973 CHILDHOOD INFECTIOUS MONONUCLEOSIS NOT ASSOCIATED WITH EPSTEIN-BARR VIRUS.

Ciro V. Sumaya and Yasmin Ench. Univ. of Texas Health Science Center, Dept. of Pediatrics, San Antonio, Texas 78284.

Non-Epstein-Barr Virus (EBV) induced infectious mononucleosis (IM) has not been adequately studied in children. In a prospective evaluation of 171 children with an illness characterized by clinical and hematologic findings for IM, 19 (11%) children had their episode unassociated with an acute EBV infection. The majority of children with non-EBV IM were <4 years old, 11 (58%), and males, 11 (58%). The spectrum of clinical manifestations in general were similar to that reported for EBV-IM in children except for a decreased rate of exudative tonsillitis in the non-EBV group, 5 (26%). Transient respiratory or hematologic complications developed in 2 children. Liver transaminases were elevated acutely and transiently in 6/10 children tested. Typical heterophil antibody responses were not detected. EBV testing indicated that 6 children had experienced this infection in the distant past; the infection in two others was of inconclusive onset. A suspected etiology was identified in 5 children: 3 had significant IgG antibody titer rises to cytomegalovirus (2 of these had the virus isolated from the urine) and 2 others had significant titer rises to Toxoplasma gondii. Children with non-EBV IM tended to be younger than that reported with EBV-IM. The non-EBV IM subgroup with suspected etiology appeared to be a major contributor to the low frequency of exudative tonsillitis. Reactivation of an EBV-carrier state provoked by the intervening etiologic agent was not documented as has been reported in adults. The majority of non-EBV IM episodes in children remains of unknown etiology.

974 α_1 PROTEINASE INHIBITOR (α_1-PI) IN BRONCHIAL SECRETIONS FROM CYSTIC FIBROSIS (CF) PATIENTS IS NOT INACTIVATED BY OXIDATION

Susanne Suter, Isabelle Chevallier, Spon. by Pierre E. Ferrier, Clinique Universitaire de Pédiatrie, Geneva, Switzerland

We have previously shown that free granulocyte elastase (GE) is present for prolonged periods in CF bronchial secretions and that this enzyme may contribute to microbial persistence by proteolysis of opsonins (J.Infect.Dis. 1984, 1986). α_1-PI, one of the most important inhibitors of GE was found to be present in an inactive state. In this study, we asked the question whether in CF bronchial secretions α_1-PI is inactivated by 1) complex formation with enzyme, 2) oxidation and/or the proteolytic activity of pseudomonas (P) elastase, a protease secreted by strains of P isolated from CF bronchial secretions. α_1-PI in 20 CF bronchial secretions was assessed by tandem crossed immunoelectrophoresis and by immunoblots and its migration pattern compared to 1) purified α_1-PI inactivated by oxidation, 2) purified α_1-PI inactivated by P elastase and 3) purified α_1-PI incubated with purified GE. In CF bronchial secretions, we found α_1-PI migrating identically to α_1-PI fragments generated by PA elastase and those generated by incubation of α_1-PI with GE, but not like α_1-PI inactivated by oxidation. We conclude that in CF bronchial secretions α_1-PI is not inactivated by oxidation, but rather by P elastase and/or GE and that this contributes to the imbalance between proteases and antiproteases.

975 BRONCHIAL SECRETIONS (BS) FROM PATIENTS WITH CYSTIC FIBROSIS (CF) CONTAIN FIBRONECTIN CLEAVING ACTIVITY

Susanne Suter, Urs B. Schaad, Isabelle Chevallier, Spon. by Pierre E. Ferrier, Clinique Universitaire de Pédiatrie, Geneva, Switzerland

It has been suggested that the degradation of cell surface fibronectin by salivary hydrolases favors colonization of the airways of CF patients with Pseudomonas aeruginosa (PA). In this study, we determined the fibronectin-cleaving and elastolytic activity of CF saliva and bronchial secretions (BS) compared to those of chronic bronchitics (CB).

Results :

		N	^{125}I-fibronectin cleavage (%)	^{3}H-Elastolytic activity(mg/18hrs)	Total protein conc.
Saliva	(CF)	24	8.2 ± 19.0	< 0.05	2.4 ± 2.1
BS	(CF)	24	39.1 ± 15.2	1.61 ± 0.85	5.8 ± 3.8
Saliva	(CB)	18	4.0 ± 9	< 0.05	1.4 ± 0.7
BS	(CB)	18	37.5 ± 15.2	0.42 ± 0.33	5.0 ± 3.6

Fragments of ^{125}I-fibronectin generated by BS analyzed with PAGE were identical in molecular weights to those generated by purified granulocyte elastase and cathepsin G. The ^{125}I-fibronectin cleaving activity in BS from CB disappeared after adequate antimicrobial treatment, whereas that in CF BS did not. We conclude that 1) the fibronectin-cleaving activity in CF BS is due to granulocyte elastase and cathepsin G and is present in significantly lower amounts in saliva ($p < 0.01$) and 2) the continuous exposure to CF airways to fibronectin-cleaving activity may favor the colonization with PA.

†976 EFFECT OF RIBAVIRIN ON VIRAL TRANSCRIPTION.

Philip Toltzis, Holly Glover, Kevin O'Connell, Jean L. Patterson. Harvard Medical School, Children's Hospital, Div. of Infectious Diseases, Boston, MA 02115. Spon. by Kenneth McIntosh.

We have examined the effect of ribavirin on vesicular stomatitis virus (VSV) RNA synthesis using a cell-free transcription system. Our prior data indicated that ribavirin had little effect on primary transcription of VSV mRNAs synthesized intracellularly, but that these RNAs were translated inefficiently. Consistent with these data, VSV cell-free transcription was inhibited only mildly (25%) by ribavirin triphosphate at 100 mg/ml. However, ribavirin diphosphate (RDP) and, to a lesser extent, ribavirin monophosphate, were 2-3 times as inhibitory at the same concentration. Transcripts synthesized in the presence of RDP were full lengthed. The inhibition by RDP could be reversed by increasing the concentration of GTP. However, reversal could also be achieved by increasing the concentration of UTP, CTP, and ATP, but not by the addition of GDP. RDP was added to a LaCrosse virus cell-free transcription assay to determine if an inhibitory effect could be established in a viral system more sensitive to ribavirin than VSV; addition of RDP to this reaction led to profound inhibition of RNA synthesis at concentrations as low as 0.1 ug/ml. These data suggest that in some viruses ribavirin may have a major direct effect on initial steps of transcription and that this effect may be mediated by the di- and monophosphorylated forms.

977 ANTIBODY RESPONSE TO HEMOPHILUS INFLUENZAE, TYPE B (HITB) PRP-D CONJUGATE VACCINE IN IMMUNOCOMPROMISED (IC) PATIENTS <2 YEARS OF AGE.

Debra A. Tristram, Julia A. McMillan, Leonard B. Weiner, A. Stephen Dubansky, Patrick McVerry (Spon. by R.Spitzer), SUNY Health Science Center, Dept. of Pediatrics, Syracuse, NY and Connaught Laboratories, Swiftwater, PA.

IC children <2 yrs represent a group at increased risk of invasive HITB infection. PRP-D conjugate vaccine (Connaught) was administered IM to 9 IC children aged 2-23 mo to assess their antibody response. Three had solid tumors (1 hepatoblastoma, 1 Wilm's, 1 neuroblastoma), 3 had sickle cell disease, 1 had AML, 1 had ALL and 1 was on immunosuppressive therapy post hepatic transplant. All cancer patients were in remission. There were no serious side effects following vaccine administration, and no children have had documented HITB infection to date. Pre and 1 mo post vaccine HITB antibody levels were measured by RIA; mean pre vaccine level was 0.025 µg/ml (range <0.012-0.12), and mean post vaccine level was 0.460 µg/ml (range <0.012-1.89). Only 2/9 children achieved a protective titer (>1 µg/ml). Of the non-responders, 4/7 were >18 mo. Three children, 16-21 mo, received a 2nd vaccine dose 1 mo after the first, and 1 responded. These data provide preliminary information regarding the response of IC children <2 yrs to PRP-D conjugate vaccine and indicate that IC children 18-23 mo do not reliably respond to a single dose of vaccine.

978 INVESTIGATION OF MYCARDIAL DYSFUNCTION IN INFANTS HOSPITALIZED WITH ENTEROVIRAL INFECTION.

Debra A. Tristram, Julia A. McMillan, Leonard B. Weiner, Cathy Sandstrom, Richard H. Strauss, Rae Ellen Kavey. (Spon. by R. Spitzer). SUNY Health Science Ctr., Department of Pediatrics, Syracuse, NY.

Although enteroviral infections have been associated with myocarditis, the importance of subclincal myocardial dysfunction (MD) caused by enteroviruses (EV) has not been investigated. From 7/83 through 9/85 we prospectively studied, for evidence of MD, hospitalized pts <16 mo of age whose illnesses were compatible with EV infection. Viral and bacterial cultures were submitted for all pts. EKG and M-mode echocardiograms (EC) were obtained within 48 hours of admission. Of the 52 pts studied, 20 had positive cultures for non-polio EV, 9 additional pts had aseptic meningitis with negative cultures, and the remainder had febrile illnesses consistent with EV. Left ventricular shortening fraction (LVSF) was <27% in 6/52 pts (4 with positive EV cultures). EC for 12 healthy control infants <6 mo old showed LVSF ≥30%. None of the 52 pts showed clinical or EKG evidence of MD. EC performed 2 weeks after hospitalization demonstrated improved LVSF in 3/6 pts who had shown MD initially. These data indicate that subclinical MD is a frequent complication of EV infection, and neither physical examination nor EKG is adequate for its detection.