

## LISTERIOSIS

### I. DESCRIPTION AND EPIDEMIOLOGY

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#### A. Overview

Listeriosis is an invasive disease caused by *Listeria monocytogenes*, a gram-positive coccobacillus that is ubiquitous in the environment and can be found in soil, water, sewage, vegetation, and silage. Domestic and wild mammals, birds, and humans may be asymptomatic carriers and serve as reservoirs. Listeriosis is considered an uncommon but important foodborne illness in the United States. *L. monocytogenes* can survive and grow in refrigerated temperatures, making control difficult. Listeriosis primarily affects persons who are elderly, immunocompromised, and pregnant; morbidity and mortality rates are high.

#### B. Listeriosis in California

There are an estimated 116 laboratory-confirmed cases of listeriosis reported annually in California. From 2013 through 2019 there were a total of 812 reported cases at an average rate of 0.3/100,000 population. During the surveillance period, 148 (18.2 percent) case-patients were reported to have died with listeriosis. Most cases of listeriosis are sporadic and not associated with an outbreak. However, California patients have been involved in multi-state outbreaks of listeriosis associated with cantaloupe, soft cheeses, caramel apples, frozen vegetables, and many where the source of infection remains unknown.

#### C. Symptoms and Clinical Presentation

Invasive listeriosis may present clinically as septicemia or meningoencephalitis. Symptoms may include fever, headache, stiff neck, loss of balance, and confusion, which can be preceded by diarrhea or other gastrointestinal symptoms. Invasive listeriosis has a mortality rate of about 20%, making it the third leading cause of death from foodborne illness in the U.S. Listeriosis disproportionately affects immunosuppressed patients and persons in the extremes of age; the most common clinical manifestations are bacteremia and central nervous system infections. Approximately 15% of listeriosis is pregnancy-associated. In pregnant women, listeriosis may present as mild symptoms or no symptoms at all, but may result in premature delivery, miscarriage, still birth, or infants born with complications.

#### D. Transmission

*Listeria monocytogenes* is most often transmitted through the ingestion of contaminated food. *Listeria* can be found in raw foods as well as foods that are contaminated after cooking or processing. *Listeria* can be present in deli meats, deli salads, dips and other ready-to-eat foods, hot dogs, soft cheeses (e.g., brie, camembert, blue veined, queso fresco etc.), refrigerated smoked seafood, and produce. *Listeria* is killed by cooking or pasteurization but may survive and grow in refrigerated temperatures. Transmission between mother and fetus/newborn can occur during pregnancy or delivery.

Notable outbreak vehicles included: [cantaloupe \(2011\)](#), [imported ricotta salata cheese \(2012\)](#), [commercial prepackaged caramel apples \(2014\)](#), [commercial soft cheeses \(2015\)](#), [packaged salad \(2016\)](#), and [imported enoki mushrooms \(2020\)](#).

### E. Incubation Period

The incubation period is highly variable but is generally from 3 to 70 days with a median incubation period estimated to be 3 weeks.

### F. Clinical Management

Clinical management decisions should generally be made by the patient's primary care physician or infectious disease specialist.

## II. COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS (CSTE) SURVEILLANCE CASE DEFINITION

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### A. Listeriosis Case Definition (2019)

The CSTE surveillance case definition for listeriosis can be found on the [U.S. Centers for Disease Control and Prevention \(CDC\) Surveillance Case Definitions for Current and Historical Conditions webpage](https://wwwn.cdc.gov/nndss/conditions/listeriosis/case-definition/2019/) (<https://wwwn.cdc.gov/nndss/conditions/listeriosis/case-definition/2019/>).

#### CSTE Position Statement

[18-ID-06](https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/2018ps/18-ID-06_FINAL.pdf) ([https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/2018ps/18-ID-06\\_FINAL.pdf](https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/2018ps/18-ID-06_FINAL.pdf))

### Clinical Description

Invasive Listeriosis:

- Systemic illness caused by *L. monocytogenes* manifests most commonly as bacteremia or central nervous system infection. Other manifestations can include pneumonia, peritonitis, endocarditis, and focal infections of joints and bones.
- Pregnancy-associated listeriosis has generally been classified as illness occurring in a pregnant woman or in an infant age  $\leq 28$  days. Listeriosis may result in pregnancy loss (fetal loss before 20 weeks gestation), intrauterine fetal demise ( $\geq 20$  weeks gestation), pre-term labor, or neonatal infection, while causing minimal or no systemic symptoms in the mother. Pregnancy loss and intrauterine fetal demise are considered to be maternal outcomes.
- Neonatal listeriosis commonly manifests as bacteremia, central nervous system infection, and pneumonia, and is associated with high fatality rates. Transmission of *Listeria* from mother to baby transplacentally or during delivery is almost always the source of early-onset neonatal infections (diagnosed between birth and 6 days), and

the most likely source of late-onset neonatal listeriosis (diagnosed between 7–28 days).

Non-invasive *Listeria* Infections:

- *Listeria* infection manifesting as an isolate from a non-invasive clinical specimen suggestive of a non-invasive infection; includes febrile gastroenteritis, urinary tract infection, and wound infection.

### Laboratory Criteria for Diagnosis

#### *Confirmatory laboratory evidence*

- Isolation of *L. monocytogenes* from a specimen collected from a normally sterile site reflective of an invasive infection (e.g., blood or cerebrospinal fluid or, less commonly: pleural, peritoneal, pericardial, hepatobiliary, or vitreous fluid; orthopedic site such as bone, bone marrow, or joint; or other sterile sites including organs such as spleen, liver, and heart, but not sources such as urine, stool, or external wounds);

**OR**

- For maternal isolates: In the setting of pregnancy, pregnancy loss, intrauterine fetal demise, or birth, isolation of *L. monocytogenes* from products of conception (e.g. chorionic villi, placenta, fetal tissue, umbilical cord blood, amniotic fluid) collected at the time of delivery;

**OR**

- For neonatal isolates: In the setting of live birth, isolation of *L. monocytogenes* from a non-sterile neonatal specimen (e.g., meconium, tracheal aspirate, but not products of conception) collected within 48 hours of delivery.

#### *Presumptive laboratory evidence*

- Detection of *L. monocytogenes* by culture-independent diagnostic testing (CIDT) in a specimen collected from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly: pleural, peritoneal, pericardial, hepatobiliary, or vitreous fluid; orthopedic site such as bone, bone marrow, or joint; or other sterile sites including organs such as spleen, liver, and heart, but not sources such as urine, stool, or external wounds);

**OR**

- For maternal isolates: In the setting of pregnancy, pregnancy loss, intrauterine fetal demise, or birth, detection of *L. monocytogenes* by CIDT from products of conception (e.g., chorionic villi, placenta, fetal tissue, umbilical cord blood, amniotic fluid) collected at the time of delivery;

**OR**

- For neonatal isolates: In the setting of live birth, detection of *L. monocytogenes* by CIDT from a non-sterile neonatal specimen (e.g., meconium, tracheal aspirate, but not products of conception) collected within 48 hours of delivery.

*Supportive laboratory evidence*

- Isolation of *L. monocytogenes* from a non-invasive clinical specimen, e.g., stool, urine, wound, other than those specified under maternal and neonatal specimens in the Confirmatory laboratory evidence section.

**Comment(s)**

- Antibody testing without additional laboratory confirmation (culture or PCR-based CIDT) is not considered sufficient to meet the case definition criteria and are not reportable to CDC.

Case Classification

**Suspected**

- A person with supportive laboratory evidence.

**Probable**

- A person who meets the presumptive laboratory evidence;

**OR**

- A mother or neonate who meets the epidemiologic linkage but who does not have confirmatory laboratory evidence.

**Confirmed**

- A person who meets confirmatory laboratory evidence

Case Classification Comments

Pregnancy loss and intrauterine fetal demise are considered maternal outcomes and are reported and counted as a single case (the mother).

Cases in neonates and mothers should be reported separately when each meets the case definition. A case in a neonate is counted if live-born.

**III. CASE SURVEILLANCE, INVESTIGATION, AND REPORTING**

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**A. Purpose of Surveillance, Investigation, and Reporting**

- To identify listeriosis outbreaks and related cases.
- To identify sources of contaminated products and prevent further transmission.
- To target high risk populations and educate people about how to reduce their risk of infection.

## B. Local Health Department (LHD) General Case Investigation Recommendations

Clinical laboratories and healthcare providers are required to report *Listeria* cases to their LHD within one working day of identification. This includes cases that are detected through culture-independent diagnostic testing (CIDT). Begin case investigation as soon as *Listeria* is reported from a clinical laboratory or healthcare provider.

Listeriosis is a rare condition that primarily affects the elderly, immunocompromised, and pregnant women, and it is important to obtain detailed exposure information for cases as soon as it is feasible. Prompt and thorough investigation of each case potentially prevents vulnerable populations from ongoing exposures to a contaminated product. Further, exposure information for all listeriosis cases helps future outbreak investigations because CDC collects this information in a national database. During investigations of suspected outbreaks, these data are used to conduct case-case analyses to determine if exposures for outbreak-associated cases are significantly greater than expected when compared to sporadic cases (for additional details, visit the [CDC \*Listeria\* Initiative webpage](#)).

Patients should be interviewed using the CDPH Listeriosis Case Report Form (CDPH 8296), which is based on the [Listeria Initiative](#) questionnaire. We request food exposure information for the 4 weeks prior to onset of illness.

If the patient is unable to provide an adequate food history, every effort should be made to interview persons who are familiar with the patient's dietary habits. It is very important to interview every patient or proxy as early as possible after identification for better recall of detailed food exposures.

If the patient is a pregnancy-associated case with a live birth, the Neonatal Listeriosis Case Report Form (CDPH 8297) should also be completed for the neonate. The mother's information should be entered and completed using the Listeriosis Case Report Form (CDPH 8296).

If the patient appears to be part of a point-source outbreak, follow your protocol for foodborne outbreak investigations. This should include notifying CDPH about the outbreak.

If you require assistance with your investigation, call the [CDPH Disease Investigations Section \(DIS\)](#) at 510-620-3434.

## C. LHD Reporting in California

### LHD Reporting Overview

Listeriosis has been a nationally notifiable disease since 1999. Confirmed and probable case-patients should be reported to CDPH. Effective January 1, 2019, CSTE updated the [listeriosis surveillance case definition](#) which includes the addition of a "probable" classification and clarification of how maternal-infant pairs are counted.

The CDPH Listeriosis Case Report Form (CDPH 8296) is required and should be used to interview all patients > 28 days old; the form is available in CaREDIE. For pregnancy-associated cases, live born neonates < 28 days old should be reported using

the Neonatal Listeriosis Case Report form (CDPH 8297), which is also available in CalREDIE. The mother's information should be entered on the standard Listeriosis CDPH 8296 form. A Spanish-language version of the *Listeria* Initiative is available upon request. Please email [listeria@cdc.gov](mailto:listeria@cdc.gov) if you would like to request the form.

#### Instructions for CalREDIE-participating LHDs:

- Enter the patient information into CalREDIE upon notification of the case by the clinical laboratory or health care provider. Select “**Listeriosis**” as “Disease Being Reported” for all patients older than 28 days. For live born neonates (< 28 days) with confirmed or probable listeriosis, select “**Listeriosis, neonatal**” condition.
- Fill out the clinical, laboratory, and epidemiology information as thoroughly as possible. If you cannot interview a patient or their proxy, please select “lost to follow-up” on the case investigation tab.
- For pregnancy-associated cases, both mother and neonate will usually be classified as confirmed or probable cases and should be reported separately (see **IV. Special Considerations, A. Classification and Reporting of Pregnancy-Related Patients and Appendix A**)
  - Maternal listeriosis patients should be entered into CalREDIE under the general listeriosis condition. The food exposure information for the neonate should be documented in the mother's listeriosis incident, even if the mother is not confirmed (the neonate is confirmed by culture or probable by culture independent diagnostic test).
  - The CalREDIE ID for the corresponding maternal or neonatal pair should be recorded on the respective clinical tabs. Prompts for this information on the maternal CalREDIE form is located in the pregnancy information section of the Past Medical History. For women infected during pregnancy, select “neonatal” as the disease case classification, below the exposure questions on the New Epi-Info tab. (See **IV. Special Considerations, A. Classification and Reporting of Pregnancy-Related Patients and Appendix A**)
- All Listeriosis and Neonatal Listeriosis case report forms are reviewed by the DIS Subject Matter Expert (SME). Listeriosis cases are not classified as confirmed or probable and closed by the state, until reviewed by the SME. Before closing a case, the DIS SME will update laboratory and outbreak information if it is available. This may require follow-up with the LHD regarding a patient or specimen that is lost to follow-up.

#### **D. Laboratory Considerations/Microbial Diseases Laboratory (MDL) Resources**

##### Laboratory Testing Overview

The diagnosis of listeriosis is made by the identification of *Listeria monocytogenes* in a clinical specimen, most commonly blood, cerebrospinal fluid, or products of conception.

Culture isolation of *Listeria* provides confirmatory laboratory evidence.

*Culture Independent Diagnostic Testing (CIDT)*: Clinical laboratories are adopting CIDT, which is the detection of antigen or nucleic acid sequences of the pathogen without culture isolation. Currently, CIDTs are not widely used to identify *Listeria*, but a CIDT positive is presumptive laboratory evidence and classified as a probable case. CIDT positives cannot be sequenced, and the patient cannot be linked to an outbreak through WGS analysis.

Antibody testing without additional laboratory confirmation (culture or PCR-based CIDT) is not considered sufficient to meet the case definition criteria and are not reportable to CDC.

*Whole Genome Sequencing (WGS)*: WGS is a high resolution molecular subtyping technique. All isolates should be forwarded to a Public Health Laboratory (PHL) for confirmation and WGS. As of January 1, 2014, clinical laboratories in California are required to send *Listeria* isolates to a PHL. The MDL and four LHD PHLs (Los Angeles, Orange, San Diego and Santa Clara) are PulseNet certified and perform WGS on all *Listeria* isolates (one isolate per person). If an isolate is closely related to two other isolates, whether it is from a clinical, food, or environmental source, the CDPH SME will review case histories and begin an investigation if epidemiologic information is available.

## IV. SPECIAL CONSIDERATIONS

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### A. Classification and Reporting of Pregnancy-Related Patients

A neonatal case or pregnancy associated case is defined as having occurred in a pregnant woman or a neonate < 28 days old. Based on the case definition (effective January 2019) mother/neonate pairs will likely be counted as two separate cases. The probable case classification for pregnancy-associated cases includes an epi-link to a confirmed or probable mother or neonate. Here are the possible classification categories:

#### Neonate is confirmed and mother is probable:

- If the neonate (< 28 days) has confirmatory laboratory evidence and the mother is negative or not tested.

#### Mother is confirmed and neonate is probable:

- If the mother has confirmatory laboratory evidence with a specimen from products of conception including the placenta, and the infant does not have confirmatory laboratory evidence, the neonate is a probable case based on epi-linkage to the mother.

#### Mother is confirmed and neonate is not a case:

- If the mother has confirmatory laboratory evidence with a specimen collected from a normally sterile site and the infant is not clinically compatible, **and** is negative or is not tested, only the mother would be classified as case.



Neonate is probable and mother is probable:

- If the neonate (< 28 days) has presumptive laboratory evidence and mother does not have confirmatory laboratory evidence.

Mother is probable and neonate is probable:

- If the mother has presumptive laboratory evidence with a specimen from products of conception including the placenta, and the infant does not have confirmatory laboratory evidence.

Mother is probable and neonate is not a case:

- If the mother has presumptive laboratory evidence with a specimen collected from a normally sterile site and the infant is not clinically compatible, is negative, or is not tested, only the mother would be classified as case.

In most of these scenarios, a separate case report form/CalREDIE record should be completed for both the mother and neonate (see **Appendix A Flowchart**). However, food exposure information should only be collected from the mother. The mother and infant case records should be manually epi-linked in CalREDIE based on IDs entered in the clinical tabs (see screenshot of Listeriosis Clinical Tab below).

**B. Other *Listeria* species**

Although rare, invasive infections can occur due to other *Listeria* species, including *L. ivanovii*. Report invasive illness caused by non-*monocytogenes* *Listeria* species through the Listeriosis form in CalREDIE (CDPH 8296).



### C. *Listeria*-based Immunotherapy

Over the last several years, *Listeria monocytogenes* has been used as a vector for cancer immunotherapy treatment. Many vaccines have been developed utilizing modified *Listeria* to generate an immune response against a variety of cancers. Many clinical trials testing *Listeria*-based cancer vaccines are ongoing and periodically, a vaccine strain of *Listeria* is detected in clinical isolates. The clinical significance of this is uncertain. If a patient with a history of receiving *Listeria*-based immunotherapy is identified as a potential listeriosis case, please contact IDB (510-620-3434) and ask for the listeriosis SME. The SME will assist with follow up and completion of the CDC *Listeria*-based Immunotherapy-Related Isolate Questionnaire.

### D. *L. monocytogenes* from non-invasive clinical sources

Isolation of *L. monocytogenes* from a non-invasive clinical specimen including stool, urine, or wounds (not including products of conception) are considered supportive laboratory evidence. These are classified as suspect cases and are not included as part of the year-end case count. However, in certain situations, such as non-invasive febrile gastroenteritis due to *Listeria* potentially associated with contaminated product, public health follow-up is warranted. *Listeria* gastroenteritis is usually recognized during point-source outbreaks, which often has a high attack rate, ranging from 50 to 100 percent. Non-invasive *L. monocytogenes* gastroenteritis affect healthy individuals and symptoms typically include fever, watery diarrhea, headache, and joint and muscle pain. Invasive infection appears to be rare, with the risk being greatest in immunocompromised, pregnant, or older adult patients. Investigation of some cases of non-invasive *Listeria* infections may provide epidemiologically relevant data. This is particularly true as febrile gastroenteritis secondary to *Listeria* infection typically occurs after ingestion of a large inoculum of bacteria from contaminated food. As such, *L. monocytogenes* isolated from a non-sterile site should be considered on a case-by-case basis. Outbreaks or clusters of any type, including febrile gastroenteritis due to *L. monocytogenes* should be investigated and reported promptly to IDB.

## IV. CASE MANAGEMENT AND CONTROL MEASURES

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There are no specific State guidelines for the management or control of listeriosis cases or contacts. No follow-up is required for sensitive occupations.

## V. APPLICABLE STATE STATUTES/BILLS

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Title 17, California Code of Regulations (CCR) Section [2500 Reportable Diseases and Conditions](#)

<https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ReportableDiseases.pdf>

Title 17, CCR [Section 2505 Reportable Conditions: Notification by Laboratories](#)

<https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/LabReportableDiseases.pdf>

## VI. ADDITIONAL RESOURCES

### A. General Information/Patient Information

- [CDC \*Listeria\* \(Listeriosis\) webpage](http://www.cdc.gov/listeria/index.html): <http://www.cdc.gov/listeria/index.html>
- [CDC \*Listeria\* \(Listeriosis\) People and Risk webpage](http://www.cdc.gov/listeria/index.html): <http://www.cdc.gov/listeria/index.html>
- [CDC National Enteric Disease Surveillance – The \*Listeria\* Initiative](http://www.cdc.gov/listeria/pdf/ListeriaInitiativeOverview_508.pdf): [http://www.cdc.gov/listeria/pdf/ListeriaInitiativeOverview\\_508.pdf](http://www.cdc.gov/listeria/pdf/ListeriaInitiativeOverview_508.pdf)

### B. References

- Heymann, DL Ed. *Control of Communicable Diseases Manual, 20<sup>th</sup> Edition*. Washington, DC, American Public Health Association, 2015
- [CIFOR \(Council to Improve Foodborne Outbreak Response\) Guidelines](https://cifor.us/products/guidelines): <https://cifor.us/products/guidelines>
- Flickinger JC Jr.et al. *Listeria monocytogenes* as a Vector for Cancer Immunotherapy: Current Understanding and Progress. *Vaccines* (Basel). 2018 Sep; 6(3): 48. Published online 2018 Jul 25.
- Barbuddhe SB, Chakraborty T. *Listeria* as an enteroinvasive gastrointestinal pathogen. *Curr Top Microbiol Immunol*. 2009;337:173-195.
- Ooi ST, Lorber B. Gastroenteritis due to *Listeria monocytogenes*. *Clin Infect Dis* 2005; 40:1327.

## VII. UPDATES

This version finalized and completed November 2021

## VIII. SUMMARY OF ACTION STEPS: LISTERIOSIS

Action	Specific Steps
<input type="checkbox"/> Begin investigation as soon as <i>Listeria</i> is reported from a clinical laboratory or healthcare provider	<ul style="list-style-type: none"> <li>• Review information in CDPH IDB Guidance, and other resources as needed.</li> <li>• Obtain and review clinical documentation, medical records, and lab reports as applicable.</li> <li>• Contact patient for interview.</li> </ul>

Action	Specific Steps
<input type="checkbox"/> Confirm case definition	<ul style="list-style-type: none"> <li>• To count as a confirmed case, laboratory confirmation that <i>Listeria</i> has been isolated by culture from a human specimen is needed. The specimen site should be sterile (such as blood, CSF, and less commonly, joint, pleural, or pericardial fluid). In the setting of pregnancy, isolation of <i>L. monocytogenes</i> from placental tissue, fetal tissue, amniotic fluid or other products of conception, or any site from neonate (e.g. tracheal aspirate).</li> <li>• Probable: A person who meets the presumptive laboratory evidence.                         <ul style="list-style-type: none"> <li><u>Mother is probable and neonate is confirmed:</u> A pregnant or post-partum woman who was not tested for listeriosis but had a <i>Listeria</i>-positive infant (&lt; 28 days).</li> <li><u>Mother is probable and neonate is probable:</u> A pregnant or post-partum woman who has presumptive laboratory evidence with a specimen from products of conception including the placenta, and the infant does not have confirmatory laboratory evidence.</li> <li><u>Mother is probable and neonate is not a case:</u> A pregnant or post-partum woman who has presumptive laboratory evidence with a specimen collected from a normally sterile site and the infant is not clinically compatible, is negative, or is not tested, only the mother would be classified as case.</li> </ul> </li> </ul>
<input type="checkbox"/> Confirm status of <i>Listeria</i> isolate	<ul style="list-style-type: none"> <li>• Ensure that the <i>Listeria</i> isolate is sent to PHL and forwarded to MDL or PHL for whole genome sequencing.</li> </ul>
<input type="checkbox"/> Attempt to identify source of exposure	<ul style="list-style-type: none"> <li>• Use the <i>Listeria</i> form in CalREDIE or posted to the CDPH form site to guide your interview, or use the protocol set by your local health jurisdiction.</li> <li>• Include as many details that may trigger memory, such as parties or special events, and inform patient that they may need to be contacted again.</li> <li>• If patient appears to be part of an outbreak, follow your protocol for foodborne outbreak investigations; this should include notifying CDPH about the outbreak. Suspected</li> </ul>

Action	Specific Steps
	<p><i>Listeria</i> outbreaks within your jurisdiction, should be reported within 24 hours to CDPH.</p>
<p><input type="checkbox"/> Report to CDPH; confirmed and probable listeriosis cases must be reported</p>	<ul style="list-style-type: none"> <li>• Complete forms CDPH 8296 and CDPH 8297 and send to SSS or create CalREDIE incident, selecting “<b>Listeriosis</b>” or “<b>Listeriosis, neonatal</b>” as “Disease Being Reported”.</li> </ul>

*If you require assistance with your investigation, call DIS at 510-620-3434*

## APPENDIX A: Flow Chart for Determining Case Classification and Form(s) for Pregnancy-Associated Listeriosis Cases

