TRANSFUSION MICROBIOLOGY

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NEWLETTER NUMBER 9

DECEMBER 1988

1. EDITORIAL

A Growing Queue of Candidate Screening Tests

In the previous edition of the Newsletter we highlighted the diversity of possible new microbiological screen tests needed to maintain the safety of the blood supply. Now, one year on, the same questions concerning the possible value of various additional tests still remain, without any clear outcome. This in itself reveals the tendentious nature of the value of introducing several of these extra screen tests.

Although several studies related to non A, non B hepatitis and the risks of transfusion are being planned or have already been started in the UK, the question of whether or not to screen UK blood donors for anti-HBc and alanaine aminotransferase still remains open. In this respect it is interesting to note that the level of non A, non B hepatitis following transfusion in the USA has indeed fallen, but as Miriam Alter[1] has pointed out, this fall pre-dated the introduction of 'surrogate' screening tests and is most likely due to the exclusion of donors at risk for contracting HIV infection and, through associated risk factors, non A, non B hepatitis. (Other articles in this issue will relate to the topic of non A, non B Hepatitis and Hepatitis C virus).

The UK Transfusion Service is still not routinely screening blood donors for anti-HIV-2. A leading article in the Lancet[2] said 'until more HIV-2 infections are found in individuals at increased risk, unselective screening of blood donors by an anti-HIV-2 test would be hard to justify'. The author also addressed the suggestion that the use of those anti-HIV-1 tests which showed a significant cross-reaction with anti-HIV-2 might be worthwhile. The author thought, however that the risk of missing HIV-1 infections 'by disturbing established and proven screening procedures may not be worth taking. For the time being, testing of donors with West African connections and exclusion of those donors who have had sexual contacts in sub-Saharan Africa are probably sufficient measures to protect recipients from HIV-2'.

The situation with anti-HTLV-1 is also under constant review. In the USA, routine donor screening is likely as soon as an appropriate test is licensed by the FDA. It seems however, that the prevalence of anti-HTLV-1 will prove to be significantly greater in the USA compared with the UK.

To move to a more parochial topic: please do not forget to send us any contributions for future Newsletters. We shall be awaiting them eagerly.

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4. A SPECIFIC TEST FOR NON-A, NON-B HEPATITIS? : SOME ANSWERS, MORE QUESTIONS

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Scientists at the Chiron Corporation (USA) have recently announced that molecular biological approaches to the isolation of a specific non-A, non-B hepatitis (NANBH) antigen appear to have borne fruit in the shape of an ELISA for antibody to NANBH; this test will be marketed by Ortho Diagnostics. Although not yet the subject of a formal report in a scientific journal, many NANBH researches (such as Dr. Harvey Alter at the National Institutes of Health, USA and Dr. Gary Tegtmeier at the Kansas City Blood Center) seem confident that we are dealing with the first specific assay for antibody to the major post-transfusion NANBH agent, termed HCV or hepatitic C virus. Dr. Alter reports complete consistency of the test with his panel of sera from patients with post-transfusion NANBH (allowing for a two month delay post infection, for antibody to HCV to develop) and at the ISBT/BBTS Conference at Wemoley Dr. Tegtmeier reported a strong association between a history of hepatitis and positivity for anti-HCV in Kansas City blood donors. Samples from two donors at the North London Blood Transfusion Centre who were implicated in transmitting NANBH were sent to the USA and were also found to be anti-HCV positive when tested blind in a panel with several other negative sera which we expected to be non-reactive.

The antigen was derived by a massive cloning programme after nucleic acid extraction from a centrifugation pellet. This was obtained under optimum conditions for virus isolation from the plasma of a chimpanzee infected with a proven human transfusion-transmissible NANBH agent. This antigen was then used in an ELISA to detect antibody as discussed above.

Even if, as seems likely, this assay proves to be specific (and sensitive) for anti-HCV, there will still be 'gaps' in our ability to detect NANBH. Some 20 to 30% of NANBH PTH is likely to be caused by another agent (which some workers claim to be in process of cloning). In addition there will be a period of some months after infection before a person infected with HCV develops antibody detectable by the assay: however the blood from such persons is likely to be infectious by transfusion for some of that period. Nor can the assay be adapted to detect IgM at present, thus leaving a circumstantial element when attempting specific diagnosis. What impact is this assay therefore likely to have on blood transfusion services in the UK? We still have no evidence that NANBH after transfusion is numerically significant except in recipients of pooled plasma products such as Factor VIII. Because of plasma-pooling, haemophiliacs receiving Factor VIII concentrates are exposed to approximately 20,000 donations per batch of Factor VIII. Hence, even if donors are screened, each pool carries a small risk of contamination by 'seroconverting' donors (as is the case with hepatitis B and Factor VIII). Nor will contamination by the 'minor' NANBH agent be prevented.

Nevertheless, heating freeze-dried UK Factor VIII at 80° for 72h appears to inactivate a high proportion (at least) of NANBH; screening might either therefore be considered 'superfluous' or sensible for reduction of the viral load piror to heat treatment. This question will require careful study and analysis. As far as individual blood or component transfusions are concerned, the rate of post-transfusion NANBH in the UK is extremely low and the contribution of post-transmission NANBH to chronic hepatitis in the UK remains to be confirmed, but few patients with chronic liver disease have a history of transfusion. If we screen for NANBH merely

because we have a specific assay for HCV as opposed to the insensitive and non-specific ALT and anti-HBc assays required in the USA, we may run the risk, ironically, of generating a demand for these same non-specific assays to fill the gap left by screening with the Chiron assay.

NANBH research is entering an interesting era when many questions associated with PTH, history of jaundice and NANBH carrier states may be at least partially clarified. However, whether the new assay, when it arrives, will have its main value restricted to diagnosis or whether it will gain acceptance as a blood donor screening assay, remains to be seen.