To the editor:

Leukocyte reduction and HTLV-I: is the glass half empty or half full?

We read with interest the recent article by Pennington et al. Based on the ability to detect Tax DNA in the blood of asymptomatic carriers with proviral loads exceeding 10^6 DNA copies/L, the authors conclude that leukocyte depletion (LD) may not provide complete protection from human T-cell leukemia virus-1 (HTLV-I) transmission by transfusion.

Lau et al. proved that cytomegalovirus (CMV)-infected blood, another example of a cell-borne viral infection, transacted with as many as 3 x 10^7 infected cells, contains a residual of 10^2 viral copies following LD, consistent with the present study’s observations. These findings were confirmed in asymptomatic seropositive donors by Dumont et al. However, in spite of the residual polymimerase chain reaction (PCR) detectability of the CMV DNA in the postfiltration blood, little controversy exists concerning the ability of LD to greatly reduce the potential for transfusion-transmitted CMV infection.

Okochi and Sato conclude that approximately 10^8 infected lymphocytes are required to transmit HTLV-I infection by transfusion. This conclusion is further supported by the fact that plasma from infected donors and the residual number of infected cells results in a reduction of 1 log_{10} less than that of native leukocytes.

Only clinical experience can confirm the extent to which LD will be effective in minimizing the incidence of transfusion-transmitted HTLV-I infection. We agree with Pennington et al. that LD will not “provide complete protection” because no precautions, including nucleic acid testing, can. However, based on the information above, we believe LD will provide significant protection and, perhaps as for CMV, protection comparable to that afforded by serologic screening. Casting the conclusion this way appears more consistent with the authors’ own data taken within the context of the available literature.

Barry Wenz and Girolamo A. Ortolano

References


Response:

Infectious dose of HTLV-I in transfusion recipients

We certainly agree with Wenz and Ortolano that leukocyte depletion (LD) reduces the risk of human T-cell leukemia virus-1 (HTLV-I) transmission by transfusion just as they agree with us that this reduction does not equate zero risk. It is therefore important to be precise as to whether we consider LD to achieve risk reduction or risk removal. In their rebuttal of our conclusions, Wenz and Ortolano quote studies regarding cytomegalovirus (CMV) and HTLV-I. We are not
To the editor:

Factor XIII activation by thrombin depends on FXIIIVal34Leu genotype

Brummel et al\(^1\) reported interesting results on different thrombin functions during tissue factor–induced whole blood coagulation. Thrombin generation, platelet activation, and activation of fibrinogen, factor V, and factor XIII (FXIII) were analyzed. FXIII activation was reported to occur slightly prior to fibrinopeptide A (FPA) release at a rate of 10.3 ± 0.9 nM/min and at a thrombin concentration of 0.84 ± 0.28 nM. However, these results by Brummel et al\(^1\) must be interpreted with caution.

FXIII activation is known to be strongly influenced by a common polymorphism in the FXIII A-subunit gene (FXIIIVal34Leu),\(^2,3\) which has been shown to be protective against myocardial infarction,\(^4\) ischemic stroke,\(^5\) and deep vein thrombosis.\(^6\) This common G>T point mutation in codon 34, exon 2 of the A-subunit gene, which codes for the Val→Leu change, is only 3 amino acids from the thrombin activation site. The Leu allele is associated with increased cross-linking activity determined by an incorporation assay\(^3,7\) and a reduced clot formation time measured by thrombelastography.\(^8\) Kinetic studies on the activation reaction of FXIII by thrombin revealed increased catalytic efficiency (k_cat/K_m) for FXIII Leu34 compared with Val34.\(^9,10\) Activation of FXIIII Leu34 occurred at a similar rate as FPA release; FXIII Val34 was activated slower.\(^9\) Based on these findings, altered fibrin structures\(^9\) and wasteful, premature FXIII activation\(^10\) have been proposed as mechanisms of the protective effect of FXIIIVal34Leu.

Knowledge of the FXIIIVal34Leu genotype in these 6 individuals taking part in the study by Brummel et al\(^1\) is essential. Because of the high allele frequency of this polymorphism (approximately 0.25 for the Leu allele\(^3\)) in the general population and the significant kinetic differences between genotypes, the Val34Leu polymorphism has to be taken into account when FXIII activation rates are studied.

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References