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TREATMENT OF STREPTOCOCCAL PHARYNGITIS WITH B.I.D. CEPHALEXIN. D.C. Anderson, S. Hollister, H. Comstock, H. Yian, D. Singer and A. Ellison, Dept. of Human Development, Mich. State Univ. (Spons. by W.B. Weil), East Lansing, Michigan.

From the private practices of Lansing community pediatricians two groups of 33 pediatric ambulatory patients with Group A β -hemolytic streptococcal pharyngitis matched with respect to age, sex, race, socioeconomic status, duration of symptoms prior to treatment, and WBC at onset of treatment were randomized into 10 B.I.D. or Q.I.D. Cephalexin treatment regimens (B.I.D. = 10-15 mg/kg/dose, Q.I.D. = 5-8 mg/kg/dose). Compliance was assured by followup phone calls and inspection of medication containers at followup visits. Excellent clinical responses and bacteriologic cure (negative culture at day 14 and 28) occurred in 31/33 B.I.D. patients and 33/33 Q.I.D. patients. One clinical and bacteriologic failure, and one bacteriologic "relapse" (positive culture on day 28) occurred in the B.I.D. treatment group. No significant toxicity occurred in any of the study patients. These findings suggest that (1) a B.I.D. Cephalexin regimen is comparable to a Q.I.D. regimen in the treatment of Group A β -hemolytic streptococcal pharyngitis, (2) further evaluations of B.I.D. Cephalexin regimens in ambulatory patients are warranted, and (3) controlled clinical trials can be practical, productive and cost-effective utilizing the private physicians' practices as a source of patient populations.

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PROTECTION OF NEWBORN RATS FROM K1 E. COLI INFECTION. Robert Bortolussi and Patricia Ferrieri, University of Minnesota Med. School, Dept. Pediatr., Minneapolis.

We have shown previously that newborn rats develop sepsis/meningitis after i.p. injection of K1 *E. coli*. The present studies examine the effect of passive immunization on infection. Pregnant rats were immunized X2 by i.v. injection of formalin-killed *E. coli* (type 07:K1:H?). Some members of subsequent litters were exchanged shortly after birth with pups from saline-immunized mothers. At age 5 days, all pups were challenged by i.p. injection of 1.2×10^7 CFU of a K1 *E. coli* strain (018ac:K1:H7). Quantitative blood cultures were obtained daily. Of 29 pups born to and nursed by K1-immunized dams, 34% and 41% had bacteremia 1 and 3 days later vs. 59% of 29 unexchanged pups from saline-immunized dams ($p > 0.05$). Mortality rates were 38% (K1) and 34% (controls) at 7 days. Exchanged animals had infection and mortality rates similar to the above. Since rat pups are able to absorb IgG (of different species) from the GI tract, other groups were given oral supplements of group B meningococcal horse serum (h.s.) which reacts with K1 antigen (Group I); normal h.s. (Group II); or water (Group III) for 2-4 days and challenged at 5 days of age. Three days later 54% of Group I had bacteremia vs. 60% of Groups II and III; however, mortality rates were 8%, 33% and 30%, respectively ($p < 0.05$). Group I had initial bacteremia with geometric mean CFU/ml 1 log lower than that of Groups II and III.

This method of maternal immunization against K1 *E. coli* gave poor protection to rat pups. Oral feeds of anti-capsular antibody favorably modified intensity of bacteremia and mortality.

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NAFCILLIN-OXACILLIN COMPARATIVE CLINICAL TRIAL. Allan M. Arbeter, Mark D. Tolpin, Sharon A. Piercy, Stephen D. Yachetti, Michele S. Danish, W. Stuart

Warren, and Stanley A. Plotkin. The University of Penna. School of Medicine and Children's Hospital of Philadelphia, Pa.

Intravenous nafcillin (N) or oxacillin (O) was administered to 114 patients, newborn to 17 years of age. Distribution of the pts included 87 studied double blind and 27 by physician preference. Physician preference pts did not alter the results. A minimum of five days of IV therapy was required for inclusion, but 60% of the pts received >10 days of therapy. The pts were monitored with serial CBC's, platelet counts, urinalysis, BUN, creatinine, SGOT, SGPT, and bilirubin. Occurrence of secondary fevers, rashes, and thrombophlebitis (TH) were tabulated.

Treatment courses were successful in 97.5%, but 4 pts died after bacteriologic sterilization. TH occurred in 17/52 N pts and 4/62 O pts. In pts over 10 years of age receiving N 14/25 developed TH. Of eight pts switched blindly from N to O because of TH, all tolerated the second drug. Three patients in each group developed severe neutropenia (WBC<1500). Seven N and 5 O pts had drug fevers. Elevated SGPT's occurred in 13/62 O and 6/52 N pts. No renal side effects were noted.

Pharmacokinetic studies were done on 12 pts of which six pts had cross-over studies on both drugs. The half-life in pre-matures was different than the older child (3.0 ± 0.9 versus 0.6 ± 0.1 hrs.) There was no difference between O or N half-lives. Volumes of distribution, and total body clearances were calculated.

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DOSE AND EFFICACY OF ARA-A IN NEONATAL HERPESVIRUS INFECTIONS. Yvonne J. Bryson, James D. Connor, and Lawrence Sweetman. Departments of Pediatrics, University of California, Los Angeles and San Diego Schools of Medicine

Ara-A has proven efficacy in Herpesvirus (HSV) encephalitis and in Varicella Zoster (VZ) infections in immunosuppressed patients. Using liquid chromatography (HPLC) and a novel bioassay method to detect ara-nucleosides and antiviral activity (AVA), we have observed a significant difference in dose responses between infants and adults. At 10 mg/kg/12 hour doses, infant plasma by HPLC contained an average of 4.5 μ g/ml ara-Hx and in 4 out of 5 samples <.02 μ g/ml of ara-A. At 20 mg/kg/12 hour doses, ara-Hx rose to average 5.6 μ g/ml with 3 of 4 ara-A values <.01 μ g/ml. At 20 mg/kg/6 hour infusion, ara-Hx averaged 8.1 μ g/ml and all plasma samples contained ara-A averaging 0.084 μ g/ml. In 2 neonates, HSV 2 disease progressed until ara-A reached >15 mg/kg/12 hour doses. At 35 mg/kg/12 hours, neonatal plasmas contained mean ara-A levels of .224 μ g/ml with CSF levels of .064 μ g/ml when measured by bioassay (sensitivity .004 - .008 μ g/ml). These compared favorably with mean ara-A plasma levels achieved in adults which were .023 μ g/ml and .119 μ g/ml at doses of 10 and 15 mg/kg/12 hour infusion respectively, with .081 μ g/ml in CSF. These findings indicate that blood levels correlated directly with the amount of drug infused and inversely with the duration of infusion, and also suggest that higher ara-A doses with potential toxicity will be required for successful treatment of the more resistant HSV 2 strains in neonates.

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MICROBIOLOGY OF RECURRENT AND CHRONIC OTITIS MEDIA WITH EFFUSION. Charles D. Bluestone, Richard H. Michaels, Keith H. Riding, Erdem I. Cantekin,

William J. Doyle, Cindy S. Poziviak. Departments of Otolaryngology and Pediatrics, Children's Hospital of Pittsburgh and University of Pittsburgh School of Medicine, Pittsburgh, Pa.

A study was conducted of 274 children who had recurrent acute or chronic otitis media with effusion or both. Forty-five percent of the ears with effusion were found to contain bacteria and 11 percent contained bacteria that were "probable pathogens" (*S. pneumoniae*, *H. influenzae*, and *S. pyogenes*). Bacteria were also found in 40 percent of the ears without effusions. The type of organism found did not vary with the age of the patient studied or the season of the year. The significance of these bacteria in the etiology of chronic otitis media with effusion remains to be demonstrated.

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EARLY RECOGNITION OF SHOCK FROM GROUP B BETA HEMOLYTIC STREPTOCOCCAL SEPTICEMIA IN THE NEONATE. Luis A. Cabal, Cindy Cristofani, Bijan Siassi, Carolyn Plajstek, J.E.

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The high mortality in neonatal Group B Beta Hemolytic Streptococcal (BHS-Gr B) septicemia may be related to difficulty in the early recognition of septic shock (SS). The objective of this study was to describe SS in 6 infants who developed BHS-Gr B sepsis at or shortly after birth. The infants (B.W.=940-2750, B.A.=27-37 wks) were studied from birth until recovery in one and death in the remaining 5. Heart rate, arterial blood pressure (ABP), central venous pressure (CVP), rectal-skin temperatures, and arterial blood gases were serially measured. During the first 10 hours, hypotension with wide pulse pressure and low diastolic pressure was consistently present. Color, skin perfusion, CVP and rectal-skin temperatures were normal. Mild metabolic acidosis was the only abnormality in the blood gases. In the 5 infants who died, CVP increased to abnormal levels. The diastolic pressure increased and the systolic pressure decreased further resulting in a narrowing of pulse pressure. Core temperature and metabolic acidosis increased while there was a decrease in peripheral perfusion and a change in the skin color to grey. SS as a result of BHS-Gr B septicemia was characterized by an early phase with pink hypotension and peripheral vasodilation. In the infants who died, grey hypotension with peripheral vasoconstriction and heart failure supervened. We postulate that recognition and therapy of the early phase of SS may prevent progression of the disease and a fatal outcome.