APPENDIX II

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Extracts from.

PRELIMINARY REPORT

SNBTS EVALUATION

OF THE

ORTHO HCV ANTIBODY ELISA TEST SYSTEM

OCTOBER 1989

CONFIDENTIAL NOT FOR PUBLICATION

SNBTS EVALUATION OF THE ORTHO HCV ANTIBODY ELISA TEST SYSTEM

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.

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 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

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%)

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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5 October 1989