Update on Emerging Infections: News From the Centers for Disease Control and Prevention

Commentator

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Editor's note: *This article is part of a regular series on emerging infection from the Centers for Disease Control and Prevention (CDC) and the EMERGEncy ID NET, an emergency department–based and CDC collaborative surveillance network. Important infectious disease public health information wit relevance to emergency physicians is reported. The goal of this series is to advance knowledge about communicable diseases in emergency medicine and foster cooperation between the front line of clinical medicine and public health agencies.*

Legionellosis—United States, 2000-2009

[Centers for Disease Control and Prevention. Legionellosis—United States, 2000-2009. *MMWR Morb Mortal Wkly Rep*. 2011;60:1083-1086.]

[Note: Because of the length of the original article, it has been abridged. Readers are encouraged to read the full original article.]

Legionnaire's disease (LD), a serious, sometimes lethal pneumonia, and Pontiac fever, an influenza-like, self-limited illness, are the 2 most common forms of legionellosis, which is caused by *Legionella* bacteria. Legionellosis cases are reported to the Centers for Disease Control and Prevention (CDC) through the National Notifiable Disease Surveillance System (NNDSS) and a Supplemental Legionnaires Disease Surveillance System (SLDSS) designed to manage surveillance data on travel-related cases and enhance outbreak detection. For this article, cases reported to NNDSS during 2000 to 2009 from the 50 states and the District of Columbia were assessed, and crude and age-adjusted incidence rates per 100,000 persons were calculated. US legionellosis cases reported annually increased 217%, from 1,110 in 2000 to 3,522 in 2009, and the crude national incidence rate increased 192%, from 0.39 per 100,000 persons in 2000 to 1.15 in 2009. Because NNDSS is a passive surveillance system dependent on case reporting by health care providers and laboratories, the actual incidence of legionellosis in the United States likely is higher. Although NNDSS does not record legionellosis cases by type, 99.5% of the legionellosis cases reported to SLDSS during 2005 to 2009 were classified as LD and 0.5% as Pontiac fever. Legionellosis surveillance was added to the population-based Active Bacterial Core surveillance system in January 2011 to assess reasons for these increases in numbers of reported cases. The increase in reported cases reinforces the need for health care providers in all parts of the United States to test and treat adults with severe community-acquired pneumonia for LD, to be vigilant for health care–associated LD, and to report legionellosis cases to public health authorities.

NNDSS data for 2000 to 2009 were used to describe legionellosis case demographics, assess seasonal patterns of legionellosis infection, and, using denominators from the 2000 US standard population[1] and US Census Bureau estimates, calculate crude and age-standardized incidence rates for the entire United States (excluding US territories) and for each of the 9 US census divisions. Only cases considered confirmed under the 2005 Council of State and Territorial Epidemiologists' legionellosis case definitions are described in this article. To be classified as confirmed, cases must be clinically compatible with legionellosis (ie, fever, myalgia, cough, or clinical or radiographic evidence of pneumonia) and meet at least 1 of the confirmatory laboratory criteria (ie, recovery of *Legionella* spp in culture, detection of *L pneumophila* serogroup 1 antigen in urine, or 4-fold or greater increase in *L pneumophila* serogroup 1–specific serum antibodies).

In 2005, the Council of State and Territorial Epidemiologists issued a position statement[2] requesting that all legionellosis cases be reported to SLDSS, but such reporting is not mandatory, and case follow-up varies by state and county according to staffing availability and perceived public health importance. For this article, SLDSS data were used to characterize diagnoses, diagnostic testing, outcomes, outbreak involvement, and recent travel. Because of potential differences in data received by SLDSS before and after the 2005 Council of State and Territorial Epidemiologists position statement, separate analyses were conducted, using cases with onset during 2000 to 2009 (NNDSS data) and 2005 to 2009 (SLDSS data).

During 2000 to 2009, the 50 states and District of Columbia reported 22,418 cases of legionellosis to NNDSS. The crude national incidence rate increased 192%, from 0.39 per 100,000 persons in 2000 to 1.15 in 2009, and the age-adjusted incidence of legionellosis in the United States increased 170%, from 0.40 to 1.08 cases per 100,000 persons. In 2000, the age-adjusted incidence varied substantially by US census division, from 0.09 cases per 100,000 persons in the west south central division to 0.73 cases in the middle Atlantic division. This disparity increased absolutely during the decade (middle Atlantic division: 2.60 cases per 100,000 persons; and west

south central division: 0.44 cases in 2009). All reporting divisions had an increase in age-adjusted legionellosis incidence from 2000 to 2001, to 2008 to 2009, ranging from a 101% increase in the west north central division to 294% in the west south central division. Nationally, 16,595 cases (74%) were in persons aged 50 years or older, and 14,255 (64%) persons were men. Legionellosis incidence increased for all age groups from 2000 to 2009, ranging from 8% for persons aged 9 years or younger to 287% for persons aged 80 years or older.

Among the 18,392 cases (82%) reported to NNDSS with available information on race, 78% were white, 19% were black, and 3% were American Indian/Alaska Native, Asian, or other. Cases tended to occur in the summer and early fall, with the June to October period accounting for 62% of the cases reported each year.

During 2005 to 2009, a total of 5,080 confirmed legionellosis cases among US residents were reported to SLDSS by 47 states, accounting for 35% of the 14,554 confirmed cases reported to NNDSS during the same period by all 50 states and the District of Columbia. An additional 82 confirmed legionellosis cases were reported among foreign visitors to the United States. A total of 1,220 (24%) cases involving US residents were travel-associated; 81% of these involved domestic travel only, and 5% involved cruise ship travel. Travel-associated cases accounted for at least two thirds of the cases reported to SLDSS from 21 states, 11 of which reported only travel-associated cases, suggesting a bias against reporting nontravel-associated cases to SLDSS from some states. Of 3,872 (76%) US resident cases with data available, 4% were associated with a known legionellosis outbreak or possible cluster. Information on clinical outcomes was available for 4,478 (88%) US resident cases, 8% of which resulted in deaths. Urine antigen tests were used to confirm 97% of US resident cases reported during 2005 to 2009. Only 5% of cases were confirmed by culture during this period, and less than 1% were confirmed by either serologic or direct fluorescent antigen testing.

Reported legionellosis incidence rates increased nearly 3-fold during 2000 to 2009. In 2009, NNDSS received 3,522 case reports, the most since legionellosis became a reportable disease in 1976.[3,4] Increased rates were observed across all age groups and geographic regions. The reported case totals likely underestimate the actual disease burden; the most recent completed US population–based study of pneumonia causes estimated that 8,000 to 18,000 persons are hospitalized each year with LD.[5]

An increasing population of older persons contributed to the increase in reported legionellosis cases. Other factors that might have contributed include an increasing population of persons at high risk for infection; improved diagnosis and reporting, possibly stimulated by the 2005 Council of State and Territorial Epidemiologists endorsement of more timely and sensitive legionellosis surveillance; and increased use of urine *Legionella* antigen testing. However, because increases in urine antigen testing began in the 1980s, its use is unlikely to account for the entire increase in legionellosis cases since 2000.[3,4]

Urine antigen tests are easy to perform and provide timely, accurate results (sensitivity 60% to 80%; specificity >99%) for detecting *L pneumophila* serogroup 1, the causative agent in 70% to 80% of LD cases.[6] In contrast, culture of respiratory samples from possible LD cases (sensitivity 20% to 80%; specificity >99%) can detect all forms of *Legionella* but has a lengthy turnaround time, and its sensitivity is highly dependent on the skill of laboratory personnel. Similarly, identifying legionellosis through paired serology (sensitivity 70% to 80%; specificity >95%) involves substantial logistic challenges, whereas direct fluorescent antigen testing for LD (sensitivity 25% to 75%; specificity >95%) can be technically demanding and can result in false positives from cross-reactions with other bacteria. Only urine antigen and serology are useful for detecting Pontiac fever, but the sensitivity of these tests for confirmation of Pontiac fever is substantially lower than that for LD.[7]

Similar to the findings of previous studies, men accounted for greater than 60% of cases, and increasing age was a major risk factor for legionellosis.[3,4] However, the finding that blacks accounted for a disproportionately high number of cases relative to their 12% share of the population was unexpected. Insufficient information is available to confirm whether these patterns might be the result of differences in underlying risk factors or exposures to *Legionella*, and the high proportion of cases in persons of unknown race limits the interpretation of the racial differences observed.

Legionellosis demonstrates seasonal and geographic variability. During 2000 to 2009, nearly all regions reported their highest proportion of cases during the summer and early fall. The reported 2009 age-adjusted legionellosis rate in the Middle Atlantic division was nearly 6 times higher than the rate in the west south central division. Whether these differences are related to the frequency of testing or reporting is unclear; nonetheless, clinicians should be particularly vigilant for possible LD during the summer and early fall and in geographic areas of relatively high legionellosis incidence. Although use of a urine antigen test for *Legionella* is recommended for cases of severe community-acquired pneumonia,[8] collection of respiratory specimens for *Legionella*-specific culture also is encouraged as a means to detect all species and subgroups of *Legionella* and enable strain identification in the event of an outbreak. Urine antigen tests and *Legionella*-specific culture also are recommended for suspected cases of health care–associated LD.[9]

The findings in this article are subject to at least 4 limitations. First, current passive surveillance systems cannot determine whether the observed increase in legionellosis cases is actual or an artifact of improved detection or reporting. Second, surveillance likely is biased toward capture of more severe LD cases in patients who are more likely to be tested for *Legionella*, missing those who have been empirically treated with antibiotics active against *Legionella* spp and those not requiring hospitalization. Third, the nonspecific symptoms of and lack of good diagnostic tests for Pontiac fever likely result in substantial underdiagnosis of this form of legionellosis. Fourth, the proportion of cases that are potentially travel associated likely is an overestimate resulting from a bias in many states toward primarily reporting travel-associated cases to SLDSS.

A better understanding of the disease burden and the epidemiology of legionellosis is important, but current passive surveillance systems cannot provide all the information required. In January 2011, active laboratory-based and population-based surveillance was launched in 10 Active Bacterial Core surveillance sites around the country. Data from this surveillance will be used to obtain population-based estimates of disease incidence; further describe demographic, seasonal, and geographic variability; and evaluate and improve legionellosis prevention efforts, such as the guidance provided by the American Society of Heating, Refrigerating, and Air Conditioning Engineers on preventing legionellosis associated with building water systems.[10]

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COMMENTARY

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Emergency physicians are the front-line providers for diagnosis and initial empiric treatment of community-acquired pneumonia (CAP). *Legionella pneumophila* can cause severe CAP with progression to respiratory failure and need for ICU admission.[1] Previous studies cite mortality rates ranging from 10% to 27% in patients not receiving appropriate empiric antibiotics on admission.[2] Diagnosis of legionellosis is often challenging because of its relatively low prevalence, symptoms and radiographic findings that are indistinguishable from other causes, and infrequency of *Legionella*-specific testing. The increase in prevalence of legionellosis, coupled with the high 8% mortality observed in this article, highlights the importance of early clinical suspicion, ordering appropriate tests, and initiation of appropriate treatment among emergency department (ED) patients at high risk for legionellosis.

Transmission of *Legionella* usually occurs through inhalation of contaminated aerosols from colonized manmade water systems such as air conditioning systems, cooling towers, hot-water systems, and whirlpools, where the bacteria thrive at temperature ranges of 20°C (68°F) to 45°C (113°F).[3] Thus, identification of the environmental source can be valuable to identify other exposed individuals. An environmental history including sick contacts, water exposures, and travel will be relevant.

Although less common than other pneumonia causes, correct management of legionellosis is important in the ED. From an epidemiologic perspective, *L pneumophila* has been identified in 2% to 8% of CAP in the United States and is arguably the most significant waterborne organism with regard to serious morbidity and mortality.[4] According to the Infectious Diseases Society of America and the American Thoracic Society consensus guidelines (IDSA-ATS), *Legionella* is the dominant atypical pathogen in severe CAP.[5] A meta-analysis review of 890 patients with CAP who were admitted to the ICU demonstrated that *Legionella* was the second most frequent pathogen only after *Streptococcus pneumoniae*.[6]

Obtaining evidence to support a specific diagnosis of legionellosis can be challenging in the ED. In addition to advancing age, male sex, geographic (middle Atlantic, east north central, New England), and seasonal (June to October) considerations highlighted in the article, additional risk factors for legionellosis from the IDSA-ATS include chronic obstructive pulmonary disease, smoking, immunosuppression, and a hotel or cruise ship stay in the previous 2 weeks.[5] Clinical symptoms and laboratory and diagnostic investigations are also nonspecific. An older study found that chronic alcohol abuse, lack of response to ß-lactam drugs, headache, diarrhea, severe hyponatremia, and elevation in serum creatine kinase levels on presentation in the ED were more frequent in CAP because of *Legionella*.[7] A more recent study attempted to create a diagnostic score that has not yet been validated.[8] The authors identified 6 parameters (each constituting 1 point), including high body temperature, absence of sputum production, low serum sodium concentrations, high levels of lactate dehydrogenase, high levels of C-reactive protein, and low platelet counts, that were independent predictors of *Legionella* CAP. Of the patients with a score of 0 or 1 point, only 3% had