INFECTIOUS DISEASES

● **980** THE ROLE OF INFLUENZA INDUCED POLYMORPHONUCLEAR LEUKOCYTE (PMN) DYSFUNCTION IN THE PATHOGENESIS OF PNEUMOCOCCAL OTITIS MEDIA. J.S. Abramson, G.S. Giebink, P.G. Quie. Univ. of Minnesota, Minneapolis.

Viral upper respiratory infection is often associated with acute otitis media suggesting that some respiratory virus compromise host defenses. We have shown that chinchillas inoculated intranasally with influenza A virus (INF) have subsequent depression of their PMN function. The role of PMN dysfunction in the pathogenesis of pneumococcal otitis media (PnOM) was studied using different intervals between intranasal pneumococcal (Pn) and INF inoculation. The incidence of PnOM was greatest when Pn was inoculated just prior to PMN dysfunction. Inoculation with Pn two days after INF produced PnOM in 7/10 chinchillas. Inoculation of Pn two days before INF, concurrent with INF and 12 days after INF caused PnOM in 12/36, 3/8 and 1/10 chinchillas, respectively. PnOM developed in 6/26 and 0/25 chinchillas inoculated with Pn or INF alone, respectively. Four through six days after INF inoculation, 13 chinchillas receiving either INF or INF + Pn had markedly depressed PMN chemiluminescence and chemotactic activity, while seven chinchillas receiving Pn alone had normal PMN function. PMN depression always preceeded clinical illness. Tympanoplasty tubes were placed in one ear of 38 chinchillas, and no difference was found in the incidence of PnOM in ventilated and non-ventilated ears. While eustachian tube obstruction contributes to the development of middle ear effusion, these results suggest that viral induced PMN dysfunction may also be important in the pathogenesis of PnOM.

981 DEPRESSED OXIDATIVE METABOLISM IN INFLUENZA VIRUS INFECTED PHAGOCYTIC CELLS. J.S. Abramson, E.L. Mills G.S. Giebink, P.G. Quie. Univ. of Minnesota, Mpls.

Susceptibility to bacterial disease following viral infection may be related to virus induced host defense dysfunction, In vitro, influenza A virus (INFA) stimulated oxidative metabolism in human polymorphonuclear leukocytes (PMN) and monocytes (MN) as measured by the chemiluminescence assay. Electron microscopy of PMN and MN incubated with INFA for 20 min demonstrated virus attached to the cell membrane and within intracellular spaces. When PMN and MN were stimulated with opsonized zymosan there was depressed peak chemiluminescence in cells pre-incubated with INFA compared to cells pre-incubated with buffer (MN: 3.6 ± .14 cpm per mn vs 19.7 ± 0 cpm per mn, $p < .001$; PMN: 12.8 ± 1.9 cpm per pmn vs 18.4 ± .9 cpm per pmn, $p < .05$). Depressed chemiluminescence also occurred in cells stimulated with phorbol myrisitate acetate which were pre-incubated with INFA compared to cells in buffer (MN: 2.6 ± .28 cpm per mn vs 6.2 ± .85 cpm per mn, $p < .05$; PMN: 1.4 ± .21 cpm per pmn vs 12.7 ± 0 cpm per pmn, $p < .001$). In vivo, depression of the PMN chemiluminescence response to opsonized zymosan and phorbol myrisitate acetate occurred in chinchillas inoculated intranasally with INFA. These animals also demonstrated depressed PMN bacterial activity for pneumococcus. These results suggest that INFA stimulation of phagocytic cell oxidative metabolism may induce cellular changes which inhibit the cells' response to subsequent particulate or soluble stimuli. Viral induced depression of phagocytic cell function could thereby contribute to increased susceptibility to bacterial disease.

982 CHANGING PATTERN OF SEPTICEMIA IN SICKLE CELL DISEASE: POSSIBLE EFFECT OF PNEUMOCOCCAL IMMUNIZATION. Joseph E. Addiego, Jr., Mark Mandel, Elliott P. Vichinsky, Bertram H. Lubin. Children's Hospital, Oakland, CA.

Since 1978 we have routinely immunized all sickle cell patients 18 mo. of age or older with pneumococcal polysaccharide vaccine (PPS). To determine if this immunization program decreased the incidence of septicemia or altered the organism responsible, we reviewed the documented septic episodes in a total of 241 sickle cell patients ages 1 mo. to 16 yrs. seen in our program from 1975-77 compared to 1978-80. The results are shown below:

	N	SS	SC	Mean Age	S.P.	H.I.
1975-77	9	9	0	2 5/12	8	1
1978-80	9	3	6	2 6/12	3	6

The number of septic episodes was the same during both periods, however, H. Influenza (H.I.) increased and Strep. pneumoniae (S.P.) decreased since 1978. Septic episodes were only found in young patients (4 yr). Only one immunized patient (PPS) developed S.P. sepsis, and that with a non-vaccine type, Type 5. Four of seven episodes of H.I. sepsis occurred in patients who had previously received PPS. There were 3 S.P. and 3 H.I. septic episodes in Hb SC patients. These results suggest a changing pattern of septicemia since beginning routine PPS immunization, H.I. rather S.P., and support our previous reports of PPS efficacy in Sickle Cell patients over 18 mo. of age. They also suggest that Hb SC patients are at significant risk of bacterial septicemia. Supported by NHLB Grant No. HL 20985-2 from NIH.

983 USEFULNESS OF SERUM C-REACTIVE PROTEIN (CRP) DURING THE NEWBORN PERIOD. Eugene Ainbender, Eresvita E. Cabatu, Dolores M. Guzman, and Avron Y. Sweet. Mount Sinai School of Medicine, Mount Sinai Medical Center, Department of Pediatrics, New York, New York.

Among 100 consecutive infants admitted to a NICU, serum CRP values ≥ 1.0 mg/dl occurred in 18 during any of the first three days of life. Of these 18 infants, 12 had one or more of these problems: intrauterine growth retardation, meconium aspiration pneumonitis, febrile mother, transient tachypnea, and low Apgar score and/or shock and/or fetal distress. Of 11 with serum CRP values ≥ 2.0 mg/dl, 8 had maternal fever, meconium aspiration pneumonitis, shock and/or fetal distress. Serum CRP values during the first 3 days of life among 35 infants of mothers with fever and/or prolonged rupture of membranes were not helpful in identifying the 2 with systemic Group B β hemolytic streptococcal disease (urine positive for antigen by countercurrent immunoelectrophoresis), there being 7 others with negative surface cultures and serum CRP values ≥ 1.0 and 3 with elevated values of 6 whose surface cultures were positive.

Serial serum CRP determinations of 10 infected neonates (7 septicemias due to a variety of organisms, 1 urinary tract infection 1 pneumonia and 1 scalp abscess) followed the expected rapid decline during successful therapy.

Serum CRP values during the first days of life are often elevated because of non-infectious causes. Accordingly, this acute-phase protein cannot be used to identify infection during the first days of life. However, it affords an excellent means of evaluating the course of infections and effectiveness of therapy among term and preterm infants.

984 THE LACK OF CROSS REACTIVITY WITH *ESCHERICHIA COLI* K100 (K100) IN THE HUMAN ANTICAPSULAR RESPONSE TO *HAEMOPHILUS INFLUENZAE* TYPE B (HIB). Porter Anderson and Richard A. Insel (Spon. by David H. Smith), University of Rochester Medical Center, Department of Pediatrics, Rochester, N.Y.

The capsular polysaccharides (CP) of HIB and K100 are polymers of ribosyl ribitol phosphate differing only in one linkage and having common (as well as unique) antigenic determinants. Animal and human antibodies (Ab) to K100 are strongly cross reactive (XR) with HIB, and exposure to K100 is thought to contribute to natural immunity of humans to HIB. The converse relation heretofore has been little examined.

Of 21 human adults responding to vaccination with HIB CP only 3 made K100-XR antibody; likewise only 2 of 11 responding children made XR Ab. In only 1 of 10 children convalescent from HIB systemic infection and 0 of 2 children asymptomatically colonized did the response include K100-XR Ab. K100 reactivity was observed in the naturally occurring anti-HIB Ab of only 3 of 21 adults but, in contrast, in 14 of 29 children. Thus K100-XR Ab in humans rarely results from exposure to HIB or its CP and must arise from K100 itself or other antigenically related stimuli. Further, humans appear likely to respond to the common determinants when exposed to K100 (although not when exposed to HIB). K100 immunogens may thus have a protective potential against HIB not manifest in corresponding immunogens prepared from HIB itself.

985 CLINICAL EFFICACY AND PHARMACOKINETICS (PK) OF MOXALACTAM (MLM) IN PEDIATRIC SKELETAL INFECTIONS. Stephen C. Aronoff, Peter V. Scoles, Michael D. Reed, Carolyn Meyers, Joseph S. Bertino and Jeffrey L. Blumer (Spon. by W.T. Speck) Case Western Reserve University, Rainbow Babies and Children's Hospital, Departments of Pediatrics and Orthopaedics, Cleveland.

The clinical efficacy and PK of the new β-lactam antibiotic, MLM, was investigated in 8 pediatric patients (8 wks.-16 yrs.) with skeletal infections. All patients received 150 mg/k/day IV in 3 divided doses for 1-4 weeks. Five children had osteomyelitis 3 with S. aureus, 1 with Serratia spp., and 1 with K. pneumoniae. Two had purulent synovial fluid without recovery of an organism. One had both osteomyelitis and septic arthritis due to S. aureus. All children demonstrated clinical improvement within 48 hrs. of the initiation of therapy. No drug-related toxicity was noted. In all cases, cultures at the termination of therapy were sterile. Ultimately, all had normal musculoskeletal function. After the initial dose and again after 3-5 days of therapy the PK of MLM were determined. A new, HPLC technique was used to measure serum concentrations. No difference in PK parameters was observed at the two time intervals. Mean peak serum concentrations were 235± 48 µg/ml and exceeded the MIC's of the separate organisms for at least 3 hrs. No drug accumulation occurred during continuous therapy. The $t_{\frac{1}{2}\beta}$ was 100±31 min. and was independent of patient age. The apparent volume of distribution was ~0.45 L/kg suggesting good tissue penetration. We conclude that MLM is a safe, effective antimicrobial agent for the treatment of skeletal infections in childhood.