

OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

ADENOVIRUS TYPE 14: NOT JUST ANOTHER URI

One April morning in 2007, a Portland-area infectious disease consultant reported that 4 of 13 patients in his hospital's medical ICU had respiratory failure, all from adenovirus infection; he found this excessive. Although adenovirus infection is not reportable, we observe its ripples through the community in reports shared by Oregon virology labs. Within a few hours, a straw poll* of Oregon hospitals revealed that many had recently cared for severe cases of adenovirus infection in patients of all ages — a finding that prompted us to gather more information. This issue of the *CD Summary* describes our findings and should arrive for your reading near the peak of the 2008 winter viral respiratory season.

CASE FINDING

Adenovirus is most frequently detected in late winter and early spring. We asked Oregon virology labs to identify and report cases confirmed during November 2006–July 2007. We reviewed case records and forwarded adenovirus isolates from our most severe cases to the federal Centers for Disease Control and Prevention (CDC) for serotyping. A few weeks later, CDC called excitedly and reported that all of the isolates from ICU patients were adenovirus serotype 14 (Ad14), an uncommon type but one CDC knew was causing unusual disease in pockets around the country.¹

ADENOVIRUS BACKGROUND

Adenoviruses are non-enveloped DNA viruses responsible for a variety of minor respiratory, gastrointestinal, and urinary tract infections. Severe manifestations such as sepsis and pneumonia are typically limited to neonates and compromised hosts, particularly hematopoietic stem-cell transplant recipients. At least 51 adenovirus serotypes are recognized, but a few account for the majority

of infections; adenovirus types 1, 2, and 5 are widespread among young children, while infection with types 3, 4, and 7 occur more often in adults. Some serotypes are also associated with specific syndromes; epidemic keratoconjunctivitis is often caused by serotypes 8, 19 and 37 and gastroenteritis with serotypes 40 and 41.

Ad14 is an uncommon serotype first described in the 1950s, but not previously reported to cause severe disease. Its identification in Portland patients prompted us to investigate all cases identified in the 9-month study period.

WHEN DID AD14 ARRIVE?

After CDC shared its technique for rapid typing of Ad14, the Oregon State Public Health Lab (OSPHL) virologists reached into the freezer and demonstrated that Ad14 had arrived in 2005 and has been the dominant serotype ever since. Although there were far more isolates in 2007 than previous years, this may not mean that there are more cases, because awareness among clinicians and virology labs rose after the cluster was identified. In addition, the techniques for identifying the viruses are becoming

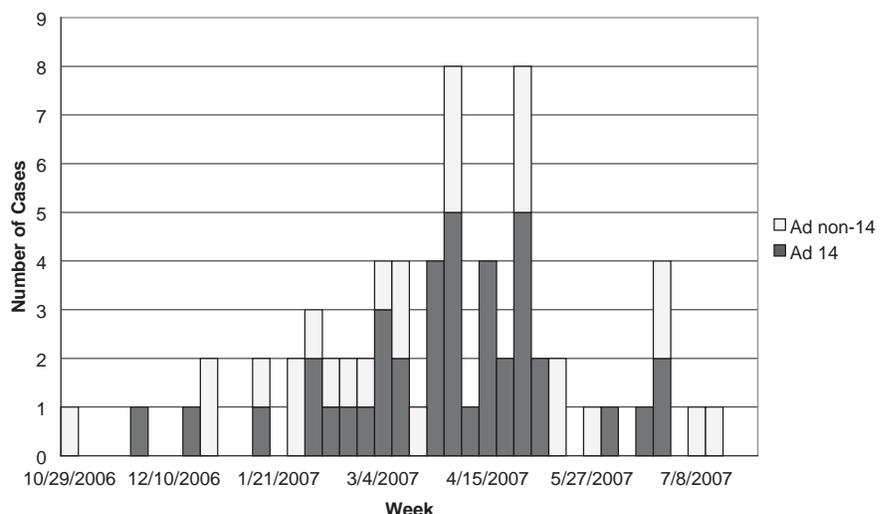
more sensitive and broader in spectrum, making year-to-year comparisons problematic.

DEMOGRAPHICS AND CLINICAL FEATURES

We defined a case as an individual with adenovirus infection confirmed by culture or polymerase chain reaction testing in an Oregon virology laboratory from November 1, 2006, through July 31, 2007. During this 9-month period, 67 adenovirus infections were confirmed in Oregon; 40 (60%) were Ad14 (Figure 1). Ad14 cases were far older on average, but neonates became ill as well; for reasons not understood,[†] three-fourths of cases (regardless of serotype) were male; and disease was scattered across seven Oregon and two Washington counties.

At 76%, Ad14 cases were almost twice as likely to require hospitalization as Ad non-14 patients (42%). Further, Ad14 patients stayed in the hospital longer than Ad non-14 patients (median length of stay 10 days vs. 3 days, respectively). Hospitalized Ad14 patients often had rocky courses; among this group (n=29), 23

Figure 1. Oregon Adenovirus Cases, 1 Nov 2006 – 31 Jul 2007



* as opposed to a primary or a caucus

† not by us, anyway



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(79%) required supplemental oxygen, 18 (62%) were admitted to an ICU, 15 (52%) required mechanical ventilation, 9 (31%) received vasopressors and 7 (24%) died. The median length of stay was 9.5 (range, 0–42) days; for the critically ill, the median length of stay in the ICU was 7 (range, 2–32) days.

Clinical characteristics and underlying disease among the Ad14 cases are found in the table. Ad14 patients suffered from a variety of underlying chronic ailments, but 53% had no history of underlying disease.

Symptoms of Ad14 were largely similar to those typically seen with Ad non-14: respiratory complaints were most common, although gastrointestinal issues were also reported. Among those requiring hospitalization, 71% were tachypnic, 48% had documented fever, and 46% were hypoxic upon admission. All hospitalized Ad14

patients had chest radiographs on admission, of which 90% were abnormal. Radiographic patterns included single-lobe (46%) and multilobe (31%) infiltrates; interstitial infiltrates (11%) and pleural effusion (15%) were less common. The radiographic appearance often progressed from single- to multilobe infiltrates and from a lobar to an ARDS pattern.

All hospitalized patients received supportive care with hydration, blood pressure support, supplemental oxygen, broad-spectrum antibiotics and mechanical ventilation as needed. The antiviral drug cidofovir was used in 6 patients, 4 of whom survived; however, the therapeutic value of this drug is uncertain, and its use was limited or halted by nephrotoxicity in all cases.

FUTURE WORK AND RECOMMENDATIONS

This season we are working with hospitals to identify adenovirus cases

early so we can pursue more detailed study to identify risk factors for infection, to understand transmission risks, and to compare adenovirus cases to patients with community-acquired pneumonia of other etiologies. Clinicians should consider testing for viral pathogens in general — and adenovirus in particular — from patients with community-acquired pneumonia of unknown cause. Although focal infiltrates on chest radiograph and hypotension are suggestive of bacterial pneumonia, Ad14 can clearly cause the same syndrome. Virology labs are aware that typing for Ad14 is available through OSPHL.

Since adenoviruses are non-enveloped and relatively resistant to disinfection, we recommend both contact (gown & gloves) and droplet (mask) precautions in the hospital.

This study did not allow us to draw any conclusions about the efficacy of cidofovir; the toxicity and potential benefit of this agent should be discussed with an infectious disease consultant.

This investigation, prompted by the observations of an astute clinician, generated national awareness of an emerging pathogen.¹ We salute our clinician partners and invite your future observations.

REFERENCE

1. CDC. Acute respiratory disease associated with adenovirus serotype 14 — four states, 2006–2007. *MMWR* 2007; 56:1181–4.

Clinical characteristics of Ad14 patients (n=38)

Underlying Condition/Illness	No. (%)
Cardiovascular Disease	15 (39%)
Hypertension	10 (26%)
Lung Disease	7 (18%)
Cancer	6 (16%)
Immunodeficiency	5 (13%)
Diabetes	4 (11%)
Any Chronic Underlying Disease	18 (47%)
Smoking	18/30 (60%)
Symptom Profile	
Fever	34 (89%)
Cough	31 (82%)
Shortness of Breath	22 (58%)
Vomiting	16 (42%)
Diarrhea	13 (34%)

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