

SURVEILLANCE AND TRANSMISSION OF ROTAVIRUS IN CHILDREN IN DAY CARE CENTERS (DCC) IN HOUSTON.

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258 children <24 months of age in 12 DCC were randomly enrolled in a prospective study of rotavirus (RV) infection. A case control study in non-DCC children was conducted simultaneously. Stool specimens were collected from every child in the DCC weekly and when diarrhea occurred. Stools were analyzed for all enteropathogens; RV was detected by a monoclonal antibody based ELISA. In the community study RV was identified in 41 of 267 children (15%) with diarrhea and 6 of 250 control children (2%). In the DCC study there were 467 episodes of diarrhea during the 2,108 child months of study (22.6 episodes/100 child months). There were 89 RV infections (4.3 cases/100 child months); 60% were asymptomatic. There were 37 DCC diarrhea outbreaks; rotavirus was identified in 8 (22%). In 42% of children with symptomatic RV infection, RV was identified in stool specimens 1-2 days before diarrhea. During the 10 month study there were 251 new entries (97% turnover rate). New entry children experienced significantly ($p < 0.001$) higher rates of diarrhea during the first 8 weeks (4.11 cases/child year), than other children in DCC (2.4 cases/child year). Analysis of stool specimens by polyacrylamide gel electrophoresis showed similar patterns in RV strains from children in the same outbreak. RV infections occur commonly in children in DCC, are readily transmitted, often are asymptomatic. Peak rates occur simultaneously in DCC and in the community. This information is important for appropriate implementation of intervention modalities such as vaccines.

DEVELOPMENT OF ANTIBODY RESPONSE TO HOST PROTEINS AS A POSSIBLE MECHANISM OF IMMUNOPATHOLOGY DURING RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION. P.A. Piedra and P.L. Ogra, SUNY at Buffalo, Children's Hospital, Dept. Pediatrics, Buffalo, NY.

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Groups of male BALB/c mice were primed intraperitoneally with uninfected HEP-2 cell cultures (HEP-2), live RSV infected cell cultures (L-RSV), or sucrose density gradient purified RSV antigen (P-RSV), in combination with alum and killed *Bordetella pertussis* as adjuvants. The animals were subsequently challenged intranasally (I/N) with HEP-2 or L-RSV. All animals developed severe pulmonary histopathology after I/N challenge with HEP-2 or RSV, regardless of whether priming immunization was carried out with infected HEP-2 cells alone or with RSV. Cellular proteins of P-RSV, HEP-2, BALB/c lung, cotton rat lung (CRL), Buffalo green monkey kidney (BGM), and human buccal epithelial cells (HBE) were separated on SDS-PAGE and tested for reactivity against the sera of these animals for immunologic cross reactivity by Western (immuno)blot procedures. Pre-immunization sera exhibited no binding to the proteins of different cells. Sera from L-RSV and HEP-2 immunized animals reacted with one or more components of all cell types tested. Significantly, however, sera from P-RSV immunized animals reacted with cellular components of HEP-2 and HBE, but not with CRL or BALB/c lung. These observations provide evidence that development of pulmonary immunopathology in RSV infection is mediated in part by the induction of autoreactive or cross-reactive antibody response to the host proteins in which virus replication occurred in this experimentally induced infection and possibly during naturally acquired or induced RSV infection in previously sensitized human infants.

COMPARISON OF VACCINE-INDUCED AND NATURAL IMMUNITY TO HUMAN CYTOMEGALOVIRUS (CMV). Stanley A. Plotkin, Stuart E. Starr, Harvey M. Friedman, and Eva Gonczol. The Children's Hospital Division of Infectious Diseases and The Wistar Institute, Philadelphia, Pa.

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A challenge study was performed to measure the protection against CMV afforded by prior natural infection or vaccination with Towne strain live attenuated CMV. Previous studies had shown that seronegative renal transplant recipients were protected by vaccine from serious CMV disease but not from infection. The challenge consisted of a fresh human CMV isolate called Toledo. A closed community of priests volunteered to participate. Twelve seronegative priests were vaccinated with Towne live virus. One year later graded doses of Toledo were administered subcutaneously to the vaccinees and to 6 seronegative and 9 naturally seropositive controls. At a challenge dose of 1000 PFU, even the naturally immune subjects became ill. At a challenge dose of 100 PFU, seronegative individuals developed CMV mononucleosis, whereas both vaccinees and natural immune subjects were protected against illness. However, at this dose half of the vaccinees became infected with the challenge virus. At a challenge dose of 10 PFU of Toledo, vaccinees and natural immune were protected against infection and disease, while seronegatives became ill with CMV mononucleosis. Neutralizing antibodies and specific cellular immune responses developed after vaccination or disease. This study demonstrates for the first time that active immunization against CMV can prevent disease in normal subjects, even when a challenge is delivered parenterally. However, resistance to CMV depends on the challenge dose and on the integrity of host immune responses.

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OUTPATIENT ADMINISTRATION OF CEFTRIAXONE TO COMPLETE TREATMENT FOR SERIOUS BACTERIAL INFECTIONS. Keith R. Powell, Steven Mawhorter, Univ. Rochester, School of Medicine and Dentistry, Strong Mem. Hosp., Dept. of Pediatrics, Rochester, New York 14642.

The pharmacokinetics and antimicrobial activity of ceftriaxone make it possible to treat serious bacterial infections with once daily intramuscular (IM) injections.

From 4/1/85 to 11/7/86, 98 pediatric patients hospitalized at Strong Memorial Hospital received ceftriaxone. Chart review indicated that 26 of these children completed antibiotic therapy as outpatients. Parents and physicians of children treated as outpatients were contacted by telephone for follow-up.

Diagnoses included: sepsis 9, meningitis 5, septic arthritis, osteomyelitis, and pyelonephritis 2 each, and brain abscess, parotid abscess, peritonitis, empyema, periorbital cellulitis, and epiglottitis 1 each. Outpatient therapy consisted of once daily IM ceftriaxone for 21 children, twice daily for 4, and twice daily either IV or IM for a child with a brain abscess. Ceftriaxone was given for 235 outpatient days (range 1-32 days per patient) and was estimated to save at least \$200 per day compared to treatment in hospital. Follow-up by telephone survey identified no drug related complications, no instances of relapse or recurrence, and a high level of acceptance by parents and physicians.

We conclude that in carefully selected cases treatment for serious bacterial infections can be completed in the ambulatory setting with considerable savings of health care dollars by using once daily IM ceftriaxone.

TRIMETHOPRIM RESISTANT (TMP^R) E. COLI IN STOOL SPECIMENS FROM CHILDREN IN DAY CARE CENTERS (DCC). Randall R. Reves, Barbara E. Murray, Mina Fong, Larry K. Pickering. The Univ. of Texas Medical School, Prog. in Infect. Dis. & Dept. Pediatr., Houston, TX

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In the U.S. *E. coli* are rarely resistant to multiple antimicrobial agents outside the hospital setting. In a recent pilot study, we demonstrated TMP^R *E. coli* in 15 of 79 children (19%) in DCC, presumably due to frequent antimicrobial drug use and fecal oral transmission. Because of these findings we determined the proportion of resistant *E. coli* in stools from 203 children in 12 DCC, 41 children not in DCC, and 66 children newly entering DCCs. All children were <24 months of age. 65 of 203 children (32%) had TMP^R *E. coli* in stools compared with 2 of 41 children (5%) not in a DCC and 5 of 66 children (8%) newly entering a DCC. The proportion of children with TMP^R *E. coli* varied from 0 in the smallest to 58% in the largest DCC. Predominant antibiograms were noted in individual centers; these antibiograms differed among centers. Total plasmid DNA detected by electrophoresis in 0.7% agarose gels were identical or similar in 3 centers where a large number of TMP^R isolates were identified, but distinct from each other and from other DCC isolates. There was an association of TMP^R *E. coli* with antimicrobial use in the 2 weeks prior to sampling. These findings extend our earlier observations of high levels of TMP^R *E. coli* in DCC. TMP^R *E. coli* in DCC may be common and appear to be related to the DCC size and prevalence of antimicrobial use. The role of DCC in the epidemiology of resistant human enteric bacteria remains to be determined.

VIRAL COFACTORS AND ACUTE RHEUMATIC FEVER. Peter C. Rowe, Neal A. Halsey, E. David Mellits, Catherine DeAngelis, Johns Hopkins University, Departments of Pediatrics and International Health, Baltimore, Maryland.

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The incidence of childhood acute rheumatic fever (ARF) declined abruptly throughout N. America starting in the late 1960s. This decline was associated temporally with the introduction of measles (ML), mumps (MU), and rubella (RU) immunization programs. To determine if there was an association at the individual level with ARF, we measured antibody titers by hemagglutination-inhibition (HI) to ML, MU, and RU and by ELISA to ML and RU in 28 patients with a past history of ARF and 51 controls matched for age, race, and sex.

% Pos.	Measles		Mumps		Rubella	
	HI	ELISA	HI	ELISA	HI	ELISA
Cases	93%	89%	86%	86%	57%*	82%
Controls	98%	88%	86%	86%	82%*	94%
GMT**						
Cases	18.3	2.1	14.1	16.7	2.5	2.6
Controls	15.8	2.1	13.7	17.4	2.6	2.6

* $p < 0.05$ ** Geometric mean titer for seropositives

The only significant difference observed was a lower rate of seropositivity to rubella by HI but not by ELISA. No differences were noted for GMT's. We conclude that ML, MU or RU infections aren't necessary cofactors in ARF pathogenesis.