IMMUNOLOGICAL RECONSTITUTION IN SEVERE COMBINED IMMUNODEFICIENCY DISEASE WITH TRANSPLANTATION FROM A NON-COMPATIBLE DONOR. Otto F.Sieber, Vincent A. Fulginiti, Brian G.Durie, Sydney E. Salmon. Univ. of Az., Coll. Med., Univ. Hosp., Depts. of Ped. and Med., Tucson.

We report the immunological reconstitution of an infant with combined immunodeficiency disease (CID) following transplantation of cells from a donor incompatible by mixed lymphocyte culture (MLC) typing.

Previous long term reconstitution in CID has been achieved by transplantation of bone marrow cells either genetically compatible by HL-A typing or more recently, in MLC.

Reconstitution has occurred in this infant with CID. No donor cells completely compatible in MLC were available. However, paternal immunocytes reactive in MLC could be eliminated in vitro with a pulse of tritiated thymidine of high specific activity. The remaining immunocytes were MLC compatible with the infant's cells. Cells were prepared in vitro in this way on three occasions (twice from peripheral blood and once from bone marrow) and transplanted intraperitoneally over a 4 month period, utilizing increasing numbers of donor cells each time.

Now at 12 months of age, the infant exhibits a moderate chronic graft versus host reaction. Immunoglobulins are normal. Cell mediated responsiveness measured in vitro by phytohemagglutinin, pokeweed, and MLC reactivity is present. Skin tests have reverted to negative. B and T lymphocytes are present. This suggests that there is a potential source of cells from non-compatible donors for reconstitution of CID.

INTERFERENCE WITH THE ALTERNATE PATHWAY OF COMPLEMENT ACTIVATION DURING TRANSPLANT REJECTION. R. Spitzer, L. Florio, A. Stitzel. State University of New York, Upstate Medical Center, Dept. of Pediatrics, Syracuse, New York 13210.

During the rejection of an allotransplant, there appears in the circulation a material which interferes with the alternate pathway of complement activation. This material also deposits on the graft and may be eluted and further purified by gel filtration. When added to normal human serum and zymosan, the rate of C3-C9 hemolytic consumption is retarded. This appears to result from an inhibition of the early steps in the alternate pathway leading to the initial generation of $C3_b$ and activation of C3 proactivator. Thus, this material can prevent C3-C9 hemolytic consumption when added to a mixture of activated properdin convertase and normal human serum. Initial activation of properdin convertase by zymosan is not affected. Separation and culture of peripheral lymphocytes from patients rejecting a transplant show that there is elaboration of the material responsible for the interference with the alternate pathway activity. Removal of 85-95% of B cells by passage over antigen-antibody-complement coated columns does not prevent this generation suggesting that T cells may be responsible. This data may, therefore, represent evidence for a link between T cell function and the alternate pathway of complement activation in graft rejection. (Supported in part by NIAMD grant AM 17376)

QUALITATIVE IMMUNOGLOBULIN (Ig) DEFICIENCY, RECURRENT INFECTIONS, AND INTACT CELLULAR IMMUNITY. Allan D. Singer, Patricia E. Byfield, Anita Weinstein, Michael Glovsky.(Intr. by Douglas C. Heiner). Harbor General Hospital, Torrance,CA and Kaiser Permanente Hospital, Los Angeles, CA.

A 10 year old female has had repeated episodes of bacterial infections including pneumonia, otitis, adenitis, and urinary tract infections. She is short, has lymphadenopathy and a protuberant abdomen. IgG=1500 mg%, IgM=430 mg%, IgA=68 mg%, IgD 18.5 mg% and IgE=14 IU/ml. Ig Subclasses, immunoelectrophoresis and complement component activity are normal. After isolating Group A streptococci from the throat and an excised node, ASO and other streptococcal antibody titers were low or undetectable. The excised lymph node showed reactive hyperplasia. Lymphocyte counts were normal. Blood is Group O and isoagglutinin titers (A and B) were absent. Responses to diphtheria, typhoid and hexavalent pneumococcal vaccine were minimal or absent. Normal numbers of B lymphocytes were determined by membrane immunofluorescence and rosettes. Spontaneous rosette formation with sheep erythrocytes was normal. In vivo delayed hypersensitivity was normal. Normal lymphocyte responses to mitogens and allogeneic cells occurred. Neutrophil (PMN) chemotaxis, mobility, phagocytosis and bactericidal activity were normal. A serum related defect in PMN opsonic and cidal activity with strep and E. coli was reversed with normal serum. The patient appears to represent a profound abnormality of antibody formation associated with recurrent infections.

THE PROPERDIN ACTIVATOR SYSTEM: A REACTION MECHANISM LEADING TO UTILIZATION OF THE CLASSICAL AND ALTERNATE PATHWAYS OF COMPLEMENT ACTIVATION. R. Spitzer, A. Stitzel. State University of New York, Upstate Medical Center, Dept. of Pediatrics, Syracuse, New York 13210.

Isolation of a new enzyme, designated properdin convertase, has allowed elucidation of a new series of reactions which taken together constitute the Properdin Activator System. At 37°, zymosan activates the isolated precursor form of properdin convertase in the absence of other factors except divalent cations. The activated, properdin convertase is present in the fluid phase and will interact with purified properdin at 37° after zymosan has been removed. Separation of these two proteins by electrophoresis on 6% polyacrylamide gel at pH 8.6 shows that the properdin has now acquired a cathodal migration and will interact directly with purified native C3 to consume over 90% of its specific hemolytic activity. When the activated properdin is added to NHS, however, not only is C3 consumed but also C3 proactivator is cleaved and the specific hemolytic activity of C_4 and C2 are consumed. Neither the cleavage of C3PA nor the consumption of C_4 or C2 will occur in sera depleted of C3 by antibody adsorption. Since C3PA, C_4 or C2 are not involved in the activation of properdin convertase or properdin, it appears that the utilization of these substances are secondary to the reactions of the properdin activator system and C3. (Supported in part by NIAMD grant AM 17376 and the N.Y.S. Kidney Disease Institute)

IMMUNOGLOBULINS IN THE AMNIOTIC FLUID AND FETUS. Allan D. Singer, Calvin J. Hobel, Douglas C. Heiner. UCLA School of Med., Harbor Gen. Hosp., Dept. of Ped., Torrance, California.

Interest in the prenatal diagnosis of hypersensitivity disorders, immunodeficiency and intrauterine infections prompted this study of relationships between immunoglobulins (Ig) in amniotic fluids (AF) and corresponding maternal and cord sera. We collected aliquots of 134 AF obtained from amniocenteses and abortions performed for other medical reasons.

The level of IgG in AF was lower than in paired cord serum even when corrected for total protein content. IgG antibodies to diphtheria toxin were detected in AF as early as 13 weeks gestation, and antibody per mg/IgG was generally similar in cord, maternal serum and AF. IgM was undetectable in all AF's even those concentrated 25x. IgD was detectable in a concentrated AF at 21 weeks of age, in which IgM and IgA were <2 mg% indicated a lack of maternal blood contamination.

In contrast to IgG, IgA in AF exceeded the corresponding cord level. AF IgA increased throughout gestation, while cord IgA remained low. Secretory component was detected in AF as early as 11 weeks. IgE constitutes a higher proportion of AF protein, than of maternal or cord serum. Both AF and cord IgE increased with gestational age. The IgE levels in paired cord and maternal sera were not correlated (correlation coefficient=.176). There was better correlation between AF and maternal IgE but best between AF and cord IgE, (correlation coefficient=.522 and $p < .01$). Secretion and active transfer appear to be important determinants of AF Ig levels.

LYMPHOCYTE STIMULATION BY HERPES SIMPLEX VIRUS (HSV) ANTIGENS IN HSV-1 OR HSV-2 INFECTED NEWBORNS AND CHILDREN. Stuart E. Starr, Siraj A. Karatela, Steven L. Shore, Aarolyn M. Visintine and André J. Nahmias. Emory University School of Medicine, Department of Pediatrics, Atlanta.

A lymphocyte stimulation assay employing HSV antigens was developed because of information suggesting that impaired cellular immunity plays a role in disseminated herpetic infection of the newborn and severe herpetic infection of immunocompromised individuals. Leukocytes were obtained by Dextran sedimentation, suspended in RPMI 1640 with autologous plasma, and incubated with HSV-1 or HSV-2 antigens and control antigens. After 6 days incubation, incorporation of H_3-thymidine over a 4 hr. period was measured.

When studied 1-3 days after the onset of clinical manifestations, four of five children with laboratory diagnosed herpetic gingivostomatitis showed no response to HSV-1 antigen and one showed three-fold stimulation. One to three weeks later lymphocytes from children with no initial response demonstrated 3-60 fold stimulation.

HSV-2 infected newborns showed significant stimulation with HSV-2 antigen and lesser responses to HSV-1 antigen. Cord lymphocytes from uninfected newborns showed no response to either antigen.