

**1002** IMMUNOREGULATION IN AN ISOLATED 12-YEAR-OLD BOY WITH CONGENITAL SEVERE COMBINED IMMUNODEFICIENCY. V.L. Paschall, L.A. Brown, E.C. Lawrence, R.A. Karol, E. Lotzova, B.S. Brown, and W.T. Shearer, Houston, TX.

We report the evaluation of *in vitro* immunoregulation in a 12-year-old untreated boy with severe combined immunodeficiency (SCID). Severely hypogammaglobulinemic, the patient was incapable of a specific antibody response to either natural substances or administered antigens. Ficoll-Hypaque-isolated peripheral blood mononuclear cells (MNL) from the patient failed to respond to pokeweed mitogen (PWM) with the normal increment in immunoglobulin-secreting cells (Ig-SC), as measured by a reverse hemolytic plaque assay. Since the patient was lymphopenic, his MNL were relatively enriched for monocytes (range = 51-81%). Removal of phagocytic cells or the addition of unrelated irradiated helper T lymphocytes resulted in enhanced, but still suboptimal response to PWM, suggesting some intrinsic defect in B lymphocyte function. Co-culture of patient MNL with normal MNL resulted in marked suppression (12% of predicted) of PWM-induced Ig-SC. Suppressor activity was unaffected by prior irradiation of patient MNL, but was substantially reversed (99% of predicted) by removal of his phagocytic cells; whereas the combination of the two procedures further reversed suppression (184% of predicted). The patient's MNL consistently demonstrated subnormal percentages of T3+ and T4+ cells and subnormal to low normal percentages of T8+ cells. These data suggest both an intrinsic defect in B lymphocyte function, and a relative excess of monocytes which could further inhibit Ig secretion by B lymphocytes. Natural killer cell function was severely depressed.

**1003** LINOLEIC ACID STIMULATION OF HUMAN T-LYMPHOCYTE CHEMILUMINESCENCE. Allen G. Peerless, Sheila R. Strom, E. Richard Stiehm, UCLA Dept. of Pediatrics, Los Angeles.

Chemiluminescence (CL) is a luminol-dependent property of concanavalin A (con-A) stimulated, nylon wool purified T-lymphocytes. Peak stimulated response (CPM x 10<sup>-3</sup> ± standard error) was 90±12, significantly (p<.001) greater than the background emission of 36±1.0. Utilizing linoleic acid (LA, 0.16 M) as both trigger and substrate in this luminol amplified system resulted in a mean peak response of 3327±1219 greater (p<.05) than the background of 41±2 and dramatically increased over the con-A induced response. Distinctive oxidative mechanisms are suggested not only by the nature of the stimulants in the reaction milieu, but altered kinetics (time to peak 2.4 minutes with con-A vs 25 with LA), differential sensitivity to anti-oxidant enzymes, and presence of the lipid peroxidative response alone in chronic granulomatous disease. We further explored lipid peroxidation in T-cells using an exquisitely sensitive luminometer (output range 0.01-10000 mV), eliminating the need for luminol. Peak and total luminescent responses (in mV) were measured in purified suspensions of T-cells and PMN:

	Peak	Total
T-cell	1.36±.27	6.25±1.49
PMN	0.1±.01	1.09±.27

p<.02, p<.05

The peroxidative potential of T-cells is further demonstrated by the superoxide dismutase resistant, LA stimulated reduction of ferricytochrome C (2.4 mM), 17.85 nM reduced per 5.0 x 10<sup>6</sup> T-cells compared to the non-stimulated background of 3.95. LA is a uniquely potent, luminol-independent trigger of T-cell CL. This phenomenon may serve as a valuable probe of cellular activation.

**1004** NEONATAL B CELL DIFFERENTIATION (DIFF). W.Pittard, K.Miller, R.Sorensen. C.W.R.U., Department of Peds., Cleveland, Ohio.

Perinatal factors influencing diff of cord blood B lymphocytes into immunoglobulin secreting plasma cells was studied in 126 neonates with gestational ages(GA) from 20-44 wks. A plaque forming cell assay measured background B cell diff and diff in response to pokeweed mitogen(PWM)plus hydrocortisone(HC). 8 infants had a GA less than 27.9 wks, 24 had GA's 28-32.9 wks, 30 had GA's 33-37.9 wks, 51 had GA's 38-41.9 wks and 13 had GA's above 42wks. The mean±SD GA was 36±5wks and B.Wt. 2400±980gm. The mean±SD background plaque formation was 98±253 and in response to PWM+HC was 7505±11874/10<sup>6</sup> cord blood mononuclear cells. B cell diff was observed in some neonates in all GA groups. The magnitude of *in vitro* neonatal B cell diff undergoes a continuous and significant(p<.002)reduction as GA increases. The influence of intra-uterine nutritional deprivation(IUGR)on B lymphocyte diff was studied, and compared to GA matched controls with a normal intra-uterine nutritional status. IUGR was not associated with a decrease in B cell responsiveness. Cesarean section and low one minute Apgar scores were associated with a significantly(p<.05)increased B lymphocyte diff. Although prolonged rupture of maternal amniotic membranes(PROM)was not singularly related to a significant increase in B cell diff, the combination of PROM and low Apgar scores(stress)was associated with a more significant increase(p<.003)than either factor alone. Thus, short term neonatal stress such as the combination of PROM and low Apgar scores has as much influence on neonatal B cell function as GA.

**1005** MODE OF DELIVERY AND NEONATAL LYMPHOCYTE PROLIFERATION(LP). W.Pittard, K.Miller, R.Sorensen, C.W.R.U., Departments of Pediatr. & Path. Cleveland, Ohio

Neonatal mitogen(M)induced lymphocyte proliferation reflects the hosts ability to develop a cellular immune reaction. Since LP and lymphokine release usually occur simultaneously and lymphokines enhance phagocytosis, LP suggests resistance to infection. To determine the influence of delivery on LP, we measured LP *in vitro* in 175 vaginally(vag) and 65 Cesarean section(CS)delivered neonates. LP/10<sup>5</sup> cord blood mononuclear cells was measured with a whole blood assay measuring tritiated thymidine incorporation(cpm). LP was significantly(p<.02)greater in neonates delivered by CS than in those delivered vag, and was more significantly increased in neonates delivered to mothers with no labor (cervical dilatation and/or effacement with uterine contractions) preceding delivery. This difference was not related to maternal anesthesia or perinatal stress (Apgar scores 6+).

	Labor(n=195)	No Labor(n=45)	p=NS
GA(wks) <sup>a</sup>	36.9±4.0	36.9±3.6	p=NS
BW(kg) <sup>a</sup>	2.6±.9	2.5±3.6	p=NS
Background <sup>b</sup>	.6±.9	.7±.5	p=.0244
Concanavalin Ab	65±49	98±61	p=.0001
Phytohemagglutinin <sup>b</sup>	45±44	80±57	p=.0000
Pokeweed mitogen <sup>b</sup>	23±17	30±15	p=.0004

Within the group of neonates delivered by CS, prior labor significantly(p<.04)decreased LP. Thus, the presence of labor prior to delivery significantly influences neonatal LP and may influence neonatal host defense.

<sup>a</sup>=mean±SD; <sup>b</sup>=mean±SD x 10<sup>3</sup>cpm/10<sup>5</sup> cord blood mononuclear cells

**1006** DiGEORGE SYNDROME AND GRAVES' DISEASE. A POSSIBLE RELATIONSHIP. A. Ham Pong, A. Cavallo, G. Holman, A. Goldman, University of Texas Medical Branch, and Texas Tech University Health Sciences Center, Departments of Pediatrics, Galveston, Texas and Lubbock, Texas.

Graves' disease is thought to be related to a defect in certain suppressor T-lymphocytes. It was of interest to discover Graves' disease in a 16 year old male with the DiGeorge syndrome. T-cell dysfunction had been documented in infancy by Kretschner, et. al (N. Engl. J. Med. 279:1295, 1968). Hyperthyroidism was documented and autoantibodies to thyroid microsomes were detected at age 13 years. Propylthiouracil treatment was begun. T-cell surface markers detected by monoclonal antibodies measured at age 14 years revealed OKT4, 34% and OKT8, 32%. After three years of antithyroid treatment, his immune status was reassessed; the number of circulating T cells (E-rosettes, 57%) and <sup>3</sup>H-thymidine incorporation following exposure to phytohemagglutinin (stimulation index (SI), 46:1) or candida (SI, 94:1) were normal.

Although T-cell function now appears to be normal it is likely that defective thymic embryogenesis in the DiGeorge syndrome resulted in inadequate T suppressor cell development and allowed for the occurrence of Graves' disease. We propose that as more patients with congenital T cell defects survive, an increased frequency of autoimmune disorders, particularly those affecting the endocrine system, will be observed.

**1007** EVALUATION OF SERUM IGE LEVELS IN TWINS AND THEIR PARENTS. Gilberto E. Rodriguez, Medical College of Virginia, Department of Pediatrics, Richmond, Va.

Serum IgE levels were measured in 394 twins and their parents. There were 116 monzygotic (MZ) twin pairs and 81 dizygotic (DZ) twin pairs. 85 twin pairs were younger than 15 years of age and 112 pairs were older. Mean IgE for MZ twins was 171.7 u/ml with a skewness of 7.7 and a kurtosis of 81.0 DZ twins had a mean of 159.7 u/ml. The sample curve was normalized by conversion to Log<sub>10</sub> IgE. Correlation coefficients for Log<sub>10</sub> are as follows:

	All Twins		MZ Twins		DZ Twins	
	T1	T2	T1	T2	T1	T2
T1	1.0000	0.6523	1.0000	0.7937	1.0000	0.4225
	P >	P =	P >	P >	P >	P =
	.00001	0.0001	.00001	0.0001	.00001	0.0001
T2		1.0000		1.0000		1.0000
		P >		P >		P >
		.00001		.00001		.00001
Fa	0.1449	0.2165	0.1727	0.2657	0.1025	0.1179
	P=NS	P=NS	P=NS	0.0680	P=NS	0.5348
Mo	0.3784	0.2734	0.3012	0.1762	0.5054	0.4520
	P =	P =	P =	P =	P =	P =
	.00005	0.0142	0.0335	0.2211	0.0044	0.0122

These results suggest a very strong genetic and maternal influence on serum IgE levels. The r value for twins < 15 y/o was 0.2563, P=0.0179 while for older twins it was 0.4771, P=0.0001 suggesting that environmental factors are more important early in life and genetic factors predominate adulthood.