

## **Legionellosis**

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#### **SLIDE 1**

Hello, my name is Greg Smith. I am a medical epidemiologist with the Communicable Disease Control Branch in the Epidemiology Section, Division of Public Health, NC Department of Health and Human Services. Today, I will be talking about Legionellosis, a modern environmental infectious disease which has emerged because of relatively recent human exposure to the agent, *Legionella*, via contaminated water aerosols.

#### **SLIDE 2**

At the conclusion of this presentation, participants should be able to 1) know the difference between Legionnaires' disease and Pontiac Fever; 2) identify high risk groups; and 3) list appropriate prevention and control measures.

#### **SLIDE 3**

In late July 1976, an outbreak of acute respiratory illness occurred in American Legionnaires who had recently attended a state convention at the Bellvue-Stratford hotel in Philadelphia. The illness was characterized by malaise, high fever, muscle aches, headache, and pneumonia, which in some cases progressed to ARDS. At the time, there was concern that the illness might be due to swine influenza virus or another novel influenza virus, but these possibilities were soon ruled out. Non-infectious etiologies involving toxic metals also were explored, but did not prove fruitful. It would eventually take six months to determine that the agent responsible for 221 cases and 34 deaths associated with the outbreak was a previously unknown bacterium, *Legionella pneumophila*. We now know that legionellosis manifests as "two clinically and epidemiologically distinct illnesses, Legionnaires' Disease, which is characterized by fever, myalgia, cough and clinical or radiographic pneumonia; and Pontiac Fever, a milder illness without pneumonia." Today, it is estimated that between 8,000 to 18,000 cases of legionellosis occur each year in the US. However, due to underdiagnosis and underreporting, only about 3,000 cases are officially reported each year in the US.

#### **SLIDE 4**

This archival photo from the Associated Press puts a personal face on the outbreak. Two of the Legionnaires in this picture succumbed to the disease.

#### **SLIDE 5**

Following the 1976 Legionnaires' disease outbreak, we learned that legionellosis may have different clinical presentations and may be caused by a variety of *Legionella* species. The most severe form of illness caused by *Legionella* species is Legionnaires Disease, which you may also find named in the literature as Legionnaires' disease, with an apostrophe. Legionnaires' disease manifests as pneumonia and may be fatal, particularly if not diagnosed early and treated appropriately. A less severe form of legionellosis is Pontiac Fever, which is characterized by a flu-like illness. Pontiac Fever does not involve pneumonia and is not fatal. *Legionella pneumophila*, the *Legionella* species most often associated with Legionnaires' disease, may also cause wound

infections, pericarditis, and endocarditis. However, such complications are uncommon and are usually associated with infection of immunocompromised hosts. *Legionella* bacteria appear as poorly staining pleomorphic (meaning variably shaped) gram negative rods. To date, 52 species of *Legionella*, encompassing 70 serogroups have been identified. About half of these species have been associated with human disease. However, the vast majority of cases are due to *Legionella pneumophila*, which has 18 currently recognized serogroups. Of these, serogroup 1 is most often associated with legionellosis.

#### **SLIDE 6**

For epidemiologists investigating illness due to a specific infectious agent, it often helps to see a picture of the agent. This slide from the CDC photo library shows a cluster of gram negative bacteria in a pulmonary tissue sample taken from a patient in the original 1976 Legionnaires' outbreak in Philadelphia.

#### **SLIDE 7**

It was later learned that *Legionella* species live and thrive in moist soils and aqueous environments. They live, grow, and reproduce within amoeba and other protozoa. Here is a wonderful micrograph showing chains of *Legionella pneumophila* within ciliated protozoa. When you hear the word Legionella, think of wet and moist environments which could serve as sources of aerosol exposure.

#### **SLIDE 8**

So far we have learned that legionellosis may be caused by a variety of *Legionella* species. These bacteria are essentially parasites which live within protozoa in nature and tissue macrophages in humans. Of all the *Legionella* species identified to date, most human disease is caused by *Legionella pneumophila*. Of all the 18 *Legionella pneumophila* serogroups, serogroup 1 causes approximately 80-90% of disease in humans.

#### **SLIDE 9**

Before continuing, let's review. *Legionella pneumophila* was identified in 1977 as the causative agent of the Legionnaires' Disease outbreak which occurred among veterans attending the 1976 Legionnaires' convention in Philadelphia. As mentioned earlier, that outbreak resulted in 34 deaths. Timely identification of *Legionella pneumophila* as the causative agent was delayed due to its slow growth in culture media. *Legionella pneumophila* requires the amino acid cysteine and other nutrients for in-vitro growth. Buffered Charcoal Yeast extract media was used to culture *Legionella pneumophila* as early as 1978 and is still used today. Following identification, a key question from epidemiologists investigating the outbreak was, "Where did this novel pathogen come from?" The hotel's cooling tower was identified as the most likely source of the bacteria. Aerosolization from the tower was the likely route of transmission.

#### **SLIDE 10**

Let's now review the clinical presentation of Legionnaires' disease or Legionnaire Pneumonia. The incubation period following exposure ranges from 2-10 days but is

most often 5-6 days. Initial symptoms include anorexia, malaise, myalgia, and headache. Within 24 hours, a fever of 102-105 F develops. Other symptoms and signs may include nonproductive cough, abdominal pain, nausea, vomiting, and diarrhea. Pneumonia may be identified clinically or radiographically. On chest X-ray, one may see patchy infiltrates or focal areas of consolidation which may progress to bilateral involvement, ARDS, and respiratory failure. The case fatality rate for Legionnaires' disease has improved since the original outbreak in 1976. Today the overall case fatality rate (CFR) is 10-15%. The majority of cases we learn about today are hospitalized. In the past, the CFR for hospitalized cases has been as high as 39%, but today the inpatient CFR is around 15%. In general, immunocompromised patients are at greatest risk of dying from Legionnaires' disease. Early diagnosis and appropriate treatment are essential in order to reduce the risk of morbidity and mortality of Legionnaires' disease.

#### **SLIDE 11**

This chest X-ray shows bilateral pulmonary infiltrates in one of the 1976 outbreak victims.

#### **SLIDE 12**

Now let's learn about Pontiac Fever or non-pneumonic legionellosis. Pontiac Fever has a usual incubation period of 1 to 2 days, but this may range from 5 hrs to 66 hrs. Pontiac Fever presents with the same initial symptoms associated with pulmonary legionellosis, which include anorexia, malaise, myalgias, headache, fever, chills and nonproductive cough. However, Pontiac Fever does not progress to pneumonia and it is not associated with death. Due to its milder clinical presentation, which is similar to many viral respiratory tract infections, Pontiac Fever is rarely diagnosed, recognized, or reported except in an outbreak setting. Patients with Pontiac Fever recover within a week. This has led some to speculate that Pontiac Fever is a clinical syndrome which results from reaction to inhaled *Legionella* antigens and not bacterial invasion.

#### **SLIDE 13**

Legionellosis is transmitted via inhalation of water aerosols containing the causative agent. In a few minutes, we will review the known sources of *Legionella*-contaminated aerosols. Before we do that, keep in mind that person-to-person transmission of legionellosis has not been documented. Also, it is important to remember that, to date, no outbreaks have been associated with swimming in rivers, lakes, or other natural bodies of water.

#### **SLIDE 14**

Continuing with the epidemiology of Legionnaires' disease, we know that the disease is associated with older age and that there is a male to female ratio of 2.5 to 1. Identified risk factors include smoking, chronic lung disease, diabetes mellitus, renal disease, malignancy, alcoholism, and a variety of immunocompromised states.

## **SLIDE 15**

Now let's look at the laboratory tests used to diagnose legionellosis. *Legionella pneumophila*, and other legionella species, may be cultured from sputum, bronchial washings, or lung tissue at autopsy. However, due to difficulties associated with obtaining a good sputum sample for culture, culturing *Legionella* species, and the fact that antibiotics are often given before obtaining culture, the sensitivity for culturing *Legionella pneumophila* is at best only 70%. Most often, legionellosis is diagnosed by urinary antigen which may be present in urine for several months after disease. The sensitivity for diagnosis of legionellosis also is not optimal because the only commercially available antigen for *Legionella* only detects *Legionella pneumophila* serogroup 1. All others are missed. The CDC recommends that only radioimmunoassay be used because latex agglutination has a high false positive rate. Legionellosis also may be diagnosed via direct fluorescent antibody (DFA) staining of lung aspirates. Again, DFA is limited due to absence of antigen specific reagents for specific serogroups and subtypes. DFA may also be falsely negative if aspirates are obtained too early in the disease. Finally, legionellosis may be diagnosed via a fourfold rise in antibody titer between acute and convalescent illness. Immunofluorescent antibody is the accepted method. ELISA is not reliable.

## **SLIDE 16**

The following four slides illustrate some of the laboratory tests used to diagnose legionellosis. This slide illustrates a culture of legionella on agar under ultraviolet light illumination.

## **SLIDE 17**

Here we see *Legionella* colonies growing on a Charcoal Yeast extract agar culture plate.

## **SLIDE 18**

These pictures illustrate Indirect Fluorescent Antibody (IFA) and Direct Fluorescent Antibody (DFA) staining of *Legionella pneumophila*.

## **SLIDE 19**

The laboratory criteria for diagnosis of a confirmed case of legionellosis include the following: 1) culture isolation of any *Legionella* organism from respiratory secretions, lung tissue, pleural fluid or other normally sterile site; 2) detection of *Legionella pneumophila* serogroup 1 via urinary antigen using validated reagents; and 3) seroconversion demonstrated by a fourfold or greater rise in specific antibody titer to *Legionella pneumophila* serogroup 1 using validated reagents.

## **SLIDE 20**

The laboratory criteria for diagnosis of a suspect case of legionellosis include seroconversion demonstrated by a fourfold or greater rise in antibody titer to specific species or serogroups of *Legionella* other than *Legionella pneumophila* serogroup 1, or a fourfold or greater rise in antibody to multiple species of *Legionella* using pooled antigen and validated reagents, and in addition, detection of specific *Legionella* antigen

or staining of the organism in respiratory secretions, lung tissue, or pleural fluid by DFA, IHC, or other similar method using validated reagents. Additionally, suspect cases may be identified via detection of *Legionella species* by a validated nucleic acid assay.

### **SLIDE 21**

The CDC and the NC Communicable Disease Control Branch use the following case definitions for Legionellosis and Legionnaires' Disease: "A suspect case of Legionellosis or Legionnaires' Disease must have clinically compatible illness and at least one of the presumptive (suspect) laboratory criteria. A confirmed case of Legionellosis or Legionnaires' Disease must have clinically compatible illness and at least one of the confirmatory laboratory criteria. In order to meet the confirmed case definition for Legionnaires' Disease, the case must have clinically or radiographically diagnosed pneumonia."

### **SLIDE 22**

CDC has defined a travel-associated case of legionellosis as any case that has a history of spending a night away from home during the 14 days prior to onset of illness.

### **SLIDE 23**

Earlier in the presentation, we learned that *Legionella pneumophila* was associated with aqueous environments. *Legionella species* are essentially ubiquitous in the aqueous environments of temperate and tropical regions of the world. Although they have been isolated from moist soils in some areas, legionellae are primarily found in natural bodies of water and man-made water supplies where they tend to grow on slimes and biofilms. *Legionella pneumophila* is hardy and can survive within a wide range of temperature and pH. In addition, it is not eradicated with chlorine at levels used in domestic water supplies. It is important to keep in mind that low or non-detectable levels of legionellae can colonize a water source and grow to high concentrations under the right conditions.

### **SLIDE 24**

As mentioned earlier, Legionellosis is caused by inhalation of the aerosolized agent. Outbreaks of illness have been associated with *Legionella*-contaminated hot water heaters and systems, hot and cold water taps, showers, hot tubs, air conditioning cooling towers, evaporative condensers, humidifiers, whirlpool spas, respiratory therapy machines, decorative fountains, dental water lines, grocery store misters, and swimming pool misters. In addition, legionellosis occasionally has been acquired following inhalation exposure to fine particulates of commercially bagged peat, peat moss and potting soil. There currently is no evidence that legionellosis is associated with home air conditioning units.

### **SLIDE 25**

The following slides illustrate some of the potential sources of exposure to *Legionella* bacteria described in slide 24. As you view these next slides, keep in mind that most persons exposed to water sources such as these, even when contaminated with *Legionella*, will not develop any signs or symptoms of clinical illness. Persons most at risk for developing disease are those with the risk factors described in slide 14. These

include smoking, chronic lung disease, diabetes mellitus, renal disease, malignancy, alcoholism and a compromised immune system due to HIV/AIDS, chemotherapy, organ transplant-associated immunosuppression, chronic steroid therapy, etc. Persons with these conditions should avoid or minimize exposure to non-sterile sources of aerosolized water.

#### **SLIDE 26**

Hot water heating systems can harbor legionellae, especially if the temperature is less than 50C/122F. When hot water heater temperatures are turned up, it is best to install scald protection faucets in order to prevent accidental burns to small children and the elderly.

#### **SLIDE 27**

Several large outbreaks of Legionnaires' disease (epidemic legionellosis) in the United States and other areas of the world have resulted from exposure of susceptible individuals to *Legionella*-contaminated aerosols from cooling towers. In an effort to reduce transmission risk associated with cooling towers, biocides are sometimes routinely added to the cooling tower water. However, this practice does not always eradicate the organism or prevent recolonization between treatments.

#### **SLIDE 28**

Other outdoor water sources which create aerosols such as these should be avoided by persons at risk for legionellosis.

#### **SLIDE 29**

In 1989, an outbreak of 28 cases of legionellosis in Louisiana was associated with exposure to water mist from a produce "fogger". Further investigation revealed that foggers, misters, and humidifiers which generate mist by ultrasonic transducers can transmit *Legionella* to humans if the water reservoir of the appliance is contaminated. The FDA has issued guidelines which specify weekly disassembly and cleaning of foggers used in grocery store settings.

#### **SLIDE 30**

Home humidifiers, especially those with water reservoirs and ultrasonic transducers, are potential sources of exposure to aerosolized legionellae. The Consumer Products Safety Commission and EPA have issued general guidelines on the cleaning and maintenance of humidifiers used in home settings.

#### **SLIDE 31**

C- Pap Machines, for people with sleep apnea, may also become contaminated with legionella. Users should follow all instructions and make sure that they use sterile water, rather than tap water, in these.

#### **SLIDE 32**

With respect to water fountains, in general, the size of water droplets associated with these fountains are relatively large and therefore less respirable than those associated

with misting devices. However, even decorative water fountains may be a source of *Legionella*-contaminated aerosols which can be inhaled by persons standing nearby. A recent North Carolina case involved a man who traveled to Florida during the 10 day period prior to onset of symptoms. A detailed history of his out-of-state activities revealed the presumptive source of his exposure – a home and garden show which showcased many decorative water fountains.

### **SLIDE 33**

In 2005, an outbreak of Legionnaires' Disease in Rapid City, South Dakota was epidemiologically linked to a decorative water fountain in the lobby of a restaurant. Eighteen cases were identified. A case control study of the first 13 cases determined that the decorative water fountain in the restaurant was the most likely source of exposure to the outbreak strain.

### **SLIDE 34**

Car wash facilities may be contaminated with *Legionella* species. In June, 2010, 9 cases of Legionnaires' disease were associated with a car-washing machine in a Spanish neighborhood. In 2008, an outbreak of Legionnaires' disease was associated with a car wash in the state of Victoria, Australia.

### **SLIDE 35**

Let's move now to case investigation and filling out the surveillance form. In addition to the standard demographic information collected on each case, it is important to document the signs and symptoms and the laboratory method of diagnosis. One of the most common errors is to not specify whether the legionellosis case was Legionnaires' disease or Pontiac Fever. Remember, Legionnaires' disease requires radiographically or clinically documented pneumonia in addition to laboratory criteria. Classify the case as "confirmed" or "probable" based on the case definition. Determine what predisposing conditions, if any, the case had. Determine what treatment was given and the clinical outcome. In order to determine possible sources of exposure, the patient or another knowledgeable person will need to be questioned carefully regarding activities during the period of interest, 2-10 days prior to the onset of symptoms. These include travel and exposure to recreational or other water sources which might be a source of inhalation exposure to *Legionella* via aerosolized mists. Local environmental health staff and industrial hygiene staff in the state Occupational and Environmental Epidemiology Branch may be helpful in determining waterborne sources of exposure, especially in outbreak situations. Exposure sources in travel-associated cases are often difficult to ascertain unless there is an outbreak or the case remembers a suspect water-associated exposure scenario during the period of interest. If a travel-associated source of exposure is suspected (e.g. a spa, whirlpool or pool at a hotel or other facility), the establishment should be contacted and the nature of the suspect exposure reported to management. If the establishment is out of state, the CD Branch should be notified to determine the best method to report this potential exposure to public health authorities out of state. Most importantly, make sure the case was not a hospital inpatient or outpatient during the period of interest. A single case of suspected nosocomially-

acquired legionellosis needs to be reported to hospital infection control and investigated immediately.

**SLIDE 36**

Preventive measures for legionellosis include proper cleaning and maintenance of cooling towers, raising the temperature of hot water systems to 60 C or higher and preventive maintenance, cleaning and inspection of hot tubs and spas, and not using tap water for respiratory therapy devices. Some hospitals routinely culture their water supply system following a nosocomial outbreak. As mentioned previously, routine environmental surveillance cultures are necessary to ensure long-term disinfection. Copper/silver ionization systems have been found to be the best long-term disinfection method for hospitals.

**SLIDE 37**

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**SLIDE 38**

CDC link