COMMITTEE OF EXPERTS IN BLOOD TRANSFUSION
AND IMMUNO-HAEMATOLOGY

LIEGE
23RD-26TH MAY 1989

NON-A, NON-B HEPATITIS
Agenda Item 5.2.2

ANALYSIS OF REPLIES TO QUESTIONNAIRE

BY

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NON-A, NON-B HEPATITIS

1. Replies to the questionnaire were received from 10 countries.

2. Examination of the replies revealed that in 4 countries routine screening of donations with ALT is being performed. These countries are the Federal Republic of Germany, France, Malta and Switzerland. Anti-HBc is routinely performed in France,

3. There are several studies being undertaken in some countries to determine the policies which should be undertaken to protect the blood supply with respect to the transmission of non-A, non-B hepatitis. These countries are Denmark, Norway, United Kingdom and Finland.

4. There is clearly an interest in the Chiron anti-HCV test and several countries are planning to conduct trials with this test.

5. There is a potential difficulty with respect to the use of the surrogate ALT and anti-HBc testing of donations with particular reference to source plasma for fractionation. The practice of routine ALT testing by the Federal Republic of Germany for many years means that plasma or its fractions, cannot be imported into that country unless the starting plasma has been ALT tested. This could have considerable implications for the standardisation of the quality requirements for plasma in 1992.

SCREENING FOR NON-A, NON-B HEPATITIS

Country	Routine Screening of Blood Donations ALT	Routine Screening of Blood Donations Anti-HBc	Selective Screening of Blood Donations ALT	Selective Screening of Blood Donations Anti-HBc	Other Remarks
Austria					
Belgium					
Cyprus					
Denmark	NO	NO	NO	NO	Trial anti-HCV (with Sweden & Finland).
Fed. Rep. Germany	YES	NO	NO	NO	
Finland	NO	NO	NO	NO	Prospective study on OHS patients to be anti-HCV tested.
France	YES	YES	NO	NO	Interest in evaluating anti-HCV test.
Greece					
Iceland					
Ireland	NO	NO	YES	NO	Interest in evaluating anti-HCV test.
Italy					
Luxembourg					
Malta	YES	NO	NO	NO	Started in 1989, < 1% abnormal.
Netherlands	NO	NO	NO	NO	Interest in evaluating anti-HCV test.
Norway	NO	NO	NO	NO	Pilot trial ALT/anti-HBc in progress.

SCREENING FOR NON-A, NON-B HEPATITIS (Contd.)

Country	Routine Screening of Blood Donations ALT	Routine Screening of Blood Donations Anti-HBc	Selective Screening of Blood Donations ALT	Selective Screening of Blood Donations Anti-HBc	Other Remarks
Portugal					
Spain					
Sweden					
Switzerland	YES	NO	NO	NO	
Turkey					
U.K.	NO	NO	NO	NO	Pilot trial ALT/anti-HBc in progress.

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TESTS FOR NON-A, NON-B HEPATITIS

Comments from selected countries:

FED. REPUBLIC OF GERMANY:

(i) Rejection for abnormal ALT was 3.65% (30 u/l) or 1.65% (35 u/l). In one series the rejection rate was 4.4%.

(ii) Donors are informed of abnormal result and advised to consult a physician. The ALT level is sent to the physician.

FRANCE:

(i) Rejection for abnormal ALT was 1.16% and for anti-HBc positives 4.6%.

(ii) The donor receives a letter containing:

(a) Significance of high ALT/ Anti-HBc positivity

(b) Advise to Consult physician for counselling.

(iii) In the absence of specific markers, it has been agreed that labile products should not be used, on the understanding that deferral might be unjustified.

(iv) There is permanent deferral of the donor if both markers are present.

(v) Plasma donations for fractionation are acceptable in some centres if one marker, (ALT or anti-HBc) are present in an otherwise healthy individual.

NORWAY:

(i) So far, clinically recognisable non-A, non-B hepatitis has been a relatively rare complication in Norway. The incidence of sub-clinical infections is unknown.

(ii) At Wleval Hospital all donations are being screened for ALT and anti-HBc. This commenced on 1st March 1989 and will continue until 31st May for ALT and 31st August for anti-HBc.

Approximately 3% ALTS are higher than 40 u/l and approximately 1% of the HBsAg negative donors have anti-HBc.

All donors with abnormal results are followed up:

The findings in this trial will be a factor in determining policy.

SWITZERLAND:

(i) Rejection for abnormal ALT is 2.06%.

(ii) Donors are informed that their donation was not used if the previous donation was also abnormal. They are advised to see a doctor.

(iii) Cannot donate blood during the next two years.

U.K.:

(i) 9000 donors from three RTC's have been tested for ALT and anti-HBc. Those with ALT greater than 45 u/l and who are anti-HBc positive have been recalled for medical assessment and further tests.

Anti-HCV tests will be performed on these donations.

(ii) A decision of the policy to be adopted will be made when the results of the study are analysed.

FINLAND:

(i) 700 patients undergoing open heart surgery have been prospectively followed with 10 samples. The study is almost completed. Eleven-twelve cases of PTH found, all but one subclinical.

(ii) This material is to be tested for anti-HCV.

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NON-A, NON-B HEPATITIS: TESTING OF BLOOD FOR INFECTIVITY

W.G. van Aken (Central Laboratory of the Netherlands Red Cross Blood Transfusion Service)

Test providing indirect evidence (ALT and anti HBc)

Since 1986 blood units in the United States are routinely tested for ALT and anti-HBc. The number of units with elevated ALT-values varies from 0.9 to 3.5%, and for increased anti-HBc-titres from 2 to 4%.

In Europe such surrogate testing for Non-A, Non-B hepatitis varies from country to country. In the Federal Republic of Germany all donors are screened for ALT since 1965. France and Luxemburg have decided in 1988 to make the testing of both ALT and anti-HBc obligatory for all blood units. In Belgium, Switzerland, Spain and Italy only part of the donor blood is presently screened with these tests. In the other European countries, surrogate testing for Non-A, Non-B hepatitis is (not yet) introduced.
The relevance, the advantages and draw-backs of this testing have been discussed previously in this Expert Committee.

Test providing direct evidence

Recently Choo et al (1) reported the successul isolation of a DNA-clone that encodes an antigen specifically associated with Non-A, Non-B hepatitis infections. They provided evidence that this clone is derived from the genome of the Non-A, Non-B hepatitis agent which was similar to the logaviridae. The authors have termed this virus, hepatitis C virus (HCV).
Using recombinant technology Kuo et al (2) have accomplished the expression of the continuous open reading frame of such a clone in yeast. In this way a polypeptide was synthetized which after solubilization and purification was used to coat the wells of micro-titer plates so that circulating antibodies to HCV in blood samples could be captured and measured. Antibodies to HCV were detected in

six of seven human sera that previously were shown to transmit Non-A, Non-B hepatitis to chimpanzees. The only negative sample was obtained from an individual in the acute phase of post-transfusion Non-A, Non-B hepatitis.

Assays of matched blood donor and prospectively obtained recipient sera from 10 well-documented cases of post-transfusion Non-A, Non-B hepatitis revealed that there was at least one positive blood donor in nine of these cases. Each of the ten recipients seroconverted against HCV during the course of the disease although in one case this was not apparent until 12 months after transfusion while in the other cases antibodies were detected within 6 months. In contrast, in individuals infected with other viral hepatitis agents seroconversion against HCV was not observed.

Concerning the specificity of surrogate tests it is of interest to note that some of the anti-HCV-positive donors had no elevated ALT concentrations or increased antibody titres to HBc. Further support for a specific association between blood-borne Non-A, Non-B hepatitis and antibodies to HCV was obtained from assays of other cases of posttransfusion hepatitis.

About 80% of such patients from Japan, Italy and the United States had circulating antibodies to HCV whereas a lower frequency (15%) was observed in acute infections.

These data suggest that HCV is an important cause of chronic Non-A, Non-B hepatitis not only in the United States but also in other parts of the world. The specific and sensitive test for antibodies to HCV may lead to the improved safety of the blood supply once this test is available for large scale use and the initial results are confirmed by others. However, it is uncertain that testing of anti-HCV alone, will be sufficient to eradicate post-transfusion Non-A, Non-B hepatitis.

References

1. Choo, Q-L.,, Kuo, G., Weiner, A. et al.
Isolation of cDNA clone derived from a blood-borne Non-A, Non-B hepatitis genome.
Science 244: 359-362, 1989.

2. Kuo, G., Choo, Q-L., Alter et al.
An assay for circulating antibodies to a major etiologic virus of human Non-A, Non-B hepatitis.
Science, 244: 362-364, 1989.

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