

806

ACUTE MEGAKARYOBLASTIC LEUKEMIA (AMKL): A UNIQUE ASSOCIATION WITH DOWN'S SYNDROME (DS) Alvin Zipursky, Marie Peeters and Annette O. Poon, Division of Hematology/Oncology, Department of Pediatrics, Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada.

AMKL has been reported in DS. We have observed recently a child with DS who developed AMKL as well as two newborn infants with Transient Leukemia (TL) which appeared to be AMKL. During a 10 year period 24 cases of leukemia (excluding TL) in DS were observed in our institute. Of them 4 were considered to have AMKL. Review of the above cases and 66 cases reported previously lead to the following conclusions: 1. Approximately 20% of leukemia (excluding TL) in DS is AMKL. 2. Approximately 20% of all leukemia in DS is TL. 3. TL in DS is AMKL. 4. Recurrence of AMKL occurs in 20% of TL. 5. The incidence of AMKL in DS is estimated to be 400 x that in normal children. These observations suggest that a specific form of leukemia, namely AMKL, has a remarkable association with DS.

809

EFFICACY OF INTRAVENOUS GAMMAGLOBULIN IN THE TREATMENT OF PNEUMOCYSTIS CARINII PNEUMONIA IN THE RAT MODEL. Frank J. Anderson, Linda L. Pifer, Carol C. Edwards, and Diane R. Woods, Dept. of Peds., Univ. of TN, Memphis, LeBonheur Child. Med. Ctr., Memphis, TN.

The efficacy of commercially-prepared IV infusions of pooled human immunoglobulin G (IVIG) was evaluated in the treatment of *Pneumocystis carinii* pneumonia (PCP) in the immunosuppressed rat model to ascertain whether such treatment might prove feasible in the management of pediatric subjects with PCP. Forty-eight rats were divided into six groups: (1) controls (C), (2) controls given IV human gammaglobulin infusions (C-I), (3) immunosuppressed rats given short-term cortisone (STC), (4) immunosuppressed rats given short-term cortisone and IV human gammaglobulin infusions (STC-I), (5) immunosuppressed rats given long-term cortisone (LTC), and (6) immunosuppressed rats given long-term cortisone and IV human gammaglobulin infusions (LTC-I). An enzyme-linked immunosorbant assay (ELISA) was employed to monitor PC-specific endogenous and exogenously administered IgG throughout the test period and toluidine blue '0' stains were performed to determine the degree of *P. carinii* infection in rat lung. Lung infection analysis showed statistical equivalence in STC, STC-I, and LTC-I. However, LTC-I lungs contained significantly fewer ($P < .05$) cysts than did LTC rats not treated with IVIG. IVIG appeared efficacious in reducing the number of cysts in the lungs of immunosuppressed rats with long-term cortisone. This study suggests a significant role for humoral immune defenses in combating PCP and warrants controlled studies in the use of IVIG in the pediatric patient with PCP.

IMMUNOLOGY

▲ 807

SYNTHESIS OF INFLUENZA A VIRUS (IAV) AND ENDOGENOUS PROTEINS IN POLYMORPHONUCLEAR LEUKOCYTES (PMNLs). Jon S. Abramson, Lisa F. Cassidy, Douglas S. Lyles, Bowman Gray School of Medicine of Wake Forest University, Department of Pediatrics and Microbiology, Winston-Salem, North Carolina.

PMNLs are well differentiated cells and are thought to have very little biosynthetic activity, however a few studies have shown that PMNLs can produce proteins when exposed to exogenous stimuli. Previous reports have also indicated that infection of PMNLs with IAV causes depression of metabolic and chemotactic responses, but the effect PMNLs have on the lifecycle of IAV has not been well defined. The present study was done to determine whether IAV can produce proteins and replicate within PMNLs. Early stages of virus-PMNL interaction were examined using binding assays with radiolabeled IAV and electron microscopy. Individual virus particles were taken up in coated pits and by 20 min were noted to be in endocytic vacuoles. Newly synthesized proteins were detected within PMNLs by incubating PMNLs with virus or buffer for 6 hours, labeling the PMNLs with ³⁵S-methionine for an additional hour, and analyzing the cell lysates by gel electrophoresis and fluorography. Host proteins were produced by buffer-treated PMNLs and both host and virus specific proteins were produced by IAV-infected PMNLs. Studies using immunofluorescent techniques combined with flow cytometry confirmed that newly synthesized viral antigens were produced by virus-infected PMNLs. Plaque assays on supernatant fluid from IAV-infected PMNLs showed that infectious progeny were not produced. These data indicate that protein production occurs in both unstimulated and IAV infected PMNLs and that IAV infection of PMNLs is abortive.

808

IgE, IgG AND IgG4 ANTIBODIES TO α -, β -, AND κ -CASEIN IN INFANTS WITH CHRONIC DIARRHEA. MFB Almeida, DC Heiner, VC Ferreira, MB Morais, U Fagundes-Neto. Harbor-UCLA Medical Center, Torrance, CA and Escola Paulista de Medicina, Sao Paulo, Brazil.

IgE, IgG and IgG4 antibodies to casein fractions were studied in 20 infants with chronic diarrhea (CD) and in 19 healthy infants (H). Mean ages were 4.6 months for CD and 5.9 for H. Mean duration of CD was 35 days. Cow milk was started during the 1st month of life in 18 of each group, duration 4.0 mo (CD), 5.1 (H). Seven of 20 CD rectal biopsies revealed colitis. Eighteen of 19 CD had abnormalities in small intestinal biopsies. All CD infants had acidic stools containing reducing substances.

Mean total IgE was higher in CD (22 IU/ml) than in H (3.1 IU/ml, $p < .01$); total IgG4 values were 87 mg/l in CD and 56 mg/l in H ($p > .1$). IgE and IgG4 antibodies to all caseins were higher in CD than H ($p < .05$). IgG antibodies to all proteins were markedly elevated in CD ($p < .001$). There was no difference in antibodies of CD infants with colitis compared to those without colitis. There was a tendency for antibodies to be higher in CD with severe small bowel changes than in those with mild.

Increased antibodies to caseins in infants with chronic diarrhea could be secondary to increased mucosal permeability or to a heightened primary immune response.

810

NEUTROPHIL DYSFUNCTION IN AUTOIMMUNE NEUTROPENIA. Kiran K. Belani, Mary E. Clay, Jean Herron, Warren E. Regeimann (Spon. by G. Scott Giebink), University of Minnesota, Department of Pediatrics, Minneapolis, Minnesota

The role of anti-neutrophil antibodies was investigated as a cause of functional abnormalities of circulating neutrophils in a child with persistent neutropenia and recurrent mouth sores. The patient's neutrophils were isolated by isopycnic centrifugation and compared with normal adult neutrophils. Functional abnormalities in the patient's PMNS included (1) decreased chemotaxis studied by under agarose method and by skin window, (2) decreased oxidative burst measured by luminol amplified chemiluminescence, and (3) decreased superoxide production measured by cytochrome C reduction assay. The ability of the patient's serum to bind normal neutrophils was determined by immunofluorescence. While the patient's serum bound normal PMNs, this binding did not interfere with their oxidative burst. In contrast, the patient's serum did not bind to his own PMNs in vitro even though his neutrophil specific antibody was anti-NAI and his PMNs were NAI positive. Therefore, the functional abnormalities of this patient's PMNs were not due to neutrophil antibody binding alone, but due to a subpopulation of dysfunctional neutrophils in circulation possibly selected out by their low affinity to the circulating autoantibodies.

811

HUMAN CORD AND NEWBORN BLOOD IS DECREASED IN NATURAL KILLER CELL CYTOTOXICITY IN COMPARISON WITH NORMAL ADULT. Lee S. Berk, George D. Georgeson, William C. Eby, Joyce L. Peabody, and Sandra Nehlsen-Cannarella. Departments of Pathology, Pediatrics and Surgery, Loma Linda University, Loma Linda, CA 92350. (Spon. by Stephen Ashwal).

Because natural killer cell cytotoxicity (NKC) is implicated in transplant rejection and we are involved in neonatal cardiac transplantation, it is important to understand normal NKC in neonates. We studied NKC in cord and newborn (2-4 days) blood from full term normal spontaneous vaginal delivery (FTNSVD) $n=40$, full term cesarean section (FTCS) $n=34$, preterm normal spontaneous vaginal delivery (PTNSVD) $n=18$ and preterm cesarean section (PTCS) $n=14$, and compared these with normal adult blood (NA), $\bar{X}=30$, (22-42 yrs). NKC was measured by a standard 4 hr 51-Cr release assay using K562 as target cells. The Student's t-test was used to determine differences in NKC. The results at the 50:1 ratio were significantly different, $p < .01$, between NA and both cord and newborn blood in all four groups. The slopes of the response curves for all these groups were also significantly different from NA, $p < .01$. Preterm categories for cord NSVD and newborn C/S were significantly lower than their respective full term category, $p < .01$. In addition, there was no significant difference between NSVD and C/S for all groups. In conclusion, cord and newborn blood in all groups studied were found to have significantly lower NKC than that of NA blood. These data provide a better understanding of normal NKC maturation in the neonate relative to transplantation and immunosuppression.