1003 SUCCESSFUL TREATMENT OF AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA) IN COMMON VARIABLE IMMUNODEFICIENCY (CVID) WITH HIGH-DOSE INTRAVENOUS IMMUNE GLOBULIN (IVIG). Frederick E. Leickly and Rebecca H. Buckley, Duke University Medical Center, Department of Pediatrics, Durham, NC 27710.
Standard therapy for AIHA with steroids, cytotoxic agents and/or splenectomy carries an even greater risk than in normals for patients with primary immunodeficiency. Because of the success of high dose IVIG therapy in immune thrombocytopenia, we treated a male with CVID and AIHA with large doses of a pH 4.0 IVIG preparation as a potentially effective means of therapy. A diagnosis of CVID (IgG 330, IgA 4, IgM 24 mg/dl) had been made at age 18 years following a history of chronic sinopulmonary disease and splenomegaly, and he was begun on I.M. gamma globulin at 100 mg/kg/mo at that time. He had no hematologic abnormalities until age 21 when he presented with acute AIHA (hgb 5.3 g/dl, haptoglobin <5 mg/dl and a 4+ positive direct Coombs). After 60 mg/d of prednisone for 2 months, his hgb rose to 12.8 and his haptoglobin to 50 mg/dl. However, his Coombs test remained 4+ positive for IgG antibody and his retic ct. was 9.7. Steroids were discontinued and therapy with 450 mg/kg IVIG was initiated and continued daily for 5 days; He was then given 100-200 mg/kg of IVIG at 4 week intervals. During this period, his hgb ranged from 12.5-14 g/dl and his retic ct. dropped to 0.5-2.3. After 7 months of IVIG therapy, his hgb is 12.6 g/dl, retic ct. 1.6%, haptoglobin 147 mg/dl and Coombs test negative. These observations provide strong support for the use of high dose IVIG in immunodeficient patients with AIHA. It is safe and a mere modification of standard replacement therapy for humoral immunodeficiency.

1004 RETICULOENDOTHELIAL ACTIVATION, DIVERSITY IN MACROPHAGE SUBPOPULATIONS. D.B. MAGILAVY, T.R. HUNDLEY, and I.M. KATONA. Children's Hospital National Center Washington, D.C. 20010 and Naval Medical Research Institute, Bethesda, M.D. 20814

The effect of C. Parvum induced RES activation on Ia and Fc expression of hepatic nonparenchymal cells (NPC) and alveolar macrophage (AM) subpopulations was studied by flow microfluorometry (FMF). DBA/2J mice were injected I.V. with 1.4 mg C.Parvum. After 14 days, NPC were isolated by collagenase perfusion of the portal vein followed by separation on Metrizamide and Ficoll-Hypaque gradients. AM from the same animals were then isolated by tracheal lavage. Fc expression was determined by incubating the cells with saturating concentration of rabbit IgG dimers followed by FITC labelled goat anti-RIg. Ia expression was determined by H2-specific FITC or biotinylated anti-Ia and Texas Red Avidin. Percentage of positive cells is shown on following table:

	AM		NPC		
	Ia+	Fc+	Ia+	Fc+	Ia+Fc+
Control	10	45	15	40	15
C. Parvum	35	50	40	40	45

The intensity of Ia expression, as determined by median fluorescence intensity (FMI), increased over 20% in both AM and NPC after C.Parvum. Although Fc expression increased in AM, the fluorescence histogram for Fc expression of Fc+Ia+ NPC became variable with an overal decreased FMI in the C.Parvum treated mice. These data suggest a differential response to C.Parvum stimulation in number of Fc surface receptors expressed among RES subpopulations

1005 IN VITRO EFFECTS OF COMMERCIAL FACTOR VIII CONCENTRATES (FC) ON THE FUNCTION OF NORMAL LYMPHOCYTES. Marie Y. Mann, C.B.Daul, W.A. Andes, and R.D. deShazo (Spon. by J.E. Lewy), Department of Pediatrics, Tulane University Medical Center, New Orleans.

Hemophiliac patients receiving FC have immunological abnormalities associated with AIDS. Although a high percentage of hemophiliacs have antibody titers to HTLV-III, the etiology of their altered immune status is unclear. We have studied the in vitro effects of FC on mitogenic responses of normal peripheral blood mononuclear cells (PBM). Ten lots of FC (including one heat-treated and two associated with cases of AIDS) from 5 manufacturers were assayed. These were added in physiological concentrations to cultures of PBM stimulated with suboptimal and optimal concentrations of PHA (2 and 50 ug/ml, respectively). Addition of these FC significantly reduced the proliferative response in a dose dependent manner. One U/ml FC resulted in an average suppression of 40% at 2 ug/ml and 34% at 50 ug/ml PHA. At 0.5 U/ml, average suppression was 35% at 2 ug/ml and 18% at 50 ug/ml PHA. Two hour pre-incubation with PHA prior to addition of FC resulted in similar suppression; however, 24 hr preincubation resulted in less suppression. Neither column-purified Factor VIII activity or antigen had significant inhibitory effects. Cell viabilities in FC cultures were similar to control cultures. These results suggest that commericially available FC contains a factor(s) other than HTLV-III which inhibits the proliferative responses of normal lymphocytes. Efforts to isolate this factor(s) are currently in progress.

● **1006** IMMUNE RECONSTITUTION IN PRIMARY IMMUNODEFICIENCIES BY INTERLEUKIN-2 (IL-2). A. Mazumder, I.C. Guerra, H.M. Rosenblatt, and W.T. Shearer, Baylor College of Medicine, Department of Pediatrics, Houston, Texas

IL-2 has been shown to have immunorestorative capabilities in some animal and human systems of acquired immunodeficiency. In this report, we present our investigations into the efficacy of recombinant IL-2 in vitro in patients with primary immunodeficiency. 4/4 patients with DiGeorge syndrome were found to have deficient NK cell function (K562 lysis was 33-58% of controls, $p < 0.01$). The DiGeorge patients also had decreased production of IL-2 after PHA stimulation (4/4 had < 50% of normal controls, $p < 0.02$). Both of these parameters, however, were improved in 4/4 DiGeorge patients up to normal levels after incubation of their lymphocytes in IL-2 for 2 days (K562 lysis was now 85-104% and IL-2 production was > 90% of the controls, with the p value versus controls now > 0.3). Lymphocytes of 7 other patients with a variety of B cell and T cell acquired and primary immunodeficiencies were tested simultaneously in these assays to determine the specificity of the improvements seen in the defects of the DiGeorge patients. Depending upon the clinical status and specific immune defect in the patients tested, their NK cell function and/or IL-2 production was deficient ($p < 0.01$). However, none of the defects seen in these 7 patients were correctable by incubation in IL-2 ($p < 0.01$). Thus, specifically in DiGeorge patients, defects in NK cell function and IL-2 production can be corrected by incubation in IL-2. It is possible that the administration of IL-2 in vivo may play a role in the immunorestorative therapy of DiGeorge patients.

† **1007** ORAL ANTI-*PSEUDOMONAS* (Pδ) IgG PROVIDE SPECIFIC IMMUNE PROTECTION AGAINST Pδ SEPSIS DURING CYCLOPHOSPHAMIDE-INDUCED LEUKOPENIA. Richard McClead, Susan Gozs (Spon. by Grant Morrow), Dept. of Peds., OSU, Columbus, OH.

We previously showed that orally-administered bovine IgG antibodies resist proteolysis and provide specific immune protection. In this report we use specific anti-Pδ bovine IgG to reduce the mortality of Pδ sepsis in an immunocompromised host. We used a leukopenic mouse model to evaluate the protective effect of orally-administered anti-Pδ bovine colostral (BCI) and human serum (HISG) IgG and three other antimicrobial factors - lactoferrin (LF), lysozyme (LZ) and lactoperoxidase (LP). Leukopenic mice (cyclophosphamide, 300 mg/kg) were fed anti-Pδ BCI, control BCI, commercial HISG, LF, LZ, LP, or a 5% glucose solution (D5W) over a 6-day period. Anti-Pδ BCI, control BCI, and HISG had anti-Pδ activity by ELISA, agglutination, and complement fixation assays. On day 4 of feedings, the mice were orally-inoculated with 10^6 Pδ. *aeruginosa* (serotype 10). Mortality was recorded 24, 48 and 72 hours later. Group survival curves were not equal ($p<0.01$; Kruskal-Wallis). Paired comparison tests for the anti-Pδ BCI and D5W groups showed a decrease in mortality of ≈50% ($p<0.05$). Groups fed control BCI or HISG, which exhibit less anti-Pδ activity, had intermediate reductions in mortality. The mortality of groups fed LF, LZ, or LP was not different from the D5W group. We conclude that oral anti-Pδ BCI reduces the mortality of Pδ sepsis in a murine model of leukopenia. We speculate that oral antibodies to enteric organisms may be an effective means of reducing the incidence and severity of gram negative sepsis in leukopenic hosts.

1008 THEORETICAL AND BIOLOGICAL CONSIDERATIONS IN SUCCESSFUL MISMATCHED BONE MARROW TRANSPLANTATION. Robert Moen, Richard Hong, E. Richard Stiehm, Ronald Billing, William Shearer, Jerry Winkelstein, and John Johnson. Madison, Los Angeles, Houston and Baltimore.

Six children with severe combined immunodeficiency disease have received bone marrow transplants from a haplotype mismatched parent. The marrow was treated by monoclonal antibody and complement prior to infusion. Complicating factors involved the presence of prior maternal graft versus host in 1, prior thymus transplantation in 1 and presence of sufficient native immunity to require ablation in one. Two children died without engraftment. The survivors have B and T cell engraftment as demonstrated by normal in vitro T cell proliferative responses, normal immunoglobulin and/or functional antibody levels except one of the patients appears to have IgA deficiency. The longest period of follow up is 20 months and the shortest is three months. In 1 patient, thymus biopsy after transplant confirmed a normal distribution of cells and the presence of a marker for dendritic cells. This marker was not present in a patient who was not successfully engrafted.

These data show: 1. Successful engraftment can be accomplished with haplotype mismatched marrow even in the face of maternal graft versus host disease. 2. Haplotype mismatched marrow can home to the host thymus and be appropriately differentiated. 3. Criteria for prior ablative therapy need to be established; thymus immunohistochemistry may be helpful in this regard. 4. Mechanisms of the immune response can be inferred from the nature of the reconstitution.