**948** INCREASED INFECTIONS IN INFANTS OF OPIATE-ABUSING MOTHERS. Ira J. Chasnoff and Kenneth Rich. Northwestern University Medical School, Departments of Pediatrics and Psychiatry, Chicago.

Although it has been suspected that infants born of drug-addicted mothers have an increased incidence of infections, it has been unclear whether this is due to social factors, increased exposure to infectious agents, or effects of the addicting drugs. Three groups of infants were followed through one year of age, and the incidence of infection was evaluated. Group A infants (N=21) were delivered to women who used heroin intravenously, Group B infants (N=15) to women who abused nonopiate drugs orally and Group C infants (N=15) to women with no evidence of drug use. There was no difference in the three groups as to maternal age, education, race, income or cigarette use. More patients in Group A had an illness during the first year of life (18 of 21) compared to Group B (7 of 15) or Group C (8 of 15) ($X^2$=7.08, $p<.01$).

| Type of Infections | Number of Episodes | | |
|---|---|---|---|
| | A | B | C |
| bronchiolitis | 9 | 3 | 3 |
| Chlamydia pneumonia | 3 | 0 | 0 |
| thrush | 8 | 1 | 1 |
| monilia diaper rash | 10 | 1 | 2 |
| otitis media | 10 | 2 | 3 |

Since groups A and B are identical in lifestyle and social environment, we conclude that maternal intravenous opiate use results in an increased incidence of infections by some as yet unknown mechanism.

**949** ABNORMAL IgG SUBCLASSES IN CHILDREN WITH SUSPECTED ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS). JA Church and W Richards, USC Sch of Med, Childrens Hospital of Los Angeles, Dept of Peds, Los Angeles, California.

A unique aspect of pediatric AIDS (PAIDS) is an additional susceptibility to infections characteristic of immunoglobulin (Ig) deficiency: otitis media, sinusitis, sepsis. To evaluate this clinical observation further, IgG subcalsses were determined in 3 infant boys with suspected AIDS and 4 adult homosexual men with AIDS. JP and PB, born at 28 and 29 weeks gestation, had received multiple blood transfusions in the neonatal period and died at 11 and 22 months, respectively, with P. carinii pneumonia The mother of a third infant, MF, has AIDS, likely acquired from her i.v. drug abusing husband. This child has lymphoid interstitial pneumonia and sinusitis. Laboratory evaluation of these infants revealed reversed T helper:suppressor ratios, decreased lymphoproliferative responses to mitogens and hyperimmunoglobulinemia G and A. JP's and PB's serum IgG levels declined as their disease progressed. In addition, JP has absent IgG2, PB had absent IgG3 and MF had absent IgG2 and IgG4. Other IgG subclasses were normal. In the 4 adult subjects, total IgG levels were increased and IgG subclasses were normal to increased.

The finding of selective IgG subclass deficiencies in PAIDS is consistent with the improvement seen in some of these patients following Ig replacement therapy. The normal IgG subclass values noted in the adult AIDS patients in association with a lack of characteristic infections indicate that Ig would not be of benefit in these patients.

**950** COMMON VARIABLE IMMUNODEFICIENCY (CVI) OF CHILDHOOD WITH AUTOIMMUNE DISEASE. M.E. Conley and Donald E. Campbell (Spon. by S.D. Douglas), Univ. of Penna. Medical School, Children's Hosp. of Philadelphia, Phila., PA.

CVI in childhood is not a well described entity. We have followed 6 children (2 males and 4 females) with this disease who have also had multiple severe, autoimmune disorders that have overshadowed infections as clinical problems. These children have all had onset of disease before 5 years of age and all have had severe growth failure. The autoimmune disorders have included ITP with autoimmune hemolytic anemia (3/6), diarrhea, malabsorption or gastritis (5/6), JRA (2/6), parotitis (2/6), chronic active hepatitis (2/6) and Guillian Barré Syndrome (2/6). All have had hypogammaglobulinemia. T and B cells have been present in the peripheral circulation, although in some cases in reduced numbers. Delayed hypersensitivity skin tests and proliferative responses to mitogens have been normal. T cell subsets, done in 4 of the patients, demonstrated an increased ratio of T helpers to T suppressors (T4/T8); 3.2 ± 0.6 vs. 1.8 ± 0.4. In vitro assays demonstrated normal or increased T cell help. When patient T cells were added to control B cells in pokeweed mitogen stimulated cultures, the number of plasma cells produced was equal to or greater than that produced when control T cells were added. In contrast, patient B cells did not differentiate into plasma cells even when supplemented with normal T cells. CVI in childhood with autoimmune disease may represent a unique syndrome which may provide new insights into understanding of B cell differentiation.

**951** CELLULAR IMMUNODEFICIENCY IN BIOTIN DEFICIENT RATS. Morton Cowan and Alyce Green. University of California, School of Medicine, San Francisco, California.

Biotin dependent multiple carboxylase deficiency, an inborn error of metabolism is associated with many clinical and laboratory abnormalities including combined immunodeficiency. We studied biotin dependent carboxylase activities and lymphocyte responses to a T cell mitogen (Con A) in biotin deficient (DEF) and biotin supplemented (CNT) pair fed Sprague-Dawley rats. Body and liver weights after 10 weeks on the deficient diet were 275 ± 25 gms. and 8.1 ± 1.4 gms. respectively for the DEF rats and 267 ± 21 and 7.4 ± 1.3 for the CNT rats. Lymphocyte Con A responses were normal in thymus (T) and spleen (S) but significantly lower ($p<.01$) in lymph nodes (LN) from DEF rats:

| | T(cpm) | S(cpm) | LN(cpm) |
|---|---|---|---|
| DEF | 258638 ± 53068 | 211387 ± 99856 | 9011 ± 3829 |
| CNT | 254909 ± 45542 | 169240 ± 69331 | 47182 ± 11158 |

Propionyl-CoA (PCC) and pyruvate (PC) carboxylase activities in DEF livers were 20% and 15% of CNT livers respectively. PCC in lymphocytes from T, S, and LN from DEF rats were 6%, 55% and 88% of CNT respectively. These results indicate: 1) T cell mitogen responses are most susceptible to biotin deficiency in the more differentiated LN; 2) PCC activity is most affected by biotin deficiency in the less differentiated T and is not the cause of depressed Con A responses by biotin deficient LN. It is possible that biotin metabolism and/or the role of biotin dependent carboxylases in lymphocytes changes with maturation and could explain the differential susceptibility of lymphocytes to the biotin deficient state.

● **952** MISMATCHED BONE MARROW TRANSPLANTATION (BMT) USING SOYBEAN AGGLUTININ (SBA) NEGATIVE MARROW CELLS. Morton Cowan, Arthur Ammann, Diane Wara, Peggy Weintrub, Henry Pabst, Natasha Martin and Nenita Arias. University of California, School of Medicine, San Francisco, California

The limitation of mismatched BMT is fatal graft vs. host disease (GVHD). We processed haplotype mismatched parental marrow with SBA to enrich for stem cells and reduce GVHD and successfully treated 6 patients with severe combined immune deficiency disease. HLA chimerism was found within 3 weeks post BMT. All the patients demonstrate T cell and 2 have evidence of B cell engraftment. T cell numbers and responses to phytohemagglutinin (PHA) and alloantigen pre and post BMT are:

| Pt # | T cell #(Pre/Post) | PHA (Pre/Post) | Alloantigen (Pre/Post) |
|---|---|---|---|
| 1 | 131/2299 | 113/23113 | 249/6058 |
| 2 | 3659/1476 | 62/18637 | 337/7616 |
| 3 | 763/37 | 46/996 | 909/3047 |
| 4 | 14/412 | 30/1057 | 38/6000 |
| 5 | 1492/4854 | 242/24 | 640/905 |
| 6 | 4500/826 | 407/2305 | 600/3390 |
| | nl >720 | nl >11750 | nl >5800 |

In #2,5,6 who required pre BMT immunosuppression for maternal GVHD, neutrophil, RBC, and platelet engraftment occurred by days 11,26,32 respectively. No immunosuppression was given post BMT. 2 patients had no GVHD, 3 had transient rash/fever, and only 1 developed persistent rash. Patients are now 3 to 17mo. post BMT. These results demonstrate that treated mismatched BMT can result in engraftment without significant GVHD and can be used for patients who otherwise have limited hope for survival.

**953** HYPEROSMOLAR MEDIATOR RELEASE FROM HUMAN BASOPHILS AND MAST CELLS. Peyton A. Eggleston, Anne Kagey-Sobotka, N. Franklin Adkinson, Jr., Lawrence M. Lichtenstein; The Johns Hopkins Hospital, Department of Pediatrics, and Good Samaritan Hospital, Baltimore, MD.

In the airway, gastrointestinal tract, renal parenchyma, and during some clinical situations, basophils and mast cells are exposed to a hyperosmolar milieu. We have shown that hyperosmolar stimuli release pharmacologically active mediators and that the process is distinct from IgE-dependent release. Significant mast cell histamine release occurs at just above physiologic levels (360 mOsm) and reaches a maximum of 12±1% at 770 mOsm; release from basophils is significant at 560 mOsm and reaches a maximum of 45±7% at 1020 mOsm. Activation of mast cells is dependent on extracellular $Ca^{++}$ but maximal release from basophils is only partially reduced in $Ca^{++}$ free buffers. Hyperosmolar buffers also increase IgE-dependent histamine release synergistically (mast cells: 460 mOsm 7±1% release; 1 µg/ml anti IgE 7±1%; both 27±4%). Prostaglandin $D_2$ ($PGD_2$) production from mast cells at 770 mOsm (69 pg/100 µl) was not different from unstimulated cells (83 pg/100 µl) despite significant histamine release (16% vs. 4% control). Furthermore, IgE-dependent $PGD_2$ production (264 pg/100 µl) was suppressed (99 pg/100 µl) in hyperosmolar buffers ($p<0.01$). The distinctive activation by hyperosmolarity and its interaction with IgE-dependent activation may have important implications for airway physiology, and the management of radiocontrast anaphylactoid reactions and clinical hyperosmolarity syndromes.