Simultaneous Infections with Different Enteric and Respiratory Tract Viruses

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Infants and young children with rotavirus (RV) or visualized adenovirus in their stools were tested for the simultaneous presence of a respiratory viral pathogen in their upper respiratory tract. Overall, at least 10.7% of 484 study subjects had such dual infections, including 8.3% of 385 RV-positive gastroenteritis patients and 24.3% of 37 RV-positive respiratory disease patients. Respiratory syncytial virus was present in 34.1% of 41 dual infections with RV and at least 40% of the 12 to 15 dual infections with visualized fecal adenovirus. Other pathogens found in the respiratory tract of patients with RV or visualized fecal adenovirus infections included influenza viruses, adenoviruses, parainfluenza viruses, rhinoviruses, and a cytomegalovirus.

In the course of studies for viral pathogens in acutely ill infants and young children with gastroenteritis or respiratory disease (1, 2, 5), we often attempted to detect viruses in specimens simultaneously collected from the respiratory and intestinal tracts. In this report, we describe the rather common finding of concurrent infections by different enteric and respiratory tract viral pathogens.

The study subjects were young pediatric inpatients and outpatients from whom a fecal and a respiratory specimen were collected within 4 days from the onset of acute diarrheal or respiratory illness and who had been found by direct or immune electron microscopy or by rotavirus (RV) enzyme-linked immunosorbent assay (ELISA) to be excreting an RV or an adenovirus in their stools (3, 7). For attempted respiratory virus recovery, respiratory specimens (from combined nasal and pharyngeal swabs) were inoculated into HEp-2, monkey kidney, WI 38, and often also human embryonic kidney cell cultures (4). Respiratory virus isolates were then identified by conventional techniques (4, 10, 11). Most of the enteritis patients also were tested by conventional bacteriologic techniques for enteric bacterial pathogens.

The original groups from which the present study subjects were derived included most infants and young children who were hospitalized at this medical center with acute gastroenteritis during the period January 1974 through September 1980 and a group of respiratory disease inpatients who, beginning in March 1974, were closely matched to the diarrhea inpatients with respect to numbers sampled, day of sampling, age in months, and similarity of laboratory study (2, 5, 6). Diagnostic specimens from inpatients generally were obtained on the first or second hospital day, and patients with nosocomial illness were excluded from the study. Outpatients from whom the present study subjects were selected also had been closely matched and were typical of infants and young children who presented to this hospital as outpatients with diarrhea or respiratory illness,

but they were arbitrarily selected as to the number sampled each month from November 1975 through September 1980.

Patients with fecal RV. Virtually all RV infections were demonstrated by direct electron microscopy of a stool specimen, and all RV infections were confirmed by ELISA. Four groups of infants and young children with enteric RV infection were tested for the concurrent presence of other viruses in their upper respiratory tract (Table 1). Excluding three patients with poliovirus in their respiratory specimens (quite likely of live virus vaccine origin), 41 (9.7%) of 422 RV-positive study subjects had at least one other viral infection. Included were 27 (8.3%) of 324 gastroenteritis inpatients, 5 (8.2%) of 61 gastroenteritis outpatients, 6 (27.3%) of 22 respiratory disease inpatients, and 3 (20.0%) of 15 respiratory disease outpatients.

Among 32 RV-positive gastroenteritis inpatients and outpatients with a non-poliovirus respiratory tract isolate, 11 yielded an adenovirus, 8 had a respiratory syncytial virus, 7 had an influenza virus (including 6 with influenza B virus), 3 had a parainfluenza virus, 3 had a rhinovirus, and 1 had a cytomegalovirus. One gastroenteritis inpatient (a female, aged 6 months) simultaneously had an enteric RV and respiratory isolates of parainfluenza 3 virus and adenovirus 1. Six of nine respiratory disease patients with RV yielded respiratory syncytial virus, whereas the remaining three had an influenza B virus, parainfluenza 3 virus, or rhinovirus infection.

Patients with fecal adenoviruses. A non-poliovirus, non-adenovirus respiratory tract viral pathogen was recovered from 4 (8.5%) of 47 gastroenteritis inpatients, 8 (50.0%) of 16 respiratory inpatients, and 12 (19.0%) of 63 total inpatients with a visualized fecal adenovirus (Table 2). Respiratory syncytial virus was recovered from 6 (50.0%) of the 12 patients with a non-poliovirus, non-adenovirus respiratory tract viral infection and from 40% of the 15 total patients (Table 2, footnote) with a non-poliovirus isolate.

Two gastroenteritis inpatients with visualized fecal adenoviruses had enteric *Salmonella* B infections, and one of these patients (previously shown in Table 1) also had an enteric RV infection. Another gastroenteritis patient with a visualized fecal adenovirus also had a visualized, noncultivable 27-nm virus in his stool specimen as well as adenovirus 2 in throat and anal swab specimens.

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TABLE 1. Virus isolates from the respiratory tract of pediatric patients who simultaneously had enteric RV infections

Respiratory tract virus	No. (%) of patients with isolates from the indicated study group				Total (422 with RV)
	Gastroenteritis inpatients (324 with RV)	Gastroenteritis outpatients (61 with RV)	Respiratory inpatients (22 with RV)	Respiratory outpatients (15 with RV)	
Respiratory syncytial	6 (1.9)	2 (3.3)	3 (13.6)	3 (20.0)	14 (3.3)
Influenza A	1 (0.3)				1 (0.2)
Influenza B	6 (1.9)		1 (4.5)		7 (1.7)
Adenovirus 1	2 (0.6)				2 (0.5)
Adenovirus 2	2 (0.6)	1 (1.6)			3 (0.7)
Adenovirus (untyped)	5 (1.5)	1 (1.6)			6 (1.4)
Parainfluenza 1	1 (0.3)				1 (0.2)
Parainfluenza 3	2 (0.6)		1 (4.5)		3 (0.7)
Rhinovirus	3 (0.9)		1 (4.5)		4 (0.9)
Cytomegalovirus		1 (1.6)			1 (0.2)
Poliovirus	1 (0.3)	1 (1.6)	1 (4.5)		3 (0.7)
Total no. of patients with a non-poliovirus isolate ^a	27 (8.3)	5 (8.2)	6 (27.3)	3 (20.0)	41 (9.7)

^a Dual respiratory tract isolates account for mathematical discrepancies.

Among the several hundred gastroenteritis inpatients and outpatients who were included in this study because they had intestinal infections with an RV or visualized adenovirus, at least 1 of every 12 had a different viral infection of the respiratory tract. Not surprisingly, in view of its importance in pediatric patients in this locale (10) and its frequent appearance during the peak months for viral gastroenteritis (1), respiratory syncytial virus was the pathogen most commonly found in the respiratory tract of patients who had an RV or visualized adenovirus in their fecal specimen. Several other common respiratory viral pathogens also were detected in study patients.

Visualized fecal adenoviruses or RVs are each only found in about 2% of our respiratory disease patients who do not have significant diarrhea (5, 6). However, among 53 such

patients in the present study, 17 (32%) were simultaneously infected with a respiratory tract viral pathogen. Five of six adenoviruses found in respiratory samples from patients with visualized adenoviruses were identified as adenovirus 1 or 2, traditional respiratory tract pathogens. Despite the fact that about 80% of the visualized adenoviruses thus far tested from the stools of our diarrhea patients are adenovirus 40- or 41-like (7), we have not found different respiratory and enteric adenoviruses to be simultaneously present in any of our study patients. However, such infections can occur (8), and several of our relevant specimens have not yet been conclusively studied. Some simultaneous enteric viral and enteric bacterial infections also were demonstrated in the present study.

In view of the relatively common simultaneous occurrence of infection by different enteric and respiratory tract pathogens, caution should be used in attributing all clinical findings to a single pathogen unless rigorous attempts have been made to exclude the possibility of one or more additional pathogens. One might be especially cautious of data which suggest that severe gastroenteritis may be caused by a respiratory pathogen such as influenza B virus (9), particularly if such data were obtained before the importance, clinical manifestations, and epidemiology of RVs were generally recognized.

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TABLE 2. Virus isolates from the respiratory tract of pediatric inpatients whose fecal samples were adenovirus positive by electron microscopy

Respiratory tract virus	No. (%) of patients with isolates from the indicated study group		
	Gastroenteritis inpatients (47 with fecal adenovirus) ^a	Respiratory inpatients (16 with fecal adenovirus)	Total (63 with fecal adenovirus)
Respiratory syncytial	2 (4.3)	4 (25.0)	6 (9.5)
Parainfluenza 3	1 (2.1)	2 (12.5)	3 (4.8)
Parainfluenza 4A	1 (2.1)	0	1 (1.6)
Influenza A	0	1 (6.3)	1 (1.6)
Rhinovirus	0	1 (6.3)	1 (1.6)
Adenovirus 1	0	2 (12.5)	2 (3.2)
Adenovirus 2	3 (6.3) ^b	0	3 (4.7)
Adenovirus (untyped)	0	1 (6.3)	1 (1.6)
Poliovirus 3	1 (2.1)	0	1 (1.6)
Total no. of patients with a non-poliovirus, non-adenovirus isolate ^c	4 (8.5)	8 (50.0)	12 (19.0)

^a One of these patients simultaneously had a visualized fecal RV.

^b One of these patients simultaneously had a visualized fecal 27-nm virus.

^c If respiratory tract adenoviruses were included, the totals would be 6 (12.8%) of gastroenteritis inpatients, 9 (56.2%) of respiratory inpatients, and 15 (23.8%) of all with a fecal adenovirus. Dual infections account for mathematical discrepancies.

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