745 IMPAIRED PULMONARY DEFENSE IN CYSTIC FIBROSIS (CF) Mary Jane Thomassen, Bernard Boxerbaum, Catherine Demko, Paula Kuchenbrod, Robert E. Wood. Rainbow Babies and Childrens Hospital, Case Western Reserve University, Cleveland, Ohio.

We studied the effect of CF serum on the phagocytic function of normal and CF human alveolar macrophages to determine if the chronic pulmonary infection in CF patients results from a defect in phagocytosis. Alveolar macrophages were obtained by fiberoptic bronchoscopy and cultured overnight on glass surfaces; the uptake of radioactive bacteria was then measured in the presence of normal or CF sera. 19 of 21 CF sera produced >30% inhibition of phagocytosis of Pseudomonas aeruginosa, and had no apparent effect on phagocytosis of Staphylococcus aureus by normal human macrophages. Alveolar macrophages from CF patients were able to phagocytize Pseudomonas in the presence of normal sera, but were inhibited by both autologous and homologous CF sera. Incubation of normal macrophages with a mixture of normal and CF serum did not reduce the degree of inhibition of Pseudomonas phagocytosis. These results suggest that CF alveolar macrophages may function normally in a suitable environment, and that CF serum contains a factor which inhibits phagocytosis of Pseudomonas. This factor is unaffected by freezing or heating at 56° for 30 minutes, and is not adsorbed onto glass. The chronic Pseudomonas pulmonary infection of CF may be due to a factor in the lung environment extrinsic to the macrophages, rather than to an intrinsic defect in the alveolar macrophages themselves.

746 DEFICIENCY OF MONOCYTE MIGRATION INHIBITION FACTOR AND IMMUNE INTERFERON PRODUCTION IN LYMPHOCYTES OF NORMAL NEWBORNS. Harland S. Winter, Yvonne J. Bryson, Sherrie E. Gard, Thomas J. Fischer, E. Richard Stiehm, UCLA Sch. of Med., Dept. of Peds., Los Angeles, Ca.

The increased susceptibility of newborns to disseminated infection may result from defective or immature lymphokine production. Thus, we assessed monocyte migration inhibition factor (MIF) and interferon (IF) production of the lymphocytes of 20 newborns (cord blood), 20 1-7 day old neonates, and 20 normal adults. Ficoll-hypaque separated mononuclear cells were stimulated with phytohemagglutinin (PHA), allogeneic lymphocytes in a mixed leukocyte culture (MLC), or Newcastle Disease Virus (NDV), and supernatants were harvested at optimal times. MIF was assessed by the inhibition of adult mononuclear cell migration under agarose; IF was assessed by micro-dye uptake of human diploid cells after encephalomyocarditis virus challenge. Mean PHA-induced MIF production in cord and newborn lymphocytes was 30 and 10% respectively of adult levels, MLC-induced MIF production was 8 and 5% of adult levels. PHA-induced (immune) IF was produced in only 1 of 20 cord bloods and 3 of 18 newborns in small amounts whereas IF was produced by all adults (mean 225 units ±2 SD). No IF was produced by MLC in newborns, cords or adults. NDV-induced (classical) IF was produced in normal amounts by adult (168±2), cord (200±2), and newborn cells (228±3). These results indicate an abnormality of cellular immunity in newborns not detected by T-cell numbers or transformation indices and suggest a mechanism for viral infection in newborns with concomitant bacterial infections and in patients undergoing graft-versus-host reactions.

747 A NATURALLY OCCURRING INHIBITOR OF LYMPHOCYTE FUNCTION FROM A CUTANEOUS LYMPHOMA. Raoul L. Wolf, Fred S. Rosen and Ezio Merler. Harvard Medical School, Children's Hospital Medical Center, Division of Immunology, Boston.

Normal T cells and null cells produced an inhibitor (SIF) of both phytohemagglutinin (PHA) induced T cell transformation (15,793 CPM of ^{3}H-thymidine incorporation reduced to 2,731 CPM - 83% inhibition) and formation of sheep red blood cell plaques (645 plaques/10^{6} cells reduced to 219 plaques/10^{6} cells) by stimulated B cells. T cells also produce a factor (LMF) which induces B cells to proliferate and synthesize immunoglobulin. Stimulated T cells produced SIF continuously by 5 days of culture while LMF production ceased after 72 hours. SIF and LMF were separated on Sephadex G200; SIF occurred predominantly in the exclusion column, and LMF exclusively in the postalbumin fraction. Serum from a man with an unusual skin lymphoma had potent SIF-like activity. That the serum SIF activity originated from the lymphoma was suggested by the fact that supernatants from skin tumor cells potently inhibited PHA-induced mitosis of normal T cells. The patient's peripheral blood lymphocytes were unresponsive to antigens and mitogens in autologous serum, but responded normally in homologous serum. This tumor appears to represent an abnormal extension of a physiological process.

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748 COMPARISON OF LASER NEPHELOMETRY (Ne) & RADIAL IMMUNODIFFUSION (RID) METHODS FOR MEASURING IMMUNOGLOBULINS (Ig) IN IMMUNE DEFICIENT (ID) PATIENTS (PTS). Lily C. Yang, Mary Ann South, Shlomo Friedman, University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, Department of Pediatrics, Philadelphia, Pennsylvania.

Previous studies have shown that in adult controls with normal Ig levels, a good correlation exists between RID & Ne. IgG, IgA & IgM levels in sera from 42, 17 & 36 respective normal children were: 100-2172 & 117-2400(r=0.81), 44-856 & 10-880(r=0.99), 41-258 & 49-350(r=0.92) by RID & Ne respectively. To measure low level Ig in ID pts by Ne linear reference curves were established having limits of detection of IgG-0.6 mg%, IgA-0.1 & IgM-0.07 mg%. IgG & IgA levels in 37 sera from 11 ID pts, 9 of whom were treated, were 42-1830 & 33-2295(r=0.88), 0-44 & 0-44(r=0.89) by RID & Ne respectively. In 13 sera from 4 pts, IgA levels were 0 & 0.25-15.6 & polymeric IgA was detected by immunoelectrophoresis(IEP), in 6 sera 0-trace & 0, in 18 sera 1.5-44 & 0.65-44 (r=0.93) by RID & Ne respectively. IgM levels in 28 sera from 5 ID pts were 0.51 & 0-36.5(r=0.87) by RID & Ne respectively. In 4 sera from 2 pts, IgM levels were 0 & 4.82-7.0 & polymeric IgM was detected by IEP, in 9 sera from 1 pt, IgM levels were 0 & 2.50-10.71 & monomeric IgM was detected by IEP, in one serum 0 & 0, in 14 sera 2.85-51.0 & 2.53-36.5(r=0.94) by RID & Ne respectively. Low levels of IgA & IgM correlate poorly in pts with selective IgA & IgM deficiencies. Laser Ne appears to be more sensitive than RID in detecting low levels of IgA & monomeric or polymeric IgM in ID pts.

INFECTIOUS DISEASE

749 CLINICAL AND PHARMACOLOGICAL EVALUATION OF CEFAMANDOLE (CM) IN NEONATAL INFECTIONS. Melanie Agbayani, Abdul J. Khan, Ponchai Kemawikasit, Kusum Kumar, Warren Rosenfeld, Delfor Salazar and Hugh E. Evans, Dept. of Pediatrics, Jewish Hospital and Medical Center of Brooklyn, N.Y.

CM is a new cephalosporine (CSP) with an expanded spectrum against gram negative organisms. 34 newborn infants (mean age 17 days, weight 3.6 kg), 32 with pustular skin infection and 2 with clinical sepsis (CS) were treated with 33 mg/kg of CM q 8 h IM for 7 days. Gentamicin was given to the 2 CS patients in addition. S. aureus (SA) was isolated in 25 cases and each was sensitive to CM. Blood cultures in all were sterile. All patients improved clinically and skin lesions disappeared by 5th day. The only side effects observed were transient elevation of SGOT (average 91, normal 40 units) in 11 and ↑ eosinophil counts (7%) in 9 cases. Coombs tests remained negative in all. Mean serum levels, half life (t 1/2) in minutes and volume distribution in ml/kg (Vd) following single doses in mg were as follows:

Dose	1/4 hr	1/2 hr	1 hr	4 hr	8 hr	t 1/2	Vd
33IM	-	74.33	50	5.5	0.76	76	502
33IV	99.25	75.25	57.5	3.65	0.68	52	269
17IM	-	35.8	19.2	2.01	0.08	60	448
17IV	52	42	22.3	1.13	-	62	460

Blood levels were higher than reported for other CSP drugs and were many fold higher than MICs required in treatment of susceptible pathogens, including SA. T 1/2 and Vds with different doses were comparable. Changes in eosinophil count and SGOT were similar to those of other CSP antibiotics.

750 DISCREPANCY BETWEEN MINIMUM INHIBITORY CONCENTRATION (MIC) AND MINIMUM BACTERICIDAL CONCENTRATION (MBC) OF PENICILLIN DEMONSTRATED IN GROUP A (GAS) AND GROUP B β- HEMOLYTIC STREPTOCOCCI (GBS). Julian L. Allen and Katherine Sprunt, Columbia Univ.,College of Physicians and Surgeons, Babies Hosp., Dept. of Pediatrics, New York. 10032.

A discrepancy between the MIC and the MBC of penicillin (pen) against GBS has been reported, suggesting that the relapses of GBS disease after treatment with conventional doses of pen may be a result of this discrepancy. In this study, we measured pen MIC and MBC levels against GBS and compared them with levels obtained for GAS, an organism that has been successfully treated for years with conventional doses of pen without evidence of relapse in normal hosts. These experiments confirmed the reports that a large MIC/MBC discrepancy exists in GBS(10 fold); however, a larger discrepancy exists for GAS(25 fold). These findings diminish the likelihood of clinical significance of the MIC/MBC ratio alone in accounting for the relative difficulty in treating GBS. Other factors, such as the lower absolute sensitivity of GBS to pen compared to that of GAS, must be playing a role: both the MIC and the MBC values were significantly higher for GBS than for GAS.