854 HETEROGENEITY OF SEVERE COMBINED IMMUNODEFICIENCY DISEASE (SCID); DEMONSTRATION OF PUTATIVE GAMMA CHAIN T CELL RECEPTOR. Rajendra N. Pahwa, Chris D. Platsoucas, Savita G. Pahwa, Stanley Schwartz, Kyogo Itoh, Constantin Ioannides, Vasco Bonini, Ragab Aoun, Neena Kapoor, Mandel Sher, Noorbibi K. Day, Robert A. Good. Dept. of Pediatrics, All Children's Hospital, Univ. S. FLorida, St. Petersburg, Florida The syndrome of SCID represents a heterogenous group of congenital lethal disorders, characterized by defects of both T and B cell systems. The patient was an eight month old female who had normal numbers of B cells, T cells and T cell subsets but with marked defective humoral and cell-mediated immunity. Using a monoclonal antibody specific for gamma chain murine T cell receptor, we were able to identify a putative second T cell antigen receptor on this patient's peripheral blood mononuclear cells (PBM) which had been propagated in-vitro with Con A, OKT3 and recombinant IL2. This molecule was shown to be associated with the T_3 antigen and was composed of two polypeptide chains with molecular weights of 56 kd and 41 kd. T cells of healthy individual propagated in a similar manner in-vitro were lacking this molecule. Investigation of pokeweed mitogen induced B lymphocyte differentiation in-vitro into Ig secreting cells was suggestive of intrinsic B cell dysfunction with normal T helper cell function and no evidence of increased suppressor cell activity. Following cytoreduction with Busulfan and Cyclophosphamide,bone marrow transplantation (BMT) was done using HLA incompatible lectin separated T lymphocyte depleted marrow from father, to correct this disorder. At 28 days post BMT there is early evidence of engraftment. These findings demonstrate further, heterogeneity of SCID.

†855 INFLUENCES OF RELATED RETROVIRUSES ON HUMAN LYMPHOCYTES. Savita Pahwa and Carl Saxinger, Dept. of Pediatrics, North Shore Univ. Hospital, Cornell Univ. Medical College, Manhasset, New York, and Laboratory of Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland.

Infection with the human immunodeficiency virus (HIV) can lead to profound perturbations of the immune system as well as to clinical disease. In contrast, two related retroviruses, the human lymphotropic virus type IV (HTLV-IV) and the Simian lymphotropic virus type III (STLV-III) have not been associated with clinical disease in their infected hosts. In this study, these viruses were band-purified and disrupted. Protein-rich preparations of these viruses were compared for their influences on functions of B- and T lymphocytes of healthy, HIV-uninfected donors. As described previously, the HIV protein preparation could induce a T-dependent, polyclonal response in B lymphocyte cultures resulting in immunoglobulin secretion. In contrast, the other two viral preparations did not cause either proliferation or differentiation of normal B lymphocytes. Pokeweed mitogen-induced B cell differentiation responses were inhibited in a dose-dependent manner with HIV but not with HTLV-IV or STLV-III. None of the viral preparations induced a blastogenic response in peripheral blood lymphocyte cultures. T lymphoproliferative responses to mitogens, antigens and allo-antigens were inhibited to varying degrees by these viral preparations, with the order of magnitude of inhibition being HIV >HTLV-IV >STLV-III. These findings suggest that there maybe marked differences between these viruses in their capacity for causing immunologic damage.

●856 ADULT-LIKE ANTIBODY (Ab) RESPONSES TO HAEMOPHILUS INFLUENZAE b (HIB) CAPSULAR POLYSACCHARIDE (PRP) VACCINE IN HUMAN INFANTS PRIMED WITH PROTEIN-OLIGOSACCHARIDE CONJUGATE VACCINES. Michael E. Pichichero, Richard A. Insel, Porter W. Anderson, U. Rochester School Med and Dent, Strong Mem Hosp, Dept. Pediatrics, Rochester, New York 14642.

Ab to PRP are protective against Hib systemic infections, but infants of age <18 mo generally do not have an adequate Ab response to the current PRP vaccine. However, sequential injections of oligosaccharides coupled to diphtheria toxoid carriers (D-ol) can induce anti-PRP Ab in early infancy. The high titers are relatively transient, but a preliminary study showed that 6 infants given D-ol at age 2, 4, and 6 mo made a high-for-age and long-lived Ab response to an injection of PRP at age 9-11 mo.

These studies have been extended to show: (1) the phenomenon is consistent--26 of 27 D-ol-primed infants had an Ab rise with a geometric mean greatly exceeding that of unprimed infants; (2) a large response to the PRP "booster" can follow even a poor response to the D-ol priming; (3) while the response to D-ol is relatively high in IgG1/IgG2 ratio, the IgG2 tends to predominate in the response of infants to the PRP booster, as it does in the responses of adults; and (4) isoelectric focusing shows that the IgG response to D-ol consists of a relatively small number of B cell clones, that the response to the PRP booster occurs by re-stimulation of these clones, and that those clones with a low pI may be preferentially reactivated.

●857 VARIABLE EXPRESSION OF B CELL FUNCTION IN FAMILIES WITH X-LINKED AGAMMAGLOBULINEMIA (XLA). Kwang H. Pyun, Hans D. Ochs, Xiqiang Yang, Ralph J. Wedgwood. Univ of Wash, Dept of Pediatrics, Seattle

XLA patients have a defect of B cell maturation involving the pre B to B cell stages. This block is not absolute since circulating immunoglobulin $(Ig)^+$ B cells may be found in XLA. To evaluate B cell function in XLA, we studied 37 patients, including 31 from 13 families with multiple affected members. Sera from 33 untreated patients contained measurable IgG, 26 exceeding 200 mg%; IgG subclasses were proportionally diminished. IgM, at low concentrations, was detected in 27; IgA1 and IgA2 in 7, and IgA1 only in 1 patient. Following immunization with bacteriophage ØX 174, 13 failed to clear antigen and to produce antibody (Ab), 2 cleared phage without making detectable Ab. Of the 22 with low Ab titers, 9 switched from IgM to IgG (IgG1-3) after repeated immunization. Six of the 13 families with multiple affected members showed discordance in their response: some did, others did not clear phage and make Ab, correlating with the number of circulating B cells. EBV induced lymphoblastoid cell lines (LCL) obtained, with difficulty, from 14/19 patients were analyzed for Ig synthesis: 7 LCL synthesized IgM, and 1 IgA1. Six LCL produced both IgM and IgG; 4 IgG subclasses were present in 1 LCL, IgG1-3 in 3 LCL, IgG1 and 3 in 2 LCL, IgG1 and 2 in 1 LCL. The amount of Ig produced was significant, although 6/14 LCL produced only 5-10% of control LCL, the quantity being highest for IgM, followed by IgG3>IgG1 >IgG2>IgG4. In contrast, mitogen stimulated peripheral blood mononuclear cells produced predominantly IgG (80% of cultures); IgM was found in only 10% and IgA in none. These studies demonstrate a broad spectrum of B cell defects in XLA, often variably expressed in members of the same family. B cells, although markedly restricted in number and function, were demonstrated in every XLA patient suggesting a broad defect of B cell maturation and differentiation into Ig synthesizing cells.

858 IMMUNOGENICITY OF VARICELLA VACCINE (VV) IN HEALTHY YOUNG ADULTS. Gerard P. Rabalais, Myron J. Levin, and Frank E. Berkowitz. Spon. by Brian A. Lauer. University of Colorado Health Sciences Center, Department of Pediatrics, Denver, Colorado

Because varicella in adults has a higher morbidity and mortality than in children, susceptible adults are a group that would benefit from VV. Since little is known about the immunogenicity of VV in adults, we studied the immune responses of ten FAMA negative (fluorescent anti-membrane antibody) adults to VV. They received 2500 plaque-forming units of Oka/Merck VV (live, attenuated) and were boosted 3 months later. A FAMA was checked one month post vaccination and every 3 to 6 months thereafter. In addition, we studied their peripheral blood mononuclear cells by stimulation index (tritiated thymidine uptake with VZV antigen) responder cell frequency,RCF,(number of mononuclear cells that respond to VZV antigen), and ability to inhibit VZV plaque formation. The mean prevaccination stimulation index was 1.6, RCF was less than 1:100,000, and VZV plaque inhibition was 4%. Post vaccination, the mean values were 71, 1:30,000, and 51%, respectively. Although all ten adults had evidence of cell-mediated immunity by one month post vaccination, three were FAMA negative until after booster, and one remains FAMA negative 12 months later. No side effects were noted, and no decrease in humoral or cell-mediated immunity was seen over the follow-up period of 3 to 21 months (mean 12 months). This vaccine seems to be immunogenic in healthy, young adults but a discrepancy may be seen between the FAMA and tests of cell-mediated immunity.

859 CYTOTOXIC LYMPHOCYTE ACTIVITY IN RHEUMATIC HEART DISEASE (RHD). Warren E. Regelmann[1], Ernest D. Gray[1], S. Zaher[3], R. Kamel[3], Aziz El Kholy[2], Zahira Abdin[3], Mohammed Monsour[2], (Spon. by Patricia Ferrieri). U of MN, Pediatrics Dept., Minneapolis, MN[1]; Egyptian Org. for Biological and Vaccine Production, Cairo, Egypt[2]; Child Health Institute[3], Free Children's RH Center, Cairo, Egypt.

Decreased peripheral blood lymphoproliferative response due to dysfunctional non-T lymphocytes and the presence of unusual antigenic structures on peripheral blood non-T cells are among the alterations in the immune system found in patients with rheumatic cardiac valvular disease. The present study examined natural killer cell activity and generation of cytotoxic lymphocytes after exposure to blastogen A in patients with RHD and age- and socioeconomic-matched controls with recurrent tonsillitis but no rheumatic history, signs or symptoms. Peripheral blood mononuclear cells (PBMNC) were obtained by isopycnic centrifugation. Fresh PBMNC were incubated with 4 concentrations of K562 erythroleukemia cell targets. Rates of target cell lysis were measured by assay of lactate dehydrogenase using a spectrophotometric assay. Natural cytotoxic activity of freshly isolated PBMNC did not differ between RHD and controls. However, the PBMNC from RHD showed significantly less cytotoxicity after they were cultured alone in media for 6 days. In marked contrast, when cultured for 6 days in the presence of streptococcal blastogen A, PBMNCs from RHD showed greater rates of target cell lysis than controls at all target cell concentrations ($P<.01$ at 8×10^4 target cells). Thus, PBMNCs from RHD patients after exposure to a purified group A streptococcal product generate markedly greater than normal cytotoxicity against a target that displays differentiation antigens but not major histocompatibility antigens on its surface.