

THE CLINICAL SIGNIFICANCE OF ESCHERICHIA COLI K1 ANTIGEN IN NEONATAL MENINGITIS. George H. McCracken, Larrie D. Sarff and Mary P. Glode, Dept. Ped., Univ. of Texas Southwestern Med. Sch., Dallas, John B. Robbins and Mark Schiffer, Bethesda, Ida and Frits Orskov, Copenhagen and E. Gotschlich, New York.

We have previously shown that 85% of *E. coli* (EC) causing neonatal meningitis possess a specific capsular polysaccharide antigen (K1) which on the basis of animal studies confers virulence to these strains. In the present study the outcome of 54 infants with EC meningitis was correlated with presence of K1 in body fluids. 45 infants had meningitis due to EC K1: 62% died or were abnormal at followup and mouse LD₅₀ values for these EC were 2 to 630 organisms. Outcome was correlated with amount and duration of spinal fluid K1:

OUTCOME	K1 UNDETECTED	AMOUNT K1	DURATION K1
Normal	7 Infants	4 µg/ml	1 Day
Abnormal	2 Infants	37 µg/ml	3.4 Days
Dead	2 Infants	117 µg/ml	2.5 Days

9 infants had meningitis due to non-K1 EC: none died and only 1 was abnormal; the EC LD₅₀ values were 767 to 390,000 organisms. 12 of 15 infants with K1 detected in serum died or were abnormal and amount of K1 in serum was 13 to 16-fold greater in these infants than in normal survivors. Capsular sialic acid (K1) content of EC and clinical outcome were correlated also.

These studies demonstrate the significance of K1 as a virulence factor for EC in neonates with meningitis.

VARIABLES INFLUENCING THE IN VITRO SUSCEPTIBILITIES OF HERPES SIMPLEX VIRUSES TO ANTIVIRAL DRUGS. M.I. Marks. McGill Univ.-Montreal Children's Hosp. Research Inst., Montreal, Quebec.

Variables of a microtiter tissue culture method for estimating antiviral susceptibility of herpes simplex viruses (HSV) were studied. Six drugs (5-iodo-2'-deoxyuridine, cytosine arabinoside, 9-B-arabinofuranosyladenine, isoprinosine, virazole and 2-deoxy-D-glucose), 3 tissue culture cell lines (primary rabbit kidney, WI-38 and rat brain), 4 inocula (10, 100, 1000 and 2000 TCD₅₀) and 11 HSV isolates were studied. Minimum inhibitory concentration (MIC) was defined as complete inhibition of cytopathogenic effect after 72 hours of incubation. There was a direct relationship between viral inocula and MIC. There were also differences between the three tissue culture cell lines and among the strains of HSV; this was independent of type. Cytosine arabinoside was the most active drug with IUdR and ara-A next; no significant cytotoxicity was encountered with these drugs. Isoprinosine, virazole and 2-deoxy-D-glucose were not effective against any of the 11 strains of HSV tested in this *in vitro* system; a comparison with previous studies indicate that activity may be cell-dependent. These results emphasize the importance of careful evaluation of *in vitro* test methods for susceptibility testing of antiviral agents against HSV.

AN OUTBREAK OF SEVERE PNEUMONIA DUE TO RESPIRATORY SYNCYTIAL VIRUS IN ISOLATED ARCTIC POPULATIONS. M.I. Marks, R.E. Morrell, R. Champlin, L. Spence. McGill Univ.-Montreal Children's Hosp. Research Inst., Montreal, Quebec.

A rapidly communicable outbreak of pneumonia was documented virologically, serologically and clinically in 2 isolated arctic populations. In addition to the two stricken communities, an additional one not apparently affected with clinical illness and a 4th, containing the major hospital and airport in the eastern arctic, was also studied. 263 patients were studied serologically and 81 specimens were obtained for virus isolation. Clinical records were kept (of the outbreak) in each epidemic area and a detailed questionnaire was completed for 140 children and their families.

Respiratory syncytial virus was cultured from 8 ill children. A seroconversion rate of approximately 50% was seen in both affected communities and in the clinically unaffected one. The epidemic in the first 2 communities was characterized by severe pneumonia and frequent hospitalization; no cases of bronchiolitis were seen. No serologic evidence of significant influenza A and B, parainfluenzae 1, 2 and 3, adenovirus and herpes simplex virus infections were found. Unusual features of this epidemic of RSV infection include the high attack rate, severe morbidity, illness manifest almost exclusively as pneumonia rather than bronchiolitis and the differences between the expression of disease in different communities.

MUCOCUTANEOUS LYMPH NODE SYNDROME (MCLS) IN THE U.S. Marian E. Melish, Paquel M. Hicks and Eunice Larson. Univ. of Hawaii, Kaula Keolani Children's Hospital (Intr. by J. Bass).

Nine children were seen with an unusual and highly distinctive symptom complex consisting of high fever for >7 days not responding to antibiotics; striking polymorphous exanthem, either morbilliform, scarlatiniform or multiforme; marked erythema of palms and soles with severe indurative edema progressing to desquamation of digits; stomatitis with fissuring of lips, diffuse mucosal erythema and strawberry tongue; conjunctivitis; and polymorphonuclear leukocytosis. Eight patients had associated cervical lymphadenopathy, 4 acute urethritis, 3 arthritis, 3 diarrhea and 2 aseptic meningitis. One child died suddenly on day 21; bilateral coronary artery thrombosis, extensive myocardial infarction, aortitis, localized arteritis and meningeal inflammation were demonstrated. Viral and bacterial studies of all patients were negative. Only 1 child developed ASO titer elevation. Children were <8 years, of both sexes and multiple races.

Patients with this unusual multisystem disease have a predictable course and resemble each other more than they resemble any syndrome recognized in the U.S. Their clinical course is indistinguishable from MCLS or Kawasaki disease widely recognized in Japan where >2200 cases have been seen. Mortality rate is 1.3% from coronary artery thrombosis. Despite extensive investigation in Japan the etiology is unknown. Recognition of these cases in the U.S. demonstrates the need for wider awareness of this significant, distinctive disease.

PRIMARY INFECTION WITH CYTOMEGALOVIRUS DURING PREGNANCY. Geo. A. Nankervis, Mary L. Kumar and Eli Gold, Case Western Reserve University School of Medicine at Cleveland Metropolitan General Hospital, Department of Pediatrics, Cleveland, Ohio

Since the majority of postnatal cytomegalovirus (CMV) infections are unrecognized, the risk to the fetus of primary CMV infection at various times during pregnancy has not been meticulously assessed. During a prospective study of over 3000 pregnant teenagers, 8 patients with primary CMV infection defined as virologic as well as serologic conversion from negative to positive, were identified and followed. Asymptomatic primary infection occurred during the 1st trimester in one patient, during the 2nd trimester in 4 patients, and during the 3rd trimester in 3 patients. All 8 infants were asymptomatic but 4 (50%) were congenitally infected; all 3 neonates of the 3rd trimester converters and one of the 4 infants of the 2nd trimester converters. The single 1st trimester converter delivered an uninfected infant at term despite cytomegaloviremia during the 1st and 2nd trimesters as well as consistent viraemia and intermittent positive throat and cervical cultures throughout her pregnancy. Placenta cultures of 6 converters resulted in one CMV isolate from an infected neonate born to a 3rd trimester converter. Primary CMV infection during pregnancy results in an infected infant in a significant percentage of patients, particularly if the infection occurs during the 3rd trimester. Nevertheless, primary CMV infection can occur during any trimester without resulting in an infant with any of the stigmata of cytomegalic inclusion disease at birth.

PATHOGENESIS OF AN ARBOVIRUS INFECTION IN FETAL, NEONATAL, AND ADULT SHEEP. James C. Overall, Jr. (Intr. by Lowell A. Glasgow), Depts. of Ped., and Micro., Univ. of Utah Coll. Med., Salt Lake City.

In order to compare the mechanisms of resistance to viral infections present in fetal, neonatal, and adult animals, we developed a model infection in sheep utilizing Semliki Forest virus (SFV), a group A arbovirus. Following IV inoculation of adult sheep with 10^{7.0} to 10^{7.5} PFU of virus, initial viral replication as reflected in the serum occurred by 12-16 hrs, with peak titers of 10^{2-10⁴} PFU/ml present at 16-24 hrs. Virus was completely cleared from the blood by 2 days as antibody became detectable in the serum. Neutralizing antibody titers reached levels of 1/2000-1/8000 by 6 to 7 days. Serum interferon was apparent by 16-24 hrs, reached peak levels of 60 to 600 units/ml, and disappeared by 2 days. Although the pattern of SFV pathogenesis following IV inoculation was similar in both fetal and neonatal lambs to that in adult sheep, virus titers in the serum reached higher levels (10^{3-10⁵} PFU/ml) and lasted longer. Antibody did not become detectable until 5 days and titers were generally lower (1/100-1/600) than in the adult. Interferon levels, however, were higher (2000-6000 units/ml) in parallel with the higher virus titers. The results indicated that in the fetal and neonatal animals: 1) virus replication, as reflected in the serum, occurred to a greater degree, 2) the higher interferon levels appeared to reflect the amount of virus replication, and 3) antibody appeared later in the serum and reached lower levels.