**709** HETEROGENICITY OF THE CLINICAL, GENETIC AND IMMUNOLOGIC FINDINGS IN HYPER-IgM SYNDROME. Catherine U. Kyong, Gabriel Virella, Charles P. Darby, Bruce E. Ponce, Maija Horsmanheimo, Lapsley G. Hope, Jean-Michel Goust, & H. Hugh Fudenberg. (Spon. by Milton C. Westphal). Dept. of Pediatrics & Immunology, Medical University of South Carolina, Charleston, South Carolina.

Hyper-IgM syndrome is characterized by recurrent pyogenic infections, depression of IgG and IgA and increase of IgM. Currently, we are studying two cases of this disorder. A.W., a 9 yr. old white female had recurrent cervical abscesses, R.S., a 3½ yr. old black male with recurrent pyogenic infections, failure to thrive, oral thrush and systemic cryptococcal infection. Both B and T cell systems were abnormal. Serum immunoglobulin determination by radial immunodiffusion in both cases showed depression of IgG and IgA and elevation of IgM. (A.W. IgG and IgA trace, IgM 1450 mg/dl; R.S. IgG 140 mg/dl, IgA 4.5 mg/dl, IgM 2640 mg/dl). Immunoelectrophoresis in A.W. showed an abnormal precipitation for IgM. Gel filtration demonstrated two populations of IgM. One is a normal high molecular weight polymer. The other is a low molecular weight IgM monomer containing light chains of K-type. Immunoelectrophoresis failed to show qualitative abnormality of IgM in R.S. Impairment of cellular immunity was demonstrated in both cases by a decrease of total and active E Rosettes and negative skin tests to Candida, SKSD, PPD, mumps and trichophyton. Incubation of both patients' lymphocytes with PHA, and Candida and PPD did not generate leukocyte migration inhibition factor. Our data indicate that there is clinical, genetic and immunologic heterogenicity in this syndrome.

**710** EFFICACY OF PLASMIN-MODIFIED INTRAVENOUS GAMMA GLOBULIN IN THE MANAGEMENT OF HYPOGAMMAGLOBULINEMIA. Daniel B. Magilavy, James T. Cassidy, David G. Tubergen, Ross E. Petty, and Keith B. McCall, Univ. of Michigan Med. Ctr., Dept. of Pediatrics, Ann Arbor and Michigan Dept. of Health, Lansing.

Commonly used replacement therapies for patients with hypogammaglobulinemia are intramuscular gamma globulin (IM-GG) and plasma. Disadvantages of the former include discomfort of the injections and occasional reactions and, of the latter, the risk of hepatitis. Intravenous gamma globulin altered enzymatically by plasmin (PT-GG) offers an alternative mode of treatment. In this study 175 infusions of PT-GG were administered to 14 patients with various forms of hypogammaglobulinemia. Our product had essentially no anticomplementary activity (1.1-1.4 CH50 units fixed/mg protein) with minimal fragmentation of the IgG molecule (<15%). Nine of the patients were studied in 2 treatment periods of 6 and 9 months with an intervening control period of 5 months on IM-GG. Frequency of infusion ranged from 2-4 weeks to maintain a serum IgG concentration of >2.5 mg/ml. Patient acceptance was uniformly positive. Eight of 11 patients maintained on IM-GG before entering the study had chronic pulmonary disease; 3 were removed from the study and placed on single donor plasma because of lack of improvement. The remaining patients had a significant decrease in number of hospitalizations and severe infections; 7 had diminution in sinusitis and otitis media. Five patients had one or more reactions (14/175 infusions). Symptoms abated rapidly with temporary interruption of the infusion. From these results we conclude that PT-GG represents a relatively safe, efficacious mode of replacement therapy in patients with hypogammaglobulinemia.

**711** EFFECT OF VITAMIN A DEFICIENCY ON THE CELLULAR IMMUNE RESPONSE. D. Mark, K.M. Nauss, R. Suskind (Spon. by J.R. Hamilton). Department of Nutrition and Food Science, MIT, Cambridge, MA.

To study the effect of Vit A deficiency on the cellular immune response, we placed twelve 21 day old Sprague-Dawley male weanling rats on a Vit A deficient diet (DEF). Pair-fed (PF) and ad libitum (AL) fed controls receiving 500 µg of retinyl acetate p.o. per wk. were simultaneously studied. Animals were considered Vit A deficient and were sacrificed when they had ceased to gain wt. Isolated splenic lymphocytes cultured for 3 days with Concanavallin A (Con A) over a range of 1 to 7 µg/ml were pulsed with tritiated thymidine ([$^3$H]-T) 18 hrs. before harvest. DEF animals and PF controls weighed significantly less ($P<.01$), had significantly smaller livers ($P<.005$), spleens ($P<.005$) had fewer splenic lymphocytes ($P<.025$) than AL controls. Splenic lymphocytes from the DEF animals were significantly less responsive ($P<.005$) to all doses of Con A than those of the PF and AL fed controls in whom the response was similar. The deficit in lymphocyte transformation was reversed within 3 days of Vit A being added to the diet. These studies demonstrate an effect of Vit A deficiency on the cellular immune response which can be differentiated from the effect of the often associated protein calorie deficit.

| | Wt gm | Serum A (mg per 100 ml) | [$^3$H]-T-CPM Non-Stim. Lymph | [$^3$H]-T-CPM Stimulated Lymph |
|---|---|---|---|---|
| DEF | 287±6* | 8±2 | 1490±335 | 15,695± 5,805 |
| PF | 283±9 | 47±3 | 2270±219 | 49,240± 8,233 |
| AL | 318±9 | 54±1 | 3780±501 | 54,659± 9,515 |
| DEF Repleted | 272±14 | 36±3 | 1232±161 | 66,403±19,774** |

*M±SEM **2µg Con A/ml

**712** HETEROZYGOUS C3 DEFICIENCY ASSOCIATED WITH A SYSTEMIC LUPUS ERYTHEMATOSUS-LIKE DISEASE. McLean, R.H., M. Lowenstein, N. Rothfield. U. Conn. Hlt. Ctr., Dept. of Pediatrics, Farmington, Ct.

We report an 18 year old caucasian male with an SLE-like syndrome and decreased serum C3 in the patient and 3 relatives. Submucosal and cutaneous hemorrhage began at age 11. An erythematous rash, arthralgias, proteinuria (512-815 mg/24 hours) and thrombocytopenia (25-38,000/mm$^3$) were detected at age 18. Serum C3, (normal 164 ± 83 mg/dL ± 2 S.D.) averaged 43 mgm/dL (range 30-60) in the propositus, 33-72 mgm/dL in the mother, 69-92 mg/dL in maternal uncle and 56 mg/dL in a first cousin. Total hemolytic complement was decreased only in propositus. Specific hemolytic C3 was below normal range (1950-2700 units/ml) only in family members with low protein C3: 1180 - propositus, 1770 - mother, 1560 - uncle and 1800 - cousin. Protein concentrations of C1q, C4, Factor B, properdin and specific functional C1, C4 and C2 were normal in propositus and the 11 family members. C1q precipitins, LE cells, antinuclear antibody, rheumatoid factor, C3 activating factor and cryoglobulins were absent in propositus. Skin biopsy showed vasculitis with IgG, C3 and C4 deposition in dermal-epidermal junction. Prednisone therapy for thrombocytopenia resulted in a transient elevation of C3. This is the first report of an associated SLE-like disease in a probable heterozygous C3-deficient individual and differs from the cutaneous vasculitis-hypocomplementemia syndrome because of 1) the absence of C1q precipitin, 2) normal early C components and 3) the familial partial C3 deficiency.

**713** NEUTROPHIL FUNCTION IN THE 28-32 WEEK HUMAN NEONATE Michael A. Medici, Christinia T.Ukrainski and Richard A. Gatti. Cedars-Sinai Medical Center, Department of Pediatrics, Los Angeles.

In vitro neutrophil function was evaluated in 28-32 week neonates and compared to similar studies of term neonates and adults. Preterm neutrophil random mobility (RM) was decreased as compared to term neonate and adult values. Phagocytosis of yeast particles opsonized with a 2.5% final concentration of autologous plasma(AP) was significantly impaired at 30 minutes in the preterm infant as compared to both term and adult neutrophils. Opsonization with 2.5% adult plasma(CP) did not normalize this parameter suggesting an inherent defect in phagocytic capacity. Increasing incubation time to 60 minutes increased the number of yeast phagocytosed by preterm and term neonates. While values for term neonates approached those of adults, preterm neutrophil phagocytosis remained significantly depressed. Chemotaxis (CX) of both preterm and term infants was below adult control values.

| | PHAGOCYTOSIS-yeast/cell AP | CP | RM-mm | CX-%† |
|---|---|---|---|---|
| 28-32 wk (11) | 3.55 (.10) | 3.89 (.19) | 0.27 (.08) | |
| Term (8) | 4.07 (.39) | 4.45 (.12) | 0.53 (.14) | 532 (338) |
| Adult (21) | 4.68 (.14) | - - | 0.53 (.11) | 1183 (781) |

These studies suggest that severely premature infants have a phagocytic defect which is independent of plasma opsonic capacity.

**714** SERUM LEVELS AND SKIN FIXATION OF TRANSFUSED IgE IN INFANTS. Michael H. Mellon, Maciej F. Tomaszewski, H. Alice Orgel and Robert N. Hamburger. University of California, San Diego. Pediatric Immunology and Allergy Division, La Jolla, California.

Six infants each requiring one or two exchange transfusions (total 8) were monitored for the level of transfused IgE in their serum and the rate of skin fixation of the exogenous IgE.

An average of over 80% of the transfused IgE was detected in the infants blood stream at the conclusion of the exchange. The persistance of the IgE in the circulation was in inverse relationship to the amount transfused. Donor IgE varied from 15 u/ml to 650 u/ml with 70% to 30% remaining in the infants' circulation after 24 hours. Skin fixation of IgE parallels its disappearance from the circulation. Maximum skin fixation was observed between 36 and 48 hours and the skin-fixed IgE persisted for the 31 days that two of the babies were able to be followed.

The normal human infant is born with a fully developed mechanism to produce an atopic reaction except for IgE antibody. Thus the IgE infused in conjunction with a transfusion can place the infant at risk of a passively transferred anaphylactic reaction for at least one month.