LAB NEWS

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Rhinoviruses: The most common cause of human illnesses

Once thought merely to be agents of the common cold, rhinoviruses are now recognized as a major viral cause of asthma exacerbations and decompensations of chronic lung disease, as well as a significant cause of lower respiratory tract infections. The advent of molecular methods has markedly improved the detection of rhinoviruses and allowed the discovery of a previously unrecognized rhinovirus group that does not grow in cell culture.

Rhinoviruses are members of the *Picornaviridae* family and have been recently re-classified as species of the Enterovirus genus (1). The 100 rhinovirus serotypes originally recovered in cell culture have been divided into species A and B. A novel group of rhinoviruses detected only by RT-PCR in patients with lower respiratory tract disease has been tentatively designated as a third species, group C (2, 3). It is now estimated that over 200 distinct rhinoviruses may exist. With no significant cross-protective immunity, it is not surprising that rhinovirus infections are so prevalent.

Season, incubation period and duration of symptoms. In temperate zones, rhinovirus infections occur year-round with a peak in September, and a second peak in late spring. The incubation period is 1-4 days and peak virus shedding coincides with the acute rhinitis. Symptoms average 7 days, but can persist for 12-14 days or more.

Upper and lower respiratory tract disease. Rhinoviruses cause approximately two-thirds of common colds, and thus are responsible for more episodes of human illness than any other infectious agent. Symptoms include profuse watery discharge, nasal congestion, sneezing, headache, mild sore throat, cough, and little or no fever.

In addition, rhinovirus has been increasingly implicated as the major viral cause of asthma exacerbations and decompensations of chronic lung disease. Rhinoviruses can also be the sole etiology of sinusitis and otitis media, can facilitate secondary bacterial infections, and have been increasingly detected in lower respiratory tract infections (4). Recently, investigators around the world have found that novel group C viruses appear to be the predominant rhinovirus species linked to hospitalizations for fever, wheezing, and lower respiratory tract disease (5).

Prolonged shedding and asymptomatic infections. By culture, rhinovirus may become undetectable at 4-5 days or may persist in low titers for up to 2-3 weeks. Using RT-PCR, rhinovirus RNA has been detected for 4-5 weeks after the onset of symptoms (6). It is possible that prolonged detection represents a series of sequential rhinovirus infections, some asymptomatic (7). Indeed, asymptomatic infections are common, occurring in 20-30% of infected persons.

Diagnostic methods. Culture is insensitive for rhinovirus groups A and B and unsuccessful for group C. Rhinoviruses are not detected by direct immunofluorescence antibody (DFA) tests. Thus, nucleic acid amplification assays have greatly increased rhinovirus detection. The Virology Laboratory introduced rhinovirus RT-PCR in 2008, but detection of rhinoviruses in clinical specimens increased substantially in 2010 when a Respiratory Virus PCR Panel replaced reflex respiratory virus cultures.

Method used. Rhinovirus PCR assays are not standardized and many are suboptimal due to the diversity and number of genotypes. The real-time rhinovirus TaqMan RT-PCR developed at the CDC is used at YNHH, is the best currently available, and has been updated to incorporate new sequence information (8).

How to order: Rhinovirus RT-PCR is part of the Respiratory Virus PCR Panel. Rhinovirus RT-PCR can also be ordered as a single test. Rhinovirus and other respiratory virus PCR tests are routinely performed once a day, 5-6 days a week.

Samples: Nasopharyngeal swabs or aspirates, tracheal aspirates and BAL samples are acceptable.

Test interpretation: Like enteroviruses, rhinoviruses are extremely common, occur in asymptomatic persons, exhibit prolonged shedding, and can occur as co-infections with other viruses or bacteria. Thus, interpretation of a positive rhinovirus PCR result and determining the role of rhinovirus in the patient's current illness can be problematic. Clinical symptoms, host risk factors, and detection of other pathogens must all be considered. Although quantitative rhinovirus viral load is not reported,

if it will affect patient management clinicians can call the laboratory to request an assessment of viral burden (low, moderate or high) based on the real-time PCR cycle threshold (C_T) value. No antiviral therapy is currently approved for clinical use.

For questions or concerns, call Marie L. Landry, MD, the Virology Laboratory Director at 688-3475 (marie.landry@yale.edu), or David Ferguson, the Laboratory Manager at 688-3524.

References

1. Landry ML. Rhinoviruses. In Manual of Clinical Microbiology, 10th edition, ASM Press (in press).
2. Lamson D, N.. et al. 2006. MassTag polymerase-chain-reaction detection of respiratory pathogens, including a new rhinovirus genotype, that caused influenza-like illness in New York State during 2004-2005. *J Infect Dis*.194:1398-402.
3. Lee W. M., et al. 2007. A diverse group of previously unrecognized human rhinoviruses are common causes of respiratory illnesses in infants. *PLoS One*. 2:e966.
4. Papadopoulos, N. G., et al. 2000. Rhinoviruses infect the lower airways. *J. Infect. Dis.* 181:1875-84.
5. McErlean P, et al. 2008. Distinguishing molecular features and clinical characteristics of a putative new rhinovirus species, human rhinovirus C (HRV C). *PLoS One*. 3:e1847.
6. Jartti T, P. et al. 2004. Persistence of rhinovirus and enterovirus RNA after acute respiratory illness in children. *J Med Virol*. 72:695-9.
7. Winther B, et al. 2006. Picornavirus infections in children diagnosed by RT-PCR during longitudinal surveillance with weekly sampling: Association with symptomatic illness and effect of season. *J Med Virol*. 78:644-50.
8. Lu X, et al. 2008. Real-time reverse transcription-PCR assay for comprehensive detection of human rhinoviruses. *J Clin Microbiol*. 46:533-9.