transmitted among NHP through fresh whole blood. 5,6,25,26 Previous reports have stressed the role of skin penetrating injuries in human acquisition of infection. 10-12 The absence of a discernible history of percutaneous injury associated with the species from which the infecting virus strain arose for 43% of participants raises the possibility that human infection with SFV may be acquired through mucocutaneous exposure to SFV-containing NHP body fluids without injury, similar to the routes of transmission of simian herpes viruses. 27 Thus, it is prudent for persons occupationally exposed to NHPs to take precautions to avoid exposure to primate saliva and other body fluids through either percutaneous injuries or mucocutaneous exposures.

Limited observations have not identified infection-associated pathology or secondary SFV transmission among humans through either intimate contact or transfusion of blood products. However, the small number of observed individuals and the limited duration of follow-up restrict our ability to draw definitive conclusions about the clinical significance of human infection with SFV and the ability of SFV to transmit secondarily. Like HTLV, the incidence of disease may be low or may follow long latency periods. It is also unknown what effect, if any, immunosuppression may have on clinical outcomes of human infection with SFV. For example, SFV replication was recently shown to expand to the small intestinal jejunum of SIVimmunosuppressed macaques, a site for significant CD4+ T cell depletion and inflammation in these animals, suggesting that SFV may play a role in the gut-associated pathology observed during progression to simian AIDS.<sup>28</sup> We caution SFV-infected persons to refrain from donation of biological materials for transfusion or transplantation pending a better understanding of the significance of human infection. 12,29 Additional observations will be necessary to further define the public health significance of zoonotic SFV infection.

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Use of trade names is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services, the Public Health Service, or the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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# 医薬品 研究報告 調査報告書

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研究報告の概

○アデノウイルス血清型14に関連した米国4州の急性呼吸器疾患(2006~2007年の報告)

アデノウイルス血清型14型(Ad14)は、希にしか報告されないが新興しているアデノウイルスの血清型株で、健常若年成人を含め全ての年齢層の患者に、重症で時に致死性の呼吸器疾患を惹起する可能性がある。2006年5月に、ニューヨーク州で生後12日目の乳児が、Ad14が原因の呼吸器疾患により死亡した。2007年3月~6月の間に、オレゴン州、ワシントン州の介護施設、およびテキサス州の空軍基地で発生した小集積事例において、合計で140名のAd14感染患者が確認された。このうち53名(38%)が入院し、24名(17%)はICUで治療を受け、9名(5%)が死亡した。全4州の患者から分離されたAd14株は、hexonおよびfiber遺伝子全長の塩基配列データは同一であったが、1955年以来のAd14レファレンス株とは区別された。このことから、米国で新たなAd14変異株が新興し感染拡大したことが示唆される。州および各地公衆衛生当局は、Ad14が原因の集団感染発生可能性に警戒すべきである。

アデノウイルスは1950年代に初めて記録され、結膜炎、発熱性上気道疾患、肺炎および胃腸疾患などの広範囲な臨床症状に関連している。新生児や高齢患者、基礎疾患のある患者では重症化の可能性があるが、健常成人では一般的に致死性感染とはならない。本報告は、米国内に感染拡大した新規病原性Ad14変異株の新興を示唆している点で異例である。Ad14感染は1955年に初めて記録され、1969年にはヨーロッパの新兵での流行性急性呼吸器疾患と関連したが、それ以降はあまり検出されていなかった。Ad14のより広域での感染循環は数年前から発生している可能性もある。

使用上の注意記載状況・ その他参考事項等

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血液を介するウイルス、 細菌、原虫等の感染 vCJD等の伝播のリスク

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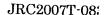
2006~2007年に、米国ニューヨーク州、オレゴン州、ワシントン州、テキサス州で合計140名のアデノウイルス血清型14感染患者が確認され、新たなAd14変異株が新興し感染拡大した可能性が示唆されるとの報告である。

日本赤十字社は、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国(入国)後4週間は献血不適としている。また、問診で呼吸器疾患などの体調不良者を献血不可としている。今後も引き続き情報の収集に努める

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November 16, 2007 / 56(45);1181-1184

# **Acute Respiratory Disease Associated with** Adenovirus Serotype 14 --- Four States, 2006--2007

Adenovirus serotype 14 (Ad14) is a rarely reported but emerging serotype of adenovirus that can cause severe and sometimes fatal respiratory illness in patients of all ages, including healthy young adults. In May 2006, an infant in New York aged 12 days died from respiratory illness caused by Ad14. During March--June 2007, a total of 140 additional cases of confirmed Ad14 respiratory illness were identified in clusters of patients in Oregon, Washington, and Texas. Fifty-three (38%) of these patients were hospitalized, including 24 (17%) who were admitted to intensive care units (ICUs); nine (5%) patients died. Ad14 isolates from all four states were identical b, sequence data from the full hexon and fiber genes. However, the isolates were distinct from the Ad14 reference strain from 1955, suggesting the emergence and spread of a new Ad14 variant in the United States. No epidemiologic evidence of direct transmission linking the New York case or any of the clusters was identified. This report summarizes the investigation of these Ad14 cases by state and city health authorities, the U.S. Air Force, and CDC. State and local public health departments should be alert to the possibility of outbreaks caused by Ad14.

#### New York

In May 2006, a fatal case of Ad14 illness occurred in New York City in an infant girl aged 12 days. The infant was born after a full-term pregnancy and uncomplicated delivery. She was found dead in bed, where she had been sleeping. The infant had been examined 3 days after birth and noted to have lost weight but was otherwise healthy. The next week she had decreased tears with crying, suggesting early dehydration. Physical activity and feeding progressively decreased during the week before her death.

Postmortem tracheal and gastric swabs from the infant were sent to the Wadsworth Center laboratory of the New Y k State Department of Health, where adenovirus was detected by polymerase chain reaction (PCR). Agenovirus also was isolated by culture, confirmed by immunofluorescence assay (IFA), and typed as Ad14 by antibody neutralization assay. Analysis at CDC identified the same unique genetic sequences in this isolate as were later identified in the Ad14 isolates from the three 2007 clusters.

Autopsy and histologic findings at the Office of the Chief Medical Examiner in New York City included presence in the lung of chronic inflammatory cells with intranuclear inclusions, consistent with adenoviral bronchiolitis and acute respiratory distress syndrome. Investigation by the New York City Department of Health and Mental Hygiene has not identified any other local cases of Ad14 illness.

#### Oregon

In early April 2007, a clinician alerted the Oregon Public Health Division (OPHD) regarding multiple patients at a single hospital who had been admitted with a diagnosis of severe pneumonia during March 3-April 6. A total of 17 specimens were obtained from patients; 15 (88%) yielded isolates that were identified by CDC as Ad14. Through retrospective examination of laboratory reports from the three clinical laboratories in the state that have virology capacity and the Oregon State Public Health Laboratory (OSPHL), OPHD identified 68 persons who tested positive (by culture, PCR, or IFA) for adenovirus during November 1, 2006-April 30, 2007. Isolates from 50 (74%) of these patients were available for further adenovirus typing at either CDC or OSPHL. Of the 50 patient isolates, 31 (62%) were identified as Ad14, and 15 (30%) were identified as another adenovirus type

ute Respiratory Disease Associated with Adenovirus Serotype 14 — Four States, 2006—2007 2/5 ページ

<u>Figure</u>); four (8%) did not test positive for adenovirus.

mong 30 Ad14 patients (i.e., all but one) whose medical charts were reviewed, 22 (73%) were male; median age as 53.4 years (range: 2 weeks--82 years). Five cases (17%) occurred in patients aged <5 years, and the remaining 0 (83%) occurred in patients aged >18 years. Twenty-two patients (73%) required hospitalization, sixteen (53%) equired intensive care, and seven (23%) died, all from severe pneumonia. Median age of the patients who died as 63.6 years; five (71%) were male. One death occurred in an infant aged 1 month. Of the 30 Ad14 cases with atient residence information available, 28 (93%) occurred in residents of seven Oregon counties, and two cases ccurred in residents of two Washington counties. No link was identified in hospitals or the community to explain ansmission of Ad14 from one patient to another.

1 comparison with the Ad14 patients, among the 12 adenovirus non-type 14 patients (i.e., all but three) whose redical charts were reviewed, nine (75%) were male. Median age was 1.1 years, and 11 (92%) patients were aged 5 years. Two (17%) adenovirus non-type 14 patients required hospitalization; no ICU admissions or deaths were ported in this group.

## **Vashington**

In May 16, 2007, the Tacoma-Pierce County Health Department notified the Washington State Department of lealth (WADOH) of four residents housed in one unit of a residential-care facility who had been hospitalized scently for pneumonia of unknown etiology. The patients were aged 40--62 years; three of the four were female. The patient had acquired immunodeficiency syndrome (AIDS); the three others had chronic obstructive ulmonary disease. All four were smokers.

he patients had initial symptoms of cough, fever, or shortness of breath during April 22-May 8, 2007. Three atients required intensive care and mechanical ventilation for severe pneumonia. After 8 days of hospitalization, ne patient with AIDS died; the other patients recovered. Respiratory specimens from all four patients tested ositive for adenovirus by PCR at the WADOH laboratory; isolates were available from three patients, and all nree isolates were identified as Ad14 by CDC. Ad14 had last been identified in an isolate from a patient from Vashington in May 2006, marking the first identification of Ad14 in the state since 2004. Active surveillance mong facility residents and staff did not identify any other cases of Ad14 illness.

#### 'exas

ince February 2007, an outbreak of cases of febrile respiratory infection\* associated with adenovirus infection as been reported among basic military trainees at Lackland Air Force Base (LAFB). During an initial investigation, conducted from February 3 to June 23, out of 423 respiratory specimens collected and tested, 268 53%) tested positive for adenovirus; 118 (44%) of the 268 were serotyped, and 106 (90%) of those serotyped were Ad14. Before this outbreak, the only identification of an Ad14 isolate at LAFB occurred in May 2006 (1).

buring February 3--June 23, 2007, a total of 27 patients were hospitalized with pneumonia (median ospitalization: 3 days), including five who required admission to the ICU. One ICU patient required attracorporeal membrane oxygenation for approximately 3 weeks and ultimately died. All 16 hospitalized patients om whom throat swabs were collected, including the five patients admitted to the ICU, tested positive for Ad14. ifteen of these hospitalized patients tested negative for other respiratory pathogens, and one patient had a sputum ulture that was positive for *Haemophilus influenzae*.

dl health-care workers from hospital units where trainees had been admitted were offered testing for Ad14, egardless of history of respiratory illness. Of 218 health-care workers tested by PCR, six (3%) were positive for d14; five of the six reported direct contact with hospitalized Ad14 patients.

revention measures implemented during the outbreak included increasing the number of hand-sanitizing stations, ridespread sanitizing of surfaces and equipment with appropriate disinfectants, increasing awareness of Ad14 mong trainees and staff members, and taking contact and droplet precautions for hospitalized patients with Ad14. leginning on May 26, trainees with febrile respiratory illness were confined to one dormitory and both patients nd staff members were required to wear surgical masks.

Cases reported postinvestigation. Since the investigation, new cases of febrile respiratory illness have continued to occur at LAFB, but the weekly incidence has declined from a peak of 74 cases with onset during the week of May 27--June 2, to 55 cases with onset during the week of September 23--29 (the most recent period for which data were available). In addition, during March--September 2007, three other military bases in Texas that received trainees from LAFB reported a total of 220 cases of Ad14 illness (Air Force Institute for Operational Health, personal communication, 2007). However, whether Ad14 spread from LAFB to these three bases has not been determined. Ad14 also was detected in April in an eye culture from an outpatient in the surrounding community who had respiratory symptoms and conjunctivitis. No link between this case and the LAFB cases was identified.

Reported by: Oregon Dept of Human Svcs. Washington State Dept of Health Communicable Diseases. 37th Training Wing, 59th Hospital Wing, Air Force Institute for Operational Health, Epidemic and Outbreak Surveillance, US Air Force. Naval Health Research Center, US Navy. Texas Dept of State Health Svcs. New York City Dept of Health and Mental Hygiene. Div of Viral Diseases, National Center for Immunization and Respiratory Diseases; Div of Healthcare Quality Promotion, National Center for Preparedness, Detection, and Control of Infectious Diseases; Career Development Div, Office of Workforce and Career Development, CDC.

### **Editorial Note:**

Adenoviruses were first described in the 1950s and are associated with a broad spectrum of clinical illness, including conjunctivitis, febrile upper respiratory illness, pneumonia, and gastrointestinal disease. Severe illness coccur in newborn or elderly patients or in patients with underlying medical conditions but is generally not lifethreatening in otherwise healthy adults. Adenoviruses are known to cause outbreaks of disease, including keratoconjunctivitis, and tracheobronchitis and other respiratory diseases among military recruits (2,3). Although adenovirus outbreaks in military recruits are well-recognized (3), infection usually does not require hospitalization and rarely requires admission to an ICU. Beyond the neonatal period, deaths associated with community-acquired adenovirus infection in persons who are not immunodeficient are uncommon and usually sporadic.

Fifty-one adenovirus serotypes have been identified (4). The cases described in this report are unusual because they suggest the emergence of a new and virulent Ad14 variant that has spread within the United States. Ad14 infection was described initially in 1955 (5) and was associated with epidemic acute respiratory disease in military recruits in Europe in 1969 (6) but has since been detected infrequently. For example, during 2001–2002, Ad14 was associated with approximately 8% of respiratory adenoviral infections in the pediatric ward of a Taiwan hospital, with approximately 40% of Ad14 cases in children aged 4–8 years manifesting as lower airway disease (7).

The National Surveillance for Emerging Adenovirus Infections system includes military and civilian laboratories at 15 sites. During 2004--2007, this surveillance system detected 17 isolates of Ad14 from seven sites (8). Ten of 17 isolates (60%) were collected from three military bases (8). Despite this surveillance, adenovirus infections often go undetected, because few laboratories routinely test for adenovirus and even fewer do serotyping. Wider circulation of Ad14 might have occurred in recent years and might still be occurring.

Further work is needed to understand the natural history of Ad14, risk factors for severe Ad14 disease, and how Ad14 transmission can be prevented effectively. Vaccines against adenovirus serotypes four and seven (i.e., Ad4 and Ad7) were used among military recruits during 1971--1999, before vaccines were no longer available. Adenoviral disease among U.S. military recruits subsequently increased (9). Ad4 and Ad7 oral vaccines have been redeveloped and are being evaluated in clinical trials. Work is ongoing to determine whether the new Ad4 and Ad7 vaccines will protect against Ad14 infection. Management of adenoviral infections is largely supportive. A number of antiviral drugs, including ribavirin, vidarabine, and cidofovir, have been used to treat adenoviral infections such as Ad14, but none have shown definitive efficacy against adenoviruses (2).

Control of adenovirus outbreaks can be challenging because these viruses can be shed in both respiratory secretions and feces and can persist for weeks on environmental surfaces. Guidelines for the care of patients with pneumonia (10) should be followed in cases of suspected adenoviral pneumonia.

Clinicians with questions related to testing of patients for adenovirus or Ad14 infection should contact their state health departments, which can provide assistance. State health departments and military facilities should contact CDC to report unusual clusters of severe adenoviral disease or cases of Ad14 or to obtain additional information

garding laboratory testing.

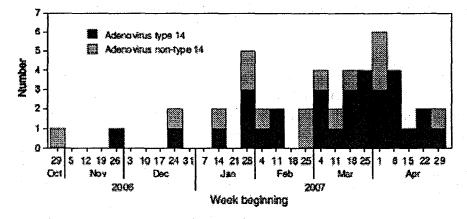
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Defined as 1) fever ≥100.5°F (≥38.1°C) plus at least one other sign or symptom of respiratory illness or 2) diagnosis of pneumonia.

## 'igure

FIGURE. Number of cases of laboratory-confirmed adenovirus (type 14 and non-type 14\*), by week of illness onset — Oregon, November 1, 2006–April 30, 2007



Confirmatory typing performed at Oregon State Public Health Laboratory or GDC.

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