

Human Coronavirus and Acute Respiratory Illness in Older Adults with Chronic Obstructive Pulmonary Disease

Gorse GJ, O'Connor TZ, Hall SL, et al (Dept of Veterans Affairs Med Ctr and Saint Louis Univ, Missouri; Dept of Veterans Affairs Cooperative Studies Program Coordinating Ctr, West Haven, Connecticut; et al)

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Background.—The clinical features and incidence of human coronavirus (HCoV) infections in chronically ill older adults need better definition.

Methods.—HCoV infection was determined on the basis of a 4-fold increase in serum antibody and the detection of HCoV by reverse-transcription polymerase chain reaction. Laboratory-documented influenza (LDI) was detected by serologic assay and culture. HCoV illnesses were compared with other acute respiratory illnesses identified by active surveillance, during the 1998–99 winter respiratory-virus season, of 2215 patients with chronic obstructive pulmonary disease who were ≥ 50 years old and who received influenza vaccines.

Results.—HCoV-229E and HCoV-OC43 were associated with 90 (14%) of 665 illnesses (HCoV-229E in 22, HCoV-OC43 in 67, and both in 1), LDI with 107 (16%) of 678 illnesses. In multivariate logistic regression analysis, myalgia was less likely with HCoV infection than with LDI (OR, 0.27 [95% confidence limit, 0.13–0.58]). A majority of these HCoV and LDI illnesses exhibited each of 11 symptoms and signs of acute respiratory illness. Spirometric results worsened most often with LDI, and many acute respiratory illnesses, regardless of etiology, were associated with hospitalization. A total of 8 illnesses were associated with HCoV-NL63, 1 with HCoV-HKU1.

Conclusions.—The frequencies of HCoV and LDI illnesses were similar. HCoV illness was less severe than LDI illness, was accompanied by multiple respiratory and systemic symptoms, and was associated with hospitalization.

► In late 2002 and early 2003, a deadly, sudden respiratory illness was reported initially from Asia and then from multiple other countries. This frightening illness, termed sudden acute respiratory syndrome (SARS), was soon found to be caused by a coronavirus, and respect for this virus, often considered a common cold virus, rose to a whole new level. In fact, there are many strains of coronavirus, and the outbreak of SARS prompted significant increased research into this RNA virus and its potential role in human respiratory problems. The authors studied acute respiratory illness (exacerbations) in more than 2200 chronic obstructive pulmonary disease (COPD) patients in one winter flu season. In this population that had received influenza vaccination, almost a third of the respiratory illnesses that winter were caused by either coronavirus or influenza virus as measured by serologic evidence of infections, culture, or polymerase chain reaction. Coronaviral infections were associated with most of the same symptoms as influenza infections, and resulted in

clinically severe enough infections to warrant hospitalization. In both groups, about one fourth of the infected patients required hospitalization. Clearly, coronavirus strains present a spectrum of human respiratory ranging all the way from colds to often-lethal SARS. It also causes a substantial number of exacerbations in COPD patients, and needs to be kept in mind when assessing and managing these patients.

J. R. Maurer, MD, MBA

Rhinovirus Disrupts the Barrier Function of Polarized Airway Epithelial Cells

Sajjan U, Wang Q, Zhao Y, et al (Univ of Michigan, Ann Arbor; et al)
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Rationale.—Secondary bacterial infection following rhinovirus (RV) infection has been recognized in chronic obstructive pulmonary disease.

Objectives.—We sought to understand mechanisms by which RV infection facilitates secondary bacterial infection.

Methods.—Primary human airway epithelial cells grown at air-liquid interface and human bronchial epithelial (16HBE14o-) cells grown as polarized monolayers were infected apically with RV. Transmigration of bacteria (nontypeable *Haemophilus influenzae* and others) was assessed by colony counting and transmission electron microscopy. Transepithelial resistance (R_T) was measured by using a voltmeter. The distribution of zona occludins (ZO)-1 was determined by immunohistochemistry and immunoblotting.

Measurements and Main Results.—Epithelial cells infected with RV showed 2-log more bound bacteria than sham-infected cultures, and bacteria were recovered from the basolateral media of RV- but not sham-infected cells. Infection of polarized airway epithelial cell cultures with RV for 24 hours caused a significant decrease in R_T without causing cell death or apoptosis. Ultraviolet-treated RV did not decrease R_T , suggesting a requirement for viral replication. Reduced R_T was associated with increased paracellular permeability, as determined by flux of fluorescein isothiocyanate (FITC)-inulin. Neutralizing antibodies to tumor necrosis factor (TNF)- α , IFN- γ and IL-1 β reversed corresponding cytokine-induced reductions in R_T but not that induced by RV, indicating that the RV effect is independent of these proinflammatory cytokines. Confocal microscopy and immunoblotting revealed the loss of ZO-1 from tight junction complexes in RV-infected cells. Intranasal inoculation of mice with RV1B also caused the loss of ZO-1 from the bronchial epithelium tight junctions *in vivo*.

Conclusions.—RV facilitates binding, translocation, and persistence of bacteria by disrupting airway epithelial barrier function.

► Rhinovirus, which is probably the most common virus causing the common cold, does not typically cause lower respiratory tract infection and does not significantly destroy the respiratory epithelium.¹ However, other respiratory