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# Adenovirus Serotype 14: One of Nature's Pathogen Cycles

Acute respiratory disease associated with emerging adenovirus serotype 14 that caused nine deaths last fall in the United States is a development worth noting, but there seems little reason to fear this strain will lead to larger ongoing outbreaks of "killer colds."

BY CHRISTOPHER J. HARRISON, M.D.

In fact, it is probably part of a natural life cycle that has been going on for millennia. We're only learning of these mutations in recent years because of active surveillance that the Centers for Disease Control and Prevention now routinely conducts at sentinel sites around the country. When the system detects something noteworthy, the findings are published in the Morbidity and Mortality Weekly Report (MMWR). Media are mining the MMWR for stories, we're seeing frequent infectious disease stories with alarmist headlines. We should be prepared to explain them to worried parents of patients.

As we know, adenovirus typically isn't a life-threatening problem. In 99% of cases it's a self-limited infection that causes conjunctivitis, rhinorrhea, exudative pharyngitis, and/or fever for 3-8 days.

Adenovirus serotype 14 (Ad14) does appear to be a bit different, though: In May 2006, a 12-day-old infant in New York died of respiratory illness caused by "Ad14." From March to June 2007, a total of 140 additional cases of confirmed Ad14 respiratory illness were identified in clusters of patients in Oregon, Washington, and Texas. Of those, 38% were hospitalized and 5% died (MMWR 2007;56:1181-4). Deaths were due to progressive pneumonias, not colds.

It's possible that Ad14 produces less frequent disease in young children than in the elderly, considering the relative ages of Ad14 patients. Among 12 cases with available medical information in Oregon, 11 (92%) of non–type-14 adenovirus patients were younger than 5 years, compared with only 5 (17%) out of 30 cases of Ad14. There was, however, one death in a 1-month-old in the Ad14 group.

But Ad14 is not new. It was initially described in 1955, and was associated with epidemic of acute respiratory disease in military recruits in Europe in 1969. According to the CDC, in 2001-2002 it was reported to be associated with approximately 8% of all respiratory adenoviral infections in the pediatric ward of a Taiwan Hospital.

However, because Ad14 hasn't been circulating in a while—it's just one of at least 42 different adenovirus strains—the current population isn't likely to be immune. While most healthy individuals are still able to mount an immune response to it, certain susceptible people will become more ill, including the very old, the very young, and those with compromised immune systems; perhaps some healthy people will have a genetic predisposition that makes them more vulnerable.

Indeed, a single nucleotide polymorphism (SNP)—one change in the DNA of a key gene—can have a dramatic effect on how a person responds to environmental or infectious triggers. Consider as an example the case of a disease that we are more familiar with than Ad14, respiratory syncytial virus (RSV) in children. Hospitalization and more severe symptoms have been demonstrated with one SNP (Pediatr. Infect. Dis. J. 2007;26:1094-8), and it's likely that similar mechanisms explain some of the variation in disease severity with other viruses as well. We're just beginning to learn about these mechanisms within the innate immune system.

In the meantime, we might want to consider obtaining viral cultures—commercially available testing systems do include adenovirus—in hospitalized pneumonia patients who do not have positive RSV or influenza rapid tests and who do not improve quickly despite appropriate supportive and perhaps empiric antibiotic therapy.

Even though we don't have a commonly used effective antiviral for adenovirus, such as oseltamivir for influenza, it can be important to be aware of cases of severe adenovirus occurring outside of the surveillance network. While Ad14 is a recent culprit, other serotypes also have been implicated in sporadic outbreaks. Also, if you have a firm viral diagnosis, you don't need to keep escalating broad-spectrum antibiotics. Adenovirus can initially mimic the high fever, leukocytosis, and ill-appearing presentation of bacterial pneumonia, particularly in young children. The x-ray findings usually are bilateral and patchy initially, but the infiltrates can become dense and appear more "bacterial" as time goes on.

Another reason to culture for adenovirus is its potential to mimic Kawasaki disease, with the nonpurulent conjunctivitis, red throat, mucositis, high fever, and swollen lymph nodes. If you can confirm that the child actually has adenovirus during the Kawasaki work-up, you can save thousands of dollars that would otherwise be spent on intravenous immune globulin (IVIG) therapy. Of course, to be really useful, you'll need to get the viral cultures early, because current culture techniques—shell vial or standard—require anywhere from 48 hours to 7 days for results to develop. Because the window of effective use of IVIG in Kawasaki disease is within 10 days of the onset of fever, getting viral cultures more than 5 days into the fever may not give you time to make the diagnosis before you will need to empirically use IVIG.

New multiplex polymerase chain reaction (PCR) technology should improve on that situation in the near future. Already in use at some teaching institutions, multiplex PCR improves the diagnostic capacity of traditional PCR by amplifying target sequences of multiple viruses all at once. The technology allows you to order a panel of 17-20 different viral tests in one batch and get the results back in a day (J. Clin. Microbiol. 2007;45:2965-70), at a cost of not much more than the $150-$200 for the current viral panel of just 6 or 7.

Another new technology on the horizon—flocked nasal swabs—will make it easier to obtain the sample from the child. Currently approved for use in adults, the swabs are made with perpendicular nylon fibers that allow you to collect epithelial cells and surrounding pathogens with a few simple twirls in the nares, a technique far more comfortable for the patient than a nasal wash. Data from the company's abstracts suggest that the sample you get from the swab is equivalent to that from the nasal wash (information available at www.copanusa.com).

These new modalities together should make viral testing as simple as taking a throat culture for the group A streptococcus bacterium, and allow us to obtain timely information that is more pertinent while the child is still sick. But at the same time we need to remind our patients—and ourselves—that in the vast majority of cases we're not talking about a "killer" disease, even with adenovirus. ■

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# Don't Rule Out Retropharyngeal Abscess in Sore Throats

BY HEIDI SPLETE
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Consider a retropharyngeal abscess when faced with a drooling child who has a severe sore throat, according to Dr. Marisol Figueira of Boston University.

"Retropharyngeal abscess is a commonly seen pathology secondary to acute infection of the throat," Dr. Figueira said in an interview. "It is a result of suppuration of the retropharyngeal lymph nodes, secondary to infection in the adenoid, nasopharynx, posterior pharyngeal wall, sinuses, and tonsils."

A high index of suspicion is needed to diagnose retropharyngeal abscess, and the diagnosis is made based on clinical manifestations and radiologic studies.

Prompt diagnosis is important, because treatment delays could lead to life-threatening complications such as a blocked airway, jugular vein thrombosis, or mediastinitis, Dr. Figueira explained in a presentation at a conference on infectious diseases held in Cambridge, Mass.

The retropharyngeal space extends from the base of the skull to the level of the T1 or T2 vertebra, and includes the space behind the muscles of the pharynx but in front of the prevertebral fascia.

An infection in the retropharyngeal space is most common in young children. Data from one 35-year review of cases at a California hospital showed that 50% of patients with a retropharyngeal abscess were younger than 3 years and 71% were younger than 6 years, Dr. Figueira said.

The abscess may follow an upper respiratory infection, group A β-hemolytic streptococcal pharyngitis (GABHS), or even trauma.

The predominant bacterial species are *Streptococcus pyogenes*, *Staphylococcus aureus*, and respiratory anaerobes (including *Fusobacteria*, *Prevotella*, and *Veillonella* species). *Haemophilus* species also are occasionally found.

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The clinical presentation can involve a spectrum of common symptoms including fever, severe sore throat, dysphagia, drooling, respiratory distress, and a muffled voice. The classic symptoms of neck stiffness and bulging of the posterior pharyngeal wall are present in fewer than 50% of patients, Dr. Figueira said.

On physical examination, the child can present with anterolateral neck swelling, hyperextension of the neck, or an enlarged cervical lymph node, she explained at the meeting, which was sponsored by the university.

Imaging is needed to confirm a diagnosis of a retropharyngeal abscess. A lateral x-ray of the neck area may show soft tissue swelling, and a CT scan of the neck can be helpful if the x-ray findings are uncertain and the clinical suspicion is high.

Immediate treatment includes airway maintenance, pain management, and hydration before admitting the child to the hospital. Consult an ear, nose, and throat specialist when the diagnosis is confirmed or if the child has an obstructed airway. The treatment plan for a retropharyngeal abscess includes incising and draining the abscess, and treating the child with parenteral antibiotics such as clindamycin or a combination of ampicillin and sulbactam.

"Prompt diagnosis and treatment of pharyngitis or upper respiratory infections will generally prevent retropharyngeal abscess," Dr. Figueira said. "Also, it is important to know that this condition can lead to laryngeal edema with possible airway obstruction, mediastinitis, and aspiration pneumonia, but with prompt treatment a patient can make a full recovery." ■