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A Monthly Newsletter Summarizing Important Advances in Transfusion

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Mechanisms of action of IVIg: Involvement of an inhibitory immunoreceptor

Human plasma-derived intravenous immunoglobulins (IVIg) are increasingly being used in the treatment of autoimmune and inflammatory diseases. Although this trend in IVIg utilization has been observed for many years, the mechanism of action of this plasma derivative in autoimmune disorders has not been completely elucidated. Jeffrey V. Ravetch's group, from Rockefeller University (New York, NY, USA), investigated on the possible contribution of a membrane receptor found on the surface of specialized immune cells in the mechanisms of action of IVIg. Using an animal model of an autoimmune disease, Samuelsson et al. report in Science magazine that the inhibitory FcγRIIB receptor is essential for IVIg to exert its therapeutic effect. These results suggest a novel mechanism of action of IVIg, and opens up new avenues of research for the treatment of autoimmune disorders.

Samuelsson, A., et al. (2001). **Anti-inflammatory activity of IVIG mediated through the inhibitory Fc receptor**. Science 291: 484-486.

A blood test for variant Creutzfeld-Jakob disease screening?

As observed for different forms of transmissible spongiform encephalopathies (TSE), variant Creutzfeld-Jakob disease (vCJD) is characterized by the accumulation of an aberrant form of the prion protein (PrP^{Sc}) within the central nervous system. The minute quantities of PrP^{Sc} present in blood during the asymptomatic phase of TSE makes preclinical detection a major technical challenge. A research group from the Roslin Institute (Edinburgh, Scotland, UK) aimed at identifying biological markers found in blood that could serve in the preclinical diagnosis of TSE. A systematic analysis of genes from blood cells of infected animal models led to the identification of a gene, *EDRF* (Erythroid Differentiation-Related Factor), whose expression level progressively declines during the asymptomatic phase of TSE diseases. Although the sensitivity and specificity of this putative screening marker have not been evaluated, its potential use as a preclinical diagnostic test deserves further attention.

Miele, G., et al. (2001). **A novel erythroid-specific marker of transmissible spongiform encephalopathies**. Nat Med 7: 361-364.

Bovine spongiform encephalopathy transmission through the IV route

Although no human cases of TSE acquired through blood transfusion have been documented, some experimental results from animal models suggest that these atypical infectious diseases could potentially be transmitted through transfusion. Indeed, the results of a collaborative effort led by Jean-Philippe Deslys (Commissariat à l'Énergie Atomique, Fontenay-aux-Roses, France) and his team indicate that the prion strain responsible for bovine TSE can be transmitted to macaques through the intravenous route. This result adds credence to the active surveillance measures in place, including blood donor selection criteria, which collectively attempt at reducing the theoretical risk of transmission through transfusion.

Lasmézas, C. I., et al. (2001). **Adaptation of the bovine spongiform encephalopathy agent to primates and comparison with Creutzfeldt-Jakob disease: Implications for human health**. Proc Natl Acad Sci U S A 98: 4142-4147.

Long-term follow-up of transfusion-associated hepatitis C

Before the advent of sensitive tests for the systematic screening of hepatitis C in blood donors, a certain number of cases of hepatitis C virus (HCV) transmission occurred through transfusion. Leonard B Seeff and coworkers, from the National Institute of Diabetes and Digestive and Kidney Diseases (NIH, Bethesda, MD, USA) undertook a 25-year follow-up study of transfusion-associated hepatitis C patients. Overall mortality among HCV-infected patients was found not to differ significantly from that of a control group of transfused uninfected patients. However, liver disease-associated mortality was higher in HCV-infected patients compared to the control group. This study underscores the chronic disease character of HCV infection, and highlights the importance of adequate medical follow-up of HCV-infected patients.

Seeff, L. B., et al. (2001) **Long-term mortality and morbidity of transfusion-associated non-A, non-B, and type C Hepatitis: A National Heart, Lung, and Blood Institute collaborative study**. Hepatology 33: 455-463.