950 ALTERNATIVE PATHWAY (AP) OPSONIC ACTIVITY OF NEWBORN (NB) SERA AS MEASURED BY CHEMILUMINESCENCE (CL). Julia A. McMillan, Roger E. Spitzer, Leonard B. Weiner, Ann E. Stitzel, Ellen C. Blinder and David A. Clark. SUNY, Upstate Medical Center, Department of Pediatrics, Syracuse, NY.

Defects in the AP of complement are thought to play a role in the susceptibility of newborns (NB) to infection. The CL assay was used to measure the ability of varying quantities of 20 cord sera to opsonize zymosan (Z). Concentrations of AP components were correlated with CL and outcome. Luminol enhanced CL was performed using adult polymorphonuclear leukocytes to react with the opsonized Z. The cord sera was found to contain 30-70% of normal concentrations of C3, factor B, properdin, β1H, and C3bINA. Mean opsonization as measured by CL was decreased for cord sera when compared to controls; however, some NB sera demonstrated normal ability to opsonize Z. Opsonic activity varied significantly only with the β1H concentration of the serum. β1H, along with C3bINA, is known to regulate the activity of C3 and factor B in the AP so that the ratio of C3+factor B/β1H+C3bINA in non-NB's is approximately 1.0. In the cord sera of 200 uninfected NB's, however, this ratio was 1.3 ($p < 0.001$) suggesting an altered regulatory mechanism for the normal NB. Eight of 9 NB's who experienced systemic infection in the first few days of life had a ratio of AP components equivalent to the non-NB's. These data demonstrate that failure to develop a typical neonatal regulatory pattern may play a role in defective opsonic activity and that CL may be used to study this activity in NB sera. The ability of NB sera to opsonize Z, however, does not predict susceptibility to infection.

● **951** IMPAIRED SPECIFIC IN VITRO ANTIBODY RESPONSES IN PATIENTS WITH ATAXIA TELANGIECTASIA (A-T). David L. Nelson and Robert Yarchoan (Spon. by R.M. Blaese). Metabolism Branch, NCI, NIH, Bethesda, Maryland.

Specific antibody responses in vitro can be induced in the peripheral blood mononuclear cells (PBMC) of >90% of normal individuals by stimulation with type A influenza viruses. Cumulative antibody synthesis is measured in 12 day culture supernatants by ELISA methodology. Antibody production requires the cooperative interaction of B-cells, T-cells, and monocytes. Antibody is expressed in units (U), 1 U being the amount of antibody present in a $1/10^5$ dilution of a pooled reference serum (approximately 2.2 ng of IgG antibody). PBMC from only 1 of 5 A-T patients made measurable antibody; this one patient made 0.7 U/ml. This is considerably less than that produced by PBMC from 6 parents of A-T patients (13.6 ± 7.7, mean ± SEM) or 14 normal controls (19.1 ± 5.5). Further studies were undertaken to examine the mechanism of non-responsiveness in 2 patients. The first patient's PBMC produced antibody when co-cultured with purified, irradiated, allogeneic T-cells and the second patient's purified B-cells produced antibody when stimulated with Epstein-Barr virus. Thus both patients had B-cells which could be stimulated to produce specific antibody. Functional monocytes were also demonstrated in the second patient since his irradiated, adherent cells reconstituted antibody production by cultures of monocyte-depleted PBMC from a normal HLA-identical sibling. These results suggest a T-cell abnormality as a cause of deficient in vitro antibody production in some A-T patients.

952 IMMUNE RECONSTITUTION IN ADENOSINE DEAMINASE DEFICIENT SEVERE COMBINED IMMUNE DEFICIENCY. Hans D. Ochs, Kenneth C. Rich, Sheldon D. Horowitz, Ted D. Groshong, Ralph J. Wedgwood, Depts. of Pediatrics, University of Washington, Seattle; Northwestern University, Chicago; University of Wisconsin, Madison; University of Missouri, Columbia.

Severe combined immune deficiency (SCID) associated with adenosine deaminase (ADA) deficiency presents an excellent model to study enzyme replacement therapy. To evaluate the effectiveness of enzyme replacement and other therapeutic regimens, we compared antibody responses to a T-dependent neoantigen, bacteriophage ØX 174 in 4 patients with ADA deficiency: one was treated with repeated red blood cell transfusions, one with a single infusion of peripheral blood mononuclear cells, one with fetal liver cells, and one with bone marrow from an HLA matched sibling. Normal antibody responses to this antigen consist of a primary IgM response followed by a brisk secondary IgG response of high titer. The antibody responses of the patients varied depending on the mode of therapy. Enzyme replacement therapy by transfusion of red blood cells, or transplantation of peripheral blood mononuclear cells, although associated with clinical improvement and partial immune reconstitution if recall antigens or mitogens were used, did not restore the antibody responses to phage: neither amplification nor IgG production occurred. The infant transplanted with fetal liver cells responded with low antibody titers but a moderate IgG response (22%) was found. Only the child treated with matched bone marrow showed a quantitatively and qualitatively normal antibody response. These results demonstrate that extrinsic enzyme replacement alone is insufficient in this syndrome and that a full set of normal uncommitted lymphoid stem cells is required for complete immune reconstitution.

953 IMMUNOGENETICS OF JUVENILE DERMATOMYOSITIS (JDMS), A COLLABORATIVE STUDY. LM Pachman, MC Maryjowski, JM Friedman, O Jonasson, RM Radvany, MA Cobb, ND Battles, WE Crowe, CW Fink, V Hanson, JE Levinson, CH Spencer, DB Sullivan, Depts. of Pediatrics, Northwestern Univ. Med. School, Children's Mem. Hospital, Chicago, Univ. of Cincinnati Med. Ctr., Children's Hosp. LA, USC Med. School, Univ. of MI Hosp., Ann Arbor, Univ. of Texas Health Ctr., Dallas, and Depts. Surg. Northwestern Univ. Med School, and Univ. of Illinois.

5 medical centers provided 90 children with definite JDMS who had the characteristic skin rash and 3 or 4 criteria: symmetrical proximal muscle weakness, positive muscle biopsy, abnormal EMG, and serum elevation of muscle enzymes. 67 white children had an increase in HLA-DR3, relative risk 3.91, corrected $p<.002$. Increased HLA-B8, relative risk 2.88, corrected $p<.005$ was also found. A marginal decrease in HLA-B7 was seen, relative risk 0.20, uncorrected $p<.01$, corrected $p<.20$. Their sera was examined for immune complexes Raji and C1q, and antibody to thyroid microsomes, gastric parietal cells, smooth muscle, striated muscle, nuclei, DNA, ENA, RNP, Sm and Pm-1. Only ANA and Raji values were significantly increased, $p<.001$, above controls. Positive sera occurred with equal frequency in those with HLA-B8 or DR3 as in children without those antigens. Supported by grants from NAIMDD & Ill. Chapter of Arthritis Foundation.

● **954** HUMORAL IMMUNE RESPONSE IN VITRO AFTER BONE MARROW TRANSPLANTATION (BMT). S. Pahwa, W. Freidrich, R. Evans, R. O'Reilly, & R.A. Good. Memorial Sloan-Kettering Cancer Center, Immunobiology Division, New York.

B cell- and immunoregulatory T cell function was investigated in polyclonal [pokeweed mitogen (PWM) driven] and antigen-specific (antigen, SRBC) antibody producing assay systems in peripheral blood lymphocytes (PBL) of 21 patients who were given BMT for hematologic disorders. Markedly deficient B cell responses were observed in the first 8-10 months after BMT and these were attributable to both B- as well as T cell dysfunction. Subsequently, while B cells became responsive in the majority of patients, T cell abnormalities persisted and hampered the successful induction of T-dependent antibody responses for an additional period of 4-6 months. Abnormalities of T cell function consisted of both excessive suppressor cell activity and decreased helper function. The former was most pronounced in the first 4-6 months after BMT. Abnormally high suppressor T cell activity and deficient helper function was noted for an extended period of time in 2 patients with chronic graft versus host (GVH) disease. Determination of surface antigen phenotype of T cells using monoclonal antibodies revealed an inverse helper/suppressor cell ratio in these patients. These findings indicate that deficient humoral immune responses in the period following BMT derive initially from B- as well as T-cell abnormalities, and later, mainly from T cell dysfunction. In chronic GVH, increased proportions of functionally active suppressor T cells may persist for prolonged periods of time.

955 TREATMENT OF CHRONIC CYTOMEGALOVIRUS INFECTION WITH INTERFERON. S. Pahwa, D. Kirkpatrick, C. Ching, C. Lopez, E. Smithwick, R. Pahwa, R. O'Reilly, P. Pasquariello, A. Korval, C. August, & R. Good. Sloan-Kettering Institute, New York, and The Children's Hospital, Philadelphia.

Treatment with human leukocyte interferon (IF) was initiated in Dec.'78 in a child (age 20 mo) with dysgammaglobulinemia type I (hyper M) and postnatally acquired CMV infection. History included pneumonias (CMV & Pn. carinii) at 5 and 8 mo, and onset of recurrent episodes of high fevers, rash, lymphadenopathy, severe oral ulcerations, and neutropenia at 1 yr age. Urine and salivary cultures repeatedly grew CMV, and inclusion bodies were present in a salivary gland biopsy. Functions of phagocytic, T, B and natural killer (NK) cells were severely depressed; NK activity could be augmented in vitro with IF. Levels of serum thymic hormones were very low. Altogether, 4 courses of IF were given (dosages varied from 2 million u/day to 1 million u 3 times/week) for periods of 10d, 28d, 80d, and 55d until Sept.'79. Plasma with high titer CMV antibody was given every 3 weeks. During IF treatment, NK normalized; excretion of CMV ceased but recurred on occasions between IF cycles. Because of severe oral and oesophageal ulcers a trial of Levamisole was initiated in Sept.'79 and a feeding gastrostomy was inserted in Dec.'79. Plasma therapy was continued throughout. Recovery of clinical and immunologic abnormalities followed. At age 3½ yr the patient has an esophageal stricture but otherwise is completely well with no recurrence of CMV. IF appears to be a useful therapeutic modality for chronic viral infection in certain immunodeficient children.