

A. Agent

Legionella is a genus of gram-negative bacterium causing legionellosis that include more than 58 different species. Twenty-five of those species are linked to human disease, with *Legionella pneumophila* being the most common. Among the 18 serogroups of *L. pneumophila*, *L. pneumophila* serogroup 1 is responsible for the majority of human infection¹.

B. Clinical Description

Legionellosis is an infection varying in severity from a mild flu-like illness called Pontiac fever to a severe and sometimes fatal lung infection (pneumonia) called Legionnaires' disease. Although extremely rare, legionellosis may also manifest at sites outside of the lungs, called extrapulmonary legionellosis. Signs and symptoms of legionellosis typically include fever, cough, myalgia, chills, weakness and headache. Legionnaires' disease however, is distinctively characterized by pneumonia and symptoms associated with pneumonia. Legionnaires' disease may also cause symptoms of the gastrointestinal and central nervous system such as diarrhea, nausea and confusion. Legionnaires' disease has a case-fatality rate of 10%. Pontiac fever is not associated with pneumonia and cases usually recover in 2-5 days without treatment¹.

C. Reservoirs

Legionella bacteria is commonly found in freshwater water sources (lakes, ponds, rivers, and moist soil) but can become a significant public health concern in man-made water systems under conditions that allow the bacteria to proliferate and reach high concentrations. Warm and stagnant water encourages the presence of biofilms, organic sediment, scale and other microorganisms that can provide the *legionella* with nutrients and protection against unfavorable conditions. Optimal legionella growth occurs between 77-113° F.

Outbreaks commonly are associated with buildings or structures that have complex water systems, like hotels and resorts, long-term care facilities, hospitals, and cruise ships.

For more information on common reservoirs in hospital settings, see <https://www.cdc.gov/legionella/wmp/healthcare-facilities/healthcare-wmp-faq.html>.

D. Mode of Transmission

Legionella is transmitted to humans when contaminated water is aerosolized and inhaled into the lungs. *Legionella* bacteria become suspended in water vapor created by shower heads, decorative fountains, misters, hot tubs, and cooling towers, to name a few. Less frequently, transmission can occur via aspiration of *Legionella*-containing water. Legionellosis is not spread via person-to-person transmission^{1,4}.

Health care-associated infections can be related to contamination of the hot water supply. Legionnaires' disease should be considered in the differential diagnosis of patients who develop pneumonia during or after their hospitalization^{1,4}.

E. Incubation Period

The incubation period for Legionnaires' disease is typically 2 to 10 days, with an average of 5 to 6 days but can occur up to 26 days. For Pontiac fever, the incubation period is generally shorter with a range of 1 to 3 days but can be as short as 4 hours¹.

F. Period of Communicability

None

G. Susceptibility and Resistance

Most healthy people exposed to *Legionella* do not get sick. The percentage of people acquiring Legionnaires' disease after exposure to an outbreak source is < 5%. Certain populations are at a higher risk of developing this disease including people with underlying chronic illness or immunocompromised patients. Factors that increase the risk of illness include ²:

- Age; 50 years or older
- Smoking
- Chronic lung disease (chronic obstructive pulmonary disease, asthma or emphysema)
- Weakened immune systems (immunosuppressive drugs, chemotherapy, transplant recipients)
- Chronic and underlying illnesses (cancer, diabetes, kidney failure, or liver failure)

H. Treatment¹

Patients with Legionnaires' disease should receive antimicrobial agents. Intravenously administered azithromycin or levofloxacin (or another respiratory fluoroquinolone) is recommended. Once the patient is improved clinically, oral therapy can be substituted. Doxycycline is an alternative agent; however, *Legionella longbeachae* often is resistant (this species is common in some geographic areas such as Australia and New Zealand). Duration of therapy is 5 to 10 days for azithromycin and 14 to 21 days for other drugs, with the longer courses of therapy for patients who are immunocompromised or who have severe disease.

Antimicrobial treatment for patients with Pontiac fever is not recommended, since symptoms result from host inflammation (not bacterial replication) and, thus, is self-limiting.

Disease Management

I. Clinical Case Definition³:

Legionellosis is associated with three clinically and epidemiologically distinct illnesses: Legionnaires' disease, Pontiac fever, and Extrapulmonary legionellosis. Clinical criteria for each of these illnesses is described below:

Clinical Compatibility	Legionnaires' disease	Pontiac fever	Extrapulmonary legionellosis
Pneumonia (clinical or radiographic)	Yes	No	No

Other clinical features	<ul style="list-style-type: none"> • Fever, myalgia, and cough are typical but not required • Additional symptoms include shortness of breath, headache, confusion, nausea and diarrhea. 	<ul style="list-style-type: none"> • Flu-like illness without pneumonia • Often with fever, chills, headache, myalgia, fatigue, malaise • Less often with cough or nausea 	<ul style="list-style-type: none"> • Clinical evidence of disease at an extrapulmonary site (outside the lungs) with endocarditis, wound infection, joint infection, graft infection.
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Laboratory Criteria for Diagnosis³

Confirmed:

- Isolation of any **Legionella organism** from lower respiratory secretions, lung tissue, pleural fluid, or extrapulmonary site by **culture** on selective media.
- Detection of any **Legionella species** from lower respiratory secretions, lung tissue, pleural fluid, or extrapulmonary site by a **validated nucleic acid amplification test (PCR)**.
- Detection of **Legionella pneumophila serogroup 1** antigen in urine using validated reagents via **urinary antigen test**.
- Seroconversion, a fourfold or greater rise in specific serum antibody titer to *Legionella pneumophila* serogroup 1, using validated reagents.

Supportive:

- Seroconversion, a fourfold or greater rise in antibody titer to specific species or serogroups of *Legionella* other than *L. pneumophila* serogroup 1 (e.g., *L. micdadei*, *L. pneumophila* serogroup 6).
- Seroconversion, a fourfold or greater rise in antibody titer, to multiple species of *Legionella* using pooled antigen.
- Detection of specific *Legionella* antigen or staining of the organism in lower respiratory secretions, lung tissue, pleural fluid, or extrapulmonary site associated with clinical disease by direct fluorescent antibody (DFA) staining, immunohistochemistry (IHC), or other similar method, using validated reagents.

Case Classification	
Confirmed	A clinically compatible case that meets at least one of the confirmatory laboratory criteria.
Probable	<ul style="list-style-type: none"> • Legionnaires' Disease: A clinically compatible case with an epidemiologic link during the 10 days before onset of symptoms. • Pontiac fever: A clinically compatible case with an epidemiologic link during the 3 days before onset of symptoms.
Suspect	A clinically compatible case that meets at least one of the supportive laboratory criteria.

Travel-associated	<ul style="list-style-type: none"> • Definite: A case that has a history of spending the entire incubation period away from home, either in the same country of residence or abroad. <ul style="list-style-type: none"> o Legionnaires' disease - 2 to 10 days prior to the onset of symptoms o Pontiac fever - 0 to 3 days prior to the onset of symptoms • Possible: A case that has a history of spending at least one night away from home, either in the same country of residence or abroad, in the incubation period prior to onset of illness.
Healthcare-associated	<ul style="list-style-type: none"> • Definite: A case with overnight (inpatient) stay at one or more healthcare facilities throughout the entire incubation period. <ul style="list-style-type: none"> o Legionnaires' disease - 2 to 10 days prior to onset of symptoms o Pontiac fever - 0 to 3 days prior to onset of symptoms • Possible: A case with overnight (inpatient) stay at one or more healthcare facilities during the incubation period but not during the entire incubation period, or that is epidemiologically linked to a healthcare facility during an outbreak investigation.

J. Import Status

Import status reflects where the *legionella* infection was acquired: in county, in state, international, out of county but in Arizona, out of state but in the U.S., or location of infection is unknown. Mark as bi-national if exposure occurred in Canada or Mexico. For more information, please refer to the MEDSIS User Guide. You can find the guide in MEDSIS Resources > MEDSIS Documentation > User Guides. However, since *Legionella* is endemic here in AZ, it is unclear if cases are definitively imported.

K. Laboratory Testing:

Laboratory diagnosis is important since pneumonia caused by *Legionella* is clinically indistinguishable from other pneumonias. The CDC recommends *Legionella* testing when a person has pneumonia or symptoms associated with pneumonia. Five diagnostic tests are validated for diagnosing Legionellosis including the urine antigen test (UAT), culture, PCR, paired serology, and direct fluorescent antibody (DFA) test. The preferred diagnostic tests are culture of lower respiratory secretions (sputum, bronchoalveolar lavage) on selective media **and** the Legionella UAT. Serological assays can be nonspecific and are not recommended in most situations. **Best practice is to obtain both sputum for culture and urine for the urinary antigen test concurrently.** Sputum should ideally be obtained prior to antibiotic administration, but antibiotic treatment should not be delayed to facilitate this process. ²

Advantages and Disadvantages for Each Diagnostic Test

TEST	ADVANTAGES	DISADVANTAGES
Culture* (of lower respiratory secretions, lung tissue or pleural fluids)	<ul style="list-style-type: none"> • Detects all species and serogroups • Clinical and environmental isolates can be compared • Confirmatory laboratory evidence for <i>legionella</i> organism 	<ul style="list-style-type: none"> • Technically difficult • Slow (>5 days to grow) • Dependent on very specific parameters • Sensitivity highly dependent on technical skill • Affected by appropriate antibiotic treatment

		<ul style="list-style-type: none"> Requires BCYE agar, which some laboratories may not have readily available
Urinary Antigen	<ul style="list-style-type: none"> Rapid (same day) <i>Legionella</i> antigens detected in urine as soon as 1 to 3 days after infection Can detect <i>Legionella</i> antigen days to weeks after antibiotic therapy Confirmatory laboratory evidence for <i>L. pneumophila</i> serogroup 1 (Lp1) (accounts for up to 84% of cases) 	<ul style="list-style-type: none"> Can only be used to detect Lp1 Does not allow for molecular comparison to environmental isolates
Serology	<ul style="list-style-type: none"> Possible to detect species and serogroups other than Lp1 Confirmatory laboratory evidence for Lp1 Supportive laboratory evidence for other types of <i>Legionella</i> 	<ul style="list-style-type: none"> Requires two samples collected 3-6 weeks apart. Must show a fourfold or greater rise in antibody titer between acute and convalescent sera samples collected 3 to 6 weeks apart Approximately 5 to 10% of the population has titer 1:≥256 (single acute phase antibody titers of 1: ≥256 do not discriminate between cases of Legionnaires' disease and other causes of community-acquired pneumonia)
DFA	<ul style="list-style-type: none"> Rapid can detect legionella in respiratory secretions and tissue samples(usually lung tissue) Possible to detect species and serogroups other than Lp1 	<ul style="list-style-type: none"> Technically difficult Reagents may be difficult to obtain Qualitative results Supportive laboratory evidence
PCR* (of lower respiratory secretions, lung tissue or pleural fluids)	<ul style="list-style-type: none"> Rapid Can be performed on pathologic specimens (usually lung tissue) Possible to detect species and serogroups other than Lp1 Confirmatory laboratory evidence 	<ul style="list-style-type: none"> Assays vary by laboratory and commercial availability may be limited in the United States Respiratory Pathogen Panels

<https://www.cdc.gov/legionella/clinicians/diagnostic-testing.html>

***Please send *Legionella* isolates from clinical specimens (sputum, transtracheal aspiration, non-respiratory sites, etc.) to ASPHL for identification within one working day⁶.** ASPHL uses RT PCR to detect *Legionella* spp., *Legionella pneumophila*, and *Legionella pneumophila* serogroup 1 and performs WGS sequencing on all *Legionella* isolates received. Prior notification to the

laboratory is requested. Isolates should be shipped on BCYE slants or plates at 4°C on cold packs. For more information on isolate submission, see [ASPHL's Guide to Laboratory Services](#)

L. Assessing Laboratory Results:

Laboratory results must be interpreted alongside medical history, physical exam, and other tests such as imaging.

Negative *legionella* results do not rule out a *legionella* infection. A *legionella* species other than the one tested may be the cause of the infection and additional testing may be required.

A positive urine antigen test (UAT), confirms a *Legionella pneumophila* serogroup 1 (Lp1) infection and if the person has symptoms consistent with pneumonia, then it is likely that the person has Legionnaires' disease. If the UAT is negative, the person may be infected by a *legionella* species other than Lp1 and a different test may be in order.

A positive *legionella* culture confirms a *legionella* infection and any species detected in the culture is identified as the cause.

A positive PCR result for the presence of a specific DNA sequence indicates a confirmed *legionella* infection with the species as the cause.

A positive DFA result is accepted as supporting laboratory evidence for Legionellosis. In conjunction with clinical evidence, a patient would be classified as suspect.

For additional information, please see CDCs [Legionnaires' Disease Diagnosis, Treatment, and Prevention](#).

M. Outbreak Definition

Legionnaires' disease and Pontiac fever outbreaks occur when **two or more people are exposed to *Legionella* in the same place and get sick at about the same time**. Outbreaks are commonly associated with buildings or structures that have complex water systems, like hotels and resorts, long-term care facilities, hospitals, and cruise ships⁷.

In a healthcare setting (acute care facility, long-term care facility, etc.), one documented case should be investigated as a potential outbreak/healthcare-associated infection until possible additional cases have been ruled out or until a source has been identified and decontaminated. For additional assistance please contact hai@azdhs.gov and legionella@azdhs.gov.

Investigation Guidelines

N. Reporting Time Frame:

Laboratories

Laboratories must submit a report within one working day after obtaining a positive test result and submit an isolate of the organism for each positive culture to the Arizona State Laboratory within one working day.

Providers

Providers must submit a report within one working day after a case or suspect case is diagnosed, treated, or detected.

Local Health Departments

Local health agencies must submit an epidemiologic investigation report within 30 calendar days after receiving a report under R9-6-202 or R9-6-203 or notification by the Department.

O. Forms

Investigation forms are available to assist with the investigation. If the case is travel-associated, the CDC case report form is required. Please attach completed forms to the MEDSIS case.

- [ADHS Communicable Disease Report Form](#) (for providers)
- [CDC Legionellosis Case Report Form](#) (required for notifying CDC of travel-associated cases with out-of-state exposure)
- [CDC Legionellosis Case Report EXTENDED Form](#) (optional for notifying CDC of travel-associated cases with out-of-state exposure)
- [CDC Legionnaires' Disease Cruise Ship Questionnaire](#)

P. Case Investigation Steps

Confirm Diagnosis

- Obtain clinical information from the health provider/medical facility
- Obtain laboratory results
- Verify laboratory and clinical criteria meet suspect or confirmed case definition. Refer to clinical case definition and laboratory criteria
- Facilitate forwarding isolates to the Arizona State Public Health Lab.

Interview Case

- Interview case or case's proxy (spouse, adult offspring, parent, etc.) to establish source of infection or possible exposures
 - Review patient's movements in the 2-10 days before onset.
 - Be sure to record a thorough travel history in the MEDSIS travel table. Include dates of travel, address and room number of lodging.
- Epidemiological investigation reports should be submitted in MEDSIS by completing the entire DSO and travel table. Note, the following fields must be filled to "complete" the investigation form:
 - Onset date
 - Diagnosis:
 - Legionnaires' Disease
 - must have pneumonia (clinical or radiographic)
 - may also have fever, myalgia, and cough. These symptoms are typical but not required; additional symptoms (e.g., shortness of breath, headache, confusion, nausea, diarrhea) may be present.
 - Pontiac Fever
 - A milder illness without pneumonia.
 - A flu-like illness, often with fever, chills, headache, myalgia, fatigue, malaise; less often with symptoms such as cough or nausea.
 - Extrapulmonary
 - Clinical evidence of disease at an extrapulmonary site. *Legionella* can cause disease at sites outside the lungs (for example,

associated with endocarditis, wound infection, joint infection, graft infection).

Determine Exposure Classification

- Travel association
 - In the 10 days before onset did the patient travel or stay overnight somewhere other than usual residence (excluding a healthcare setting)?
 - Definitely travel-associated: History of spending the entire incubation period away from home (≥ 10 days) prior to onset of symptoms.
 - Possibly travel-associated: History of spending at least one night away from home in the incubation period (2-10 days) prior to onset of symptoms.
 - Not travel-associated: No history of travel with an overnight stay in the incubation period (2-10 days) prior to onset of symptoms.
- Healthcare association
 - Healthcare Information Inpatient ONLY (within 10 days before onset)
 - Definitely HAI: Patient with overnight (inpatient) stay at one or more healthcare facilities during the entire incubation period (2 to 10 days before onset of symptoms for Legionnaires' disease or 0 to 3 days for Pontiac fever).
 - Possibly HAI: Patient with overnight (inpatient) stay at one or more healthcare facilities during the incubation period (2 to 10 days before onset of symptoms for Legionnaires' disease or 0 to 3 days for Pontiac fever) but not during the entire incubation period.
 - Not HAI: A patient with no overnight (inpatient) healthcare visits in the incubation period (2-10 days prior to onset of symptoms for Legionnaires' disease or 0 to 3 days for Pontiac fever).
 - Pneumonia
 - Did the patient have clinical/radiographic pneumonia?
 - Nebulizer
 - Within the 10 days before onset, did the patient use a nebulizer, CPAP, BiPAP or any other respiratory therapy equipment?
- **If the case is travel-associated, please fill out the CDC report form** with as much information as possible and attach to the MEDSIS case.
 - [Legionellosis Case Report Form](#)
 - This information is used to notify CDC and other states of possible exposure to *legionella* within that state in order to help identify any possible clusters.
- If the case is healthcare-associated, patient hospitalized or resides in a healthcare facility continuously for ≥ 10 days before onset of *Legionella* infection, contact hai@azdhs.gov and legionella@azdhs.gov for assistance.

Conduct Contact Investigation

- Others are only at risk if they are exposed to the same source of *legionella* exposure.
- An enhanced investigation should take place to identify and confirm the source(s) of exposure and identify other cases among groups of people at high risk or in healthcare settings.

Isolation, Work and Child Care Restrictions

Standard Precautions are recommended.

Case Management

- Provide education on reservoirs for *Legionella* and how to reduce possible risks and home exposures in the future.
- If the case is healthcare-associated, surveillance efforts for additional cases should be enhanced by the infection control official at the facility. See *Special Situations* section below for more information.

Contact Management, including Susceptible Contacts

None; unless required as part of an active investigation with the state and/or CDC.

Environmental Measures

- Should additional cases be identified with the same source of exposure within a 12 month period of time, an outbreak investigation should be considered including environmental activities to confirm the source(s).
 - [Processing Environmental Samples: CDC Laboratory Protocol](#)
 - [CDC Sampling Procedure and Potential Sampling Sites](#)
- It should be noted that in the absence of clinical disease, routine environmental testing is not recommended. Low levels of *legionella* bacteria can and do exist in water systems without resulting in disease.

Q. Outbreak Investigation Guidelines

Refer to the [ADHS Outbreak Investigation Guide](#) for information on managing an infectious disease outbreak investigation. For comprehensive guidance on conducting a Legionnaires' disease outbreak investigation, consult the *ADHS Legionnaires' Disease Outbreak Response Protocol*.

- Refer to the general outbreak guidelines section for details on investigating an outbreak or healthcare acquired infection and utilize the ADHS outbreak definition.
- If case(s) meets outbreak definition, report suspected outbreak to ADHS via outbreak module protocol (see general outbreak guidelines section for details).
- [Case Investigation Prioritization Matrix](#)
- Contact hai@azdhs.gov and legionella@azdhs.gov for assistance.

Special Situations

R. Special Situations

The majority of Legionnaires' disease outbreaks are associated with travel (hotels, resorts, cruise ships) or healthcare settings (hospitals, long-term care facilities).² Because health-care settings represent highly susceptible populations and outbreaks among travel-related cases are difficult to detect, careful collection and reporting information ensures that steps can be taken to prevent further exposure. Contact hai@azdhs.gov and legionella@azdhs.gov for assistance.

Hospitals, Healthcare Facilities

- Healthcare-associated legionellosis³:
 - **Definite:** A case with overnight (inpatient) stay at one or more healthcare facilities throughout the entire incubation period.

- for Legionnaires' disease of 2 to 10 days
 - for Pontiac fever of 0 to 3 days before the onset of symptoms
 - **Possible:** A case with overnight (inpatient) stay at one or more healthcare facilities during the incubation period but not during the entire incubation period, or that is epidemiologically linked to a healthcare facility during an outbreak investigation.
- For a single case of healthcare-associated *legionella*:
 - Communicate with facility Infection Preventionist
 - Retrospective case finding (lab lookback)
 - 12 months prior to onset date
 - Prospective surveillance
 - 6 months after onset date
 - Test healthcare-associated pneumonia cases for *legionella* by culture and urine antigen
 - Review facilities water management plan to identify any gaps or measurements outside of normal range that could have led to *legionella* growth
 - [Toolkit: Developing a Water Management Program](#)

Travel, Hotels/ Resorts, Cruises

- Arizona residents with out-of-state exposure to legionella need to be notified to the CDC. Complete one or more of the following case report forms and attach to the MEDSIS case.
 - [Legionellosis Case Report Form](#)
 - [Legionellosis Case Report Form](#) (extended)
 - [Legionnaires' Disease Cruise Ship Questionnaire](#) (section 1)
- For residents of other states who acquired legionellosis while traveling in Arizona, ADHS receives notifications from CDC and conveys them to the LHD in which the travel accommodation is located for their records.
 - LHD should keep record of travel notifications and follow up with facilities as needed if multiple cases are found to be associated with the same facility.
- Contact legionella@azdhs.gov for assistance

References

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5. Arizona Department of Health Services. In: Case Definitions for Reportable Communicable Morbidities: 2022. 2022 [cited 2022Feb24]; Available from:

<https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf>

6. ARIZONA LABORATORY REPORTING REQUIREMENTS
<https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/communicable-disease-reporting/lab-reporting-requirements.pdf>
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Additional Information & Resources

Centers for Disease Control and Prevention:

- Legionellosis Resource Site
 - <http://www.cdc.gov/legionella/index.html>
 - Investigation Tools for Clusters and Outbreaks of Disease
- <https://www.cdc.gov/legionella/health-depts/inv-tools-single/travel-identify-report.html>
Legionellosis – United States, 2000 – 2009 (MMWR, 08/2011)
 - http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6032a3.htm?s_cid=mm6032a3_e%0d%0a

Council of State and Territorial Epidemiologists

- Legionellosis Position Statement
 - <http://www.cdc.gov/legionella/health-depts/inv-tools-single/cste-position-statement.html>

Hospital-Associated Infection Resources

- CDC Special Considerations for Healthcare Facilities
 - <https://www.cdc.gov/legionella/wmp/healthcare-facilities/index.html>
- Water Management in Healthcare Facilities
 - <https://www.cdc.gov/legionella/wmp/healthcare-facilities/water-mgmt-facilities.html>
- Preventing Legionnaires' Disease: A Training on Legionella Water Management Programs (PreventLD Training)
 - <https://www.cdc.gov/nceh/ehs/elearn/prevent-LD-training.html>
- Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). MMWR 2004; 53(RR03):1-36.
 - <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5303a1.htm>