

Rhinovirus Causes More Infections Than Thought

Early infection with rhinovirus appears to increase the risk of children later developing asthma.

BY TIMOTHY F. KIRN
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ASPEN, COLO. — The molecular DNA techniques of the past few years have shed much new light on rhinovirus infection, including the fact that rhinovirus causes more lower respiratory tract infections than previously thought and that there may be a possible connection between early infection and asthma.

The new techniques, most of which utilize polymerase chain reaction technology, allow the virus to be detected and identified much more precisely than before. Some serotypes of rhinovirus cannot be cultured, said Dr. Adriana Weinberg, the medical director of the clinical virology laboratory at the University of Colorado Hospital, Denver.

Studies using these techniques now have shown that rhinovirus is associated with both bronchiolitis and pneumonia, Dr. Weinberg said.

In one study of 239 hospitalized Finnish children with bronchiolitis, rhinovirus was the second most common virus recovered from children who were less than 1 year of age (42%), just behind respiratory syncytial virus (54%). In the children who were older than 1 year, rhinovirus was more common than respiratory syncytial virus (*Emerg. Infect. Dis.* 2004;10:1095-101).

A few studies have looked at rhinovirus infection in children with community-ac-

quired pneumonia (CAP). Those studies have shown that 24% of children less than 5 years of age with CAP tested positive for a rhinovirus infection. Among school-age children, 45% of pneumonia cases had a rhinovirus infection, Dr. Weinberg said.

None of the studies had control subjects, Dr. Weinberg said. There are few studies of lower respiratory tract infection and rhinovirus that do. Moreover, in many cases, the study children did have mixed infections, either another virus or a bacterial infection.

Therefore, while this information about rhinovirus and lower respiratory tract infection is obviously important, it is not necessarily in context yet, Dr. Weinberg said.

In general, mixed infections are thought to have the most severe morbidity and symptoms. And in one study that did look at whether infections were mixed or only rhinovirus and whether the “mixed” was another virus or bacteria, there was not much difference in the rates of the recovery from other viruses or bacteria—for the lower age groups at least (less than 14 months)—in the subjects who were symptomatic with a lower respiratory tract infection, compared with those who were asymptomatic, she said.

That argues that the rhinovirus is playing some role, because the rates of rhinoviral infection were different in the symptomatic and asymptomatic patients, Dr. Weinberg said.

Regarding the asthma association, Dr. Weinberg again said that there are a collection of studies that have made this observation; that is, that early infection with rhinovirus appears to increase the likelihood a child will later develop asthma.

Some of the studies have tracked the cohorts since birth, and some have been case-control studies. They have ranged in size from 100 patients to 1,314 patients and have tended to have fairly rigorous criteria for diagnosing asthma.

One theory about why rhinovirus infection would predispose toward asthma is that the infection causes some kind of physical remodeling in a developing and evolving respiratory tract. Another is that early infections prime the dendritic cells of the immune system to be hyperreactive.

Taken together and individually, the studies have suggested that severe and/or repeated lower respiratory tract infections before age 2-3 years increases the prevalence of asthma 10 times. That compares with a five-fold increase the studies have found for respiratory syncytial virus.

Of course, none of these studies provides any explanation about how this association would fit with the other, contradictory epidemiologic studies suggesting that children have increased risk of asthma when they are protected from certain infections and exposures.

“A lot of work remains to be done to fully understand the mechanism and to fully determine whether early rhinoviral infections are a cause of asthma,” Dr. Weinberg commented.

Recent work also showed that infections with rhinovirus can be severe, she

noted. In a big study of the antiviral oseltamivir for influenza treatment, it was found that 19% of the patients enrolled, based on their symptoms, actually had rhinovirus infection. In those patients, the drug was not effective, but the clinical presentation was extremely similar, the investigators noted.

“Rhinovirus is much more serious than we used to think—at least in terms of morbidity,” Dr. Weinberg said.

A number of facts that were known previously about rhinovirus have been confirmed by modern study, according to Dr. Weinberg.

- Those facts include the following:
- ▶ Rhinovirus accounts for about 30%-50% of all “common colds.”
- ▶ Rhinovirus is highly contagious. About two-thirds of individuals exposed to the virus will acquire an infection and develop symptoms.
- ▶ The incubation period is about 12 hours.
- ▶ The duration of symptoms of an infection usually last 2-3 days, but in 25% of cases can last up to 2 weeks.
- ▶ By age 4, most individuals have had about five infections with rhinovirus.

Dr. Weinberg also noted that human rhinoviruses, of which there are about 100 different serotypes, do not have a lipid coat, which means they are not affected by sterilization using organic solvents like soap or alcohol. Instead, if one wants to clean surfaces that have been around someone with rhinovirus, one has to use something acidic. “You may want to decontaminate objects with lemon juice or vinegar,” she said. ■

Strep Throat Risks Called Exaggerated, Tx Rationale Changed

BY TIMOTHY F. KIRN
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ASPEN, COLO. — The risk that a sore throat will lead to rheumatic fever has always been vastly exaggerated, and it may be lower now than it once was. In fact, the risk is one of the major myths of medicine, Dr. Michael Radetsky said at a conference on pediatric infectious diseases sponsored by Children’s Hospital, Denver.

That means any approach—rapid antigen test or culture, or empiric treatment or not—can be justified, said Dr. Radetsky, a pediatric infectious diseases consultant from Albuquerque, N.M.

“The whole issue of strep disease is now shifting from an issue of real medicine—meaning treating real disease—to an issue of relationship with the family,” he said.

Last year, a group at Michigan State University, East Lansing, attempted to develop a rule for when to use a rapid antigen test versus when to culture a patient with pharyngitis for group A hemolytic streptococcus (GAS) infection, based on a cost analysis. Their investigation is very enlightening, Dr. Radetsky said.

The article raises “every serious issue that if we had time we would be thinking about, regarding what we should do about the entire issue of looking for strep

throat,” he said. The first interesting facet of this study is that in their analysis the researchers found that there are no current, accurate estimates for calculating the risk and incidence of peritonsillar abscess or acute rheumatic fever.

To develop their risk estimate of acute rheumatic fever, they had to go back to 1961, to the outbreak in New York City in which there were 2 cases among 608 cases of untreated GAS—for an incidence of 0.328% (*Pediatrics* 2006;117:609-19).

Since then—according to the available, albeit scanty, evidence—the incidence of GAS has been reduced by 98%. So the investigators multiplied 0.328 by 2%, which gave them a current estimate of a risk of acute rheumatic fever of 1 in 15,000 cases of untreated disease. Of those, only 10% will have complications and 1% will die, while treatment appears to reduce the risk of acute rheumatic fever by 88%, the study concluded.

“That was their estimate; I don’t think anyone has done it better,” Dr. Radetsky said.

The incidence of peritonsillar abscess, also never well studied, has been estimated at 0.5%-3%, and treatment of pharyngitis appears to reduce the incidence by only one-sixth or one-ninth, the investigators said.

They concluded in their analysis that treatment needed to be based on some kind of testing, because treating everyone and treating no one were not cost-effective. But, whether a rapid test or a culture is used depends on the costs, which vary in different areas.

But Dr. Radetsky said the study needs to be given deeper consideration.

The study shows that the risk of any kind of complication in a patient is extremely low.

The rationale for treating streptococcal pharyngitis has evolved over the years, he noted. Initially, it was to prevent rheumatic fever. Then it was to prevent peritonsillar abscess. Now it is also justified to enhance recovery and prevent contagion.

But, treatment has been shown not to speed recovery much, and treating to prevent contagion also is not likely to make much difference, because it is estimated that for every patient with a sore throat who sees a doctor, four to six people do not. Moreover, 15% of schoolchildren at any one time are carriers of GAS, so it is more likely that any one patient with GAS will acquire it at school than that they will be the source of an outbreak.

Given those facts, the physician has two obligations regarding GAS, Dr. Radetsky said.

One is to practice in whatever way fosters the therapeutic relationship with a patient and his or her family.

The second is to confine antibiotic use.

He recommended using a culture rather than a rapid antigen test or not testing at all to confine antibiotic use. That way, you give the patient a few days to get better before prescribing. To the family, the physician can explain that, even if the child does have GAS, waiting a few days will give the child a better opportunity to develop immunity to that particular serotype.

Moreover, treating with a second- or third-generation cephalosporin for 5 days, instead of using penicillin for 10 days, reduces the use of antibiotics and probably has superior efficacy, at least according to one recent metaanalysis (*Pediatr. Infect. Dis. J.* 2005;24:909-17).

“You have just cut the number of days on antibiotics in half,” he said.

Dr. Radetsky also advocated using the technique of the deferred prescription, to be used only if the culture comes back positive or if the patient gets worse.

“The justification for doing what we do is becoming slimmer and slimmer, so that the continued pursuit of group A streptococcal pharyngitis is really driven by an outdated notion of risk, and a self-perpetuated habit,” he added. ■