The "Common Cold" in Frail Older Persons: Impact of Rhinovirus and Coronavirus in a Senior Daycare Center

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OBJECTIVE: To evaluate the incidence and impact of rhinovirus and coronavirus infections in older persons attending daycare.

DESIGN: Prospective descriptive study.

SETTING: Three senior daycare centers in Rochester, New York.

PATIENTS: Frail older persons and staff members of the daycare centers who developed signs or symptoms of an acute respiratory illness

MEASUREMENTS: Demographic, medical, and physical findings were recorded on subjects at baseline and during respiratory illness. Nasopharyngeal specimens for viral culture as well as acute and convalescent sera for coronavirus 229E enzyme immunoassay (EIA) were obtained for all illnesses.

RESULTS: During the 44 months of study, 352 older persons experienced 522 illnesses. Thirty-five (7%) of 522 cultures were positive for rhinovirus and 37 (8%) of 451 serologies were positive for coronavirus 229E infection. The clinical syndromes associated with rhinovirus and coronavirus infection were similar and characterized by nasal congestion, cough, and constitutional symptoms. No patient died or was hospitalized, but approximately 50% had evidence of lower respiratory tract involvement. The average illness lasted 14 days. During the same period, 113 staff developed 338 respiratory illnesses. Eight percent were identified as coronavirus and 9% as rhinovirus. Cough, sputum production, and constitutional symptoms were significantly more common among older persons.

CONCLUSIONS: Rhinovirus and coronavirus 229E are common causes of moderately debilitating acute respiratory illnesses among older persons attending daycare. **J Am Geriatr Soc 45:706–711, 1997.**

Respiratory tract infections are the source of significant morbidity and mortality in older persons. Viruses, such as influenza and respiratory syncytial virus (RSV), have been shown to be the cause of serious disease in this age group.[1] Less is known about the impact of rhinoviruses and coronaviruses, the causative agents in the majority of "common colds."[2] Approximately 20 to 40% of upper respiratory tract infections (URIs) in adults are caused by rhinoviruses, and 5 to 15% are caused by coronaviruses. More than 100 serotypes of rhinoviruses and two major serotypes of coronavirus (229E and OC43) have been identified.[3-4] Reinfections with both viruses occur throughout life, in part because of multiple serotypes and incomplete immunity.[5-7] While these infections lead to significant time lost from work and school, they generally do not result in serious disease in children or young adults.[8-12] Rates of acute respiratory tract infections diminish with advancing age, most likely as a result of less frequent exposures.[13] However, frail older persons attending adult daycare centers may represent a special population at increased risk of infection and at risk for complications from these common infections.[14] The purpose of this study was to evaluate prospectively the prevalence and clinical features of rhinovirus and coronavirus 229E infections in frail older persons attending senior daycare.

METHODS

Subjects

Volunteers were recruited from three sites of a senior daycare program in Rochester, New York. These facilities allow frail older persons who are nursing home-eligible by New York State Medicaid standards to be maintained at home by providing comprehensive medical and social services. All attendees of the daycare program were recruited to take part in the study. Daycare participants were scheduled to attend the center, on average, 3.5 days per week, with a minimum of once a week. Ill subjects were encouraged to attend the program for evaluation by center physicians. In addition, all staff members with direct contact with older participants were also recruited for the surveillance study.

Study Design

Informed consent was obtained from volunteers upon entrance into the daycare program. If volunteers were unable to provide informed consent, consent was obtained from their legal guardians. Baseline information, including medical history and demographics, were obtained from daycare participant's medical records. Subjects were examined at base-

line, and arterial oxygenation saturation (SaO$_2$) was measured percutaneously by pulse oximetry (Ohmeda-Biox IV-Boulder, CO). Baseline serum samples were collected from daycare participants and staff members.

Surveillance for acute respiratory illnesses took place between January 30, 1992, and October 2, 1995. Possible respiratory illnesses among daycare workers or attendees were reported by the daycare staff to the project nurse for evaluation. An acute respiratory illness was defined as nasal congestion, sore throat, new or increased cough, wheezing, sputum production, or respiratory difficulty with or without fever. Illness evaluations consisted of a directed history and physical exam, measurement of SaO$_2$, and nasopharyngeal swab for viral culture. Subjects were evaluated each day they attended the center until symptoms resolved. End of illness was defined as resolution of symptoms and physical findings. If participants were well upon return to the center after an absence of several days, they were questioned as to when symptoms resolved. Staff members who became ill answered brief questionnaires and had nasopharyngeal cultures taken. Four-week convalescent sera were obtained from as many staff and participants as possible. Viral cultures and sera were not collected from asymptomatic individuals.

Laboratory Methods

Viral Cultures

Nasopharyngeal swabs were performed by gently rubbing the posterior nasal turbinates and posterior pharynx with cotton tip swabs. Swabs were placed in veal infusion broth, transported to the laboratory on ice, and inoculated onto WI-38 cell cultures (Biowhittaker, Walkersville, MD) within 6 hours of collection. Tubes were incubated at 33°C on roller drums and observed for 10 days for cytopathic effect (CPE). Rhinovirus infection was identified by typical CPE and confirmed by acid lability testing.

Serology

Serologic evidence of coronavirus infection was defined as a greater than 4 rise in coronavirus-specific IgG as measured by enzyme immunoassay (EIA). Coronavirus antigens were prepared by expanding coronavirus 229E virus in WI-38 cells. At the point of visible CPE, monolayers were scraped, and cellular material was pelleted in a Sorvall at 500 g for 15 minutes. Pellets were resuspended in 0.5% NP40, and suspensions were sonicated every 15 minutes for 1 hour. EIA plates were prepared by coating 229E antigen to Immulon round bottom plates in bicarbonate buffer and stored at 4°C overnight. Control plates were prepared by using uninfected WI-38 cell lysates prepared by the above procedure. Acute and convalescent sera was added in serial 2-fold dilutions from 1:400 to 1:102,400 in duplicate to control and antigen plates. Serum IgG was detected with alkaline phosphatase conjugated goat a human IgG followed by substrate. Coronavirus titer was defined as the highest titer with an optical density (O.D.) $\geq$ 0.100 and at least twice the O.D. of the control plate.

As part of an ongoing surveillance project for respiratory infections in the daycare centers, all nasal specimens were cultured for other viruses (influenza, RSV, parainfluenza, enteroviruses), and all sera were tested by EIA for influenza A and B, parainfluenza, and RSV infection. Details of these methodologies and the results of this project will be presented in a future publication.

RESULTS

During the 44 months of study, 352 older daycare attendees were enrolled and participated in the surveillance project for a mean of 43.6 ± 33.7 months. All illnesses were evaluated with viral cultures, and 451 of 522 specimens (86%) had acute and convalescent sera available for coronavirus EIA.

Both coronavirus 229E and rhinovirus infections were identified in approximately 7% of all illnesses. Viral cultures were positive for rhinovirus in 35/522 (6.8%) specimens and coronavirus serology was positive in 37/451 (8.0%) paired sera tested. Sixty-one subjects experienced 72 separate infections. Fifty persons had a single infection, and 11 subjects had multiple infections. Three subjects had two different rhinovirus infections, two subjects had two episodes of coronavirus infection, and six people had one rhinovirus and one coronavirus infection each during the study period. Six individuals had evidence of concurrent mixed viral infections. Four persons had 4-fold rises in both RSV and coronavirus titers. Two subjects, one with coronavirus infection and one with rhinovirus, had serologic evidence of parainfluenza infection. Thus, in 32 illnesses, coronavirus 229E was the sole pathogen identified, and in 34 illnesses, rhinovirus was the only organism found. The clinical features associated with illnesses were analyzed only in cases where either coronavirus or rhinovirus was the only agent identified.

Coronavirus 229E infections were identified most commonly during the winter and early spring whereas rhinovirus activity was sporadic but tended to be more frequent in the summer and fall (Figure 1). Interestingly, when coronavirus was circulating, rhinovirus activity nearly ceased. While no clear outbreaks of infection occurred at any daycare center, periods of viral activity typically involved small clusters of three to six older persons and several staff members. Clusters of rhinovirus or coronavirus infections were not infrequently preceded by an ill staff member. In the spring of 1995, a 4-week period of increased coronavirus activity at one center, involving seven people, was preceded by 2 days with a coronavirus-infected staff member.

The mean age of the 61 subjects who experienced illnesses was 78.5 ± 7.1 years old. The demographics and clinical characteristics of the group that became infected were reflective of the group as a whole except that diabetes was less common in the infected group (11 vs 27%, $P = .01$) (Table 1). Approximately two-thirds of subjects had underlying cardiac disease, and 21% had chronic pulmonary disease. In addition, there were no significant differences between the group infected with rhinovirus compared with the group infected with coronavirus.

The clinical syndromes produced by coronavirus 229E and rhinovirus were nearly identical (Table 2). Most illnesses were characterized by nasal congestion, cough, and constitutional symptoms. Low-grade fever was not uncommon, but temperature of 101°F or greater occurred in only three subjects, two with coronavirus and one with rhinovirus. Although subjects generally recovered without significant sequelae, illnesses lasted, on average, 14 days. Approximately 50% of illnesses were associated with evidence of lower respiratory tract involvement as defined by the presence of sputum production, shortness of breath, new wheezing and/or new rales on exam. Thirty-six percent complained of
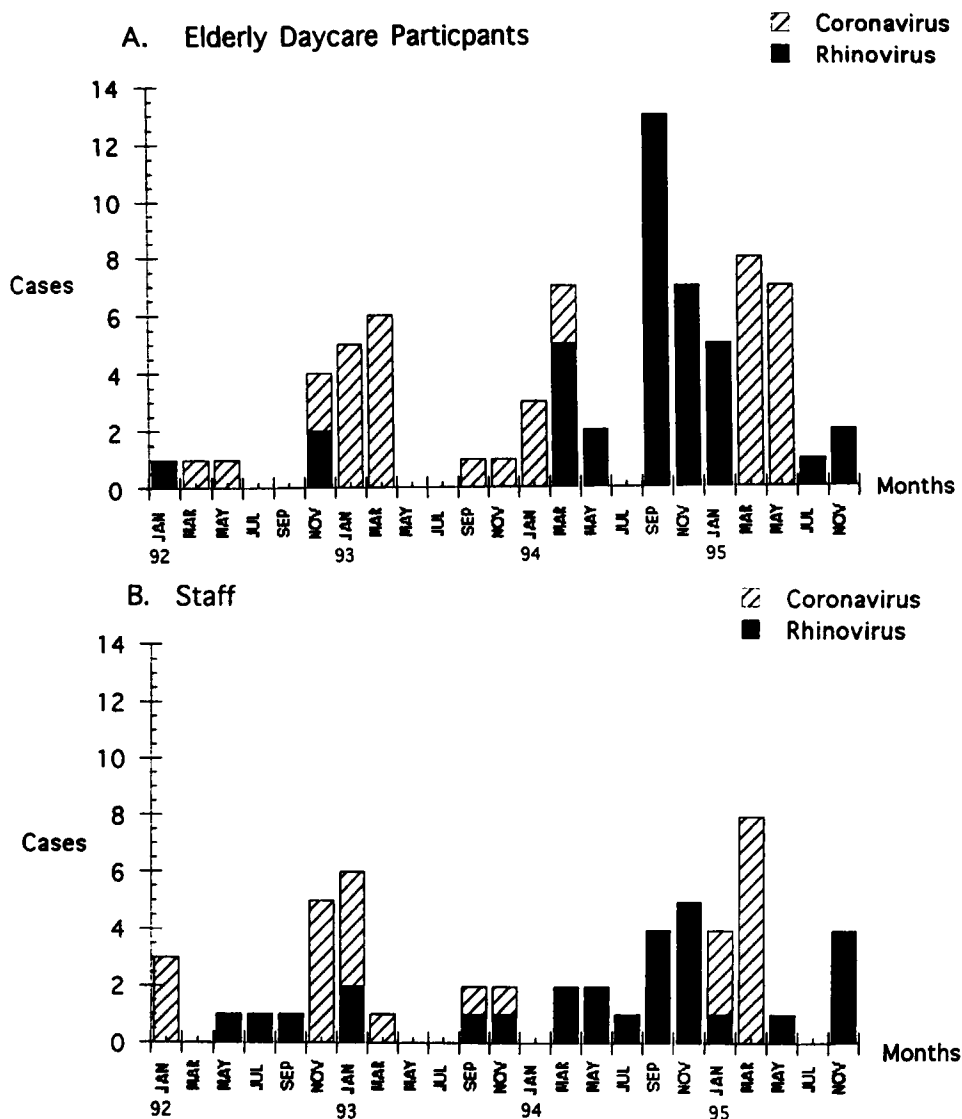
A.   Elderly Daycare Particpants

B.   Staff

Figure 1. Distribution of rhinovirus and coronavirus 229E infections among olderl participants and daycare staff during the 44-month study period.

feeling short of breath. Twenty-two percent had wheezing, and 46% had rales found on auscultation of the chest. Notably, few subjects had wheezing (3%) or rales (13%) on baseline examinations. Although mean SaO_2 measurements for the group dropped only a modest amount from 95.3 ± 1.9 at baseline to 94.2 ± 2.0, P = .003 when ill, seven individuals had a greater than 4-point drop in SaO_2 during illness. One individual with coronavirus had a fall in SaO_2 from a baseline of 95% to 89% while ill. Four illnesses were evaluated with chest roentgenograms, of which three were normal and one showed congestive heart failure. Nine percent of subjects with rhinovirus and 16% with coronavirus received bronchodilators. Antibiotics were frequently prescribed in both groups (Table 3). One individual with rhinovirus infection was hospitalized and treated for congestive heart failure with complete recovery. No deaths occurred. Of note, the six illnesses associated with RSV or parainfluenza were not significantly different from those with rhinovirus or coronavirus alone.

When individuals with underlying cardiac or pulmonary disease were compared with those without, no significant difference in the severity of rhinovirus or coronavirus infections was noted. Wheezing was found to be equally prevalent in those with chronic lung disease as in those without pulmonary problems (23 vs 22%). Subjects who developed wheezing during their illnesses were symptomatic slightly longer (15.3 ± 6.6 days vs 12.4 ± 5.9, P = .095) and received antibiotics much more frequently (86% vs 33%, P < .001) than those who had no evidence of bronchospasm.

During the same time period, 113 staff members developed 338 respiratory illnesses (Figure 1B). The mean age of staff members was 35.0 ± 7.4 years. Twenty-six of 301 (8.6%) tested seropositive for coronavirus infection, and 28 of 338 (8.3%) had a rhinovirus isolated during an acute illness. Five persons (3 coronavirus and 2 rhinovirus) had evidence of mixed viral infections with either influenza A, B, or RSV.

Symptoms associated with infection were similar when staff and participants were compared (Table 3). However,

Table 1. Daycare Participant Characteristics

	Subjects with Illness (n = 61) No. (%)	Subjects without Illness (n = 291) No. (%)
Sex		
Female	43 (70)	181 (62)
Male	18 (30)	110 (38)
Race		
White	57 (93)	246 (85)
Black	3 (5)	38 (13)
Hispanic	1 (2)	6 (2)
Living situation		
Alone	29 (48)	148 (51)
Spouse	14 (23)	69 (24)
Adult family	16 (26)	72 (25)
Young children	2 (3)	2 (0.7)
Medical conditions		
All pulmonary	13 (21)	53 (18)
COPD	8 (13)	42 (14)
All cardiac	40 (66)	225 (77)
CHF	10 (16)	59 (20)
Diabetes	7 (11)	79 (27)

Table 2. Clinical Features of Illnesses in Older Participants*

	Rhinovirus N = 33 No. (%)	Coronavirus N = 31 No. (%)
Symptoms		
Constitutional	30 (91)	28 (88)
Nasal congestion	29 (88)	27 (84)
Sore throat	15 (45)	8 (25)
Hoarse	16 (48)	14 (44)
Cough	31 (94)	30 (94)
Sputum production	17 (52)	21 (66)
Shortness of breath	13 (39)	11 (34)
Signs		
Rhinorrhea	28 (85)	24 (75)
Rales	14 (42)	17 (53)
Wheezes	8 (24)	7 (22)
Temp >99.5°F	6 (18)	9 (28)
Therapy		
Antipyretic	16 (46)	20 (63)
Decongestant	3 (9)	1 (3)
Cough suppressant	14 (40)	14 (44)
Bronchodilator	3 (9)	5 (16)
Antibiotics	14 (40)	15 (47)
Hospitalization	1 (3)	0

* Clinical data missing from 1 rhinovirus and 1 coronavirus.

cough, sputum production, and constitutional symptoms were significantly more common among older persons. Twenty percent of daycare staff missed work secondary to rhinovirus or coronavirus illnesses.

Table 3. Clinical Features of Rhinovirus/Coronavirus Infections Among Staff Compared with Older Participants

	Elderly n = 66 No. (%)	Staff n = 44 No. (%)	
Nasal congestion	56 (85)	42 (95)	NS
Sore throat	23 (35)	23 (52)	NS
Hoarse	30 (45)	21 (48)	NS
Cough	61 (92)	28 (64)	$P < .001$
Sputum	38 (58)	10 (23)	$P < .001$
Dyspnea	24 (36)	11 (25)	NS
Constitutional	58 (94)	39 (61)	$P < .001$
Fever	15 (23)	10 (23)	NS

DISCUSSION

This study represents the largest series to date of prospectively identified cases of coronavirus 229E and rhinovirus infections in older persons. Our data show that both viruses are common in the daycare setting, and although infections did not generally result in serious complications, many were clinically significant with prolonged symptoms and evidence of lower respiratory tract involvement.

Relatively little information has been reported on the impact of these common viruses in frail older populations. In a study of acute respiratory infections in nursing home patients by Nicholson et al., 12 persons were identified as having coronavirus infection by EIA, and three had evidence of lower respiratory involvement.[15] In the same study, 11 individuals were found to have rhinovirus infection, one of whom had lower respiratory tract disease. In our previous study of 14 nursing home residents with rhinovirus infections, all illnesses were mild, with only 21% complaining of sputum production and 14% noting shortness of breath. No patient was hospitalized or died.[16]

In contrast, in a recent report by Wald et al. describing an outbreak of rhinovirus infection that affected 35 institutionalized older persons, a high percentage (66%) of subjects had lower respiratory tract symptoms, and 52% had new abnormalities on lung exam.[17] Persons with underlying lung disease had more severe illnesses, with two individuals requiring hospitalization, one radiographically documented pneumonia, and one death secondary to respiratory failure. Although all participants of the present study recovered without serious sequelae in contrast to our previous study in the nursing home, these subjects were more seriously ill. Similar to the study by Wald and colleagues, our current subjects frequently had evidence of lower respiratory tract involvement with new auscultatory findings, symptoms of dyspnea, and a drop in arterial oxygen saturation. Additionally, subjects were ill for approximately 2 weeks compared with the usual 2 to 4 days of illness in the young healthy adult. It is also note worthy that, during this era of increasing antimicrobial resistance, antibiotics were prescribed during 50% of illnesses caused by rhinoviruses and coronaviruses.

Rhinovirus and coronavirus infections have only rarely been found to be the cause of pneumonia in adults, even in severely immunocompromised patients.[3,7,10,18] However, both viruses have been implicated as a precipitating factor in exacerbations of asthma and COPD.[19-22] Consistent with

the published literature, no older subjects in our study had evidence of invasive disease or pneumonia. This contrasts sharply with infection with influenza, RSV, or parainfluenza in older persons where rates of pneumonia can be high and excess mortality rates have been noted.[1,23–25] The relatively milder illnesses associated with rhinoviruses and coronaviruses likely reflect the biological characteristics of these viruses. Rhinovirus replicates poorly at core body temperature of 37°C and appears to produce symptoms via chemical mediators rather than direct viral invasion.[26] Although less well studied because of fastidious growth requirements, coronaviruses also do not appear to cause significant damage to respiratory epithelium. The lower respiratory signs of wheezing and rales without evidence of pneumonia in our patients suggest that these viruses cause disease in older persons by aggravating preexisting congestive heart failure or inducing bronchospasm.

The incidence of rhinovirus and coronavirus 229E infections in the daycare centers was found to be nearly identical. Since we tested only for one of the two most common serotypes of coronavirus infection and the incidence of 229E and OC43 are roughly equivalent, it is possible that the number of illnesses attributable to coronavirus may actually have been double what was reported. The small intermittent clusters of infections in staff and participants at each center suggest that these viruses were introduced into the centers from outside sources. However, once introduced, some element of nosocomial spread is also likely because of close contact between staff and older persons. The daycare policy that encourages participants to attend daycare so they can receive medical attention from the on-site physicians may have influenced the overall incidence of infection in the daycare. However, this concern must be balanced with the need to provide medical care to this very debilitated group of older persons. The daycare center requires that employees with febrile illnesses and/or uncontrolled respiratory symptoms stay out of work until symptoms resolve. However, many of the common respiratory viruses do not cause fever or severe symptoms in young healthy persons, and, therefore, most healthcare workers suffering from upper respiratory illnesses do not miss work. Because many individuals, both staff and participants, will be experiencing 'colds' and be in close contact throughout the winter months, good infection control practices in daycare centers are critical.

Most respiratory viruses, with the exception of influenza viruses, require relatively close contact for transmission.[27] Rhinoviruses can be transmitted either by fomites and autoinoculation or by aerosol spread.[28,29] Although less information is available about the transmission of coronavirus, it is likely they are also spread by fomites and close contact.[2] Many authorities in the field of pediatrics feel that control of respiratory infections in children's daycare centers is nearly impossible because of the nature of young children's activities.[30] However, in senior daycare centers, the outlook for infection control may be more hopeful. Since transmission of these agents is caused, in part, by fomites, careful handwashing may interrupt spread.[27] In addition, architectural design of centers with attention to square feet per resident and adequate ventilation may be important for future control of respiratory infections.[31]

In summary, coronavirus 229 and rhinoviruses were found to be common causes of acute respiratory illnesses among the staff and participants of a senior daycare program.

Although illnesses were not as severe as those associated with other viral pathogens such as influenza and RSV, older subjects were moderately debilitated by these infections. Attention should be paid to basic infection control principles to limit spread of these common viruses.

ACKNOWLEDGMENTS

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