

Legionnaires' Disease

by

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Abstract

Legionnaires' disease is an infectious disease caused by a gram negative bacillus called *Legionella pneumophila*. This bacterium is found in the natural environment and normally conducts its life cycle by infecting amoebas. *L. pneumophila* can also infect humans and reproduce inside monocytes, alveolar macrophages, and polymorphonuclear leukocytes. The signs and symptoms of Legionnaires' disease include: fever, chills, cough, headache, malaise, confusion, and pneumonia. There are approximately 8,000-18,000 persons diagnosed with Legionnaires' disease each year in the United States.

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Introduction

In the summer of 1976, there was an outbreak of a previously unknown pneumonia that made news headlines throughout the world. This outbreak occurred at an American Legion Convention hosted at the Bellevue Stratford Hotel in Philadelphia. There were 221 people who contracted the previously unknown type of bacterial pneumonia. Thirty four people subsequently died from the pneumonia. The bacterium was identified in 1977 when the investigators of the Center for Disease Control in Atlanta were able to isolate the bacterium from the infected patients and also the air conditioning system of the Bellevue Stratford Hotel. The bacterium was named *Legionella pneumophila* (Roy 2002). *L. pneumophila* is a gram negative

bacillus that is found commonly in the natural environment. These bacteria enter amoebas, in the same manner as they enter human lung cells, to conduct their life cycle in the natural environment. *L. pneumophila* is able affect humans because it is more resistant to chlorine than other gram negative bacteria (Nester et al 2001). Thus, *L. pneumophila* reproduces very well in warm stagnant waters and has been cultured from the plumbing of warm water systems, cooling towers, and air conditioning systems of buildings (MD Consult 2002). Cases of Legionnaires' disease have been attributed to the respiration of contaminated aerosols from air conditioners, nebulizers, showers, and whirlpools (Nester et al. 2001). Approximately 8,000-18,000 people in the United States are afflicted with Legionnaires' disease each year (MD

Consult 2002). The highest percentage of Legionnaires' disease occurs during the summer months because this is the time of year when air conditioning systems in large buildings are used the most (NIEHS 2002). Legionnaires' disease is not spread through direct contact, but it can be spread through drinking contaminated liquids or inhaling the bacterium after someone has coughed or sneezed. Outbreaks are usually confined due to the chance of inhaling the bacterium after someone has coughed or sneezed is low because the bacteria are in such a low concentration. Outbreaks usually occur when a water system has become infected with very high concentrations of *L. pneumophila*. People with exposure to the contaminated water system become infected with *L. pneumophila*, and can develop Legionnaires' disease (MD Consult 2002).

Signs, Symptoms, and Risk Factors

There are many signs and symptoms that occur due to infection of *L. pneumophila*. The signs and symptoms include: fever, chills, cough, headache, malaise, confusion, and pneumonia (NIEHS 2003). Approximately 25% of patients will also experience symptoms such as nausea, vomiting, diarrhea, and abdominal pain (Nester et al 2001). Many Legionnaires' disease patients, who have been treated and released from hospitals, will often have lingering symptoms that include fatigue, energy loss, and difficulty concentrating for several months following treatment (Lin 2002). The death rate of people who contract Legionnaires' disease is between five and fifteen percent (NIEHS 2003). Even though the mortality rate for Legionnaires' disease seems high, patients who do not have any underlying health problems and are treated with appropriate antibiotics at the onset of pneumonia have very high recovery rates. Patients who have weakened immune systems are at high risk

for dying from Legionnaires' disease. Patients with weakened immune systems include patients with cancer, renal disease, AIDS, and organ transplant recipients. Even though patients who have weakened immune systems would seem to be the likely population to have the highest incidences of Legionnaires' disease, the most common risk factor of persons who contracted Legionnaires' disease was heavy cigarette smoking (Lin 2002).

Diagnosis

Symptoms of Legionnaires' disease usually appear within two to ten days after exposure to *L. pneumophila*. The most common symptoms of Legionnaires' disease include very high fever and pneumonia (Lin 2002). *L. pneumophila* detection requires very specific tests which are not normally ordered when a patient presents with symptoms of fever or pneumonia. So, physicians have to be aware of *L. pneumophila* to order the specific tests needed to diagnose Legionnaires' disease (MD Consult 2003). *L. pneumophila* requires a very specialized media called *Legionella* media to be cultured. An antibody test can be conducted on a patient's blood sample. The antibodies will bind to the *L. pneumophila*, if present, in the patient's blood. Then, the antibodies can be detected using a fluorescent microscope. There is also a urine antigen test available that can detect the presence of *L. pneumophila* in the urine (Lin 2002).

Treatment

L. pneumophila is a type of bacterial that makes a special enzyme called β -lactamase. This enzyme is able to break down β -lactam rings, which are the active ingredients of many penicillin and cephalosporin based antibiotics. When the β -lactam ring is broken down, then the bacteria become resistant to these types of antibiotics (Nester et al 2001). Many other types of antibiotics,

which are usually effective against other types of bacteria that cause pneumonia, are not effective against *L. pneumophila*. The reason why most antibiotics are not effective against *L. pneumophila* is because most antibiotics cannot enter the respiratory tract cells or alveolar macrophages. Newer classes of antibiotics have become available to treat Legionnaires' disease. The newer classes are called macrolides and quinolones. The macrolides include azithromycin, and the quinolones include ciprofloxacin, levofloxacin, and gemifloxacin, and moxifloxacin. These drugs are very effective in treating Legionnaires' disease because they are able to penetrate the respiratory tract cells and alveolar macrophages to kill the *L. pneumophila* where it is located (Lin 2002).

Mechanism of Entry into Cells

L. pneumophila is an intracellular pathogen that enters into human monocytes, alveolar macrophages, and polymorphonuclear leukocytes in order to replicate. The mechanism of entry is unique to *L. pneumophila*. This type of phagocytosis has been termed as coiling phagocytosis or pseudopod coiling (Horwitz 1984). When *L. pneumophila* enter the cells, they cause the cytosol to swirl around the enveloped bacteria. This phenomenon appears as if the bacteria are rolling inside the cell while coils of cytosol are formed around each bacterium. Coiling phagocytosis occurs with live and also formilin-killed, glutaraldehyde-killed, and heat-killed *L. pneumophila* (Horwitz 1984). *L. pneumophila* is endocytosed by host macrophages. The macrophages secrete complement (C3). The C3 will bind to the major outer membrane protein (MOMP) of *L. pneumophila*. The complement receptors, CR1 and CR3, present on the host cell, bind to the C3b and cleave it into the active form C3bi (Horwitz 1992). The receptor-ligand

interaction of CR1 and CR3 with C3bi initiates pseudopod coiling by activating tyrosine kinase and protein kinase C. The activation of these two enzyme initiates the polymerization of actin and promotes the bacteria's entry into the cell (Coxon et al 1998). Upon entry into the host cells, *L. pneumophila* forms vacuoles that move through the cytosol. After approximately one hour after entry into the cells, the vacuoles become surrounded by smooth vesicles and mitochondria. Within four hours after entry into the host cell, the vacuoles are completely surrounded by rough vesicles and mitochondria. Then approximately eight hours after entry, the vacuoles are completely surrounded by the host cell ribosomes (Horwitz 1983). Then the ribosome-lined vacuoles enter the host cells' endoplasmic reticulum (ER). Once the vacuole is inside the ER, then the *L. pneumophila* is safe from lysosomal degradation. Lysosomes are cellular organelles that breakdown vacuoles containing bacteria. It is believed that the *L. pneumophila* evade lysosomes because their vacuoles are surrounded by cellular organelles such as: smooth vesicles, mitochondria, and ribosomes. In addition to being safe from lysosomal degradation while inside the ER, the ER contains a rich supply of peptides that are the energy source of multiplying *L. pneumophila* (Roy and Tilney 2002). Replication occurs while inside the ER. The generation time of *L. pneumophila* is approximately two hours. Eventually the bacteria cells become so numerous that they cause the host cell to lyse. These bacteria will invade other cells and the process will continue (Horwitz 1983).

Conclusion

An outbreak of Legionnaires' disease is potentially a very dangerous situation because it could cause a large number of

deaths if patients are not treated quickly and appropriately. Physicians should always consider Legionnaires' disease when an outbreak of pneumonia occurs. Also, Legionnaires' disease should be included in a differential diagnosis if a patient has pneumonia. Specific tests are available in order to diagnose Legionnaires' disease, and antibiotics are very effective in treating Legionnaires' disease by killing *L. pneumophila* (Lin 2002).

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