Into the occult: Strategies for preventing transfusion-transmissible infections

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Transfusion services all over the world are constantly trying to improve blood safety and to reduce the residual risk of transfusion-transmissible infections (TTI). Current mandatory tests to detect TTI in India include testing for human immunodeficiency virus 1 and 2 antibodies, hepatitis B surface antigen (HBsAg), hepatitis C virus antibodies, syphilis, and malaria. Studies from Europe and America suggest that the addition of nucleic acid testing (NAT) will increase the detection rate of the transmissible viral infections, thereby increasing safety of blood transfusion [1–6]. In India, NAT is not mandatory although several major blood banks have already included this in their screening profile.

The article by Sodhi et al. [7] in this issue of the *Journal* highlights this question. Six percent of their 150 patients who had multiple transfusions developed evidence of hepatitis B virus infection, with seven of the nine patients developing clinical viral hepatitis. The authors showed that testing stored serum samples from the blood donor for antihepatitis B core (HBc) antibody and HBV DNA quantitation by real-time polymerase chain reaction (PCR) detected HBV infection in six of the nine donors. HBV DNA was detected in four of them; the two others having only IgG anti-HBc. In the other three patients, they concluded that the source of hepatitis B infection was other than the transfusion. The prevalence of HBsAg in healthy blood donors, as reported in their paper was 0.56 %.

Sensitivity and specificity of the currently used fourth-generation enzyme-linked immunosorbent assays are much better than the earlier versions but it is clear that they fail to detect donors in the window period and with occult infections without detectable levels of circulating HBsAg. It has been suggested that the addition of anti-HBc testing may be a cost-

effective strategy, though there have been reports of occult infection in anti-HBc-negative individuals. Therefore, without NAT testing, the addition of anti-HBc as a routine practice would only lead to a higher rate of discard of blood units as the rate of anti-HBc positivity in blood donors is 10 %–20 % [8].

There are excellent research studies and detailed reviews [1–6] from Europe and America which clearly showed that the addition of NAT increased the rate of detection of viral infections in potential donors. NAT is now mandatory in screening potential donors in many of these countries. From India, a detailed multicentre evaluation of NAT was published in 2008 involving eight large blood banks from metropolitan centers [9]. It was reported that eight additional infected donors were detected out of a total 12,224 samples. The highest yield was for HBV infection (6/8) [9]. There are a few other reports from India [10–15] which also show that the addition of tests to detect nucleic acids (NAT or PCR) increased the yield of donors who are hepatitis B positive. In China and Taiwan, with a high endemicity of hepatitis B, the addition of NAT increased the detection of occult carriers [16, 17]. It must however be emphasized that NAT does not replace serological tests for TTI since HBsAg-positive samples could be NAT negative. In one of the studies from India, 84 samples which were seroreactive for HBsAg were NAT negative [9].

There are two possible strategies for NAT testing, individual donor testing and minipool testing. In countries where the prevalence of HBV infection is low, minipool strategy is adequate while in high-prevalence countries to which India belongs, individual donor testing is recommended [10, 18]. There has been considerable debate regarding the necessity to make NAT mandatory in all blood banks but the significant increase in the cost of NAT tested blood is possibly the major factor which has prevented implementation across all sectors.

In a country with approximately five million blood donors and around 50 million hepatitis B carriers, the first line of defense against TTI is the full evaluation of the risk of the

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donor by good history taking. Unarguably for the individual patient, NAT screened blood is ideal for detecting window period and occult infections. Most of the large hospitals in urban centers have already started using NAT screening in their blood banks. Should NAT be statutorily implemented throughout India? The money available for public health and public hospital services is limited and the debate is still ongoing to decide whether this should be invested in implementing NAT or in improving hospital-based practices. The fact that it was concluded in this article that transfusion was not the cause of infection in one third of the patients who developed post-transfusion hepatitis B could further fuel this debate. As the aim of good screening practice in blood banks is to provide safer and better blood products, the actual benefit vs. cost of NAT implementation across all blood centers in India has to be determined so that patients, whether requiring single or multiple transfusions, might be at least residual risk of getting a TTI.

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