901 RIBAVIRIN THERAPY IN CRITICALLY ILL CHILDREN Janet A. Englund, Henry H. Balfour, Jr., Univ. of Minnesota, Dept. Pediatrics, Mpls, MN.

There was a remarkable incidence of respiratory syncytial virus (RSV) in the 1985-86 winter season. The aerosolized antiviral ribavirin was used in 22 patients with suspected or proven RSV disease. Patients were enrolled if they had disease compatible with RSV and evidence of RSV by culture or antigen detection (RSV-Ag). All patients were seriously ill at initiation of therapy, with 82% requiring intensive care and 64% on assisted ventilation (vent.). Underlying medical conditions included prematurity (30%), immunocompromise (23%), pulmonary or cardiac disease (45%), and bacterial infection (9%). Mean duration of ribavirin therapy was 18 hours daily for 6 d. Therapy was discontinued according to clinical improvement, as well as negative RSV cultures and/or RSV-Ag. Twenty of the 22 patients had confirmatory evidence of RSV. Mean time required for diagnosis by RSV-Ag was 0.5 d. vs. 12 d. by culture. Compared with culture, sensitivity of RSV-Ag was 82% and specificity 96% when not receiving antiviral therapy. Premature infants and those with immunodeficiency or infections responded clinically within 2-3 d. of therapy (mean=2 d. on vent.), whereas those with cardiac or pulmonary disease had a delay in clinical improvement until 5-7 d. after initiation of therapy (mean=5 d. on vent.). There were no deaths or serious complications even in pts. receiving assisted vent. during a portion of ribavirin therapy. In this non-controlled study, specific antiviral therapy was rapidly instituted in a group of high risk patients with clinical and laboratory evidence of improvement.

902 H. INFLUENZAE B (H.I.B.) CAPSULAR POLYSACCHARIDE-DIPHTHERIA TOXOID CONJUGATE VACCINE (PRP-D): A FIELD TRIAL IN FINLAND. Juhani Eskola, Heikki Peltola, Aino Takala, Helena Kayhty, Eija Kela, Pirgo-Riitta Ronnberg, P. Helena Makela. (Spon. by Martha Lepow), National Public Health Institute, Helsinki, Finland.

A field trial with a new HIB conjugate vaccine, PRP-D, was initiated in Finland in January 1986. Infants born after October 1, 1985 are offered PRP-D in an open study according to their birthdate. Those born on odd days receive PRP-D at 3, 4, 6 and 14 months and those born on even days, at 24 months. All children receive the routine vaccinations: DPT at 3, 4, 5 and 24 months, IPV at 6, 12 and 24 months and MMR at 14 months. A cohort of these children has been followed serologically. Geometric mean antibody concentrations of anti-PRP antibody by radioimmunoassay at the ages of 3, 4, 6 and 7 months are 0.12, 0.10, 0.10 and 0.45 ug/ml respectively. PRP-D does not have an adverse effect on the antibody response to the routine vaccines. During the first 10 months over 90% of infants in the country have been enrolled. Side effects (local soreness, fever, irritability and other minor reactions) have been rare in the over 20,000 children vaccinated with PRP-D. Based on age-specific attack rates in Finland we have calculated that if the protective efficacy of PRP-D is over 50%, we will be able to demonstrate it by April 1987.

903 IMMUNE RESPONSE TO NONTYPABLE HAEMOPHILUS INFLUENZAE Howard Faden, Jung J. Hong, Deborah Krystofik, Joel Bernstein, John Stanievich, Linda Brodsky, Pearay L. Ogra. SUNY, Children's Hospital, Departments of Pediatrics and ENT, Buffalo, N.Y.

The antibody response to nontypable Haemophilus influenzae (NTHI) was determined in the normal population and in children with otitis media by an immunodot assay. Preliminary studies confirmed the specificity and IgG nature of the antibody measured. The mean antibody titers for individuals in various age groups were as follows: newborn 25,600; 0.5 years (y) 3,200; 1 y 6,400; 1.5 y 6,400; 2 y 6,400; 4 y 25,600; 6 y 25,600; 10 y 25,600; adult 25,600, a serologic pattern remarkably similar to infection with Haemophilus type B. The antibody response in the systemic circulation of young children with otitis media reflected the titer of the corresponding normal age group. In contrast, the level of antibody in the middle ear fluid reflected prior exposure to NTHI. For example, the antibody titer in the middle ear fluid during the first episode of otitis media with NTHI was negligible (< 25). During the second episode, the antibody titer rose to approximately 100 in the middle ear fluid of the infected ear while the titer in the noninvolved ear remained low. Recurrent otitis media resulted in very high titers of antibody in the middle ear fluid (1600) while simultaneous systemic antibody levels continued to reflect age-specific normal values. These data suggest that children do not produce significant systemic antibody to NTHI until four years of age. However, local antibody production in the middle ear mirrors prior sensitization to NTHI.

904 IMMUNOLABELING OF ANTIBIOTIC-TREATED GRAM-NEGATIVE BACTERIA. Pat M. Flynn, Jerry L. Shenep, Francis Gigliotti, and Donna Davis. St. Jude Children's Research Hospital and University of TN, Memphis, TN (sponsored by Walter T. Hughes).

The use of cross-reactive antibodies to the core polysaccharide (CPS) of E. coli J5 to protect against the toxic effects of Gram-negative bacterial sepsis has been proposed. However, it has been shown that conserved lipopolysaccharide (LPS) epitopes on viable cells are not necessarily available for binding by cross-reactive antibody. To test the hypothesis that these conserved epitopes become available for binding after exposure to bacteriolytic antibiotics, immunoelectron microscopy of control and antibiotic-treated bacterial cells was performed using a murine monoclonal antibody. M1B1 is an IgG directed to the CPS of LPS and binds purified LPS from E. coli K1:07 strain C94, but not viable cells, as demonstrated by a radiolabelled binding assay. Binding of M1B1 to control and antibiotic-treated C94 cells was detected with a gold bead-labelled goat anti-mouse antibody. M1B1 did not bind to intact C94 cells, but, after exposure to moxalactam, M1B1 bound to disrupted areas on the cell surface and to intracellular contents extruding from lysed cells. Specificity of M1B1 binding to LPS was confirmed using an irrelevant monoclonal antibody. We conclude that sequestered LPS epitopes within bacteria become exposed after antibiotic treatment. Exposure of these common epitopes may facilitate therapeutic intervention using cross-reactive antibodies.

905 POLYMYXIN B AS ADJUVANT THERAPY FOR OVERWHELMING GRAM-NEGATIVE BACTERIAL SEPSIS. Pat M. Flynn, Jerry L. Shenep, and Dennis C. Stokes. St. Jude Children's Research Hospital and University of TN, Memphis, TN (sponsored by Walter T. Hughes).

Polymyxin B (PMB) is a surface-active agent and antibiotic which ameliorates the adverse effects of endotoxin. Sodium deoxycholate (NaD), a surface-active agent present in bile, also protects against endotoxin. To determine if either of these agents is efficacious in Gram-negative bacterial sepsis compared to antibiotics alone, 36 New Zealand White rabbits were infected by intraperitoneal injection of mucin-enhanced E. coli K1. One hour after infection all animals were treated with moxalactam, 100 mg/kg, and were then randomized in groups of three to receive either saline, PMB 0.21 mg/kg/hr, or NaD 1.0 mg/kg/hr. Blood was sampled prior to infection and hourly thereafter and assayed for bacterial colony-forming units, plasma endotoxin, arterial blood gases and complete blood counts. Heart rate, mean arterial blood pressure (MAP), and core body temperature were monitored continuously. Although levels of bacteremia and endotoxemia were similar in all three groups, the PMB group had significantly higher MAP, pH, and bicarbonate concentrations than the control group ($p<0.05$). Rabbits receiving NaD fared no better than controls. This work shows that PMB effectively blocks some of the physiologic responses to endotoxin and provides support for a clinical trial of PMB in patients with overwhelming Gram-negative sepsis.

† 906 H. INFLUENZA B IMMUNIZATION OF CHILDREN WITH SICKLE CELL DISEASES. Arthur L. Frank, Richard J. Labotka, Lisa R. Frisone, Sudha Rao, Patrick H. McVerry, Joel S. Samuelson, Helen S. Maurer and Ram Yogev. Univ. of Illinois Coll. of Med. Dep't Pediatrics, Northwestern Univ. Medical School, Dep't Pediatrics, Cook County Hospital, Chicago and Connaught Labs, Swiftwater, PA.

H. flu B vaccine is recommended for children 1.5-6 yrs with sickle cell anemia but the adequacy of their response is unknown. We immunized 55 children age 1.5-5.6 yrs (mean 3.6) with sickle cell syndromes, ss, sc or s-thal using two vaccines alternately, single blind (25 patients PRP; 30 PRP-D). The vaccine groups were similar in age, sickle diagnoses and vaccine-to-post-serum interval (28-57 days, mean 40). Coded pre and post sera were tested by radioimmunoassay for ug/ml of anti-PRP antibody.

The geometric mean titer (GMT) for the entire group of children rose 48 fold from 0.126 (PRP, 0.158; PRP-D, 0.104) to 6.16 (PRP, 2.45 or 16 fold vs. PRP-D, 12.88 or 123 fold; p=.006, p=.001 for fold rise difference). A total of 34 children (16 PRP; 18 PRP-D) with pre titers <0.125 rose 80 fold from a GMT of 0.045 (PRP, 0.046; PRP-D, 0.044) to 3.60 (PRP, 1.35 or 30 fold vs. PRP-D, 8.51 or 195 fold; p=.019, p=.025 for rise). Eighty-eight, 68 and 28% of PRP children and 100, 97 and 60% of PRP-D children achieved titers of ≥ 0.1, ≥ 1.0 and ≥ 5.0 respectively. Only 5% or 16% of the total group ended up with possibly inadequate titers <0.1 or <1.0 respectively.

Thus both vaccines were immunogenic in most sickle cell children and are likely to protect. However, PRP-D appears to be more immunogenic than PRP in our population at 1-2 mos after vaccination.