Listeriosis

A. Agent:
Listeria monocytogenes is an anaerobic gram-positive rod-shaped bacterium[1,2].

B. Clinical Description:
In adults, invasive disease caused by *Listeria monocytogenes* manifests most commonly as meningitis or bacteremia; infection during pregnancy may result in fetal loss through miscarriage or stillbirth, or neonatal meningitis or bacteremia[1-3]. Other manifestations can also be observed[1-3]. Infections in healthy persons may appear as self-limiting diarrheal illness or mild flu-like illness[3]. It may cause abortion, preterm delivery, or fetal death in pregnant women[1-3]. Meningoencephalitis onset may be sudden with fever, headache, nausea, vomiting, and signs of meningeal irritation[1,3]. Endocarditis, granulomatous lesions in the liver and other organs, localized internal or external abscesses, and pustular/papular cutaneous lesions may also occur[1]. ~30% case-fatality rate in infected newborns[9].

C. Reservoirs:
Reservoirs for *L. monocytogenes* are soil, decaying vegetation, silage, water, mammals and fowl[1,5].

D. Mode of Transmission:
L. monocytogenes may be acquired by the fetus in utero or during delivery[1-4]. Pregnant women are 10 times more likely to be infected than other people[2]. *Listeria* is most often transmitted through ingestion of contaminated foods[1-4]. It may also be transmitted through contact with infected animals or birds[1,2]. Person-to-person transmission has also been reported in neonatal nosocomial outbreaks[1]. *Listeria* tends to multiply in refrigerated foods that have been contaminated[1-4]. Foods implicated in outbreaks include unpasteurized milk, soft cheeses, deli meats, prepared meats like hot dogs, and raw fruits and vegetables such as cantaloupe[1-4].

E. Incubation Period:
Varies; The incubation period for invasive disease is longer for pregnancy-associated cases (2–4 weeks or occasionally longer) than for nonpregnancy-associated cases (1 to 14 days). The incubation period for self-limiting, febrile gastroenteritis following ingestion of a large inoculum is 24 hours; illness typically lasts 2 to 3 days[2]. Range of 1-7 weeks[5].

F. Period of Communicability:
L. monocytogenes may be shed for months in the stool of infected persons, although person-to-person transmission is rare[1]. Mothers of infected newborns may shed *L. monocytogenes* for 7-10 days after delivery and listeria has been isolated from human milk.

G. Susceptibility and Resistance:
Those most at risk include pregnant women and their newborns, adults aged 65 or older and people with weakened immune systems. Other people can be infected with *Listeria*, but they rarely become seriously ill[4]. There is no evidence of immunity after infection[1].

H. Treatment:

No controlled trials have established the drug(s) of choice or duration of therapy for listeriosis. Combination therapy using ampicillin and a second agent in doses appropriate for meningitis is recommended for severe infections. An aminoglycoside, typically gentamicin, usually is used as the second agent in combination therapy[2]. If alternatives to gentamicin are used, susceptibility should be confirmed because resistance to trimethoprim-sulfamethoxazole, fluoroquinolones, linezolid, or rifampin occasionally has been reported. In the penicillin-allergic patient, options include either penicillin desensitization or use of either trimethoprim-sulfamethoxazole or a fluoroquinolone, both of which have been used successfully as monotherapy for *Listeria* meningitis and in the setting of brain abscess.[2]. Treatment for invasive infections without meningitis for 14 days is usually effective[2]. For meningitis cases, most experts recommend 3 to 4 weeks of treatment[2].

Disease Management

I. Clinical Case Definition[6]:

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 ≤ 28 days. Listeriosis may result in pregnancy loss (fetal loss before 20 weeks gestation), intrauterine fetal demise (≥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.

J. Laboratory Criteria for Diagnosis[6]:

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.

*For listeriosis, a CIDT should only include PCR or other nucleic acid amplification test (NAAT) assays. Serological tests should not be considered evidence of infection.

Epidemiologic Linkage[6]

For probable maternal cases:

- A mother who does not meet the confirmed case criteria, **BUT**
- Who gave birth to a neonate who meets confirmatory or presumptive laboratory evidence for diagnosis, **AND**
- Neonatal specimen was collected up to 28 days of birth.

For probable neonatal cases:

- Neonate(s) who do not meet the confirmed case criteria, **AND**
- Whose mother meets confirmatory or presumptive laboratory evidence for diagnosis from products of conception, **OR**
- A clinically compatible neonate whose mother meets confirmatory or presumptive laboratory evidence for diagnosis from a normally sterile site.

Case Classification[6]	
Confirmed	A person who meets the confirmatory laboratory criteria.
Probable	A person who meets the presumptive laboratory criteria for diagnosis; OR A mother or neonate who meets the epidemiologic linkage but who does not have confirmatory laboratory evidence.
Suspect	A person with supportive laboratory evidence.

Criteria to Distinguish a New Case from an Existing Case[6]

As a rule of thumb, a case should not be counted as a new case if laboratory results were reported within 6 months of a previously reported infection in the same individual. However, as

noted in the 2018 CSTE position statement, there is currently insufficient data available to support a routine recommendation for criteria to distinguish a new case of listeriosis from prior reports or notifications. Duplicate or recurring reports of listeriosis in an individual should be evaluated on a case-by-case basis.

K. Classification of Import Status:
Import status reflects where the *Listeria* 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 infection was acquired in Canada or Mexico or food was consumed from Canada or Mexico and was not purchased in a U.S. store during the exposure period. For more information, please refer to the MEDSIS User Guide. You can find the guide in MEDSIS under: Resources → MEDSIS Documentation → User Guides.

L. Laboratory Testing[1-3]:
Gold standard – Confirmation of isolates from a normally sterile site, such as blood, CSF, amniotic fluid, placenta, or fetal tissue.

Serological tests are considered unreliable.

TEST[7]	SPECIMEN & TRANSPORT[7]	TESTING AVAILABILITY[7]
Culture	CSF, blood, amniotic fluid, placenta, meconium, vaginal secretions, respiratory, skin, mucous swab, or stool	Commercially available
PCR	Vaginal and stool samples	Not widely available; may become more common
Confirmation of isolates	Sterile: Blood, cerebrospinal fluid, amniotic fluid or placenta. Non-sterile: meconium, vaginal secretions, respiratory, skin or mucous swabs. Specimens should be transported as soon as possible. Ship specimen at 4°C. See below	ASPHL
Whole Genome Sequencing (WGS)	ASPHL will conduct WGS on all L*isteria* isolates	ASPHL

- Specimens from sterile sites (blood, cerebrospinal fluid, amniotic fluid or placenta) should be transported as soon as possible. If processing is delayed, specimens should be held at 35°C in an incubator for no longer than 48 hours.
- Specimens from non-sterile sites other than stool (meconium, vaginal secretions, respiratory, skin or mucous swab) require prompt handling. If processing is delayed, the materials should be kept at 4°C or frozen at -20° C if testing delays are expected to exceed 48 hours.
- Reference cultures can be transported on Nutrient Agar slants or other non-glucose containing agar.
- ASPHL maintains the ability to test highly suspect environmental and food specimens if needed. For guidance on what types of specimens to collect and what media to use, contact the ASPHL Environmental Microbiology Department.

See Arizona Department of Health Services (ADHS) Guide to Laboratory Services: Microbiology: https://www.azdhs.gov/preparedness/state-laboratory/public-health-microbiology/index.php

M. Assessing Laboratory Results:
Whole Genome Sequencing (WGS) is completed at ASPHL. WGS yields serotype information and genetic information that allows for cluster and outbreak detection.

N. Outbreak Definition:

- Diagnosis or detection of two or more individuals from different households and families who experience an illness clinically compatible with *Listeria* infection, at least one with laboratory-confirmed listeriosis, after eating a common food or food from a common source.
- An unexplained, unexpected increase in cases of laboratory-confirmed *Listeria* infection that is clustered by time, place, or person.
- Most outbreaks of *Listeria* infection are identified using whole genome sequencing (WGS). An outbreak investigation is triggered when *Listeria* isolates from two or more individuals whose specimens were collected within 60 days of each other are determined to be highly related by WGS.

NOTE: See Infectious Disease Outbreak Investigation and Management webpage for additional information/guidance.

Investigation Guidelines

O. Time Frame[8]:
Submit a report within 24 hours**; investigation should be initiated *within 24 hours*** of initial report. ***Listeria* case investigation form must be completed within 7 days of initial report** and submitted to CDC by ADHS Epi. Outbreaks should be entered into MEDSIS Outbreak Module within 24 hours of report.

P. Forms:

- Please refer to the Department-provided formats for submitting Epidemiologic Investigation Reports for guidance on the required fields and forms for each morbidity.
- ADHS Reporting and Investigation Forms: https://www.azdhs.gov/preparedness/epidemiology -disease-control/index.php#investigations -forms

Q. Investigation Steps:

Confirm Diagnosis

- Contact health care provider/facility to obtain demographic and clinical information.
- If case was hospitalized, obtain medical records including admission notes, progress notes, lab report and discharge summary.
- Refer to case definition to verify case classification.
- Facilitate forwarding specimens to the ASPHL.

Conduct Case Investigation

- The purpose of the case investigation is to identify potential sources of infection. Ask especially about the following exposures in the 3-70 days prior to onset:
  - Consumption of unpasteurized milk or dairy products
  - Consumption of prepackaged, ready-to-eat meat (e.g., hot dogs, turkey, bologna)
  - Consumption of refrigerated, prepared foods, or any foods from a deli

- Consumption of dried, preserved or traditionally prepared meats (e.g., sausage, salami, jerky) or preserved, smoked, or traditionally prepared fish
- Contact with farm animals or animal products

- Report electronically through MEDSIS; and use the CDC Listeriosis Investigation Form (see link to form in section P, above) to conduct your investigation. Attach the completed form to the MEDSIS case when complete.
    - *Listeria* case investigation form must be completed within 7 days of initial report and submitted to CDC by ADHS Epi
- The ADHS Foodborne Disease Epidemiologist, Environmental Health Food Safety Program Manager, and Medical Director are available as resources.

Conduct Contact Investigation

- With the exception of mother-to-fetus/newborn, person-to-person transmission of listeriosis is rare. Identifying and investigating asymptomatic contacts is generally not necessary.

Initiate Control and Prevention Measures

- A decision about testing suspected food items can be made in consultation with ADHS Foodborne Disease Epidemiologist and the Environmental Microbiology Department at ASPHL.
- In the event that food service, child care center, or public supply is implicated in transmission, coordinate through the proper regulatory agency.
- Provide education and advise people at higher risk, such as pregnant women and persons who are immune compromised, to avoid high-risk foods.

Isolation, Work and Child Care Restrictions

With the exception of mother-to-fetus/newborn, person-to-person transmission of listeriosis is rare. To prevent the possible spread in child care and health care settings, enforce strict hand washing. Food handlers, child care providers, and healthcare professionals with diarrhea should be excluded from work while symptomatic.

Case Management

- When infection occurs during pregnancy, antibiotics given promptly to the pregnant woman can often prevent infection of the fetus or newborn.
- Educate case on measures to avoid future illness and its transmission. Educational resources can be found at https://azdhs.gov/preparedness/epidemiology-disease-control/foodborne/index.php#listeriosis

Contact Management

Antimicrobial therapy of infection diagnosed during pregnancy may prevent fetal or perinatal infections and its consequences.

Notifications

- Maintain communication with all associated partners in the investigation process to ensure coordination of efforts.
- Organize, collect and report data utilizing the CDC *Listeria* Initiative Case Report Form.
- Report data electronically via MEDSIS or by fax if necessary, including:

- All essential data that was collected during the investigation, especially data that helps to confirm or classify a case. Remember to verify that all key Disease Specific Observation fields are filled out.
- For epi-linked cases, please include the MEDSIS ID of the related case in the case notes section.

- If appropriate, work with Public Information Officer to ensure appropriate and timely dissemination of public information.
- ADHS will notify CDC and federal regulatory agencies (FDA, USDA).
- ADHS will forward the CDC *Listeria* Initiative Case Report Form to CDC – **within 7 DAYS of initial report.**

R. Outbreak Guidelines:

Special Situations

Refer to the Outbreak Guide in the Infectious Disease Investigation Manual. For complete guidelines to investigating foodborne outbreaks, consult the ADHS Foodborne and Waterborne Disease Outbreak Investigation Resource Manual.

NOTE: See Infectious Disease Outbreak Investigation and Management webpage for additional information/guidance.

S. Special Situations:

Pregnancy-Associated Cases:

- When infection occurs during pregnancy, antibiotics given promptly to the pregnant woman can often prevent infection of the fetus or newborn[2].

Additional Information & Resources

ADHS Guide to Laboratory Services: Microbiology:
https://www.azdhs.gov/preparedness/state-laboratory/public-health-microbiology/index.php

Foodborne and Waterborne Disease Outbreak Investigation Resource Manual:
http://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/foodborne-waterborne-disease-outbreak-manual.pdf

CDC Listeria:
http://www.cdc.gov/listeria/

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