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DO THIRD-GENERATION CEPHALOSPORINS HAVE A ROLE IN GRAM-NEGATIVE CNS INFECTIONS? Ellen G. Chadwick, Stanford T. Shulman, Ram Yogeve. Northwestern U. Med. School, Children's Mem. Hosp., Dept. of Pediatrics, Chicago.

The role of third-generation cephalosporins in pediatric gram-negative CNS infections remains undefined. Therefore, we reviewed our experience with these drugs in 42 patients (ages 19 days to 11 years) with ventriculitis complicating hydrocephalus (14), or meningitis (28), 30 treated with moxalactam and 12 with ceftriaxone. Moxalactam dosages were 50-100 mg/kg q 8 hrs for 10-29 days, and ceftriaxone 50 mg/kg q 12 hrs for 10-31 days. Etiologic agents included *H. influenzae* type b (25), *E. coli* (8), *klebsiella* (6), *E. cloacae* (2), and *salmonella* (1). Median minimal inhibitory concentrations of moxalactam and ceftriaxone respectively for hemophilus were 0.055 and 0.003 µg/ml, and for enteric bacilli were 0.45 and 0.12 µg/ml. Levels in CSF or ventricular fluid ranged from 18-60 µg/ml for moxalactam and from 8.9-13.7 µg/ml for ceftriaxone. The bacteriologic cure rate was 100%. Clinical cures were demonstrated in 41/42 patients, with one patient unevaluable. No significant clinical side effects were noted; one patient had transient eosinophilia. The only complications were 2 patients with oral candidiasis and one with enterococcal ventricular superinfection. No bleeding problems or significant diarrhea were encountered. Because of the safety and efficacy of moxalactam and ceftriaxone in the treatment of both gram-negative enteric and hemophilus CNS infections in children, these agents may now represent the drugs of choice for such infections.

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IMPAIRED PYROGEN PRODUCTION BY FETAL AND NEWBORN RABBIT LEUKOCYTES. Kathleen H. Chance, Michael E. Miller, Boyd W. Goetzman, Anthony T. Cheung, Department of Pediatrics, University of California, Davis, CA

Since newborns often do not respond to infection with fever, their white cells may not be capable of producing pyrogens. We investigated this possibility in leukocytes obtained from 23 and 26 day gestation fetal rabbits and term (31-33 days gestation), 2 day old, 4 day old, and adult rabbits. Their leukocytes were incubated with *E. coli* endotoxin and the resultant supernatants, possibly containing pyrogen, were injected into adult rabbits (recipients) whose rectal temperatures were being monitored. Blood samples were drawn from the recipients before and 2 1/2 hours after the injection for the determination of total neutrophil counts. The recipients developed fever following supernatant injections of leukocyte preparations from some fetal, term, and 2 day old rabbits, and all 4 day old and adult rabbits. When there was no febrile response, there was nevertheless a 2 to 4 fold increase in the total neutrophil count. Both the PMN and febrile responses were suppressed by administering pregnant adult plasma to the recipient.

The apparent impaired pyrogen production by leukocytes from younger animals may explain their failure to develop fever with infection. While generation of insufficient or incomplete pyrogens are possible mechanisms, the transplacental transfer of a maternally produced inhibitor appears more likely.

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INCREASED LEUKOCYTE ALKALINE PHOSPHATASE IN SICK NEONATES. Kathleen H. Chance, Elliot Goldstein, Boyd W. Goetzman, William Lippert, and Richard M. Donovan, School of Medicine, Dept. of Pediatrics and Internal Medicine, University of California, Davis.

Alkaline phosphatase (LAP) and myeloperoxidase (MPO) were evaluated in polymorphonuclear leukocytes (PMNs) from neonates using a computer-assisted cytospectrophotometer. This method allowed quantitative enzyme determinations within each PMN. Population distributions were determined for 100 individual cells. Of the 10 infants studied, 8 were ill, 3 with congenital pneumonia and 5 without proven infection, and 2 were well pre-term infants. PMNs were obtained from all during the first week of life and from 5 during the third week, as well. The 8 ill infants showed a broad distribution of LAP activity in their PMNs in the first week of life, with 75.4±25.2% (x±S.D.) of PMNs having LAP activity greater than the 95th percentile of our adult controls. By the third week of life, the percent of PMNs had significantly diminished to 35.6±33.9% (x±S.D.) (p < .05). The 2 well preterm infants in the first week of life had only 7±4% (x±S.D.) of PMNs with activity greater than the 95th percentile for adult controls. The distribution of MPO activity did not differ from adult controls in any infant.

In summary, we found increased PMN LAP activity in the first week of life in sick neonates with and without infection as compared with adults and well neonates. Decreasing LAP activity in the third week of life corresponded with clinical improvement. Thus, differences in intracellular LAP activity appear to be due to pathologic rather than maturational processes.

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GRAM-NEGATIVE BACTEREMIA DOES NOT INCREASE ALBUMIN OR BILIRUBIN CONTENT IN BRAINS OF ADULT RATS. Shu Chen, William J. Cashore, and William Oh. Brown Univ., Women & Infants Hosp., Dept. of Ped., Providence, RI

The risk of bilirubin-related brain injury may be increased by perinatal or neonatal infection. To determine whether Gram-negative bacteremia acutely increases transfer of bilirubin and albumin from blood to brain, 6 adult rats were injected with 10⁸ *E. coli* to produce positive blood cultures, and then infused while awake with bilirubin (BR) and ¹²⁵I albumin (ALB) via indwelling catheters for 180 minutes. 3 of 6 rats with positive blood cultures had lethargy or temperature instability during the experiment. At 180 mins, the animals were sacrificed for brain BR and ALB concentrations. Compared to 5 controls, there were no differences in serum or brain BR and ALB in the bacteremic rats, as shown in the table:

	Whole Blood pH	Serum BR,mg%	Serum ALB,gm%	Brain BR,µg/gm	Brain ALB,µg/gm
Control	7.31±0.10*	8.3±4.2	3.6±0.4	0.60±0.27	215±59
Septic	7.37±0.02	5.1±2.3	3.2±0.5	0.51±0.18	194±167

*Means±S.D.

In the adult rat, bacteremia does not cause acute changes in permeability of the blood-brain barrier to bilirubin or albumin. If sepsis does increase the risk of bilirubin injury to the central nervous system, systemic metabolic or circulatory changes due to sepsis or acute effects of endotoxin, rather than acute bacterial effects on the blood brain barrier, may be more likely reasons for this association.

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DIARRHEA ASSOCIATED WITH *E. COLI* PRODUCING SHIGA-LIKE CYTOTOXIN. Thomas G. Cleary, Jeff Mathewson, Larry K. Pickering, Phil Johnson, Lindsey Wood, Donna Morgan, Charles D. Ericsson, Herbert L. DuPont. Prog Infec Dis and Dept of Pediatrics, Univ of Texas Med Sch at Houston.

College students spending the summer in Mexico were studied for the development of diarrhea. Stool specimens were collected from sick and asymptomatic students. 188 episodes of gastroenteritis were evaluated for salmonella, shigella, campylobacter, enteropathogenic *E. coli*, enterotoxigenic *E. coli* (ST,LT), giardia, *E. histolytica*, and cryptosporidium. 53 episodes occurred for which no etiologic agent could be defined. *E. coli* isolated from these students and asymptomatic students were assayed for adherence to HEP-2 cells and production of Shiga-like toxin. HEP-2 adherent *E. coli* were isolated from ill students more frequently than from those who were well (p < 0.05). 50% of strains from sick students with no known etiology were positive for Shiga-like toxin while only 27% of *E. coli* from asymptomatic individuals were positive. Strains that were positive for Shiga toxin tended to be positive for HEP-2 adherence and strains that were negative for Shiga or HEP-2 tended to be negative for the other marker (p < 0.02). HEP-2 adherence and Shiga toxin production correlated with presence of gastroenteritis in individuals who had no previously described enteric pathogen. This is the first evidence that Shiga toxin production by *E. coli* may commonly cause enteritis.

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INHIBITION OF STREPTOCOCCAL GROWTH BY HUMAN BLOOD AGAR. Janice L. Cockrell, (Sponsored by Harold Maurer), Department of Pediatrics, Children's Medical Center, Medical College of Virginia, Richmond, Virginia

It is generally accepted that the ideal culture plate medium for Group A beta-hemolytic streptococci (GABHS) is 5% sheep's blood agar (SBA), with human, rabbit or horse blood being acceptable substitutes. During a recent study of acute pharyngitis conducted in Costa Rica, because of a relative unavailability of sheep's blood, human blood agar plates were utilized. After 29 of 30 throat cultures were negative for GABHS in spite of excellent growth of other organisms, sheep's blood agar was obtained, and a standard GABHS strain (J174A4) from the American Type Culture Collection was reconstituted. Sheep and human blood agar plates were inoculated, then incubated both aerobically and anaerobically. After 24 hours of incubation, poor colony growth with minimal hemolysis was noted on both the aerobic and anaerobic human blood plates, with excellent growth and beta hemolysis on SBA. Frozen samples from the 30 original throat cultures were subsequently grown on SBA and typed by means of latex agglutination. Four specimens in addition to the original positive culture were confirmed as positive for GABHS. One was suspicious but could not be isolated for confirmation. Preliminary data suggest that human blood agar is not an acceptable substitute for SBA as some lots may contain factors which may inhibit growth of GABHS.