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COMPARISON OF ORAL AND PARENTERAL GENTAMICIN (G) IN THE PREVENTION OF ENTERALLY-ACQUIRED PSEUDOMONAS (PS) SEPSIS. Richard E. McClead, Mary Lentz, Michael Brady, Mario Marcon, Milap Nahata, William Barson, Ohio State University, Children's Hosp., Dept. of Pediatrics, Columbus, Ohio.

We evaluated the protective effect of oral and parenteral G in the leukopenic mouse. C3H/HeN mice were made leukopenic by injection of cyclophosphamide. Mice were either gavage fed (po) or injected (ip) with G in 5% glucose water (D5W) at 5, 10, or 15 mg/kg/day (days 1-7). On day 4 the animals were orogastrically inoculated with Ps. aeruginosa, immunotype 7 (ATCC #27318) in D5W. Survival of treatment groups were compared by 2-way ANOVA.

RESULTS:

GROUP	N	G DOSE	ROUTE	PS INOCULUM	15 DAY % SURVIVAL
I	10	5 mg/kg	po	1 x 10^6 cfu	20%
II	10	10 mg/kg	po	1 x 10^6 cfu	40%
III	10	15 mg/kg	po	5.7 x 10^6 cfu	70%
IV	10	5 mg/kg	ip	1 x 10^6 cfu	20%
V	11	10 mg/kg	ip	5.7 x 10^6 cfu	73%
VI	10	15 mg/kg	ip	5.7 x 10^6 cfu	70%
VII	10	--	--	5.7 x 10^6 cfu	40%

The MIC of G for PS is 2 µg/ml. Protection by G is significantly related to dose [$F(2,55)=5.65$, $p=0.0059$]. Prophylactic G is more protective at 15 mg/kg/day than 5 mg/kg/day ($p<0.05$). Interestingly, oral G is as protective as parenteral G when given at equivalent doses. **CONCLUSION:** Prophylactic oral and parenteral G are effective in the prevention of enterally-acquired Ps sepsis in a leukopenic mouse model.

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INHIBITION OF E.COLI DNA SYNTHESIS BY HYPOCHLOROUS ACID MAY MODEL THE BACTERICIDAL ACTIVITY OF PHAGOCYTES Susan M.McKenna and Kelvin J.A. Davies (Spon by Robert L. Baehner) University of Southern California and Children's Hospital of Los Angeles, Institute for Toxicology & Depts of Biochem & Peds, Los Angeles

Phagocytic cells exert a rapid, selective inhibition of bacterial growth, followed by a more gradual degradation of cell components. Hypochlorous acid (HOCl), a product of the "Oxidative Burst", has been proposed as the agent responsible for bactericidal activity. HOCl, however, is generally characterized as a potent oxidant with nonselective destructive activity against all biomolecules. We designed a series of experiments to test the ability of HOCl to inhibit E.coli growth in a discrete or selective manner. Our data indicate that at physiological concentrations (10-50µM) HOCl exerts an irreversible bacteriostatic effect without coincident membrane disruption or extensive protein breakdown. Protein synthesis (incorporation of ^{3}H-leucine) declines gradually over 15-30min, suggesting a secondary role in bacteriostasis. In contrast, DNA synthesis decreases by 50-80% in 1min, and by as much as 95% within 5min. E.coli ($5x10^8$ cells/ml) ±50µM HOCl were used to measure intracellular accumulation of ^{3}H-thymidine (5mCi/ml) as well as incorporation into newly-synthesized (acid precipitable) DNA. Our data show that impaired incorporation of radioactivity precedes the decline in accumulation. We suggest that HOCl may, indeed, function as a selective bactericidal agent in phagocytes, and may act by inhibition of DNA synthesis.

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ECMO THERAPY FOR INFANTS WITH OVERWHELMING SEPSIS. Marilea K. Miller, Andrea Lotze, Penny Glass, Billie L. Short George Wash. Univ. Sch. Med. Children's Hospital National Medical Center, Dept. Pediatrics, Wash. DC

Neonates with fulminant bacterial infections can die in septic shock despite aggressive medical therapy. From 6/84 to 11/86, 10 infants with septic shock were treated at CHNMC with veno- arterial extracorporeal membrane oxygenation (ECMO). All infants had failed to respond to conventional intensive medical management and met ECMO entry criteria predictive of > 80% mortality risk. Diagnosis was by positive blood cultures in 7 infants. One infant had negative blood cultures but Wellcogens were positive for GBS antigen. Two infants had negative cultures, but perinatal hx's were compatible with septic shock. Eight infants had total WBC's <6,600 prior to ECMO. All ten infants survived with ECMO therapy. Morbidity among these infants included: (1) ICH in 4 infants, 2 which were severe; (2) oxygen dependence beyond one month in 3 infants. The risk of ICH was higher in the septic shock infants than in our ECMO population in general (40% vs 26%). Likewise, the risk for chronic lung disease was higher in the septic shock infants than in our ECMO population (30% vs 15%). In our experience ECMO is a valid therapy for infants with septic shock unresponsive to other therapies.

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IMPAIRED NATURAL IgG2 ANTIBODY (AB) RESPONSE TO POLYSACCHARIDE ANTIGENS AND DECREASED Km(1)-A2m(2) ALLOTYPES IN CYSTIC FIBROSIS (CF). R.B. Moss, Y.P.Hsu, N.J. Lewiston, G. deLange. Department of Pediatrics, Stanford University, Stanford, CA and Netherlands Red Cross Central Transfusion Laboratory, Amsterdam.

We recently described impaired IgG2 Ab responses to P. aeruginosa (PA) lipopolysaccharide in CF patients without PA infection (Pediatr Res 20:453, 1986). To investigate the basis for this defect, we measured natural IgG and IgG1-4 Ab levels to H. influenzae polyribophosphate (PRP) and tetanus toxoid (TT) by quantitative monoclonal Ab-based ELISA in 24 adult CF patients and 20 controls. Immunoglobulin allotypes were determined on 154 CF patients and 110 controls. The TT IgG Ab response was predominantly IgG1. CF and control subjects had similar TT IgG and IgG1 Ab levels. The PRP IgG Ab response was predominantly IgG2. In contrast to TT results, CF patients had subnormal levels of PRP IgG Ab compared to normal (geometric mean = 1.14 vs 2.32 mcg/ml, respectively, 2 tailed $p=0.004$, Mann Whitney U test). PRP IgG2 levels were also depressed in CF patients ($p=0.03$). CF patients had a lower prevalence of Km(1) ($p<0.025$, X^2 with continuity correction) and A2m(2) ($p<0.05$) than controls: G2m(n) and other allotype prevalences were similar. Impaired IgG2 Ab responses to certain polysaccharide-encapsulated microbes may predispose CF patients to endobronchial infection and lead to production of nonopsonizing isotype responses. A possible immunogenetic basis for impaired IgG2 Ab response is suggested by lower Km(1) allotype prevalence, while the role of A2m(2) is unknown.

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THE NATURAL HISTORY OF CMV EXCRETION BY CHILDREN IN GROUP DAY CARE. Jody R. Murph and James F. Bale, Jr. (Spon. by Charles Grose). University of Iowa College of Medicine, Departments of Pediatrics and Neurology, Iowa City, Iowa.

Cytomegalovirus (CMV) frequently infects young children who attend group day care. Although congenitally infected children excrete CMV for extended periods, the natural history of CMV excretion among children who acquire CMV in day care is unknown. To determine the acquisition rates and duration of CMV excretion among such children, we sampled the urine and saliva of 65 children in a single day care center at 3 to 6 mo. intervals over a 2 yr period. During the study period, 23 children (35%) excreted CMV in urine and/or saliva. The duration of CMV excretion ranged from 4 to 24 mo., with a mean of 9.73 ± 1.47 (SE) mo. for urine (N=10) and 8.33 ± 0.87 mo. for saliva (N=8). Among children who were initially CMV negative the mean age at onset of CMV excretion was 26.8 mo. The mean duration of excretion for children who remained in the study until CMV excretion ceased was 11.48 mo. for urine and 10.88 mo. for saliva. Children who excreted CMV tended to enter day care at an earlier age (7.7 mo. for CMV excretors vs. 10.1 mo. for non-excretors) and spent more hrs per week in day care (43.6 hrs vs. 37.8 hrs). At the initial sample collection CMV-excreting children were younger than non-excretors (26.8 mo. vs. 35.0 mo.) ($p=0.02$). However, there was no correlation between age at which children began to excrete CMV and the duration of excretion in urine ($r=0.075$) or saliva ($r=0.339$). These results indicate that children in day care who acquire CMV excrete the virus for many months and are thus a substantial reservoir of infection for exposed adults.

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FIRST CLINICAL TRIAL WITH SABIN INACTIVATED POLIO VACCINE. Jody R. Murph, Charles Grose, Gilbert J. Cuthbertson, Christina Mickiewicz, Steve Mento, and Frank Cano. University of Iowa, Department of Pediatrics, Iowa City and Lederle Laboratories.

During Phase I of this study 39 males, 20-43 years of age with a history of previous polio immunization, were screened for antibody to poliovirus. 49% (19/39) had no detectable neutralizing antibody to at least 1 of the 3 poliovirus types at ≥ 1:8 and 31% (12/39) were negative at ≥ 1:4. 12 subjects seropositive at ≥ 1:4 received either 0.25, 0.5 or 1.0 ml of a highly potent inactivated poliovaccine manufactured from Sabin-strain attenuated poliovirus with D antigen content of 40:25:70 units/ml for types 1, 2 and 3 poliovirus respectively. Approximately 6 months later, 9 subjects previously identified as seronegative to at least 1 type of poliovirus despite a history of adequate polio vaccination, entered Phase II of this study. These subjects received 0.5 ml of the Sabin-strain IPV and had antibody determinations at 2, 4, 7 and 30 days post vaccination. In the first trial this vaccine was safe and highly immunogenic (see Table). All seronegative Phase II subjects also responded to the vaccine. The immune status of these individuals with waning antibody continues to be of concern, particularly in view of the recent outbreak of polio in Finland.

Mean Reciprocal Antibody Titers to Sabin IPV (0.5 ml)

	Phase I			Phase II		
polio type	1	2	3	1	2	3
prevaccine	39	17	58	0	0	0
7 days post	--	--	--	102	181	297
30 days post	1161	373	5344	453	181	211