

685**IMMUNOGLOBULIN SECRETING CELLS IN THE BLOOD AND TONSIL OF NORMALS AND PATIENTS WITH IMMUNODEFICIENCY.** R.M. Blaese, J. Grayson, E.C. Lawrence and A.V. Muchmore.

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Using a new assay to detect lymphoid cells actively secreting immunoglobulin (Ig), we have evaluated blood and tonsil from normals and blood from patients with immunodeficiency for the presence of lymphocytes secreting IgG, IgA, IgM and IgE. Ig secreting lymphocytes (IgSL) were enumerated using a "reverse plaque" assay which detects cells secreting Ig by the lysis of sensitized indicator erythrocytes in the presence of developing antisera specific for each Ig class. Normal blood contained a mean (N=20) of 179 IgG-SL, 148 IgA-SL and 159 IgM-SL per 10^6 lymphocytes. Tonsils were found to contain significantly more IgSL with a mean (N=11) of 3311 IgG-SL, 571 IgA-SL, 642 IgM-SL, and 19 IgE-SL per 10^6 lymphocytes. Five patients with the Wiskott-Aldrich syndrome had normal numbers of IgSL for each class despite abnormal serum Ig levels. Four patients with selective IgA deficiency had normal IgG and IgM-SL but no detectable IgA-SL either fresh from the blood or after 6 days of culture with pokeweed. 14 patients with hypogammaglobulinemia had essentially no Ig-SL for any class. However, several of these patients developed a normal Ig-SL response following culture with pokeweed. Measurement of Ig-SL provides a useful tool to study the differentiation of B lymphocytes and their disorders in human disease.

688**CELL MEDIATED IMMUNE DEFECTS IN MALNOURISHED HOSPITALIZED U.S. CHILDREN.** J.M. Carney, M.S. Warner, W.J. Byrne, T.C. Borut, M.E. Ament, E.R. Stiehm.

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Severe protein calorie malnutrition is characterized by profound depression of cell mediated immunity. We studied 28 hospitalized U.S. children with various degrees of malnutrition to determine if similar defects existed. Ages ranged from 6 wks to 20 yrs. All had weights less than the fifth percentile for age. Chief diagnoses were chronic diarrhea(7), gastroesophageal reflux (4), Crohn's disease(4), and anorexia nervosa(3). Thirteen/28 eventually required hyperalimentation.

10/28 (36%) had marked depression (<50%) of T lymphocytes (E-Rosette Forming Cells - E-RFC). 5/10 had depressed PHA transformation (Index <40). 8/10 were <2 years. 3 pts had albumin <3gm/dl, 5 had hgb <10gm%. One 2 month old boy had decreased lymphoid tissue, decreased granulocytes and severe infection.

5/28 (18%) had mild decrease of E-RFC(50-60%). PHA index was low in 3 of these pts. 2 had hgb <10gm%, and 1 had alb <3gm/dl. No severe infections were seen.

13/18 (46%) had initially normal E-RFCs. All these had normal albumins; 3 had low hgb. E-RFC decreased to <50% in 3 pts, including one who had candida sepsis.

We conclude that depressed T cell function occurs in malnourished U.S. children, may precede clinical infection, and is associated with young age, chronic diarrhea, and wts less than the fifth percentile. Hyperalimentation may be of value in correcting this defect.

686**COMPLEMENT-MEDIATED DESTRUCTION OF LYMPHOCYTES AND LYMPHOBLASTS: INHIBITION IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL).** Glenn H. Bock, Ann E. Stitzel, Joan R. Urmsom, Kate W. Rittenhouse and Roger E. Spitzer.

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Previous data have shown that sera from patients with ALL contain a material which will block the activation of C3 by both the classical and alternative pathways. An in vitro assay was established to test whether or not this "inhibitor" will prevent complement-mediated killing of normal peripheral lymphocytes (L) or bone marrow-derived malignant lymphoblasts (LB). This assay utilizes L or LB as a target cell, antilymphocyte globulin, and serum; cell death is measured by the uptake of 5% eosin. With normal human serum (NHS), the extent of killing of L or LB depends upon the concentrations of target cells, antibody, and serum as well as the time of incubation at 37° C. Using optimal conditions with ALL sera or with NHS to which purified "inhibitor" has been added, the average killing was decreased by 64%. Increasing Ab concentration two fold, serum concentration five fold or the time of incubation three fold did not completely correct the defect with ALL sera. This "inhibitor" is present in NHS and appears to function by modulating the biologic activity of C3. At diagnosis or relapse, patients with ALL may be deregulated in the elaboration of this material. The resultant excess of the "inhibitor" apparently leads to blockade of the effects of antibody and complement in eliminating tumor cells.

689**BREAST FEEDING AND PREVENTION OF ATOPIC ECZEMA.** R.K. Chandra. Memorial Univ. of Newfoundland, Janeway Child Health Centre, Dept. of Pediatrics, St. John's, Newfoundland.

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The offspring of parents suffering from atopic disease are at higher risk of developing eczema, asthma and other manifestations of allergy compared with children of non-atopic parents. In a group of 31 such "high risk" neonates, breast feeding was employed as the exclusive form of infant feeding for the first 8 weeks or longer after birth. Followup for 12 to 36 months (mean 20.6 months) showed the development of clinical eczema in 4, compared with 19 of 31 matched controls fed cow's milk formula. Serum IgE concentration at one year of age was elevated in the artificially fed (121 + 39 IU/ml) and normal in the breast fed (17 + 8 IU/ml). The incidence of positive radioallergosorbent test for IgE antibodies to cow's milk, complement activation in vivo after challenge with cow's milk, and of respiratory disease characterized by bronchospasm, was higher in the cow's milk fed group. These data confirm the positive beneficial effect of breast feeding in the prevention of atopic disease in early childhood.

687**ADENOSINE DEAMINASE DEFICIENCY WITHOUT IMMUNODEFICIENCY.** William Borkowsky, Anne A. Gershon, Rochelle Hirschhorn. N.Y. Univ. School of Medicine, Depts. of Medicine and Pediatrics, N.Y.C.

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A 20 month old male child was diagnosed as having adenosine deaminase (ADA) deficiency during N.Y. State-mandated neonatal screening. At age one month he had tonsils, a normal WBC and differential, a thymic shadow, and normal bony structures, despite confirmation of his enzyme defect on repeated testing (less than 1% of normal ADA and increased adenosine in RBC). Throughout his life he has had normal numbers and distribution of lymphocytes, normal responses to pokeweed mitogen, phytohemagglutinin, and Con A, and a normal mixed lymphocyte reaction. Following immunization he developed antibody and/or positive in vitro responses to diphtheria, tetanus, and polio antigens.

Skin tests with DNCB and diphtheria toxoid yielded hyper-sensitivity responses. Except for accentuated transient physiologic hypogammaglobulinemia, he has had normal immunoglobulins and complement. Except for several brief episodes of otitis media and an upper respiratory infection his general health has been excellent, and his growth and development have been normal.

Genetic heterogeneity for ADA deficiency may account for the spectrum of clinical manifestations, ranging from Severe Combined Immunodeficiency to normal immunologic function.

690**LYMPHOCYTE SUBPOPULATIONS AND FUNCTIONS IN COMMON VARIED IMMUNODEFICIENCY.** Ranjit K. Chandra. Memorial Univ. of Newfoundland, Janeway Child Health Centre, Dept. of Pediatrics, St. John's, Newfoundland.

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The clinical and immunological profile of 30 cases with common varied immunodeficiency were analyzed. The common modes of presentation were recurrent or severe infection and allergy. There was a wide variation of immunoglobulin (Ig) levels and of the Ig class affected among patients and their family members. Within individual patients, the Ig concentrations were largely constant, but in 9 children, the levels fluctuated over a wide range. Rosette-forming T cells were reduced in number in one child. The number of B lymphocytes bearing surface Ig was reduced in 2 patients, of pre-B lymphocytes in the bone marrow in 1, and of T cells bearing receptors for IgM-Fc in 3 of 14 patients studied. The number of T cells bearing receptors for IgG-Fc was increased in 3 cases. Suppressor cell activity was demonstrated by coculture of lymphocyte subsets from the patients and healthy adults in one instance. Mitogen-induced lymphocyte DNA synthesis was reduced in 2 children. The study showed the heterogeneity of pathogenetic mechanisms that may underlie the syndrome of common varied immunodeficiency.