

MDHHS Legionellosis Surveillance and Investigation Protocol

Note:

While this document is currently finalized, changes driven by national programs are anticipated in the near future. These changes include the provision of communications strategies and recommendations as well as modifications to the criteria used to determine case definitions.

This document will be updated as those become available.

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Legionellosis Overview

Occurrence

An estimated 8,000 to 18,000 cases of Legionnaires' disease are hospitalized each year in the United States. In general, the number of cases reported has been on the rise over the past decade. This may reflect a true increase in the frequency of disease due to several factors (e.g., older U.S. population, more at-risk individuals, aging plumbing infrastructure, climate). It may also be a result of increased use of diagnostic testing or more reliable reporting. Cases may occur throughout the year but are more common in the summer and fall. Warmer temperatures and increases in precipitation are associated with an increase in cases. The rate of reported Legionnaires' disease cases in the U.S. tends to be higher in the Mid-Atlantic and Northeastern Central regions than in the south and west.

Clinical Description

Legionellosis is associated with two clinically and epidemiologically distinct illnesses:

- **Legionnaires' disease**, which is characterized by fever, myalgia, cough, and clinical or radiographic pneumonia
- **Pontiac fever**, a milder illness without pneumonia

Causative Agent

Legionellae species are Gram-negative, non-spore-forming, rod-shaped, aerobic bacilli. There are over 50 species within the family Legionellaceae; species *Legionella pneumophila* serogroup 1 is most commonly associated with disease. Other types of *Legionella* (e.g., *micdadei*, *bozemanii*, *longbeach*, *dumoffi*, etc.) have been isolated primarily from immunosuppressed patients.

Reservoir

Legionellosis is a waterborne disease. Man-made water supplies that aerosolize water, such as potable water systems, cooling towers, whirlpool spas, and decorative fountains, are the common sources for transmission. Conditions that are favorable to *Legionella* growth include warm water temperatures, stagnation, scale and sediment, and low biocide levels.

Incubation

The incubation period for Legionnaires' disease is most commonly 2–10 days, with an average of 5–6 days, but has been reported to be up to 26 days in rare cases. For routine surveillance

purposes, exposure histories are collected for the 2–10 days prior to onset. However, in outbreak settings where it is important to consider a wide range of possible sources, use of a 14-day incubation period is standard. But public health officials have reported incubation periods up to 26 days under rare circumstances that may be related to the immune status of the patient at the time of the exposure or the nature of the exposure.

Transmission

People are exposed to *Legionella* when they breathe in a mist or vapor (small droplets of water in the air) containing the bacteria. Less commonly, *Legionella* can be spread via aspiration of drinking water into the trachea (windpipe) and lungs instead of down the digestive tract. People at increased risk of aspiration include those with swallowing difficulties. In general, *Legionella* does not spread from one person to another.

At low levels of contamination, most healthy people will not develop illness when they come into contact with the *Legionella* bacteria, or they may develop the milder form of illness, Pontiac fever.

High-Risk Groups

Most healthy people do not become infected with *Legionella* after an exposure. People at higher risk of getting sick include the following: older people (usually 50 years or older); current or former smokers; people with a chronic lung disease (e.g., chronic obstructive pulmonary disease or emphysema); people with a weak immune system from diseases like cancer, diabetes, or kidney failure; and people who take drugs that suppress (weaken) the immune system, such as after a transplant operation or chemotherapy.

Legionellosis Case Definition (CDC/CSTE 2005)

Laboratory Criteria for Diagnosis

Confirmed

- By culture: isolation of any *Legionella* organism from respiratory secretions, lung tissue, pleural fluid, or other normally sterile fluid.
- By detection of *Legionella pneumophila* **serogroup 1** antigen in urine using validated reagents.
- By seroconversion: fourfold or greater rise in specific serum antibody titer to *Legionella pneumophila* **serogroup 1** using validated reagents.

Suspected

- By seroconversion: 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).
- By seroconversion: fourfold or greater rise in antibody titer to multiple species of *Legionella* using pooled antigen and validated reagents.
- By the detection of specific *Legionella* antigen or staining of the organism in respiratory secretions, lung tissue, or pleural fluid by direct fluorescent antibody (DFA) staining, immunohistochemistry (IHC), or other similar method, using validated reagents.
- By detection of *Legionella* species by a validated nucleic acid assay (PCR).

Nearly all cases are identified by urinary antigen testing, not culture. Urinary antigen tests specifically for *L. pneumophila* serogroup 1, which causes the majority of illness. However, urinary antigen tests will be negative if the person is infected with another species or serogroup (non- pneumophila serogroup 1) of *Legionella*.

A single serum antibody titer (acute draw during illness, no convalescent draw) is not diagnostic for legionellosis. If the acute titer is 1:256 or higher, a repeat convalescent titer should be drawn 2-4 weeks after the acute titer to check for a four-fold rise in antibody levels. Studies have found up to 20% of the general population may have *L. pneumophila* serogroup 1 antibody titers of 1:128 or greater.

Lower respiratory specimen cultures are vital for linking a case to a potential environmental source, particularly in outbreak settings. Investigations of outbreaks of Legionnaires' disease rely on both clinical and environmental culture isolates.

Case Classification

Suspect: a clinically compatible case that meets at least one of the presumptive (suspect) laboratory criteria.

Confirmed: a clinically compatible case that meets at least one of the confirmatory laboratory criteria.

Travel-associated: a confirmed or suspect 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 10 days before onset of illness.

Healthcare-associated:

- **Definite healthcare-associated:** case-patient was hospitalized or a resident of a long-term care facility for the entire 10 days prior to illness onset.
- **Possible healthcare-associated:** case-patient had exposure to a healthcare facility for a portion of the 10 days prior to illness onset.

Reporting and Investigation Responsibilities

Per the Michigan Public Health Code, physicians and laboratories are required to report suspect or confirmed cases of legionellosis within 24 hours of diagnosis or discovery to the appropriate local health department (LHD).

Within 24 hours of receiving a report, the LHD will enter the case information into the Michigan Disease Surveillance System (MDSS), if not entered by the lab or physician, and begin case follow-up. The LHD will complete the disease-specific Legionellosis form in MDSS.

Additionally, MDHHS requests that all clinical isolates—and environmental isolates obtained during an outbreak investigation—be sent to the MDHHS Bureau of Laboratories for Whole Genome Sequencing (WGS). If a contractor/consultant is utilized for environmental sampling during an outbreak investigation, a special request from the LHD to obtain isolates may be required.

MDHHS Surveillance

MDHHS staff review cases reported into MDSS monthly. Run a statewide 5-year epi curve monthly to monitor for any large increase in the number of cases. If a community-acquired case has been in MDSS for more than 30 days since referral and has had no follow-up (i.e., still marked as new), contact the LHD.

MDHHS staff will monitor reported cases monthly for common exposures prior to illness onset, such as, any out-of-state travel or hospitalizations in the 10 days prior to onset.

- **Travel-associated cases**—If the case has out-of-state travel overnight to a public place (e.g., campground, hotel, etc.), MDHHS Epidemiology will report the case to the Centers for Disease Control and Prevention (CDC) at travellegionella@cdc.gov. People staying at private residences (e.g., stayed at sister's house, etc.) are not reported to CDC (exception: individuals with overnight stay at a public rental home, such as an AirBnB). Notification to CDC should include basic demographics (age, sex, residency), onset date, lab testing results, hospitalization status, if the person survived or died, where the person traveled (city, state, name of accommodations and address if available), dates of travel and dates of stay in the accommodations, details of the travel (what they did, any exposure to pools, showers, decorative fountains, hot tubs, lakes, etc.), and any information on underlying conditions that may have made the person more susceptible to infection.

- **Healthcare-associated cases**—Monitor in-state cases monthly for common healthcare exposures in the 10 days prior to illness onset. A full investigation should be performed when (1) one case of definite healthcare-associated Legionnaires' disease is identified; and (2) when two or more cases of possible healthcare-associated Legionnaires' disease are identified within 12 months of each other.

Case Investigation

Sporadic Cases

Case investigation is undertaken by the LHD where the ill individual resides. MDHHS recommends the following investigation steps at the LHD level:

- Enter the case into MDSS within 24 hours of notification if not already entered by provider or lab
- Contact the diagnosing hospital ICP or physician to:
 - Verify that the diagnosis meets the case definition (meets confirmed or suspect clinical AND laboratory criteria)
 - Verify and record the illness onset date. An accurate illness onset date is important for the determination of the patient's potential environmental exposures (if missing or as needed). In certain circumstances, the LHD medical director, attending physicians, and MDHHS may be consulted to determine an appropriate onset date.
 - Collect any additional information about the clinical course of illness.
 - Recommend additional testing, as needed (e.g., if serology is done, a convalescent serum must be drawn 2-4 weeks after the initial acute drawn).
 - Request a respiratory culture be performed on *Legionella*-specific media. If the hospital lab is uncertain about their capability or unable to perform the culture, the clinical respiratory specimen may be sent to the MDHHS Bureau of Laboratories for culture.
 - If a culture has already been performed by the hospital, any positive *Legionella* isolates should be forwarded to the MDHHS State Laboratory.
 - Note discharge date and outcome; if case still hospitalized, check back with hospital until discharge.
 - Verify whether the case was previously hospitalized, in a long-term care facility, or had other healthcare exposure during the 10 days prior to onset (if missing or as needed).
 - LHD's with a high burden of legionellosis or an LHD experiencing an increase in cases from baseline should consider completing the MDHHS Supplemental Questionnaire to identify potential exposures.

- Conduct an interview as quickly as possible with the case or proxy (family member or designee if the patient is too ill to complete an interview) and enter data into the MDSS record. Interviews should be completed and entered into MDSS within one week. If case is still hospitalized, close case as Completed-Follow-up. Complete when discharged to capture outcome and verify incubation period exposure history. Update MDSS record. Upload any medical records as attachments in the MDSS Notes section.

Suspected Outbreak or Increase in Cases

An outbreak is defined as two or more cases who have been exposed to the same hospital, long-term care facility, hotel, or job site, for example, at about the same time¹. All LHDs should follow an outbreak response protocol and a suspected outbreak should be reported within 24 hours of detection to MDHHS (Regional Epidemiologist or MDHHS Legionellosis subject matter experts). If an LHD is seeing an increase in reported cases from baseline levels, the [MDHHS Supplemental Questionnaire](#) can be used to collect additional information on potential common exposures. If there is a marked increase in cases in a county, MDHHS recommends the LHD notify providers in their area (via the Michigan Health Alert Network (HAN) and blast fax) to emphasize the collection of accurate onset dates along with *Legionella*-specific culture specimens concurrently with a urine antigen test. A culture must be collected in order to perform WGS testing and may be used to potentially link clinical and environmental specimens in identifying the likely source of an infection.

¹The timeframe for defining an outbreak may vary depending upon the circumstances. MDHHS and the CDC defines outbreaks associated with:

- travel
- [healthcare](#)
- potable water systems in other [buildings at increased risk](#) for *Legionella* growth and transmission

as two or more cases associated with the same possible source during a 12-month period. This definition increases sensitivity of outbreak detection, especially for outbreaks involving potable water, and helps account for periodic changes in risk (i.e., due to seasonality). Note that under certain circumstances, the timeframe under consideration may be shorter, such as during cooling tower outbreaks, which tend to be more explosive and of shorter duration (e.g., 3 months).

Determine the jurisdictional lead for the outbreak

- i. Localized: Single jurisdiction outbreaks** (involving 1 LHD) - These are typically point source events or otherwise contained (small-to-moderate) numbers of cases associated with a common potable water source.

Lead Agency

- The LHD in whose jurisdiction the outbreak is occurring takes the lead role in the investigation unless they are unwilling or unable to do so. As all outbreaks are reportable, the outbreak should be reported to MDHHS and a NORS Waterborne form should be completed within 60 days of the first onset of illness. The NORS Waterborne form and guidance can be found at <https://www.cdc.gov/nors/forms.html>.
- Perform epidemiologic investigation.
- Perform environmental investigations as indicated by epidemiologic information.

Develop and distribute public messaging regarding identified outbreak.

Role of MDHHS

- When notified by an LHD that a local outbreak is identified or suspected, MDHHS staff provide technical consultation and recommendations, if requested.
- Ongoing information sharing and follow-up communications with the LHD are sought and encouraged by MDHHS staff for monitoring of the outbreak, coordination of specimen collection and testing, and the associated control actions taken by the LHD, until the infection incidence returns to endemic levels. Additional assistance or guidance, including some of the steps listed below for more complex outbreaks, may be necessary on a situational basis.
- If needed additional input is needed, contact subject matter experts at the CDC Legionellosis Surveillance & Outbreak Response NCIIRD/DBD/Respiratory Diseases Branch.

- ii. Outbreaks requiring joint investigation with MDHHS support** (exceeding the resources of 1–2 LHDs). These outbreaks include moderate or substantial numbers of cases in one or two nearby jurisdictions, or alternatively an outbreak contained within one community but the exposure occurred outside of that local jurisdiction (i.e., ill persons

residing in one LHD, but exposure in another). These scenarios typically necessitate a comprehensive supporting, but *non-leading*, role by MDHHS.

Lead Agency/Agencies

- Co-led by 1–2 LHDs where the outbreak is initially centered and/or where the exposure has occurred unless they are unwilling or unable to do so.
- A NORS Waterborne form should be completed within 60 days of the first onset of illness. The NORS Waterborne form and guidance can be found at <https://www.cdc.gov/nors/forms.html>.
- Perform epidemiologic investigation.
- Perform environmental investigations as indicated by epidemiologic information.
- Develop and distribute public messaging regarding identified outbreak.

Role of MDHHS

- MDHHS provides specific technical support and resources but does not assume lead role in the investigation.
- This may transition to include a joint lead with the MDHHS if the situation becomes more extensive, or at the request of the LHDs involved.
- Upon request, MDHHS will host an initial conference call or meeting with the LHD agencies involved to share available information and to collaboratively determine the next steps and which agencies will be responsible for each action. A projected frequency schedule of additional calls (if needed) can be decided during the initial call along with who will host the subsequent call(s).
- Liaise with other partners to coordinate interagency communication and share pertinent information.
- Assist with review and analysis of collected data as requested by the LHDs involved.
- The role of the MDHHS Regional Epidemiologists' include (1) helping to assess which LHDs may request or need assistance with timely case follow-ups and questionnaire administration; (2) providing necessary assistance and resources as part of the MDHHS response.

- If needed additional input is needed, contact subject matter experts at the CDC Legionellosis Surveillance & Outbreak Response NCIRD/DBD/Respiratory Diseases Branch.

See additional steps under **Widespread: Multijurisdictional/Multistate outbreaks**, which may apply depending on the outbreak scenario.

iii. Widespread: Multijurisdictional/Multistate outbreaks within Michigan (requiring multilevel coordination)

Lead Agency

- The MDHHS may assume the lead role in overseeing and coordinating the epidemiologic investigation among multiple Michigan LHDs.

Role of MDHHS

- Per agreement between all involved LHD's, MDHHS can arrange and lead outbreak conference calls with the participating investigative teams, as needed (e.g., LHDs, healthcare facilities).
- Work with LHD investigative partners to expand surveillance for additional cases by conducting the following steps: a) enhanced or targeted review of the existing Surveillance Systems; b) issue interagency, medical community, and public notifications to stimulate reporting of potentially related cases; and c) triage calls from the lay public about compatible illnesses that may be linked to the outbreak
- Review laboratory status of each case to determine whether all laboratory-confirmed cases have applicable specimens forwarded to the MDHHS Bureau of Laboratories for further analyses and characterization. Coordinate with the LHD and MDHHS Bureau of Laboratories to contact clinical or reference laboratories and facilitate shipping of any needed specimens. For cases that are not laboratory confirmed, assess feasibility and options for testing.
- Review WGS data as applicable. Provide epidemiologic and subject matter expertise regarding Legionellosis, such as baseline frequency, seasonal fluctuations in occurrence, natural reservoirs or known sources, information regarding historical outbreak associations, and other relevant information that may guide the initial investigation. Share information with investigation partners and medical community.

- Develop case definition(s). For laboratory-confirmed outbreaks, include outbreak strain characteristics such as pathogen typing and molecular subtyping in the case definition algorithm.
- Work with LHD's to develop a working outbreak hypothesis based on information collected, and update/revise with new information as needed.
- Establish an "outbreak identifier" used in the MDSS record for each case matching the case definition. This identifier code will typically be the WGS pattern designation or name of the suspected source.
- Develop and implement investigative tools and methods as needed. These typically involve use of a [MDHHS Supplemental Questionnaire](#) or outbreak-specific questionnaire. Disseminate the tools to the investigative team(s).
- Assist LHDs with interviews and case investigations, upon request. Verify that completed outbreak and supplemental questionnaires have been uploaded to the MDSS. MDHHS will contact LHD regarding any cases without an uploaded supplemental questionnaire within three business days of MDSS case report.
- As appropriate, notify subject matter experts at the CDC Legionellosis Surveillance & Outbreak Response NCIRD/DBD/Respiratory Diseases Branch.
- For multijurisdictional outbreaks with coordination needs, outbreak investigation materials may be posted to a dedicated HAN folder [Documents/Local Health/CD Investigations/Name of outbreak] for easy access for LHD investigators (communicable disease nurses, Health Officers, Medical Directors, and Emergency Preparedness Coordinators). The materials will include the outbreak questionnaire, a listing of outbreak-related cases reported by jurisdiction, and an aggregate outbreak summary. An epi curve and map may also be provided.
- Work with Regional Epidemiologist network to assess which LHDs may request or need assistance with timely case follow-ups and questionnaire administration.
- Coordinate data collection, analyze case questionnaire data, and summarize relevant findings. Share findings among stakeholders.
- Prepare updates for MDHHS Administration and Public Information Officer, as needed, and coordinate messaging with other investigative partners (CDC, LHDs, healthcare facilities, hotels).

Environmental Samples for Testing

Because *Legionella* bacteria are common in the environment in water sources, the general understanding is that if environmental samples are taken there is a reasonable likelihood that the bacteria may be found. Without clinical specimen culture isolates from patients there is no way to definitively link environmental specimens to the clinical specimens to determine the source of the infection. In the event of a recognized outbreak, MDHHS will coordinate with the LHD to have environmental specimens collected by the LHD tested at the MDHHS Bureau of Laboratories (with approval by MDHHS Epidemiology) or help the LHD identify a private lab. Specimens should be collected after appropriate epidemiologic assessment, environmental assessment, and sampling procedures have been completed.

MDHHS cannot recommend specific private laboratories to do environmental testing at citizens' residences. MDHHS can advise individuals that there are private environmental labs that will perform this testing for a fee. Again, the individuals should be educated that *Legionella* bacteria are common in water environments at low levels. The potential for transmission of legionellosis infections depends on the strain of bacteria, level of bacterial contamination (CFUs), mode of transmission, and any underlying health conditions that may make an individual more susceptible. Single-family or small multi-family residences are not generally recognized as sources for legionellosis infections. Larger building water systems are more likely to be colonized, amplify and transmit the bacteria causing infections. The CDC maintains a website with ELITE certified laboratories in the United States that have demonstrated proficiency in the isolation of *Legionella*. This can be found at: <https://wwwn.cdc.gov/elite/Public/EliteHome.aspx>

For more information on environmental sampling during an investigation or outbreak, please see the MDHHS Legionellosis Outbreak Guide (release TBD) .

General Control and Prevention Measures

Risk of infection can be reduced through implementing control measures to remove *Legionella* from the water that has been identified as the source of infection. MDHHS staff will support LHD efforts to identify those common sources where remediation can be effective. MDHHS will work to facilitate the identification of appropriate guidance documents and/or appropriate remediation activities based on current scientific literature and best practices. MDHHS will support continued surveillance activities to assess the effectiveness of remediation. Large or complex facilities will likely need to engage an environmental consultant or company that specializes in *Legionella* remediation and building water management.

High-risk facilities should develop and utilize water management programs to reduce the risk of *Legionella* colonization and transmission within their facilities. Water management resources developed by the CDC can be found at:

<https://www.cdc.gov/legionella/wmp/index.html>

Reference and Resources

Control of Communicable Diseases Manual. Heymann. D., ed., 20th Edition. Washington, DC, American Public Health Association, 2015.

Case Definitions: CDC National Notifiable Diseases Surveillance System (NNDSS)
<https://wwwn.cdc.gov/nndss/conditions/>

CDC ELITE Program website:

<https://wwwn.cdc.gov/elite/Public/EliteHome.aspx>

CDC *Legionella* website: <http://www.cdc.gov/legionella/index.html>

Developing a Water Management Program to Reduce *Legionella* Growth and Spread in Buildings: A Practical Guide to Implementing Industry Standards. CDC. March 2016.

MDHHS Legionellosis Guidance for Clinicians and Laboratories. May 23, 2016

http://www.who.int/water_sanitation_health/dwg/admicrob4.pdf