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PRELIMINARY REPORT

SNBTS EVALUATION

OF THE

ORTHO HCV ANTIBODY ELISA TEST SYSTEM

OCTOBER 1989

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Introduction

"Non-A, Non-B (NANB) hepatitis" is a collective term for hepatitis in which hepatitis A virus (HAV), hepatitis B virus (HBV), cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) have been excluded as causal agents.

Recently workers at Chiron have published data suggesting that a togavirus like agent, tentatively termed "hepatitis C virus" had been isolated from a chimpanzee known to have been infected with non-A, non-B hepatitis. Using cloning techniques, these workers were able to produce recombinant proteins to which sera from patients convalescing from parenterally transmitted non-A, non-B hepatitis reacted. Although Chiron developed a radioimmunoassay for this antibody, the enzyme linked immunosorbent assay (ELISA) was developed by Ortho in conjunction with Chiron.

Clinical trials of the Ortho ELISA test were completed by July 1989.

In June 1989, Professor JD Cash arranged with Ortho to obtain kits for the SNBTS to evaluate. It was agreed that the West of Scotland BTS would carry out this evaluation. Meetings were held with Professor JD Cash, Dr R Mitchell, Dr BC Dow, Mr A Barr and Dr J Gillon to select appropriate categories for inclusion in the trial. Proforma were sent to all RTCs to allow them to select available samples from their library. By the start of August all RTCs had sent their contributions to the West of Scotland RTC and testing commenced on 2.8.89 using the manufacturer's protocol.

Reagents Supplied - Two batches: Lot Nos DEV 89038 and HCV 101

Equipment Supplied - None

Equipment Used - 2 Multichannel Pipettes (50-250 ul)
2 Ortho PiPoints
2 Gilson 20 ul Pipettes
4 Reagent Troughs
1 LEEC Incubator (37°C)
1 Skatron 96 well Washer
1 Dynatech Spectrophotometer

Objectives

This evaluation had several objectives:

1 To determine the prevalence of anti-HCV in the Scottish blood donor population and identify any geographical variation.

2 To ascertain the relevance of surrogate markers such as alanine aminotransferase (ALT) and anti-HBc.

3 To determine the efficiency of the test in the examination of sera from patients with alleged post-transfusion non-A, non-B hepatitis along with the implicated donations.

4 To examine donors who, after donating were found to be in "high risk" groups, such as HBsAg positive and anti-HIV positive.

5 To ascertain whether the marker was prevalent in donors who admitted to having had a jaundice episode at some time in the past but after the age of 12 years.

6 To determine the prevalence of the marker in selected patient groups, such as haemophiliacs and multi-transfused individuals.

7 To ascertain the longevity of the antibody by testing serial samples from reactive donors.

8 To examine various blood products to determine the suitability of the test in screening fractionated blood products.

9 To determine batch to batch variations between kit lots.

Results

Random Blood Donations

A total of 2745 random blood donations from three SNBTS regions, North East (Aberdeen), East (Dundee) and West (Glasgow) were tested (Table 1).

Only 15 (0.55%) initial screen positive results were obtained. Repeat testing, in duplicate, showed 13 (0.47%) to be repeatedly reactive (Table 2).

The repeatedly reactive rate was highest in Glasgow donors (0.55%) and lowest in Aberdeen donors (0.35%) but this difference was not statistically significant.

All 2745 donations had been tested for alanine aminotransferase (ALT) levels in an exercise conducted in 1987 and 1988 using the BDH EPOS system. Only one (donation 804373) of the 15 initial screen positive donations had an abnormal ALT level - 281 IU/l.

The initial screen positives for Dundee and Glasgow were tested for the presence of anti-HBc by Corab (Abbott Laboratories). None were reactive for anti-HBc.

Table 1

RESULT OF TESTING RANDOM BLOOD DONATIONS

Region	Number Tested	Initially Reactive	Repeatedly Reactive
Aberdeen	855	3	3 (0.35%)
Dundee	814	5	4 (0.49%)
Glasgow	1076	7	6 (0.55%)
TOTAL	2745	15	13 (0.47%)

Table 2

RESULTS OF REPEAT TESTS ON INITIAL SCREEN POSITIVE

AMONGST 2745 RANDOM BLOOD DONORS

RTC	Donation	Initial Result			Repeat Results				ALT IU/l
		Kit	Test OD	Cut Off	Kit	Test OD	Test OD	Cut Off	
Aberdeen	960834	D	1.907+	0.505	D	>2+	>2+	0.498	<45
	866005	D	1.090+	0.524	D	0.772+	0.771+	0.498	<45
	865934	D	0.962+	0.498	D	1.109+	1.057+	0.510	<45
Dundee	683976	H	0.833+	0.432	H	0.843+	0.787+	0.450	<45
	684035	H	0.741+	0.450	H	0.015-	0.016-	0.423	<45
	684127	H	0.496+	0.436	H	0.774+	1.148+	0.423	<45
	684252	H	0.890+	0.417	H	1.582+	1.624+	0.423	<45
	684392	H	1.077+	0.413	H	1.776+	1.904+	0.421	<45
Glasgow	718813	D	0.712+	0.459	D	0.691+	0.638+	0.476	<45
	776423	D	1.443+	0.478	D	1.412+	1.385+	0.459	<45
	804373	D	1.742+	0.481	D	>2+	>2+	0.459	281
	820575	D	0.587+	0.513	D	0.605+	0.592+	0.519	<45
	718946	D	1.321+	0.484	D	0.089-	0.084-	0.517	<45
	719023	H	0.987+	0.421	H	1.028+	1.297+	0.429	<45
	719028	H	>2+	0.421	H	>2+	>2+	0.429	<45

D = DEV 89038
H = HCV 101

Donors With Evidence Of Abnormal Liver Function Tests

Table 3 depicts the results of anti-HCV tests on the various groups of donors with evidence of abnormal liver function tests.

a) Plasmapheresis Donors

The Plasmapheresis donors tested were known to have had either an abnormal aspartate aminotransferase (AST) (Aberdeen) or alanine aminotransferase (ALT) (Glasgow and Edinburgh) at some time in the past. The latest sample available was tested in the Glasgow and Aberdeen groups whereas the index and later donations (when available) were tested in the Edinburgh group.

Only one repeatedly reactive sample was found amongst the Aberdeen plasmapheresis donors giving a 0.65% prevalence. No reactive samples were found in the Glasgow donors, whilst 3 Edinburgh donors were positive on initial screening. Two of the three Edinburgh donors were repeatedly reactive - one of which was an index sample and the other a later sample from a donor whose index sample was unavailable.

b) Random Blood Donors

In 1987-1988 an SNBTS evaluation of the BDH.EPOS method of ALT testing was carried out on random blood donor sera. Three (2.7%) repeatedly reactive samples were found in 112 Glasgow donors with raised ALT levels. Similarly, one (2.9%) repeatedly reactive sample was found in 35 Edinburgh donors with raised ALT levels, whereas 20 Dundee donors with raised ALT levels failed to react.

When the ALT cut-off point was raised to a level of 2.5 times the upper limit of normal (ULN) - a value regarded as indicative of hepatitis - a greater proportion of Glasgow donors were shown to be reactive (16%). None of the 5 Edinburgh and Dundee donors with these high ALT levels were reactive.

These latter results contrast with an ALT study performed by Dr B Dow in 1980 to 1985 when around 10,000 random blood donors were ALT tested. Either index or later samples were still available from 36 blood donors shown to have ALT levels indicative of hepatitis in this study. Nineteen (53%) were shown to be repeatedly reactive.

The anti-HBc status of these donors was already known (Table 4). Examination of this data indicated that of the anti-HBc positive group 75% were anti-HCV reactive whereas only 42% were anti-HCV reactive in the anti-HBc negative group.

It should be pointed out that the increased prevalence of anti-HCV reactivity in this group of donors was probably related to the particular donor sessions which these individuals attended. Most of the 36 donors were prison donors and many of them were subsequently identified as being intravenous drug abusers. Prison sessions were discontinued in 1983 whilst AIDS guidelines precluded past or present drug abusers by 1985.

Table 3

RESULTS OF TESTING DONORS KNOWN TO HAVE HAD ABNORMAL LIVER FUNCTION TESTS

Plasmapheresis Donors	Region	Number Tested	Initially Reactive	Repeatedly Reactive
AST raised	Aberdeen	153	1	1 (0.65%)
ALT raised	Glasgow	54	0	0
ALT raised	Edinburgh	69	3	2 (2.9%)

* Random Donors	Region	Number Tested	Initially Reactive	Repeatedly Reactive
ALT >45 IU/l	Glasgow	112	3	3 (2.7%)
ALT >45 IU/l	Edinburgh	35	1	1 (2.9%)
ALT >45 IU/l	Dundee	20	0	0
ALT >2.5xULN	Glasgow	12	2	2 (16%)
ALT >2.5xULN	Edinburgh	4	0	0
ALT >2.5xULN	Dundee	1	0	0

** Random Donors	Region	Number Tested	Initially Reactive	Repeatedly Reactive
ALT >2.5xULN	Glasgow	36	19	19 (53%)

ULN = Upper limit of normal

* 1987-88 Study

** 1980-85 Study

Table 4

THE RELATIONSHIP BETWEEN A RAISED ALT, ANTI-HBc AND ANTI-HCV REACTIVITY AMONGST RANDOM BLOOD DONORS (1980-1985)

Group	A/HBc Status	Number Tested	A/HCV	
			Initially Reactive	Repeatedly Reactive
Donors of donations with ALT levels >2.5 x ULN	Negative	24	10	10 (42%)
	Positive	12	9	9 (75%)
	TOTAL	36	19	19 (53%)

ULN = Upper limit of normal

Blood Donors Found To Be In "High Risk" Groups

Table 5 shows the results of anti-HCV tests on blood donors who may be considered to be in "high risk" groups because of HBV or HIV markers or because they have admitted to a past episode of jaundice when they were older than 12 years of age.

Twelve (35%) of 34 anti-HIV positive donors were shown to be repeatedly reactive for anti-HCV. Ten of these reactive donors were known to be intravenous drug abusers or contacts. The others included a donor who had apparently been infected with HIV in Africa and another donor alleged to have been infected because of homosexual activities. Not all those admitting to intravenous drug abuse were positive. Indeed, three Edinburgh donors who admitted drug abuse were non reactive for anti-HCV.

Five (6.4%) of 78 HBsAg positive donors were shown to be repeatedly reactive for anti-HCV. One of the five donations was from a donor who was also anti-HIV positive.

Surprisingly, none of the 37 Edinburgh donors with anti-HBc nor any of the 63 high titre anti-HBs (>10 IU/ml) donors were reactive for anti-HCV.

West of Scotland donor forms for May 1989 were scanned to identify donors who had admitted to a past history of jaundice at an age older than 12 years - 110 donors were identified and only 1 (0.9%) was shown to be repeatedly reactive for anti-HCV.

Table 5

RESULTS OF ANTI-HCV TESTS ON BLOOD DONORS IN "HIGH RISK" GROUPS

Groups	Region	Number Tested	Initially Reactive	Repeatedly Reactive
Anti-HIV Positive	All	34	13	12 (35%)
HBsAg Positive	All	78	5	5 (6.4%)
Anti-HBc Positive	Edinburgh	37	0	0
Anti-HBs Positive	Dundee/ Glasgow	63	0	0
Jaundice History (Age >12 years)	Glasgow	110	1	1 (0.9%)

Non-A, Non-B Post Transfusion Hepatitis

Samples were available from reported non-A, non-B hepatitis cases as far back as 1977. Unfortunately, not all cases had a complete collection of implicated donations and where these were unavailable the latest donation from implicated donors were included. Similarly, only a few patients samples were available for examination in the study.

Table 6 shows the summary of tests performed on reported cases of non-A, non-B post-transfusion hepatitis (NANB PTH).

a) Patients

Fifteen NANB PTH patients were tested (12 from Glasgow, 1 Belfast, 1 Inverness, 1 Edinburgh) and 5 (33%) were shown to be positive (all from Glasgow).

1 X3/77 was a reported NANB PTH case with a 10 week incubation. Of the 2 donors implicated only a later sample from one was available and this proved to be negative.

2 X2/81 was a NANB case in a renal dialysis patient who had received 6 units of blood over a period of 2-5 months prior to his acute hepatitis episode. No index donations were available but later samples were available from 4 of the donors and all were anti-HCV negative.

3 X5/82 was a haemophiliac child reported to have had NANB PTH. No donor investigation was carried out in this survey.

4 X10/82 was a NANB PTH case reported in a woman who had cardiac surgery together with 7 transfusions, 2 months previously. Index donations were available from 6 of the transfusions and all were clearly negative. A later sample was available from the donor of the missing donation and although this donation was negative using the HCV test kit, a retest using the Dev test kit showed this donation to be repeatedly reactive. Results of testing subsequent donations from this donor will be reported later.

5 X5/86 was an Intravenous Immunoglobulin recipient who was reported as a NANB PTH case. Two samples were available from this patient. The first sample was repeatedly reactive whilst the second sample proved to be on the negative side of the cut off with kit HCV 101 but weakly positive with the Dev test kit.

b) Donors

Samples of sera from donors in 28 cases of non-A, non-B hepatitis were fully investigated using either the index or a later sample from each donor. A total of 111 donor samples were tested. Only 6 donors (Table 6) were identified as being anti-HCV repeatedly reactive. Assuming that all reported cases of NANB PTH were due to HCV and that the agent responsible was transfusion transmitted rather than by another mode of spread then only 21% of cases had a donor identifiable as being anti-HCV reactive. It is theoretically possible that individuals positive for anti-HCV could lose this antibody over a period of time and therefore testing later donations rather than the index donation may show a poorer solution rate. Similarly, as anti-HCV is known to take several months to develop in certain cases, it is possible that testing index donations may not reveal those donors who have still to develop anti-HCV.

Nevertheless, of the 6 "resolved" cases, 3 from Glasgow were interesting:

X4/83 was a NANB PTH case in an 18 year old woman who developed PTH 2-3 months after a 5 unit transfusion. One of the 5 index donations was shown to be repeatedly reactive.

X5/83 was a NANB PTH case in a 24 year old woman who developed PTH 2 months after a 2 unit transfusion. Both index donations were unavailable but later donations from both implicated donors were tested and a 1989 donation from one of them was shown to be repeatedly reactive.

X10/85 was a NANB PTH case in a 33 year old woman who was a blood donor in 1984 and was shown to be negative for anti-HCV at that time. This patient received 3 units of blood 6 weeks prior to her hepatitis. Samples from the index donations were available for the study and one of these was shown to be repeatedly reactive.

Table 6

SUMMARY OF A/HCV TESTS PERFORMED IN REPORTED CASES OF NON-A, NON-B POST-TRANSFUSION HEPATITIS (NANB PTH) AND IMPLICATED DONORS

Category	Region	Number Tested	Initial Screen Positive	Repeatedly Reactive	
NANB PTH Patients -	Glasgow	12	5	5	
	Belfast	1	0	0	
	Inverness	1	0	0	
	Edinburgh	1	0	0	
	TOTAL	15	5	5(33%)	
					No of Cases
Implicated Donors In NANB PTH -	Belfast	5	0	0	2
	Inverness	2	0	0	1
	Dundee	8	1	1	2
	Glasgow	68	3	3	15
	Edinburgh	28	2	2	8
	TOTAL	111	6	6	28 cases

Transfusion Recipients

Table 7 depicts the result of testing various patient groups, all of which had received many units of blood or blood products.

Of the West of Scotland haemophiliacs 63% were shown to be repeatedly reactive for anti-HCV.

Surprisingly few (3%) of the home dialysis patients or multitransfused patients were shown to be reactive for anti-HCV. None of the intravenous immunoglobulin recipients gave a positive result although it should be noted that these recipients were selected either because of a raised ALT at some point in the past or because they were recipients of a batch of intravenous immunoglobulin said to have transmitted NANB hepatitis.

Table 7

TRANSFUSION RECIPIENTS

Category	Region	Number Tested	Initially Reactive	Repeatedly Reactive
Haemophiliacs -	Glasgow	146	92	92 (63%)
Home Dialysis Patients -	Glasgow	64	2	2 (3.1%)
Intravenous Immunoglobulin Recipients -	Aberdeen	11	0	0
	Glasgow	23	0	0
	Edinburgh	1	0	0
	TOTAL	35	0	0
Multi Transfused Patients -	Dundee	23	0	0
	Inverness	10	1	1
	TOTAL	33	1	1 (3.0%)

Protein Fractionation Centre Preparations

All plasma preparations and heat-treated factor VIII material were shown to be non-reactive for anti-HCV.

All 10 Intravenous Immunoglobulin preparations were shown to be repeatedly reactive (Table 8).

This latter finding prompted us to examine further examples of immonoglobulin preparations. Dr Cuthbertson (PFC) supplied both intramuscular and intravenous immunoglobulins, some of which had been prepared from a relatively small number of donors. Again, all proved to be repeatedly reactive.

These results suggested that the high concentration of immunoglobulin in these products may have produced false positive results. However, as a few of these products were implicated in possible cases of NANB PTH it was decided to dilute all intravenous immunoglobulin preparations 1 in 10 in phosphate buffered saline (PBS) to attain physiological levels of immunoglobulin. All samples gave negative results by the manufacturer's criteria (Table 9).

Table 8

PFC PREPARATIONS

Preparation	Number Tested	Initially Reactive	Repeatedly Reactive
Plasma Preparations	30	0	0
Z8 (80°C)	10	0	0
NY (65°C)	5	0	0
IV Immunoglobulin	10	10	10
IV Immunoglobulin	8	8	8
IM Immunoglobulin	10	10	10

Table 9

RESULTS OF TESTING VARIOUS A/HCV REACTIVE INTRAVENOUS IMMUNOGLOBULIN PREPARATION AT NEAT AND 1:10 DILUTION

IV IgG		Neat	1:10
CY	6.001	1.663 +	0.119 -
CMV	5.002	0.903 +	0.024 -
CY	8.005	1.740 +	0.173 -
CY	7.004	1.734 +	0.169
GL	6.001	0.970 +	0.064 -
T	9.002	1.490 +	0.107 -
T	5.001	1.419 +	0.068 -
GL	6.001	0.755 +	0.055 -
N	4.003	1.528 +	0.157 -
N	5.021	0.967 +	0.078 -
N	7.022	1.086 +	0.111 -
N	6.014	1.264 +	0.125 -
N	9.050	1.416 +	0.085 -
N	8.033	1.024 +	0.033 -
N	7.021	1.099 +	0.073 -
CY	6.003	1.317 +	0.054 -
N	9.058	1.367 +	0.120 -
CY	8.005	1.427 +	0.224 -

CUT-OFF = 0.425
KIT HCV 101

Dilution Studies

The fact that 1 in 200 random blood donors were reactive for anti-HCV (Table 1) made the negative finding on the plasma preparations from 1000 donors rather surprising (Table 8). It was therefore decided to investigate the effect of dilution on several of our anti-HCV positive donor sera. Eleven samples were tested neat and diluted 1:10, 1:100 and 1:200 in the manufacturer's negative control serum. Table 10 shows the result of this exercise.

Donation 718813 which was shown to be repeatedly reactive with the Dev kit was negative using the HCV 101 kit. Of the 10 other positives only one donation (804373) was positive at a 1:10 dilution and none were positive at 1:100 and 1:200 dilutions.

Table 10

RESULTS OF TESTING VARIOUS A/HCV REACTIVE DONATIONS AT VARIOUS DILUTIONS

Donation	Neat	1:10	1:100	1:200
820575	0.467 +	0.034 -	0.023 -	0.025 -
718813	0.292 -	0.139 -	0.030 -	0.029 -
719023	1.141 +	0.098 -	0.041 -	0.032 -
719028	> 2 +	0.158 -	0.038 -	0.028 -
684392	1.635 +	0.270 -	0.031 -	0.029 -
684252	1.432 +	0.104 -	0.032 -	0.066 -
683976	1.568 +	0.192 -	0.021 -	0.025 -
684127	0.825 +	0.044 -	0.028 -	0.021 -
804373	> 2 +	> 2 +	0.414 -	0.252 -
776423	1.176 +	0.053 -	0.026 -	0.025 -
111191	> 2	0.280 -	0.038 -	0.035 -

CUT-OFF = 0.425
KIT HCV 101

Batch To Batch Variation

During the evaluation reactive samples from one batch were retested as a single test with the other batch. Immediately it was noticed that one sample (718813) which gave consistent "positive" reactions against batch Dev failed to react on three occasions with batch HCV (Tables 2 and 10).

This observation made us critically review the optical densities (OD) of the test batches. It was noted that in the Dev kit the OD of most negative results were below 0.1 whereas in the HCV kit this figure was 0.05. This finding suggested that the Dev kit was likely to be more sensitive than the HCV kit. All results with the latter batch were reviewed and 29 donations were identified which had results between 50% and 100% of the cut-off (ie negative by manufacturer's criteria).

All 29 samples were repeat tested with the Dev batch and 11 were found positive on initial screen (Table 11). Only 2 of these samples (Dundee 684100 and Glasgow 20138) had negative results on repeat testing. One sample was of particular interest. This sample (Edinburgh anti-HIV positive 256275) was an initial screen positive when originally tested with the HCV kit but was not reactive on later duplicate testing. As Table 11 shows this sample was repeatedly reactive using the Dev kit.

Earlier and later donations from repeatedly reactive donors were tested in parallel with both kits (Table 12). This exercise confirmed our suspicion of a variation in sensitivity between the two batches (see Donors 1, 3, 4, 5, 6 and 7).

Donor 6 was of further interest because of involvement in a NANB PTH case in 1982. The 1982 sample was unavailable for testing but samples collected between 1983 and 1989 showed variable results with apparent loss of antibody between 1987 and 1988. It is possible that the negative results in this period of time could be interpreted as in a "grey-zone."

An apparent loss of antibody activity was shown in Donor 2.

Table 11

RESULTS OF REPEAT TESTING SAMPLES IN A GREY ZONE WITH HCV 101 BY THE ORIGINAL DEVELOPMENTAL KIT

Category	Region	Donation	HCV 101 Kit Test OD	Cut-Off	Dev kit Test OD	Cut-Off	Repeat Results	ALT
Random Donor	Glasgow	719047	0.267-	0.419	0.930+	0.464	+ +	<45
Random Donor	Glasgow	820669	0.422-	0.434	1.097+	0.464	+ +	126
Random Donor	Dundee	684100	0.370-	0.436	0.662+	0.464	- -	3
Raised ALT Random Donor	Glasgow	776790	0.388-	0.420	0.465+	0.464	+ -	50
NANB PTH Implicated Donation	Glasgow	109638	0.240-	0.427	0.609+	0.464	+ -	
1980-85 Raised ALT Donor	Glasgow	20138	0.352-	0.428	0.483+	0.464	- -	
HIV Positive Donor	Edinburgh	254296	0.269-	0.416	0.545+	0.464	+ -	
HIV Positive Donor	Edinburgh	256275	0.497+	0.416NR	0.481+	0.464	+ +	
HBsAg Positive Donor	Edinburgh	425420	0.250-	0.416	0.622+	0.464	+ +	
Known A/HCV Positive	Glasgow	419233	0.308-	0.419	0.782+	0.464	+ +	
Known A/HCV Positive	Glasgow	IVIgMED	0.377-	0.419	0.600+	0.464	ISFT	

NR = Non-repeatable

ISFT = Insufficient serum for test

Table 12

Comparison Of The Dev And HCV Kits With Donations From Known Repeatedly Reactive Donors

	DEV89038	HCV101
Donor 1		
770404/87	0.732+	0.281-
*777850/87	1.128+	0.413+
925510/88	0.497+	1.302+
931449/88	0.910+	0.860+
936549/88	0.822+	0.367-
Donor 2		
*820575/87	1.117+	0.438+
213144/89	0.236-	0.215-
Donor 3		
*820669/87	0.506+	0.282-
Donor 4		
*776790/87	0.490+	0.165-
927069/88	1.217+	1.531+
935854/88	1.988+	1.375+
942817/88	1.542+	>2+
194090/89	1.296+	>2+
Donor 5		
735719/87	0.888+	0.266-
711913/87	0.954+	0.303-
*719047/87	0.875+	0.297-
885360/88	0.810+	0.304-
997632/89	0.720+	0.328-
Cut Off	0.453	0.409

* Index Donation

Table 12 (Continued)

	DEV89038	HCV101
Donor 6 (X10/82)		
*109638/83	0.477+	0.249-
674490/87	0.184-	0.221-
875086/88	0.382-	0.361-
854055/88	1.117+	0.619+
133827/89	0.550+	0.430+
141973/89	0.726+	0.429+
Donor 7		
*718813/87	0.712+	0.292-
112148/89	0.504+	NT
Donor 8		
*776423/87	1.443+	1.176+
226371/89	0.651+	NT
Donor 9		
*804373/87	1.742+	>2+
226591/89	>2+	NT
Donor 10		
*685648/87	NT	>2+
955395/88	>2+	NT
Donor 11		
*719023/87	NT	1.141+
163023/89	>2+	NT
176087/89	1.363+	NT
Donor 12		
*719028/87	NT	>2+
163032/89	>2+	NT
Cut Off	0.453	0.409

* Index Donation

NT = Not Tested

CONCLUSIONS

In this study approximately 1 in 200 random blood donors were shown to be anti-HCV positive, whilst only 3% of the multi-transfused groups were positive. This could suggest that only a proportion of anti-HCV positive donations are actually infective. Unfortunately, the Ortho test would only have prevented 21% of the NANB PTH cases - a somewhat lower figure than reported elsewhere. Perhaps this is due to our cases of NANB PTH being due to another agent(s).

The correlation between a raised ALT and anti-HCV was noted amongst random blood donors. This was more obvious in the population tested prior to HIV donor screening. It is possible that self exclusion of donors has reduced the prevalence of the HCV marker in our donor population.

Compared to other ELISA tests, the Ortho anti-HCV ELISA had relatively few initial screen positives which were negative on repeat testing. Most random donors had test ODs less than 0.1 with the Dev kit and less that 0.05 with the HCV kit. The use of a "grey area" with the test, whilst possibly identifying weak true positive samples may also flag samples with cross-reacting antibodies.

Dilution studies suggested that very few donors have particularly strong levels of circulating antibody. Therefore, the use of the Ortho test in screening products at fractionation centres may be of limited value.

From the limited evaluation carried out, the Ortho HCV ELISA test has been shown to have an acceptable specificity. The apparent dimunition in the sensitivity of HCV kit when compared to the Dev kit is worrying. This underlines the need to check the sensitivity and specificity of kits before routine use. If batch variations are continued to be seen a weakly positive Quality Control sample may be required as a "minimum" cut-off. The test itself was "user friendly" but in large scale donor testing major consideration should possibly be given to automated sampling.

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WTD/ 2389

5 October 1989