1080 INFLUENCE OF DOSAGE INTERVAL ON THE IN VITRO ACTIVITY OF CHLORAMPHENICOL AGAINST H. INFLUENZAE(HI). Mark D. Greenfield, Roger D. Toothaker, Arnold L. Smith. Children's Orthopedic Hospital and Medical Center, Dept. of Pediatrics, Dept. of Pharmaceutics, Univ. of Washington, Seattle.

Controversy remains regarding the effect of dosing interval(τ) on the efficacy of antibiotics. Usually the antibiotic dose is based on static MIC/MBC determinations and dosing interval on pharmocokinetic data acquired through clinical studies. If smaller doses at more frequent intervals have equivalent bactericidal effect, high peak concentrations can be avoided. This study compares the effect of different τ's of chloramphenicol tested against a type b HI (MIC 0.8 µg/ml) in a dynamic in vitro dilution model. High dose (HD) and low dose (LD) simulations were compared using equivalent elimination half-life, area under the drug concentration vs. time curve, and drug concentration at steady state, but differing C_{max} and τ(8.4 µg/ml q 6h or 4.8µg/ml q 2h in HD and 1.6 µg/ml q 6h or 0.98 µg/ml q 2h in LD). The HD simulations showed faster rate and greater total bacterial killing. For both HD and LD, total bacterial reduction and area under the bacterial concentration vs. time curve were comparable for τ=2h or τ=6h. Although total bacterial reduction in 12h was equivalent in LD, more bacteria were killed in the first 9h of study with LD q 6h in comparison to q 2h. These data suggest that total drug given, not C_{max} or τ determine the maximum degree of bacterial killing, and that toxicity could be minimized with equal effect using dosage regimens with minimal concentration fluctuations. Animal studies are in progress to determine whether the in vitro data are reproducible in vivo.

1081 CEFTAZIDIME (CAZ) VERSUS CEPHALOTHIN, CARBENICILLIN AND GENTAMICIN (KCG) AS THE INITIAL THERAPY OF THE FEBRILE NEUTROPENIC (F/N) PEDIATRIC CANCER PATIENT. Linda Granowetter, Heidi Wells, and Beverly Lange. Children's Hospital Cancer Research Center, Philadelphia, PA.

In a randomized trial we compared an extended spectrum cephalosporin (CAZ) and multidrug therapy (KCG) in F/N patients aged 5 mo. - 20 yrs. Of 107 evaluable episodes, 45 were documented infections (13 bacteremias: 6 gram (+); 7 gram (-)). Sixty-two episodes were due to fever of unknown origin (FUO). Results are defined as success alone (SA), success with modification (SM: addition of antifungal, TMP-SMX, erythromycin, or vancomycin), cross-over (X: due to microbiologic failure or toxicity), or failure (F: death due to infection). Results over 15 months are shown:

	FUO					Documented Infection				
Regimen	#	SA	SM	X	F	#	SA	SM	X	F
KCG	33	27	4	1	2	26	14	10	1	1
CAZ	29	20	7	1	1	19	10	6	3	0

FUO failures were due to fungal superinfection despite early empiric Amphotericin. One cross-over (CAZ to KCG) was due to persistent hypotension: staph aureus bacteremia (CAZ resistant) was subsequently proven. The overall outcome with KCG and CAZ are similar. However, the increasing re-emergence of serious gram (+) infection may necessitate the addition of broader gram (+) coverage in patients treated with CAZ.

●1082 PREVENTION OF E. COLI K1 INFECTION BY MATERNAL IMMUNIZATION WITH MANNOSE-SENSITIVE (MS) PILI FROM E. COLI K1 OR KLEBSIELLA PNEUMONIAE. Nicholas G. Guerina, T. Woodrow Kessler, Sol Langermann, Victoria J. Guerina, Herbert W. Clegg, and Donald A. Goldmann. Harvard Medical School, Children's Hospital, Dept. of Pediatrics, Boston, Massachusetts

We have purified and characterized MS pili from E. coli (EC) K1 and Klebsiella pneumoniae (KP). These pili were found to be chemically and serologically similar. In vitro adherence of both ECK1 strain C94 and KP strain Fader to oropharyngeal cells was inhibited by purified MS pili from either strain. When pregnant rats were immunized with purified MS pili from either strain C94 or strain Fader, high levels of colostral and milk anti-pilus antibody were produced as determined by ELISA. The average milk titers with C94 pilus immunization were 3,000 for IgG and 2,000 for IgA; with Fader MS pili, titers were 2,500 for IgG and 2,000 for IgA. Pre-immune titers were undetectable. Infection with strain C94 was prevented in neonatal rats suckled by dams immunized with Fader as well as homologous MS pili:

Challenge bacteria	Vaccine preparation	Bacteremia rate
ECK1 C94	Buffer vehicle control	24/81 (30%)
ECK1 C94	ECK1 C94 MS pili	0/84 (0%)
ECK1 C94	KP Fader MS pili	0/86 (0%)

The highly significant heterologous protection ($p<0.001$), coupled with recent serological studies, suggest that life-threatening ECK1 infection may be prevented by a vaccine composed of MS pili from a small selection of clinical isolates. KP may colonize and invade in a manner similar to ECK1, so vaccination with the same selection of MS pili may also prevent KP sepsis.

1083 VIRALLY INDUCED MEMBRANE PERMEABILITY CHANGES AS A POSSIBLE LINK BETWEEN INFLUENZA B AND REYE'S SYNDROME. Mina Gurevitz, Irene T. Schulze, Ella M. Swierkosz, Max Q. Arens, and Kathleen B. Schwarz (spon. by Thomas Aceto, Jr) St. Louis University School of Medicine, Cardinal Glennon Memorial Hospital for Children, Dept. of Peds and Microbiol, St. Louis, MO.

The mechanism by which viral infection can lead to the multiple metabolic derangements characteristic of Reye's Syndrome is not understood. The possibility that influenza virus could induce changes in membrane permeability to nutrients ordinarily concentrated within the cell was examined. Madin Darbin canine kidney (MDCK) cells were infected by egg grown influenza B virus by two routes: at physiological conditions, pH 7.4, 37°C; and adsorption at 0°C followed by brief exposure to pH 5.0, 37°C. Control cells were mock-infected with allantoic fluid. Transport (uptake and release) of phosphate (Pi) 2-deoxyglucose (dGlc) and α-aminoisobutyric acid (AIB) were measured at various intervals 0 to 10 hours after infection. At physiological pH, Pi uptake by infected cells was inhibited ($p< 0.01$) at 0 to 2 hours as compared to controls. Uptake of AIB was also inhibited ($p< 0.01$) at 2 hours. The uptake of all nutrients was higher at 6 to 10 hours in infected cells as compared to controls ($p< 0.01$). When release of Pi and dGlc was measured, there was no difference between infected cells and controls at 0-10 hours. At low pH, fusion occurred in infected cells, but not in control cells. Fused infected cells demonstrated both significantly increased release and diminished uptake of nutrients compared to controls. Thus influenza B virus can induce changes in host cell membrane permeability that may have important implications for cell metabolism.

●1084 RIMANTADINE TREATMENT OF INFLUENZA A IN CHILDREN Caroline B.Hall, Christine L.Gala, Raphael Dolin, The Elmwood Pediatric Group, University of Rochester Medical Center, Departments Pediatrics and Medicine, Rochester, NY

Rimantadine (Rim) has appeared to be more effective than amantadine in vitro and in animal Flu A infections and better tolerated in adults. However rimantadine has not been studied in children. Thus, Rim was compared to acetaminophen for treatment of Flu A infections in children from private practice. Patients received Rim (3mg/lb/d to 200 mg/d)(Rim group) or acetaminophen (q.i.d.) (A group) for 5 days. Patients were examined and nasal washes obtained daily for 7 days by home visits. 91 patients were enrolled. 71 had Flu A/H3N2 by culture. 69 were analyzed: 37 in Rim, and 32 in A groups (mean age 6.6 & 4.2 yr). Severity of illness on day 1 was equal in both groups but reduction in mean fever, cough, sore throat and malaise was greater in first 3 days in Rim group ($p<.01$ on day 2 or 3). Similarly, mean symptom score was less in Rim group on day 2 ($p<.05$) and d. 3 ($p=.006$). Amount of Flu A shed was also less on d. 2-3 in Rim group with significantly fewer shedding on d. 2 ($p=.03$). But % of Rim group shedding after d. 5 increased slightly in contrast to A group, such that significantly more Rim patients shed on d. 6-7. Also Rim patients had significantly longer duration of shedding and more had an increase in their symptom score on or after d. 5 ($p<.04$). Rim was well tolerated. Possible side effects were not significantly different in the two groups. Thus, treatment with Rim produced greater reduction in fever, symptoms and shedding over first 3 days than did acetaminophen, but shedding was prolonged after the end of therapy.

1085 NONSPECIFIC VAGINITIS (NSV) FOLLOWING SEXUAL ABUSE IN CHILDREN. Margaret Hammerschlag, Marinella Cummings Brinda Doraiswamy, Phyllis Cox, William McCormack (Spon. by L. Finberg), SUNY, Downstate Medical Center, Department of Pediatrics and Medicine, Brooklyn, New York

NSV, one of the most common causes of vaginitis in adults, is a polymicrobial infection in which vaginal anaerobes act synergistically with Gardnerella vaginalis. The diagnosis is made by examination of the vaginal secretions for clue cells, the development of a fishy odor after the addition of 10% KOH and a pH≥4.5. To determine if NSV may occur in sexually abused children, we obtained vaginal washes from 31 abused and 28 control children, 2.5 to 13 years of age. A wash was considered definite for NSV if it contained both clue cells and odor; possible if it contained either clue cells or odor. We did not use pH since the normal range has not been standardized in prepubertal girls. Possible NSV (odor only) was found in only 1(4%) control. She was asymptomatic and her f/u exam was normal. Only 1 abused child had possible NSV (odor) detected at the initial exam, ≤ 48 hours after the episode of abuse, whereas 8(26%) developed definite(4) or possible(4) NSV at the f/u visit ≥ 7 days after the episode of abuse or rape. Five of these girls developed either a new vaginal discharge or dysuria; 3 were treated with metronidazole with resolution of the symptoms and reversion of the vaginal wash to normal.

These findings suggest that NSV is uncommon in normal children and that it can be acquired after sexual abuse. NSV was the most frequent cause of vaginitis in the abused girls in this study Examination of a vaginal wash for clue cells and odor should be part of the routine evaluation of sexually abused children.