.

5. A dose response relationship is unlikely.

6. There was a lack of association between donor ALT levels and anti-HBc status. The two tests appeared, therefore, discriminating to unrelated donor populations and the two non-specific markers appeared to act as independent variables.

7. The receipt of anti-HBc positive blood did not correlate with the biochemical severity or persistence of the hepatitis.

8. Both ALT and anti-HBc have a high level of false positivity; 70-88% of recipients of blood with high ALT levels or anti-HBc positive do not develop NANB hepatitis.

9. The incidence of anti-HBc in the donor population studied was 103/2549 (4%). In other studies this has been as high as 8% (7,8).

10. It was estimated that approximately 40% of transfusion associated NANB hepatitis could be prevented by routine screening of donations for ALT and anti-HBc.

No comparable study to the above has been carried out in the U.K. Some screening has taken place for anti-HBc has taken place in two RTC's in England and one in Scotland.

At the Bristol RTC the incidence of anti-HBc in donors in a limited study in the mid 1970's was 0.5% (Fraser, personal communication). A series of 1853 British born new blood donors attending the Edgware RTC who had not lived or worked in Countries where HBV infection was common and who were HBsAg negative were tested for anti-HBV markers; 25 (1.4%) were anti-HBc positive (10). Of these, 18 were positive for anti-HBs and/or anti-HBc. In a second similar series at the same RTC carried out in 1983/4 an incidence of 0.82% was found. (Howell and Barbara, personal communication). Of 395 donors from the general public in the West of Scotland, 4 were found to be anti-HBc positive (1%), three

of whom were also positive for anti-HBs. This compared with an incidence of 6% in a prison population (11).

In 1985 the Manchester R.T.C. carried out anti-HBc tests on 6163 random donor samples and found 27 positive for anti-HBc only and 7 positive for anti-HBc and anti-HBs (0.6%).

MATTERS FOR CONSIDERATION

1. **Incidence of Transfusion Associated NANB Hepatitis in the U.K.**

   The best estimate of incidence from published data is 3%. If one assumes that the 2.3 million donations in the U.K. are transfused to 750,000 recipients annually, (possibly a more accurate assessment should and could be made), then one would expect 22,500 icteric or anicteric cases of NANB hepatitis each year. If the morbidity pattern of the disease is similar to that in the U.S.A. then one might expect half of these patients to have chronic ALT elevation and 10%, i.e. 2250, to develop cirhosis.

2. **Projected value of ALT and anti-HBc screening in prevention of transfusion associated NANB Hepatitis**

   If 30-40% of NANB hepatitis could be prevented by the use of the above tests, then the reduction in the number of cases would be 6750-900 per year and by extrapolations; 675-900 cases of cirhosis.

   Some qualifications should be made to (1) and (2) above.

   (a) The course of the chronic disease in NANB hepatitis is mild and, therefore, many cases probably remain undiagnosed even when cirrhotic changes occur. This, I feel certain is why we have not been aware of what appear to be quite serious statistics. Of course, one must also bear in mind that approximately 50% of patients die of their primary disease within one year of transfusion, and this presumably applies in the U.S.A.

   (b) The incidence of NANB hepatitis has been determined in the U.S.A. often with multiply transfused patients and in the TTV there was clearly dose relationship. Even in the two U.K. studies the patients in the second one (6) received an average of 6.28 units each.

   (c) The data from the U.S.A. is from transfusions administered in the 1970's and early 1980's and even the more recent studies in the U.K. were undertaken before attempts to encourage self-selection of donors.

   (d) One must question, therefore, whether the incidence of transfusion associated NANB hepatitis is as high now as the estimates suggest.

3. Effect of ALT and Anti-HBc Screening on Blood Collection

   From the evidence available in the U.K. one might expect that ALT screening will cause the loss of 0.7-0.9% of donations and anti-HBc in the order of 1%.

   Presumably there will be some overlap in the ALT and anti-HBc results but one might expect a loss of donations of approximately 1.5-1.75%.

Again, some qualifications need to be made:

(a) The data is largely from the time period before self-exclusion of donors for HIV infection and it is important to determine in a new study, perefably carried out in three Centres in England - Bristol,

Edgware and Manchester have been suggested, by the routine screening of 3000-4000 donations in each Centre how many donations are rejected. Preferably, also one Centre in Scotland should join the study.

All Centres should work to a common protocol and analysis of the results should yield information from which a prediction of loss of donations throughout at least England and Wales, can be estimated.

(b) The method for ALT estimation must be clearly defined and the means of determining the lower cut-off determined. (Note the AABB and the American Red Cross recommend the lower cut-off to be determined as:

antilog (log mean + (2.25 x SD log values).

Other topics for discussion:

Estimate life

(1) The cost of implementing ALT and anti-HBc screening

(2) The effect of screened donations in lessening the occurrence of NANB hepatitis from fractionated products derived from pooled plasma. Heat Haem.

(3) If routine screening was introduced how would donors be managed? and Recalls.

H.H. GUNSON
OCTOBER 1986

ADDENDUM

Since this report was prepared the following data has been received:

ALT Testing:

1. North London RTC

ALT levels in 319 plasmapheresis donors

			%
ALT normal		233	73
ALT raised	10%	60	18
ALT raised	50% occasions	12	3.8
ALT raised	100% occasions	14	4.2

ALT levels of the 86 donors above:

31-35 iu/l	22
36-40	20
41-45	6
46-50	12
51-55	2
46-50	2
51-55	1
56-60	3
61-65	7
66-70	4
-71	7

Upper limit of normal - 30 iu/l

2. Manchester RTC

ALT levels on 535 plasmapheresis donors

ALT normal	496	
ALT raised	39	(7.2%)

Upper limit of normal - 40 iu/l

3. North London RTC

1986 ALT testing on 2023 random donors

Conclusions:
(i) there is a skewed distribution with a long tail
(ii) there would appear to be a need for a lower cut-off for females compared with males
(iii) taking the U.S. cut-off of 45 iu/ml (for both females and males), 65 males and 8 females were above this level, i.e. 73 out of 2023 (3.6%).

30 randomly selected donations with raised ALT levels were screened for anti-HBc - 2 were positive.

4. South London RTC

1985-1986 ALT testing on 1257 plasmapheresis donors

ALT normal (i.e. 50 iu/l)	1213	
ALT raised	44	(3.6%)

These figures indicate that there would be a high rate of rejection of donations than indicates by the U.K. data given on page 2 of the report.

Anti-HBc Screening

North London RTC (March 1985)

6000 unselected donors:

first time donors anti-HBc positive	-	9 out of 1200	(0.75%)
established donors anti-HBc positive	-	27 out of 4800	(0.6%)
	Total	36 out of 6000	(0.6%)

These figures are identical to those found at the Manchester RTC (page 4 of the report).

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