Evaluation of a Panel of Monoclonal Antibodies to D and Exploration of the Synergistic Effects of Blending IgG1 and IgG3 Antibodies on Their in vivo Biological Function

Transfusion 1999;39:1005–1011

The anti-D immunoprophylaxis program has not only strongly reduced the incidence of Rh haemolytic disease of the newborn but also the most important source of polyclonal anti-D, which still is the prophylactic product at present. Monoclonal and anti-D from hybridoma cell lines may become an acceptable alternative and clinical efficacy of individual monoclonal anti-Ds is being evaluated in several centres. The authors evaluated 20 monoclonal anti-Ds by investigating their in vitro biologic and serologic activity. The bioassays used were lymphocyte (K cell) antibody-dependant cellular cytotoxicity (ADCC), monocyte ADCC and monocyte chemiluminescence which together reflect the processes involved in the in vivo destruction of anti-D-sensitised red cells. Six antibodies, 3 IgG1 and 3 IgG3, were selected to study the effect of blending in the three assays. Several blends displayed greater activity in the three assays than their component parts in the range of 6–124%. There was no evidence of functional blocking effects. The blends containing both IgG1 and IgG3 were the most functionally active as were blends containing antibodies against different epitopes.

Hepatitis C Virus Transmission by a Blood Donation Negative in Nucleic Amplification Tests for Viral RNA

Lancet 2000;355:41–42

One problem concerning the transmission of viruses by blood transfusion is that recently infected donors go through a phase of viraemia before developing antibodies. This problem is greatest with HCV, which has a window period of 12 weeks. This led to a decision by the European Community that all plasma-derived products must be HCV, which has a window period of 12 weeks. This led to a decision by the European Community that all plasma-derived products must be

Prospective Investigation of Transfusion-Transmitted Infection in Recipients of over 20,000 Units of Blood

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The purpose of this study was to follow up recipients of 20,000 units of blood to identify infections transmitted by blood transfusion. Twenty-two London hospitals participated. The patients were adults who had recently been transfused. Further blood samples were taken at 9 months and were tested for markers of hepatitis B and C, HIV and human T cell leukaemia/lymphoma virus type I and II (HTLV) infections. Recent infections were distinguished from pre-existing infections by comparison with blood samples taken before transfusion. Of the 9,220 recruited patients 5,579 recipients of 21,923 units of blood were followed up. No transfusion-transmitted infections were detected. Thus, the incidence of transfusion-transmitted infections was 0 in 21,043 units (95% confidence interval for risk 0–1 in 5,706 recipients) for hepatitis B; 0 in 21,800 units (0–1 in 5,911 recipients) for hepatitis C; 0 in 21,923 units (0–1 in 5,944 recipients) for HIV, and 0 in 21,902 units (0–1 in 5,939 recipients) for HTLV. Three patients acquired hepatitis B during or after hospital admission but not by blood transfusion; 176 had pre-existing hepatitis B infection. Sixteen patients had pre-existing hepatitis C, and 5 had HTLV. It is concluded that the current risk of transfusion-transmitted infection in the United Kingdom is very small, but patients in hospital may be infected by other sources than transfusion. A considerable percentage of patients have pre-existing infections.

Solvent/Detergent-Treated Plasma Has Decreased Antitrypsin Activity and Absent Antiplasmin Activity

Blood 1999;94:3922–3927

Solvent/detergent (S/D)-treated plasma is currently marketed by the American Red Cross as a virally inactivated alternative of fresh-frozen plasma (FFP). The serpin-type serine proteinase inhibitors control major plasma proteolytic cascades, including coagulation, fibrinolysis, inflammation and complement activation. These inhibitors have a flexible reactive site loop that can convert from the active conformation to the inactive latent or polymerised conformation when exposed to heat or detergents. The authors have compared the conformational stability and inhibitory activity of three plasma serpins – antithrombin, antitrypsin, antiplasmin – in S/D plasma and FFP. In S/D plasma, virtually 100% of the antiplasmin and approximately 50% of the antitrypsin are in either the latent or the polymerised conformation and lack inhibitory activity, while in FFP only the active conformation...
is present. Interestingly, antithrombin is not affected by S/D treatment and remains fully active. These data demonstrate that S/D plasma is not simply a virally inactivated equivalent of FFP. The lack of antiplasmin activity and the decreased antitrypsin activity suggest that S/D plasma may not be as effective as FFP for the treatment of bleeding in patients with systemic activation of proteolytic cascades, such as disseminated intravascular coagulation and sepsis, acquired fibrinolytic states and large volume blood replacement. Clinical studies to directly compare the therapeutic efficacy of FFP and S/D plasma for the treatment of these conditions are needed.

L. Crisa, V. Circulli, K.A. Smith, et al.

**Human Cord Blood Progenitors Sustain Thymic T-Cell Development and a Novel Form of Angiogenesis**

Blood 1999;94:3928–3940

Haematopoietic progenitor cells in cord blood (HPCB) have become an important alternative for allogeneic bone marrow transplantation, particularly in children. Cord blood has been found to be a rich source of progenitors of the erythroid, myeloid and B cell lineages. Whether HPCB engrafting in the bone marrow space also comprises T cell progenitors capable of trafficking to the thymus and of reconstituting a functional thymopoiesis in young recipients is unknown at present. The authors show that HPCB engrafted in the bone marrow of immunodeficient mice sustain human thymopoiesis by generating circulating T cell progenitors capable of homing to and developing in a human thymic graft. Surprisingly, development of HPCB in this in vivo model extended to elements of the endothelial cell lineage, which contributed to the revascularisation of transplants and wound healing. These results demonstrate that human cord blood progenitor cells can reconstitute thymus-dependent T cell lymphopoiesis and show a novel role of progenitor cells derived from cord blood in angiogenesis.

B. Ludewig, A.F. Ochsenbein, B. Odermatt, et al.

**Immunotherapy with Dendritic Cells Directed against Tumor Antigens Shared with Normal Host Cells Results in Severe Autoimmune Disease**


Dendritic cells are the antigen-presenting cells par excellence and in fact are essential for the induction of a primary immune response. A recent development in transfusion medicine is the use of dendritic cells to enhance the immune response against weak antigens, e.g. tumor antigens. To this purpose, dendritic cells are pulsed with the antigen and then transfused to the patient. A danger of this therapy might be that if the tumor antigen is also expressed in peripheral non-lymphoid organs, it might cause severe autoimmune disease, because of the abnormally strong immune response against antigens that are normally ignored by the immune system.

The authors, using a mouse model, show that indeed severe autoimmune disease may develop in such a situation. Fatal autoimmune diabetes developed in transgenic mice expressing the target tumor antigen also on the β islet cells of the pancreas or severe arteritis, myocarditis and eventually dilated cardiopathy when arterial smooth muscle cells an cardiomyocytes expressed the transgenic tumor antigen. These results reveal the delicate balance between tumor immunity and autoimmunity and point out important limitations for the use of not strictly tumor-specific antigens in antitumor vaccination using dendritic cells.

A. Schuh, W. Atoyebi, T. Littlewood, et al.

**Prevention of Worsening of Severe Thrombocytopenia after Red Cell Transfusions by the Use of Leucocyte-Depleted Blood**


It has long been recognized that the transfusion of large quantities of blood, as well as smaller transfusions of 1–5 units, may lead to significant decreases of the posttransfusion platelet count. A fall in platelet count may be very serious in patients who are already severely thrombocytopenic. The authors measured platelet counts before and after red cell transfusions in 30 patients with anaemia and severe thrombocytopenia resulting from haemato logic diseases. There was a mean reduction of 1.1×10⁹/l (p=0.43) in the platelet count after transfusion of 2–3 units of leucocyte depleted red cell concentrates (20 patients). However, there was a mean reduction of 2.7×10⁹/l (p=0.03), ≈ 10%, in the platelet count after transfusion of non-leucocyte-depleted red cell concentrates (10 patients). The findings-suggest that the forthcoming introduction of universal leucocyte depletion of red cell concentrates will minimize the worsening of thrombocytopenia that occurs in severely thrombocytopenic patients receiving standard non-leucocyte-depleted red cell concentrates.