926 THE EFFECT OF PHENYTOIN ON IMMUNOGLOBULIN (Ig) PRODUCTION. Mark Holbreich and Anthony R. Hayward (Spon. by Richard B. Johnston, Jr.) Nat. Jewish Hosp. and Univ. of Colo. School of Med., Dept. of Peds., Denver, Co.

Patients treated for epilepsy with phenytoin develop a significant fall in serum IgA. We investigated this association because it may be a model for selective IgA deficiency. Phenytoin (20μg/ml) was added to human lymphocyte cultures stimulated by pokeweed mitogen (PWM). After 6 days in culture lymphocyte proliferation was measured by thymidine incorporation. B-cell differentiation and relative proportions of IgG-, IgM- and IgA- containing plasma cells (PC) were measured by counting PC in cytocentrifuge preparations stained for Ig.

Thymidine uptake ($\bar{x}$ ±SEM, n=6)		PC$\times 10^{-3}$/well ($\bar{x}$, ± SEM, n=6)		%Ig-bearing PC (%, ± SEM, n=5)	
Control	Phenytoin	Control	Phenytoin	Control	Phenytoin
4832(1498)	5008(1374)	55(12)	34(8)	IgG 47(3)	46(11)
p=NS		p=0.05		IgM 37(4)	34(3)
				IgA 16(2)	20(2)
				p=NS for each	

These results suggest that phenytoin at therapeutic levels does not interfere with PWM-stimulated thymidine incorporation. B-cell differentiation to PC was reduced but isotype distribution was unchanged. This latter finding is consistant with the published observation that IgG and IgM, as well as IgA, are lowered in some patients on phenytoin. The predominance of the in vivo effect on IgA may be due to a genetic predisposition, interference with T-cell cooperation needed for B-cell production of IgA, or direct interference by the phenytoin molecule in the biochemical basis of B-cell differentiation and proliferation.

● **927** RESTRICTED DIVERSITY OF THE LIGHT CHAIN OF HUMAN ANTIBODY (Ab) TO THE CAPSULAR POLYSACCHARIDE (CP) OF *HAEMOPHILUS INFLUENZAE* TYPE B (HIB). Richard A. Insel and Steven Schuster (Spon. by David H. Smith). University of Rochester Medical Center, Department of Pediatrics, Rochester, New York.

Previous studies by others have suggested that HIB infection above age 18 months and a delayed maturation of the infant's Ab response to HIB-CP may be associated with particular Km allotype antigens of the kappa light chain. To better understand the mechanism of this association, the light chain type distribution of anticapsular Ab induced by HIB-CP immunization and HIB infection was determined by an enzyme-linked immunosorbent assay. The light chain of immunization-induced antibody was predominantly of the kappa chain type in 19 of 25 adult sera and almost exclusively kappa chain in 9 of these sera. Kappa chain restriction did not correlate with the pre-immunization light chain type distribution nor the post-immunization antibody level. Restriction persisted up to 30 months after immunization. The convalescent sera of 9 of 10 patients recovering from HIB disease showed kappa chain restriction. In contrast, antibody to tetanus toxoid and the CP of *S. pneumoniae* type 3 in both groups of sera did not show light chain restriction. This light chain restriction of anticapsular Ab may be a partial explanation of the described association of delayed maturation of immunity to the HIB-CP with particular Km allotype antigens.

928 IS A SERUM INHIBITOR RESPONSIBLE FOR THE HIGH INCIDENCE OF SEVERE COMBINED IMMUNODEFICIENCY (SCID) IN NATIVE AMERICANS? James F. Jones, Linda Minnich, Vincent A. Fulginiti, Univ. of Arizona, University Hosp., Dept. of Pediatrics and Pathology, Tucson.

The incidence of SCID in one American Indian tribe approximates 1/3500 live births. In an ongoing attempt to evaluate this unexplained phenomenon, serum from 3 patients with SCID was examined for inhibition of normal lymphocyte response to mitogens and antigens. Responses were diminished from 33 to 99.9% with PHA, Con A, and PWM, and 22% with C. albicans when patient serum or plasma was substituted for AB plasma. If patient sera and AB sera were both present, inhibition ranged from 13-91%. A 24-hour incubation period was required to prevent removal of the inhibitory effect by washing of normal cells. Washing of patient cells did not restore function. The inhibitor effect was diminished after temporarily successful treatment with cultured thymus fragments in 2 patients, and following plasma and RBC infusion. Heterologous RBCs and PMNs, but not lymphocytes, adsorbed the inhibition activity. PMN function (chemiluminescence) was not altered by the sera. Analysis of the purine pathway by F. Schmalsteig (Galveston) showed the presence of ensymes and no toxic metabolites. Inhibitor activity was not removed by dialysis nor heating at 56°C for 30 min., and was always present in multiple samples. Serum from one of 4 caucasian SCID patients (courtesy of A. Goldman) suppressed only the Con A response. The relation of this inhibition to the etiology of SCID in these patients is uncertain, but additional studies are warranted.

929 INCOMPLETE LYMPHOCYTE DIFFERENTIATION IN B CELL LINES FROM IMMUNODEFICIENT PATIENTS. James F. Jones, Hans D. Ochs, Frank L. Meyskens. Univ. of Ariz., Depts. of Pediatrics and Medicine, Tucson, Univ. of Wash., Dept. of Pediatrics, Seattle.

EBV-infected cell lines from 31 immunodeficient (ID) patients and 1 normal individual, and 7 spontaneous cell lines from cancer patients were assayed for terminal deoxynucleotidyl transferase (TdT) activity. TdT is found primarily in pre-T cells in bone marrow, thymus, and in some acute leukemias; it is not present in mature circulating B or T cells. Twenty-nine lines were studied with and without ATP, a specific TdT inhibitor, and 11 lines without ATP. As a reference, 8402 cells (T cell line) had 0.400 units (U) of activity with >80% inhibition. Seven of 11 lines had 0.018 to 0.095 U of activity; 4 of these were from ID patients. Twelve of 29 lines had TdT activity with 8 having >50% inhibition; TdT values ranged from 0.006 to 0.037 units. The 4 lines without inhibition of TdT ranged from 0.007 to 0.01 U. All of the T cell leukemic lines (including 8392) contained TdT and were inhibited by ATP; the Burkitt's line was negative. Of the ID patients, 3/10 common variable ID, 3/7 ADA + SCID (1 ATP neg.), 1/1 Bruton's and 1/1 Wiskott-Aldrich were positive. All ataxia telangiectasia (4), X-linked agammaglobulemia with hyper-IGM (3), ADA negative SCID (2), and normal cell lines were negative. The presence of TdT in B cell lines from selected ID patients suggests persistence of abnormal lymphocyte differentiation in certain ID states.

930 ABNORMAL NK CELL AND SUPPRESSOR CELL ACTIVITY IN SICKLE CELL DISEASE. Joseph Kaplan, Wayne State University School of Medicine, Children's Hospital of Michigan, Department of Pediatrics, Detroit.

Abnormalities in the number or functional activity of regulatory T cells could contribute to deficiency of humoral immune factors which render children with sickle cell diseases (SCD) highly susceptible to overwhelming bacterial infections. Children with SCD are reported to have increased numbers of T cells with receptors for IgG, a population containing natural killer (NK) cells and suppressor cells. We have tested the functional activity of such cells in 15 children with SCD. NK cell activity was measured in a 3 hour chromium-release assay against target cell K562. Suppressor cell activity was assayed by quantitating concanavalin A-induced suppression of pokeweed mitogen-stimulated B cell Ig production. NK cell lysis of K562 at the low effector target ration of 10/1 was somewhat decreased in SCD compared to controls, but the difference was not statistically significant (16% vs 25%, $p>0.1$). However, the plateau value of maximum lysis at high E/T ratios was significantly lower in SCD children (42% vs 63%, $p<0.02$) suggesting that they may have increased numbers of cells which inhibit NK activity. Con A-induced suppressor cell activity was also significantly lower in SCD children than in controls (56% vs 89%, $p<0.01$). These alterations in NK cell and suppressor cell activity in children with SCD may be related phenomena caused by a common underlying mechanism, and may contribute to their increased susceptibility to infection.

● **931** NEWBORNS HAVE DIMINISHED NATURAL KILLER CELL ACTIVITY. Joseph Kaplan, Robert O. Bollinger, and Thomas C. Shope. Wayne State University Medical School, Department of Pediatrics, Children's Hospital of Michigan, Detroit.

Natural killer N(NK) cells appear to be an important first line of host defense against viral infections. Because a decrease in the number or functional activity of such cells could contribute to the increased susceptibility to virus infections which occurs in the newborn period, we sought to compare the NK cell activity of newborns and adults. Blood lymphocytes from 11 newborns and 9 normal adults were tested for spontaneous cell mediated lysis against standard tumor target cell line K562 in a 4 hr. chromium-release assay. The NK activity of newborn lymphocytes was considerably less than that of adult lymphocytes. At effector/target ratio 33/1 the mean % specific lysis by newborn vs adult cells was 9% vs 45% ($p<0.001$). Moreover the plateau level of maximum lysis at high effector/target ratios was significantly lower for newborn lymphocytes (29% vs 90%, $p<0.001$) suggesting that newborn lymphocytes contain cells which inhibit NK lytic activity. In support of this, newborn lymphocytes caused 20% inhibition of adult NK cell activity when present in the ratio of 1 newborn to 8 adult lymphocytes. The diminished NK activity documented here may be a major factor rendering newborns susceptible to overwhelming viral infections.