THE ROLE OF Fc FRAGMENT RECEPTOR IN IMMUNE INJURY TO HUMAN PLATELETS INDUCED BY PROTEIN A OF STAPHYLOCOCCI. J. Hawiger, S. Steckley, D. Hammond, C. Cheng, S. Timmons and R. M. Des Prez. Vanderbilt University and VA Hospital, Nashville, TN, USA.

The ability of the Fc fragment to trigger an immune injury to human platelets challenged with immune complexes or aggregated IgG was mainly observed in plasma-free medium. We now show that immune injury to human platelets in autologous plasma when Protein A-bearing staphylococci were added to the system. Protein A, a cell wall constituent of pathogenic staphylococci interacts with the Fc fragment of IgG making it reactive with the membrane receptor. Aggregation and release of [3 H]serotonin from human platelets suspended in autologous plasma occurred when at least two Protein A-bearing staphylococci were added per one platelet. Partial stripping of Protein A by trypsinization reduced the extent of platelet injury. When Protein A was solubilized and isolated by affinity chromatography, release of [3 H]serotonin by soluble Protein A-IgG complexes occurred only in plasma-free medium. Using radiolabelled Protein A, we demonstrated that release of [3 H]serotonin was paralleled by the binding of [125 I]Protein A-IgG complexes to platelet membrane. This binding was dependent on the Fc fragment and its receptor since the removal of the Fc fragment abolished the binding of Protein A to platelets. Thus, immune injury to human platelets has been demonstrated in two systems: (1) when Protein A was in solid phase, i.e., attached to staphylococci, platelet injury by Protein A-IgG occurred in plasma, and (2) when Protein A was in fluid phase, i.e., isolated from staphylococci, injury occurred only in plasma-free medium. Both mechanisms required the Fc fragment of IgG to interact with the membrane receptor on human platelets.

COMPLEMENT-DEPENDENT ACTION OF HLA-SPECIFIC ANTIBODIES ON HUMAN PLATELETS.

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HLA-antibody-induced platelet alterations are mediated by (a) complement-independent (Heinrich et al, Brit. J. Haematol., 35, 443, 1977) and (b) complement-dependent mechanisms. To prove the latter hypothesis platelet-rich plasma (PRP) of HLA-typed donors was incubated with HLA-specific sera and various inhibitors of platelet function (prostaglandin- E_1 (PGE $_1$), acetyl-salicylic acid (ASA), N-ethyl maleimide (NEM), adenosin, 2-desoxy-glucose + antimycin A (2-DOG + ANT.A)), furthermore an inhibitor of complement activation (cobra venom factor (CVF)) and EDTA or heparin known to interfere with platelet function and complement activation. Methods: Platelet aggregation (Born), 14 C-serotonin release and 51 Cr release. Results: Contrary to collagen- and thrombin-induced platelet alteration, PGE $_1$, NEM, ASA, adenosin and 2-DOG+ANT.A exhibited only moderate inhibition of antibody-induced platelet alteration. However, EDTA, heparin and CVF+PGE $_1$ strongly inhibited antibody-induced platelet alteration. The results support the concept of two pathways for specific HLA-antibody action on platelets: (a) a complement-independent mechanism resulting in aggregation and release and (b) a complement dependent, lytic mechanism.

IMMUNOLOGICAL ABNORMALITIES IN CHILDHOOD CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP).

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Chronic ITP, unlike acute ITP, may be the result of an underlying immunologic disorder. To examine this possibility 3 children, and their families (totalling 13 members) were studied in an attempt to identify underlying abnormalities in cellular and humoral immunity. All 3 patients had their disease for more than 1 year. All had shortened platelet life spans. None were receiving drugs, and none had had their spleens removed. In these patients, 2 of 3 were found to have decreased numbers of T lymphocytes and PHA reactivity; 2 of 3 had dysgammaglobulinemias; 1 of 3 had decreased isohemagglutinins, and all 3 had abnormal reactivity to a variety of intradermal antigens. In the family members these same abnormalities were found with increased frequency. 6/13 were found to have decreased numbers of T lymphocytes and PHA reactivity; 6/13 dysgammaglobulinemias and 1/13 decreased isohemagglutinins. In addition, autoantibodies such as a biologically false positive serological test for syphilis, and antithyroid antibodies were also found. A parent of one of the probands, and 2 asymptomatic siblings of another were also documented to have shortened platelet life spans in the presence of normal platelet counts. The HLA antigens, A3 and B7 were found in all 3 families. These 2 HLA antigens have previously been documented to occur with increased frequency in a variety of "auto-immune" disorders. These studies demonstrate that chronic ITP occurs in families with immunologic defects, and suggests that this disease has a genetic rather than an exclusively environmental basis.