967 REJECTION OF BONE MARROW TRANSPLANT (BMT) AND RESISTANCE OF ALLOANTIGEN REACTIVE CELLS TO IN VIVO DEOXYADENOSINE (DAD) IN A PATIENT WITH ADENOSINE DEAMINASE (ADA) DEFICIENCY

Morton J Cowan, Kevin Shannon, Diane W Wara, Arthur J Ammann, University of California, School of Medicine, Department of Pediatrics, San Francisco and OakNoll Naval Hospital, Oakland, CA

A soybean agglutinin processed haploidentical BMT was performed in a child with severe immunodeficiency and ADA deficiency who lacked a histocompatible donor. Because of significant alloreactivity in mixed lymphocyte culture (MLR) and to avoid chemotherapy we used DAD, which in ADA deficiency is metabolized to dATP and is thought to cause the immunodeficiency. We assessed the in vitro effects of DAD on bone marrow erythroid and myeloid colony formation (CFU-E, BRU-E, CFU-C) in normals, the patient and the donor. There were no differences among the 3 groups studied and increasing concentrations of DAD resulted in equivalent suppression of colony formation. Also, addition of EHNA (an ADA inhibitor) resulted in nonspecific inhibition of colony formation in all groups. Based on these results the patient received an infusion of DAD with increasing doses up to 200 mg/day. Erythrocyte (E) dATP rose from 200 nm/ml packed E to 900 while ATP remained at 300 nm/ml packed E. Suppression of the MLR did not occur. After the BMT the DAD infusions were continued for 1 month. Evidence of transient engraftment occurred at 2 weeks but did not persist. These results suggest that DAD/dATP inhibition of lymphocyte function is not the only mechanism in ADA deficiency and/or there are residual lymphoid cells resistant to elevated dATP.

● **968** **IMMUNE-SPECIFIC GAMMA INTERFERON (IFN) PRODUCTION CORRELATES WITH LYMPHOCYTE BLASTOGENESIS.** A. D'Andrea, S. Plotkin, S.D. Douglas, R.A. Polin. Dept. of Peds., Univ. of Pa. Sch. of Med., and The Children's Hosp. of Phila., Phila., PA.

Gamma IFN is produced by human mononuclear cells in culture from seropositive donors in response to cytomegalovirus (CMV), herpes simplex virus, mumps virus, and varicella zoster virus (VZV) antigens. The recent availability of an RIA for gamma IFN (IMRX™, Centocor Inc., Malvern, PA) makes gamma IFN production a potentially more rapid and sensitive measure of cell-mediated immunity than a six day blastogenesis assay. Mononuclear cells were obtained from 32 healthy adults (18 CMV seropositive (S+) and 14 CMV seronegative (S-)) by Ficoll hypaque gradients and cultured in triplicate in microtiter plates containing either CMV, VZV, tetanus antigen or phytohemagglutinin (PHA). Lymphocyte blastogenesis (^{3}H thymidine uptake) and gamma IFN were determined on day 6. The mean stimulation index (SI) of S+ (10.01 ± 9.46) was significantly greater than S- individuals (1.04 ± 0.67) ($p < 0.001$). Similarly, the gamma IFN stimulation index, defined as the concentration of gamma IFN (NIH units/ml) induced by viral antigen divided by the concentration induced by control antigen, was 93.82 ± 111.45 for (S+) and 2.49 ± 2.25 for (S-) ($p < 0.005$). Significant increases in gamma IFN also occurred with VZV and tetanus antigens. In 3 (S+) and 3 (S-) individuals, gamma IFN was assayed daily. Significant levels of gamma IFN (> 10 NIH units/ml) were observed for S+ individuals at 24 hours with peak levels at 4 days. No detectable levels of IFN (< 2 NIH units/ml) were observed in (S-) individuals during the six day incubation. In conclusion, mononuclear cell production of gamma IFN in a sensitive assay for CMI and is readily detectable in vitro as early as 24 hours.

● **969** CHARACTERIZATION OF IL2-DEPENDENT MARROW T PRECURSOR CELLS. Hans-Michael Dosch, Toshifumi Hibi and Gordon B. Mills. Research Institute, Hospital for Sick Children, Division of Immunology, Toronto, Ontario, Canada.

T helper precursor cells have been well characterized in human bone marrow. These cells require exposure to thymic epithelium or its products for their acquisition of functional activity. We now describe a population of marrow resident T suppressor precursor cells which require exposure to IL2 for their functional maturation. This population is completely distinct from helper cell precursors. It expresses T8 and TAC (IL2 receptor) determinants and acquires E receptors, T3 determinants and suppressive activity towards immunoglobulin secreting B lymphoid cells after as little as 4 hours of incubation in the presence of cell line derived or recombinant IL2. Helper precursors, in contrast, are $T4^+/T8^-/TAC^-$ and on density gradients they are separated as large buoyant cells from the small, dense suppressor precursors. In 2 patients with SCID, IL2 dependent T precursor cells appeared only late following thymic epithelial transplantation, after small numbers of T lymphocytes had appeared in marrow and circulation. We propose a model where pathways of extrathymic T cell differentiation are preceded by and dependent on the initiation of intrathymic T cell development. With about 10^{11} IL2 dependent T suppressor precursor cells present in an adult bone marrow, these cells may play an important role in immune homeostasis.

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970 A NEW INACTIVATED CONCENTRATED POLIOMYELITIS VACCINE

J. Drucker, B. Montagnon, M. Roumiantzeff
Institut Merieux, Lyon, France

A new inactivated polio vaccine produced on Vero Cells in a microcarrier system on an industrial scale has been used in a concentrated form to immunize children. A review of the different clinical trials of this vaccine in a two or three dose schedule is presented. Tolerance, potency and efficacy will be discussed.

971 THE ROLE OF LYMPHOCYTES IN THE MURINE MODEL OF ROTAVIRUS GASTROENTERITIS. Joseph Eiden, Robert Yolken, Howard Lederman, Steven Vonderfecht. Departments of Pathology and Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21205.

Rotaviruses are major etiologic agents of diarrhea in man and many animal species, but symptomatic infection occurs mainly in young individuals. The murine model of rotavirus infection was used to investigate whether lymphocyte-dependent mechanisms primarily determine age-related susceptibility to rotavirus infection. Mature, athymic, nude mice were infected per os with rotavirus, and their clinical course and antibody response were followed. Nude mice and normal controls were both very difficult to infect, even though the viral inoculum used was 10^4 greater than that required to infect newborn mice. Of those mice successfully infected with virus (3/7 nudes and 8/11 controls), none became symptomatic. The duration of virus excretion was similar in nude and normal mice, but nude animals did not mount an antibody response like normal controls. Additionally, newborn nude mice cleared rotavirus infection in a manner similar to age-matched controls. These studies suggest that lymphocyte response and antibody production are not necessary for adult mice to recover from rotavirus infection.

Rotavirus Infection of Adult Mice

	Nudes (# positive/total)	Normals (# positive/total)
Diarrhea	0/7	0/11
Antibody response	0/7	8/11 ($p < .001$)
Antigen excretion	3/7	8/11

● **972** PLACENTAL TRANSFER OF ANTIBODY: CORRELATION WITH SUBCLASS COMPOSITION. M.S. Einhorn, A. Quinn and P.G. Shackelford, Wash.Univ.Sch.of Med.,St. Louis

Previous studies indicate that IgG1 concentrations are higher in cord than in maternal sera whereas IgG2 is thought to cross the placenta less well. Transfer of specific subclasses has not been related to the concentrations of specific antibodies of differing subclass composition. Therefore, we measured the concentration of IgG1 and IgG2 and of IgG-anti-tetanus toxoid (TT), IgG-anti-H.influenzae, type b capsular polysaccharide (PRP) and anti-group A streptococcal carbohydrate (GAC) in 16 paired maternal (M) and cord (I) sera. Measurement of IgG1 and IgG2 was performed by a competetive radioantigen binding assay. Measurement of anti-TT, anti-PRP and anti-GAC was accomplished with an IgG-solid phase RIA, an IgG-ELISA, and a radioactive antigen binding assay, respectively. Previous studies have shown that anti-TT of adults is 90% IgG1, anti-PRP is 40% IgG1, 60% IgG2, and anti-GAC is 90% IgG2. By paired t-test, mean IgG1 was higher in I than M sera ($p < .001$), mean I/M=1.78±.59. IgG2 was not different in I and M sera, mean I/M=0.98. Anti-TT was higher in I than M ($p=0.002$), mean I/M=2.228±1.17 and anti-GAC was not different, mean I/M=1.07±.63. Anti-PRP was lower in I than M sera ($p=0.05$), mean I/M=0.88. Thus, IgG1 but not IgG2 is selectively transferred across the placenta. As a result, anti-TT (predominantly IgG1) is higher in infant than maternal sera, whereas anti-GAC (predominantly IgG2) is not. The reason for lower concentrations of anti-PRP in I than M sera is unclear.