954 DELAYED SERORESPONSE TO EBV INFECTION IN AN INFANT WITH AIDS PRODROME. James C. Fackler, Patricia T. Mildvan, Richard F. Ambinder, William H. Adler & James E. Nagel. Johns Hopkins School of Medicine, Dept. of Pediatrics, & National Institute on Aging, Baltimore, MD

A 7 mo. old girl, born to an IV drug dependent mother, presented with chronic diarrhea, impaired growth, hepatosplenomegaly & generalized lymphadenopathy. Serum immunoglobulins were elevated, but lymphocyte mitogen responses & T cell subsets were normal. EBV genome was detected in the saliva & in a spontaneous cell line grown from the patient's lymphocytes, however, anti-EBV antibody titers (VCA-IgM, VCA-IgG, EA & EBNA) were < 1.10. Following recovery from an episode of S. pneumoniae meningitis at age 10 mo. lymphocyte mitogen responses were decreased & T cell subsets abnormal (T4/T8 = .3). Serum anti-EBV antibody remained undetectable until age 14 mo. (VCA-IgG 1:400). At 16 mo. this rose to 1:2560 and EA-R was 1:20. Specific antibody to tetanus, diphtheria, pneumococcus and HTLV were present. Persistent tachypnea with a diffuse interstitial infiltrate developed at 11 mo. & did not respond to treatment with trimethoprim-sulfa. Lung biopsy tissue showed a peribronchiolar lymphocytic infiltration consistant with EBV pneumonitis. Confirmation by DNA hybridization is pending. Pulmonary symptoms were unchanged by IV acyclovir. The patient's lymphocytes continue to readily form EBV^+ lymphoblast lines. These data indicate that despite chronic, symptomatic, infection this child with an AIDS prodrome has developed a minimal antibody response to EBV. The relationship of EBV to the etiology of the AIDS prodrome is unknown.

955 IMMUNOSUPPRESSION BY NEONATAL APOLIPOPROTEIN E Trudy M. Forte, Linda Curtiss, Paul Davis, and Orsolya Genzel (Spon. by Bertram Lubin) Donner Laboratory, Univ. Calif., Berkeley, Dept. Immunology, Scripps Clinic, La Jolla and Children's Hosp. Med. Ctr., Oakland, CA.

Recent reports have suggested that in adults certain lipoproteins, particularly those carrying apolipoprotein (apo) E and apo B, play a role in suppression of the immune system. We have investigated the ability of lipoproteins from umbilical cord blood (CB) to suppress immune response. CB lipoprotein concentrations are lower than those of adult, i.e., the low density lipoprotein (LDL) level in CB is 30% that of adult while the high density lipoprotein (HDL) level is 50% of adult. Apo E concentration in CB is 2-fold higher than adult (5.8±2.5 mg/dl vs. 3.1±0.9 mg/dl). The ability of LDL and HDL to inhibit mitogen-stimulated ^{3}H-thymidine uptake in adult peripheral blood mononuclear cells (PMC) was used as an in vitro test system to study immunosuppression. Relative to adult lipoproteins, CB LDL and HDL were 2 to 4 times more potent in inhibiting PMC proliferation. Radioimmunoassay showed a strong correlation between amount of apo E in CB LDL and HDL and PMC inhibition. Selective removal of apo E-containing lipoproteins decreased significantly the inhibitory effect in CB LDL and eliminated almost completely inhibition by HDL. Results indicate that CB lipoproteins containing apo E in association with apo B and AI are capable of suppressing the immune response. Since the fetus is an allograft to its mother, the relatively high apo E levels may have a functional significance in the establishment of self and maintenance of the fetus in utero.

956 ONTOGENY OF DEVELOPMENT OF PHA-INDUCED GAMMA INTERFERON (IFN) PRODUCTION BY LYMPHOCYTES OF NORMAL INFANTS AND CHILDREN. L. Frenkel*, Y. Bryson; UCLA Sch. Med., Dept. Pediatrics, Los Angeles, Ca.

The increased severity of infections in young infants may be due to immaturity of the neonatal immune system. Studies have shown that lymphocytes from 1-7 day old infants make normal adult levels of alpha IFN, but have impaired production of PHA-induced gamma IFN. This impairment has been shown to be primarily due to a functionally immature neonatal macrophage. Gamma IFN production is important in recovery from viral infections and can also be used as a marker of macrophage function in infants. To determine the ontogeny of gamma IFN production in vivo, we obtained blood from 40 healthy children (age 1 day to 12 yrs), and 13 adult controls. Whole blood (adjusted to $2x10^5$ lymphs/ml) was incubated with PHA-A in RPMI for 48 hrs, and supernates assayed for IFN expressed in International Units (IU) by protection of WISH human aminon cells from encephalomyocarditis virus challenge. All adults (13) produced IFN geometric mean titer (GMT) 114 IU (range 25-756 IU). In comparison healthy infants ages 0-75 days exhibited markedly decreased gamma IFN with only 8/26 producing any detectable IFN (range 0-480 IU), GMT 2.75 IU ($p<.01$). Infants from 75-180 days of age produced gamma IFN at intermediate levels of 0-240 IU GMT=50 (N=6). Adult levels of gamma IFN were produced by 7/8 children >180 days old (180 days-12 yrs) levels 0-980 IU, GMT=177 IU (N=8). This impaired gamma IFN production in infants $\leq 2\frac{1}{2}$ mos. of age may represent a functionally immature macrophage system and may help explain the increased morbidity and mortality from bacterial and virus infections (particularly herpes simplex virus) in young infants.

957 NEONATAL AND PLACENTAL MACROPHAGES (MØ) SURFACE ANTIGEN EXPRESSION. D.M. Glover, C.B. Wilson, (spon. by A. Smith), Child. Ortho. Hospital and Univ. of Wash., Dept. of Pediatrics, Seattle.

The fetus and newborn are afflicted by infections that suggest a relative impairment in immunity; MØ play an important role in the immune response by clearing and processing foreign material. We compared surface epitopes necessary for antigen (Ag) presentation on neonatal cord blood MØ, fetal tissue MØ from the placenta, and adult blood MØ. Blood MØ were isolated by conventional methods. Placental MØ were obtained by enzyme digestion, density gradient separation, and selective adherence. Surface Ag expression was determined by indirect fluorescence microscopy using monoclonal antibodies towards: 1) Monomorphic HLA-DR determinants 7.2, L112 or 12.2; 2) a MØ surface epitope associated with enhanced accessory cell function-MØ 120; and 3) a human MØ marker F13. Viability of blood MØ was ($\bar{x} \pm$ S.D.) 91±5.3 and of placental MØ was 84±8 (NS); non-specific esterase and F13 staining were 90±4 and 87±4 and were comparable for each MØ type. Comparable and persistent expression of HLA-DR and MØ 120 were found for each MØ type.

	Adult Blood MØ			Cord Blood MØ			Placental MØ
Hrs. in cult.	0	24	96	0	24	96	0-24
HLA-DR (N=3-9)	89±4	89±2	87±7	89±4	90±7	86±5	84±7
MØ120 (N=3-10)	40±10	44±10	37±4	49±9	40±14	41±9	54±11

F.A.C.S. analysis of 0 and 96 hr. adult and cord MØ gave parallel but somewhat lower values. Thus, newborn MØ have the relevant surface phenotypes for Ag presentation; further investigation is needed to define functional correlates.

● **958** STRUCTURAL BASIS FOR THE MULTIPLE FUNCTIONS OF SECRETORY COMPONENT. RM Goldblum, CS Woodard, JB Splawski, and RM Denney, University of Texas Medical Branch, Galveston, Texas, Departments of Pediatrics and Human Biological Chemistry & Genetics.

Secretory component (SC) plays a central role in the mucosal immune system. This polypeptide serves as the epithelial cell receptor and transporter for polymeric IgA (pIgA) and protects IgA from proteolysis. To evaluate the structural basis for these functions, we produced a large panel of monoclonal antibodies to human free SC (FSC) and SC bound to secretory IgA (bSC). We examined the reactivity of these antibodies with FSC, bSC and reduced and alkylated sIgA (R-A sIgA) by ELISA, and to membrane SC on a colon carcinoma cell line (HT29) by immunofluorescence.

Twenty one of 22 antibodies from fusions in which sIgA was the immunogen bound preferentially to bSC, while 19 of 25 antibodies from FSC fusions were specific to FSC. These specificities were confirmed by reactions with complexes formed in vitro from pIgA and FSC. Few antibodies reacted with both FSC and bSC. Further testing with R-A sIgA allowed definition of at least 5 groups of epitopes on SC. Only a portion of antibodies reactive with one of these epitope groups mediated intense membrane and cytoplasmic immunofluorescent staining of HT29 cells.

These results are consistent with the synthesis of SC as an intergal membrane protein. The frequency of unique epitopes on the various physical forms of human SC indicates that this peptide undergos marked changes in tertiary structure or becomes integrated into surrounding structures. These modifications may be related to the various functions of SC.

959 SUCCESSFUL BONE MARROW TRANSPLANTATION IN DIGEORGE SYNDROME. Alan B. Goldsobel, Guillermo R. Mendoza, E. Richard Stiehm, UCLA, Dept. of Pediatrics, L.A.,CA.

DiGeorge syndrome is a congenital immunodeficiency disorder with variable degrees of T cell immunity. Immunologic reconstitution with fetal thymic tissue or hormones has shown varied success, and appropriate tissue is difficult to obtain.

A patient with DiGeorge syndrome presented at day 3 with hypocalcemia, seizures, Tetralogy of Fallot, and typical facies. Thymus shadow was absent on X-ray. Parathormone level was low. Evaluation at 26 weeks showed normal lymphocyte count, T cells 16% by E rosette, 1% by pan-T cell monoclonal antibody, B cells 65%, IgG 277 mg/dl, IgM 61 mg/dl, IgA 0, IgE 15 IU/ml, isohemagglutinins present at titer 1:1. Phytohemagglutinin (PHA), antigen and allogeneic stimulation were flat. Factor thymic serique was present at 1/4 (low), thymosin α_1 was 700 pg/ml (normal).

Because of the profound T cell defect with antibody defect, we performed bone marrow transplant (BMT) with 1.16×10^9 nucleated cells/kg from her HLA,A,B,C matched, DR mismatched, MLC nonreactive brother without conditioning. There was no evidence of GVH disease. PHA stimulated lymphocytes now show XY karyotype and T cells are 43% by E rosette. EB virus stimulated B cells are 29/30 XY, but DR type is unchanged. Immunoglobulins are normal, antibody and in vitro proliferative response to injected antigen are present.

This experience indicates that little thymic function is necessary for successful BMT, but does not determine whether there has been central or peripheral reconstitution.