● 1069 LIVE ATTENUATED VARICELLA VACCINE IN CHILDREN WITH MALIGNANCIES. Ziad M. Shehab, Kristen A. Weigle, Clementina F. Geiser, Philip A. Brunell; U. of Texas HSC; Dept. of Pediatrics, San Antonio, TX.

Children with leukemia or lymphoma have clinical responses of varying severity to natural varicella or varicella vaccine (VV) virus infection. A study was designed to determine the factors influencing response to VV. Ten patients in remission off chemotherapy (CT) and 3 patients in remission on maintenance CT have been studied thus far. In the latter group, CT was discontinued 1 week prior to and 1 week following administration of OKA strain VV. Thus far all patients have seroconverted as determined by measurement of antibody against membrane antigen at 30 days. Titers ranged from 1:4 to 1:512. Six months following VV, all 5 vaccinees tested still had detectable antibody. Three to 67-fold increases in lymphocyte stimulation by varicella-zoster virus (VZV) were noted in all VV recipients at 30 days as compared to pre-vaccination. Fever related to vaccine or vesicular rash were not observed. VZV was not recovered from blood, throat and urine cultured on 2 occasions per vaccinee. Evidence of spread to contacts was not found as none of the 49 family contacts including 10 susceptibles had rises in antibody. Additional patients in remission on CT are being studied in an effort to correlate clinical or immune responses and spread to contacts with vaccinee's immunologic status, type of disease, chemotherapy, and other characteristics. This information will be useful in predicting which patients with malignancies can safely and effectively be immunized with VV.

1070 SERUM ANTIBODY RESPONSES TO LIPOPOLYSACCHARIDE (LPS) IN CHILDREN WITH HAEMOPHILUS INFLUENZAE TYPE B (HIB) MENINGITIS. Jerry L. Shenep, Robert S. Munson, Jr. and Dan M. Granoff, Washington Univ. School of Medicine, St.Louis.

We employed ELISA to measure antibody response to LPS in paired sera from 24 patients with Hib meningitis (mean age 13.8 mos). The results were compared to serum titers of 24 control children (mean age 15.2 mos). LPS was prepared from 12 CSF isolates and analyzed by SDS-PAGE. Size heterogeneity was observed, but all molecules were low molecular weight, indicating the absence of long O-antigen chains. At least 4 serologically-defined determinants were observed. Three LPS preparations containing all identified determinants were used for measurement of antibody. In acute sera, 12 of 24 meningitis patients had IgM titers $\geq$1:250, and 12 of 24 had IgG titers $\geq$1:1000. These titers were not significantly different in control children (8 of 24, and 12 of 24, respectively). Young children with meningitis responded as well to LPS as older children: 11 of 17 patients <12 months had $\geq$4-fold increases in IgG and/or IgM antibody compared to 4 of 7 patients $\geq$12 months. In contrast, there was a highly significant inverse relationship between antibody concentration in acute sera and ability to respond to LPS. 10 of 12 patients with initial IgG titers <1:1000 had $\geq$4-fold increases in IgG antibody compared to only 1 of 12 with acute titers $\geq$1:1000 ($p < .001$). Of 8 infants that failed to show serum anticapsular antibody responses (<70 ng/ml), 5 had >4-fold increases in LPS antibody. Thus human infants are more responsive to some Hib LPS determinants than to the type b capsule but the data do not allow distinction between protective and nonprotective antibody.

1071 INDOMETHACIN IMPROVES HEMODYNAMIC AND CLOTTING STUDIES IN E.coli SEPSIS. Billie L. Short, Michael Gardiner*, John R. Fletcher*(spon. Gordon B. Avery)George Washington Univ., Children's Hospital National Medical Center, Washington D.C., and Naval Research Institute, Bethesda,Md.*

Sepsis remains one of our major unresolved problems. The prostaglandin synthetase inhibitor, indomethacin(IND) improves survival in endotoxin and sepsis models. However, the protective mechanisms are unknown. We injected the peritoneum of 70 male rats(250-300g) with 1.25×10^{10} E.coli organisms(LD_{80}). After 1hr. 35 controls received IP injection of 2cc normal saline, and the other 35 received IP IND 3mg/kg(2cc). Survival was increased from 17% in the controls to 43% in the IND group($p<.02$). To investigate the possibility that IND improves survival by attenuating the circulatory and clotting abnormalities, we performed the following study in 25 additional rats, measuring mean arterial pressure(MAP) by carotid artery cannulation.

	Time Hrs.	n	WBC	Plate-lets	Hct %	PT sec	PTT sec	Fibrin-ogen mg%	II %	V %	VII %	VIII %	MAP mmHg
BASE	0	10	4314	862,160	38	16	22	158	100	100	60	7	148
C	3	10	2097	184,200	42	20	37	68	87	50	43	3	113
IND	3	5	699*	298,800	40	17*	29	99	96	59	47	6	139*

(All control values were sig. from baseline;*sig. from control) ($p < .05$)

We conclude that IND decreases coagulation and hemodynamic abnormalities in gram negative sepsis and shock. This agent may become a useful adjuvant to therapy.

● 1072 ALTERED PATHOGENICITY OF ACYCLOVIR (ACV) RESISTANT HSV FROM AN IMMUNODEFICIENT CHILD. Cornelia D. Sibrack, Laura T. Gutman, Catherine M. Wilfert, Colin McLaren, David W. Barry. Duke Univ. Med. Ctr., Dept. of Ped., and Wellcome Res. Labs, Durham, NC. The frequency and clinical significance of drug-resistant herpes viruses occurring in clinical settings requires thorough investigation. We have studied over 100 HSV isolates from a variety of sources and have found one group, from a 15 month boy with adenosine deaminase deficient type of severe combined immunodeficiency, which was resistant to both ACV and IUDR. During a 6 week hospitalization he received topical ophthalmic, parenteral and oral ACV for treatment of herpetic keratitis and cutaneous lesions involving face, hands and perirectal areas. Early treatment courses resulted in dramatic clinical improvement but later recurrences were characterized by chronic lesions unresponsive to ACV despite serum levels up to 6 mcg/ml. After death from Pseudomonas sepsis and pneumonia, postmortem tissues, although HSV-positive, showed no evidence of viral cytopathic effect. A 100-fold decrease in sensitivity to ACV was noted between early and late isolates. Thymidine kinase activity was normal in sensitive but absent in resistant isolates. Reduced apparent pathogenicity in man was paralleled by a 100-1000-fold decrease of these isolates in their virulence (as determined by PFU/LD_{50} and PFU/MID_{50} ratios) in normal, hairless and nude mice by intracerebral and cutaneous innoculation. Cutaneous infection caused by the resistant virus was less severe or produced low-grade, chronic, lesions rather than acutely fatal infections. Antiviral resistance can occur in selected clinical situations but diminished sensitivity may be associated with diminished virulence.

1073 MOLECULAR ANALYSIS OF CYTOMEGALOVIRUS INFECTIONS IN HOSPITALIZED INFANTS: Stephen A. Spector (Spon. by James D. Connor). University of California Department of Pediatrics, San Diego.

Recent studies show that 14-30% of newborn infants with prolonged hospitalizations in intensive care nurseries (ICNs) develop infections with cytomegalovirus (CMV). These infections can be associated with fever, hepatitis and pneumonia. Maternal-infant transmission at the time of birth, and acquisition of CMV through blood products appear to be the major routes of viral transmission. Although most cases of CMV infections occur sporadically in ICNs, our surveillance program has identified several clusters of 2 to 4 infants excreting CMV at the same time in one ICN. These multiple groups of infants with temporally related nosocomial CMV infections suggest that infant-infant transmission of CMV may occur. Using restriction endonuclease analyses, I have compared the DNA fragment migration patterns of the CMV isolates of infants with epidemiologically related infections. In addition, the viruses of a nosocomially infected baby and his mother who developed a primary CMV infection after the discharge home of her infant were compared. At present the analyses indicate that no 2 infants excreting CMV were infected with the same strain virus. However, the DNA digestion pattern of the mother's isolate is identical to her infant's CMV strain. These findings suggest that although nosocomially infected infants are capable of transmitting CMV to other individuals that the risk of infant-infant CMV transmission in ICNs is low with routine methods of handwashing and isolation.

1074 A PATHOGENIC FACTOR IN CONGENITAL CMV INFECTIONS (C-CMV). Sergio B. Stagno, Robert F. Pass, Meyer E. Dworsky, and Charles A. Alford. University of Alabama Medical School, Department of Pediatrics, Birmingham, Alabama.

To better define the role of primary (PMI) and recurrent (RMI) CMV infections in the pathogenesis of C-CMV a longitudinal study of both middle (MI) and low (LI) income pregnant women was initiated. Susceptibility to CMV at the onset of pregnancy was 39% (1630 of 4130) in MI women and 16% (399 of 2375) in LI women. In these two groups, newly acquired infections were confirmed in 0.7% and 1.5% of serosusceptibles, respectively. Interestingly, independent from economic strata, PMI lead to C-CMV in only 36% of cases. However C-CMV after a recurrence in previously infected women occurred in 0.2 and 1.4% of infants born to MI and LI women respectively. This dissimilarity accounts for the major difference in the overall incidence of C-CMV between these two populations (0.2% vs. 0.8%).

From this and previous studies we have identified 19 and 17 infants whose C-CMV resulted from primary and recurrent maternal infections respectively. Thus far, disease has occurred in only 3 infants (one fatal) and all belong to the former group. Also increased IgM in cord sera and the quantity of CMV shed in urine of these infants up to 4 months of age, were significantly higher among those infected after PMI.

These observations indicate that PMI does not always result in C-CMV nor does it cause acute or delayed morbidity in all infected infants. Yet, its pathogenic potential may be significantly higher than RMI.