0049

U.K. ADVISORY COMMITTEE ON TRANSFUSION TRANSMITTED DISEASES

Anti-HCV Tests on Blood Donations

1. Consideration has been given to the introduction of routine anti-HCV tests on blood donations at two meetings of the Committee on 8th January 1991 and 25th March 1991.

2. Proposals for the schedule of anti-HCV tests have been agreed and those are summarised in the flow chart (Appendix I).

   The procedures proposed for testing are similar to those used in the detection of other infectious markers.

3. **ALT testing**

   It will be noted that there is a recommendation for an ALT test to be carried out on all repeatable anti-HCV positives. This suggestion was made on the basis that a raised ALT might indicate, in the absence of a positive result in the confirmatory tests for anti-HCV, the presence in the sample of another virus which could transmit non-A, non-B hepatitis.

   Since these proposals were put forward, however, some doubt has been cast upon the usefulness of this test. It has been known for many years that ALT tests are not specific. Also, in studies on patients recently published there was poor correlation between HCV antibody status and ALT (van de Poel et al, Lancet 337: 317-319, 1991; Contreras et al Lancet 337: 753-757, 1991).

   The view has been put forward that the purpose of anti-HCV testing is to detect those donors who may transmit hepatitis C and that ALT testing only confuses this issue. It may be a useful test as part of the investigation of liver function in donors who are confirmed anti-HCV positive, but that to perform ALT tests at an earlier stage might be counter-productive.

   The question of ALT testing will be reviewed at the next meeting of the Committee.

4. **Confirmatory testing**

   The Virologists who were offering confirmatory testing met on 12th February 1991 and made the following recommendations.

   4.1 Samples which are repeatably positive with the anti-HCV ELISA test should be referred to a confirmatory laboratory.

4.2 The samples will be tested with RIBA-2 and other serological tests at the discretion of the confirmatory laboratory.

4.3 RIBA-2 reactives and indeterminates would be tested by PCR.

5. **Follow-up**

5.1 RIBA-2 reactive, PCR positive donations would be reported as anti-HCV confirmed, HCV RNA detected. The index donation would be discarded and arrangements made for the donor to be counselled, the tests repeated and medical care offered.

5.2 RIBA-2 indeterminate, PCR positive would be reported as anti-HCV not confirmed, HCV RNA detected. The index donation would be discarded and arrangements made for the donor to be counselled and medical care offered.

5.3 RIBA-2 negative would be reported as anti-HCV not confirmed. A sample from the next donation should be sent for confirmatory tests. The index donation would be used for plasma for fractionation and the donor could remain on the active panel, but used only for plasma for fractionation.

5.4 RIBA-2 reactive (or indeterminate) PCR negative would be reported as anti-HCV confirmed (or anti-HCV not confirmed), HCV RNA not detected. A sample from the next donation should be sent for confirmatory tests. The index donation would be used for plasma for fractionation and the donor could remain on the above panel (subject to the results of the second set of confirmatory tests), but used only for plasma for fractionation.

6. **Comments on confirmatory testing and follow-up**

6.1 In the multi-centre trial, of the 69 repeatably positive results with the 1st generation ELISA, the 6 RIBA positives were all PCR positive and the RIBA negatives were PCR negative. The number of concordant results of RIBA positive and PCR positive to statistically justify the statement that all RIBA positives will be PCR positive are too few. At least 70 such correlations would be required.

On the other hand, the PCR is technically difficult to perform, the viral RNA does not store well in plasma and the test is very expensive. The logistics of storing frozen samples of plasma awaiting RIBA test results also presents difficulties. It would be

difficult to use a negative PCR result with confidence to reassure donors that they did not suffer from chronic liver disease.

It is important that more PCR tests are performed to confirm the correlation with RIBA-2. With the proposed extension of the trial an estimated 60,000 donations will be tested for anti-HCV. This should give approximately 300 repeatably positive anti-HCV ELISA tests. Carrying out RIBA-2 and PCR on these samples may help to solve this problem.

6.2 The interpretation of the RIBA-2 indeterminates is difficult to assess. It is this group of tests where PCR might be most helpful. It is good advice that such tests should be repeated on the next donation since it will be difficult to advise donors when counselling.

6.3 Retention of donors on the panel who are repeatably positive for anti-HCV, but RIBA-2 negative for the use of their plasma for fractionation is uneconomic when the red cells have to be discarded. Asking such donors to become plasmapheresis donors would be an excellent way to use their services, but as costings are received at the Directorate it is apparent that most RTCs cannot recover the costs of apheresed plasma.

6.4 From the multi-centre trial it is known that Ortho and Abbott ELISA tests identify two overlapping populations of repeatable positives, although the confirmed positives (RIBA-2 positive, PCR positive) were all positive with both tests. The effect of this will be that donors may be found repeatably positive in one RTC using a particular test and even if RIBA-2 negative their services may be dispensed with (see para. 6.2), whereas the same donor in another RTC using a different test would give a negative result and continue to donate for all products.

This situation is a cause for concern since even if the confirmatory laboratory used ELISA tests different to that used in the RTC and obtained a negative result, it is difficult to issue the red cells and particularly the platelets from such a donation because of the time taken to obtain the results of confirmatory tests.

For an RTC to have two different tests available, again, would not be economically viable. Also much more work is required to be certain that true positives will be positive with all tests - they should be otherwise a test will be giving false negatives. However, borderline positives may be reactive with one test whilst another, which is slightly less sensitive, may fail to react.

7. **Recommendations for routine anti-HCV tests on blood donations**

7.1 Anti-HCV ELISA tests should be performed according to the flow chart appended to this report.

7.2 Further discussions are required with respect to ALT tests.

7.3 The basic confirmatory tests should be the use of ELISA tests as appropriate and RIBA-2 assay.

7.4 It is important that PCR is evaluated but since its value is as yet controversial this should be funded separately as a research project.

8. **Plasma for fractionation**

8.1 Plasma for fractionation should be anti-HCV negative.

8.2 The plasma from donations which are repeatably positive with ELISA anti-HCV, but RIBA-2 negative can be used for fractionation.

8.3 The plasma from donations which are RIBA-2 positive or indeterminate must not be used for fractionation.

Conflicts with 5.4, above.

H.H. GUNSON
10.5.91.