●1026 PATHOGENESIS OF PARAINFLUENZA VIRUS (PV)-INDUCED CROUP: ROLE OF DEFICIENT REGULATION OF CELL-MEDIATED IMMUNE RESPONSE AND IGE PRODUCTION. R. Welliver*, M. Sun, D. Losi, SUNY and Children's Hospital, Buffalo, N.Y.

We studied children with croup (C) or upper respiratory illness (URI) alone due to PV to determine if abnormalities of immune regulation play a role in the pathogenesis of C. The presence of PV-specific IgE in nasopharyngeal secretions (NPS) was determined by an ELISA test. Whole blood lymphocyte transformation (LTF) responses to PV antigen were determined in vitro, and histamine was added to LTF assays in order to determine the degree of suppression of PV-specific LTF responses.

As expected, patients with C had significantly greater titers of PV-specific IgE in NPS than patients with URI alone (mean titer = 4.2 ± 1 vs. 1.6 ± 1, $p<0.05$). LTF responses to PV antigen were also greater in patients with C than in patients with URI (mean stimulation index = 3.7 ± 0.8 vs. 2.6 ± 0.4, $p<0.01$). The addition of histamine at 10^{-8} and 10^{-6} M to LTF assays resulted in a 70% suppression of the LTF response at each histamine concentration in URI patients, but only in a 36% and 40% suppression, respectively, in C patients ($p<0.05$). For the entire study group, the magnitude of histamine-induced suppression was inversely correlated with the peak titer of PV-IgE produced ($p<0.01$). Reduced function of a suppressor cell regulating both IgE production and lymphoproliferative responses to PV antigen may underlie the pathogenesis of PV-induced croup, and links this disease to bronchiolitis and to atopic disease states.

†1027 THE ROLE OF INTERLEUKIN 2 IN THE NEONATE. Karl Welte, James B. Bussel, Margaret W. Hilgartner, and Roland Mertelsmann. N.Y. Hospital-Cornell Med. Ctr., New York City, Dept. of Pediatrics, and Memorial Sloan-Kettering Division of Hematopoiesis.

The development of the Interleukin 2 (IL2) system of secretion and response via proliferation has not been well defined in neonates. We report the results of cord blood testing of 13 term neonates investigating T cell proliferation in response to PHA and OKT3, IL2 production, and response to exogenous highly purified IL2. The table divides the patients into 3 groups:

PATIENTS	N	PHA	PHA+IL2	OKT3	OKT3+IL2	IL2(OKT3)
nl PHA, nl OKT3	6	165	171	93	161	1.4
nl PHA,↓OKT3	6	127	135	16	130	0.4
↓PHA↓ OKT3	1	26	81	3	80	<0.2
TOTAL	13	137	147	51	140	0.9

It is clear that neonates have good responses to PHA but variable responses to OKT3 (group 1 vs. group 2). These depressed responses to OKT3 correct exuberantly to normal with exogenous IL2 and the IL2 measured in supernatants is significantly lower in group 2 patients than in group 1, suggesting that IL2 receptors are present on the cell surface but IL2 is not secreted. This discrepancy has previously been seen only in patients recovering from bone marrow transplantation and may help explain development of the immune system in neonates and implies a possible therapeutic role of IL2. Further studies in progress include clinical comparison of groups 1 and 2, identification of anti-OKT3 binding (OKT3 is part of the antigen recognition complex) and the role of macrophages/IL1.

1028 VIRAL IMMUNE RESPONSES OF PROFOUNDLY DEAF STUDENTS AGED 19. Lowell L. Williams (Sponsored by Dwight A. Powell) Dept. Pediatrics. Ohio State University College of Medicine. Columbus, Ohio.43205

We compared the viral-specific immunity of 6 profoundly deaf students born in 1964 with congenital rubella(CR) with that of 10 same-aged students profoundly deaf from other causes(OD). No defects other than hearing loss and mild retinitis were present. We measured GAM immunoglobulins(Ig),viral-specific antibodies(Ab) and in vitro lymphocyte stimulation indices (SI) against 7 heat-killed viruses, etiologically linked with deafness. The presence of prostaglandin-dependent lymphocyte suppression was determined by SI after indomethacin (IMC) addition.

CR vs OD students had lower mean rubella Ab titers (1:29+9 vs 1:52+29, p=0.05) and lower mean rubella SI (3.5+2 vs 22.9+11; p< 0.001). Rubella SI were not increased after IMC in the CR group. SI against other viruses were comparable in the CR and OD students. In contrast to the CRs, 9 of 10 ODs had increased SI to one or more viruses after IMC,indicating suppressor activity. Normal levels of Ig were present in all CRs but only 3 of 10 ODs.

The finding of immune tolerance against rubella virus in the CR group is a recognized event following intrauterine exposure to the virus. We demonstrate its persistence for at least 19 years. The finding of IMC-abrogated suppressor activity and altered Ig in these OD students suggests that their deafness, if virally-associated, differs in timing, or involves immunologic responses different from those following congenital rubella.

†1029 RESISTANCE OF GROUP B STREPTOCOCCI(GBS) TO KILLING BY OXYGEN METABOLITES. Christopher B. Wilson, William M. Weaver.(sponsored by A. Smith) Child. Ortho. Hospital and Univ. of Washington, Dept. of Pediatrics, Seattle, WA.

Known risk factors for early onset GBS sepsis include lack of specific antibody, density of maternal colonization and prematurity. An additional proposed risk factor, is decreased production of microbicidal oxygen metabolites by phagocytes of susceptible newborns(NB). However, GBS lack catalase, produce and release H_2O_2, and thus should be readily killed by phagocytes with a diminished respiratory burst. Surprisingly, GBS III were equally or more resistant than Staph aureus (SA) to reagent H_2O_2(60 min assay, n=5-7): $\log_{10}$ cfu/ml at none, 10^{-3}M, 5×10^{-3}M, 10^{-2}M H_2O_2 for GBS=7.1,7.3,5.9,3.1* and for SA=7.2,6.6,4.5*,4.4*-(*$p < 0.001$ vs none). Results with other strains of GBS were similar; Group A strep were more susceptible. Neither GBS nor SA were killed in 60 min by a xanthine oxidase-acetaldehyde - Fe^{++} - EDTA system by a flux of 0.7 nmoles O_2/ml/min; both were killed by 3.5 nmoles O_2/ml/min. Killing of both was inhibited by omission of Fe^{++} or EDTA and by addition of mannitol, catalase or superoxide dismutase, suggesting that hydroxyl radical (OH·) played a major role in microbicidal activity and was active at concentrations ~ 2 $\log_{10}$ less than H_2O_2. Although GBS lacked catalase, GBS compared to SA contained more glutathione(G) (68.2 vs 0.2 nmoles/mg) and G reductase (44.2 vs 1.3 nmoles/mg/min); SOD and G peroxidase were comparable. G may protect GBS from H_2O_2 and OH·. Defective phagocyte production of oxygen radicals, particularly OH· as reported by Ambruso(Ped 64:722,1979), may contribute to the NB's susceptibility to GBS.

●1030 INTERLEUKIN 2(IL2) AND MACROPHAGE ACTIVATION FACTOR (MAF) PRODUCTION BY NEWBORN LYMPHOCYTES. Christopher B. Wilson, Judith Westall. (sponsored by A. Smith) Children's Orthopedic Hospital and Medical Center and University of Washington, Dept. of Pediatrics, Seattle, WA.

The neonate (NB) is susceptible to severe infection with intracellular pathogens such as Toxoplasma gondii (T), resistance to which is mediated by lymphokine (MAF) induced macrophage (Mφ) activation. We have previously reported decreased production of MAF by NB lymphocytes from cord and peripheral blood, decreased responsiveness of newborn Mφ to newborn but not to adult MAF, and that MAF appears to be γ-interferon. Since γ-interferon production is IL2 dependent, we assayed IL2 production by Con A stimulated cord and adult blood mononuclear cells (MC). MC supernatants were assayed for IL2 by measuring ^{3}H-thymidine incorporation by an IL2 dependent CTLL cell line. Although lymphocyte transformation was comparable (Adult = 37822 ± 5795, NB = 38418 ± 2105 cpm, n=11), NB lymphocytes produced more IL2 (Adult= 543 ± 126, NB = 2414 ± 631 units/ml, n = 11, $p < 0.005$). In contrast, NB sups did not inhibit replication of T in Mφ (T per vacuole at 20h-control = 5.0 ± .3, + NB sups = 4.2 ± .3, NS) whereas adult sups did (T/vacuole = 2.9 ± .2, $p < 0.05$, n = 3). Unstimulated cord and adult MC did not release IL2 or MAF. These results suggest a disassociation between IL2 production and release of MAF by cord lymphocytes, which may contribute to the NB's susceptibility to infections with intracellular pathogens.

†1031 **HUMAN PLACENTAL CELLS AS REGULATORS OF LYMPHOCYTE FUNCTION.** Raoul L. Wolf (Spon. by Samuel P. Gotoff); Pritzker School of Medicine, Univ. of Chicago; Michael Reese Hosp. & Med. Cntr; Dept. Peds.; Chicago.

A normal fetus is an allograft, yet is tolerated by maternal immunological mechanisms. We have used soluble inhibitory factor (SIF) to study this phenomenon. SIF, a product of normal T lymphocytes and of the JEG-3 choriocarcinoma cell line, blocks proliferative and antibody-producing responses of mononuclear cells.

The villous surface of 5 normal human placentae was digested with collagenase to free cells that were predominantly multinucleated giant cells. After 5 days of standard culture, we assayed cell-free conditioned culture medium (CdM) for SIF content by measuring suppression of [^{3}H] thymidine incorporation ([^{3}H]TD-I) into lymphocytes stimulated by low-dose phytohemagglutinin. Significant suppression ($p<0.001$) was noted: 25,847±8,007 cpm (mean±SD) was reduced to 359±272 cpm by full-strength CdM and to 3,474±1,949 cpm by half-strength CdM.

SIF can be characterized by a noncovalently linked subcomponent, lipid suppressor substance, which was isolated from SIF in CdM by extraction into organic solvents and by thin-layer chromatography. SIF also appears to suppress lymphocyte response via a subpopulation of mononuclear cells. SIF-CdM likewise induced the development of cells that suppressed [^{3}H]Td-I from 30,625±3,013 cpm to 14,487±1,496 cpm.

Normal placental multinuclear cells thus release an SIF-like substance into culture fluid. Our findings support the hypothesis that the placenta modifies maternal immunologic mechanisms of rejection.

Aided by Basil O'Connor Starter Research Grant #5-347, March of Dimes Birth Defects Foundation.