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EUROPEAN HEALTH COMMITTEE (CDSP)

21th meeting

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Extract from the report

of the

COMMITTEE OF EXPERTS

on

BLOOD TRANSFUSION AND IMMUNOHAEMATOLOGY (SP-HM)

10th meeting

Rome, 19-22 May 1987

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12.3 Non-A, Non-B Hepatitis - testing of blood for indirect evidence of infectivity

A synthesis of replies received from members of the SP-HM to the questionnaire on Non-A, Non-B Hepatitis (NANB) was presented by Dr. H GUNSON. These replies clearly show that this issue is in general given careful consideration by most blood transfusion services. The general impression is that the incidence of NANB-Hepatitis is rather low, but varies widely between different regions. The value of "surrogate-tests" such as ALT and anti-HBC has been studied by various groups but there is doubt about their cost/effectiveness. Prof. H WEISE remarked that ALT-testing has been used in the Federal Republic of Germany for more than 20 years. The reduction in NANB-hepatitis was estimated at about 29% according to Prof. H WEISE, while approximately 1.2% donors were lost. However, controlled studies have thus far not been performed.

Dr H HEISTO (Norway) told the committee that in his Transusion Centre 494 new donors were tested for ALT in the period 1 February to 30 April 1987. Ten had an increased value (40 U/L 37° C). This would represent 2% in a normal population. All 494 donors were also tested for HBs antibody and HBs antigen. All the ten donors with increased ALT were negative for HBs antigen. One of them had HBs antibody.

Dr C HÖGMAN (Sweden) reported that experience in Sweden regarding the "surrogate" testing of plasmapheresis donors indicated quite large variations within one donor. He expected that anti-HBC testing would be introduced for first time donors in Sweden. However the experience with ALT-testing was less favourable and for the moment there was no proposal to introduce compulsory screening.

Dr B HABIBI (ISBT) presented the following data to the committee:

Analysis of data from 16 reports amongst current literature reveals:

a. a wide variation in the prevalence of NANB-Hepatitis as defined by a persistently elevated ALT, ranging from 1.6% in an Australian study to 18.2% in a French one.

b. an overall incidence of 8.34% in 6126 transfused patients versus 1.85% in 5776 hospitalised non-transfused "control" patients.

A hitherto unpublished prospective study in cardiac bypass surgery patients in Toulouse and Lyon (France) has shown an incidence in 7.1% in 112 patients having been transfused with unselected blood, 2.4% in the 248 patients having received normal ALT blood, and 24.2% in the 173 patients having received at least one unit blood with high ALT levels.

The mean rate of donor "loss" based on the study of ALT and anti-HBC markers in 10168 donors from various geographical areas of France has been predicted to be 4.6% for donors with anti-HBC, 1.3% for donors with ALT levels higher than twice the normal and 6.73% for donors with one or both markers.

It must be emphasised that decision making on this issue can be neither carried out uniformly as between different countries, non based on clear-cut scientific data. Among arguments supporting introduction of ALT and anti-HBC testing, Dr HABIBI stressed the following issues:

- based on American and some French studies, a significant proportion of transfusion-related NANB hepatitis should apparently be prevented;

- no specific test is currently available to identify virus carriers;

- ALT testing in blood donors might represent a valuable contribution of blood transfusion centres to public health through counselling of donors;

- the evidence already published of efficacy of such screening policies raises ethical issues on the initiation of additional randomised studies;

- the reduction in health costs of treating chronic hepatitis might well balance those generated by this screening policy.

Dr. HABIBI informed the meeting that based on these considerations the viral hepatitis study group of the French National Blood Transfusion Society had recommended the implementation of both ALT and anti-HBC testing among blood donors in France. He further indicated that a decision of the French public health authorities on this subject was expected in the forthcoming months.

Prof. W G VAN AKEN then presented his report on NANB hepatitis and specifically mentioned the preliminary data from a study in multi-transfused patients in Amsterdam which should allow incidents of NANB Hepititis.

Dr. H GUNSON told the committee that in the United Kingdom a study on a cohort of donors in four centres had been proposed. Each donor would be ALT and anti-HBC tested and those with abnormal results would be assessed clinically in order to try and establish their potential risk in respect of the transmission of NANB hepatitis. This study would also yield important information on the loss of donors and donor management. Proposals for a prospective study on patients transfused with blood with normal and raised ALT levels had not received eithical approval.

Dr. J LEIKOLA (Finland) reviewed the literature of the last eight years concerning this topic. He concluded that many of these studies lack definitions of hepatitis and control populations. Also there are discrepancies between epidemiological data and the results of small scale studies. He expressed his opinion that a decision to introduce "surrogate" testing should be based exclusively on data available or obtained from a given country or region. In Finland a prospective study in five hospitals will be started to establish the value of such "surrogate" tests for the prevention of post-transfusion NANB Hepatitis. In the discussion Dr HABIBI pointed out that the prevalence of NANB Hepatitis in non-transfused hospital patients in the United States is about 2%. In Japan 0.6% of hospitalised non-transfused patients have elevated ALT levels.

After ample discussion on this topic, it was decided that a working group comprising Prof. VAN AKEN, Dr. GUNSON, Dr. HABIBI and Dr. LEIKOLA would prepare a brief report and if possible define recommendations.

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Later this working group reported as follows:

Many factors are involved in the incidence of transfusion associated NANB Hepatitis. There is a geographical variation with a tendency for a higher prevalence in the Southern European countries. However, in all countries blood transfusions are transmitting NANB Hepatitis, most commonly recognised by a persistent elevation of liver enzymes. The disease may run a symptomless sub-clinical course, but in some cases there is chronic disease resulting in microscopical evidence for cirrhosis and very occasionally the disease is fulminating and rapidly fatal.

The argument for introducing tests to reduce the incidence of NANB Hepatitis has been supported by the prediction that up to 10% of infected patients with persistent elevation of the liver enzymes will eventually suffer from cirrhosis. If the clinical course of the disease in blood donors is similar to that in recipients of blood, out of the estimated number of carriers in the United Statates an appreciable proportion could develop serious liver disease. Such estimations are not consistent with the hepatitis epidemiology in the United States and there is a possibility therefore, that a healthy carrier state may exist for the agents responsible for NANB Hepatitis.

There is no specific test available for the detection of the viral agents which cause NANB Hepatitis, nor does it appear that a specific test will be available in the foreseeable future. The only possibility for reducing the incidence NANB Hepatitis therefore appears to the use of non-specific tests. In this context, ALT and anti-HBC testing of blood donors has been proposed and it has been predicted in the United States that this will lead to a 35% reduction in the incidence, but not to the prevention of transfusion associated NANB Hepatitis. United States routine screening of donors for ALT and anti-HBC has started. With respect to European countries, ALT testing was performed in Switzerland for a short period during the 1950s, but it was discontinued. It has been undertaken in the Federal Republic of Germany and in Italy since 1965, but it is not possible to evaluate its effectiveness in the prevention of transfusion associated NANB Hepatitis. A prospective study in two centres in France has shown that ALT values significantly correlated with the transmission of NANB Hepatitis and the data confirmed the United States data. In Sweden, longitudinal ALT testing of plasmapheresis donors showed that ALT levels varied considerably within one and the same individual, which limited the value of ALT testing.

The prevalence of anti-HBC in blood donors varies in different countries and a range of 0.7% - 40% has been observed. Some studies in France have shown significant correlation between transmission of NANB Hepatitis and presence of anti-HBC in donors, but other studies have failed to do so.

Apart from Belgium, the Federal Republic of Germany, some Italian regions and Luxembourg, no other member countries of the Council of Europe are routinely using ALT tests on blood donations at the present time. However, a national working party in France has now recommended the introduction of both ALT and anti-HBC tests; anti-ALT testing may also be commenced in Sweden. A possibility exists with anti-HBC testing, that tests could be restricted to existing and new blood donors but not repeated on all blood donations after a donor has been found anti-HBC negative.

Two studies are proposed. In Finland a prospective study of patients undergoing open heart surgery who are to be assessed for the development of NANB Hepatitis and in the United Kingdom there are proposals to ALT and anti-HBC test a cohort of blood donors in four centres. Those donors who have a raised ALT and are anti-HBC positive will be recalled and assessed for their potential in transmitting NANB Hepatitis.

On the basis of this information the working group concluded that:

1. The use of non-specific test for the purpose of reducing the incidence of transfusion associated NANB Hepatitis and its possible value as a public health measure remain controversial issues.

2. If a stance is taken that blood should have maximum safety then the tests would be introduced but the benefits derived from this testing would not be uniform throughout every country. Also, there is no guarantee that, in a given country, there will be a significant reduction in the transmission of NANB Hepatitis.

3. The introduction of non-specific tests could lead in some countries to a severe depletion of blood donors which may compromise the blood supply and this is a factor which must be taken into account.

4. When non-specific testing is introduced in a country, provision must be made for the interviewing, counselling and further medical examination and treatment which may be required for donors found to have a raised ALT or who are anti-HBC positive.

5. The committee cannot give a general recommendation on the introduction routinely of non-specific tests for evidence of NANB infectivity of blood donors. Individual countries will have to assess the situation locally and decide on the appropriate action to take.