

Listeriosis

Listeriosis,
Listerellosis,
Circling disease

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Importance

Listeriosis is caused by several species of *Listeria*, bacterial organisms that live as saprophytes in the environment but occasionally cause disease in a wide range of vertebrates including mammals, marsupials, birds and reptiles. These organisms are most often ingested in food, where they can proliferate even at refrigeration temperatures. Most illnesses are caused by *Listeria monocytogenes*, but *L. ivanovii* is found occasionally, and there are rare reports of clinical cases caused by other species of *Listeria*.

In humans, *L. monocytogenes* is most important as a cause of pregnancy losses in healthy women, and septicemia or central nervous system (CNS) disease in people who are immunosuppressed, debilitated, newborn or elderly. Clinical cases are uncommon in healthy, nonpregnant people and the associated syndromes are not usually life-threatening; however, rare serious illnesses can have a high case fatality rate, as listeriosis may not be suspected and the appropriate treatment may be delayed. Sporadic clinical cases and outbreaks of listeriosis are also seen in animals. They occur most often in herbivores fed silage, but carnivores and omnivores can also be affected. As in humans, reproductive losses, CNS disease and septicemia are the most serious syndromes. Predisposing factors for listeriosis are poorly understood in animals, and many affected animals seem to be healthy.

Etiology

Listeriosis is caused by members of the genus *Listeria*, a Gram positive bacterial rod in the family Listeriaceae. *L. monocytogenes* is the primary pathogen in humans and animals, but *L. ivanovii* is found occasionally, and there are rare reports of clinical cases caused by *L. seeligeri*, *L. grayi* (which includes the former *L. murrayi*) and *L. innocua*. Isolates of *L. monocytogenes* can differ in virulence. While all 13 serovars of this organism are potentially virulent, serovars 4b, 1/2a, 1/2b and 1/2c are thought to account for more than 95% of the clinical cases in humans, and serovars 4b, 1/2a, 1/2b and 3 are reported to be common in animals. As of 2019, there are no reports of clinical cases caused by *L. welshimeri* (although fecal shedding was reported in one person) or by newly recognized or proposed species such as *L. marthii*, *L. rocourtiae*, *L. weihenstephanensis* and *L. fleischmannii*.

Species Affected

A wide variety of vertebrates, including mammals, birds, reptiles, amphibians and fish, can develop subclinical infections and shed *Listeria* in the feces. Clinical cases are seen most often in cattle, sheep and goats, but they have also been reported in other ruminants (e.g., water buffalo, deer, reindeer, antelope, moose), South American camelids, rabbits (*Oryctolagus cuniculus*), rodents (e.g., guinea pigs, chinchillas, rats), horses, pigs, dogs, cats and farmed mink (*Neovison vison*). Cases are reported occasionally in captive or free-living wild mammals and marsupials. Some species that have been affected include nonhuman primates, several species of wild hares (*Lepus* spp.), foxes, a pet sugar glider (*Petaurus breviceps*), cougars (*Felis concolor*), serval (*Felis serval*), leopards (*Panthera pardus*), a raccoon dog (*Nyctereutes procyonoides*), common brushtail possums (*Trichosurus vulpecula*), common ringtail possums (*Pseudocheirus peregrinus*) and a red-necked wallaby (*Macropus rufogriseus*). Birds with listeriosis have included poultry (chickens, turkeys, geese, ducks), game birds (e.g., red-legged partridges, *Alectoris rufa*; pheasants, *Phasianus colchicus*; willow grouse, *Lagopus lagopus*), canaries (*Serinus canaria*), parrots, budgerigars (*Melopsittacus undulatus*), a cockatiel (*Nymphicus hollandicus*), a merlin (*Falco columbarius*), a snowy owl (*Bubo scandiacus*) and other species. A few clinical cases have been reported in reptiles including inland bearded dragons (*Pogona vitticeps*) and farmed alligators but, to date, listeriosis is not known to affect amphibians or fish.

L. monocytogenes is responsible for most clinical cases in animals, but *L. ivanovii* has been reported in approximately 10% of the cases in ruminants. The latter organism also occurs occasionally in other species such as chinchillas. *L. innocua* was found in two cases of encephalitis, one in a bull and one in a ewe.



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Zoonotic potential

Humans usually acquire *Listeria* from food and not directly from animals; however, unpasteurized milk and uncooked meat can contain organisms, and zoonotic infections occasionally occur after direct contact with sources such as the placenta or fetus. *L. monocytogenes* causes most clinical cases in humans, but rare cases caused by *L. ivanovii*, *L. seeligeri*, *L. grayi* and *L. innocua* have been reported. Most, though not all, of the latter organisms were found in people who were immunocompromised.

Geographic Distribution

Listeria, including *L. monocytogenes*, are ubiquitous organisms that can be found worldwide.

Transmission

Listeria spp. are mainly acquired by ingestion, but they can also enter the body by other routes including inhalation or inoculation into broken skin or the eye. Their primary reservoirs are soil and decaying vegetation, where they grow as saprophytes, but they can also be found in many other environmental sources, such as plants and water. The infective dose for *L. monocytogenes* is thought to be high (approximately 100,000 bacteria/g food) in healthy, nonpregnant humans, who can eat many *Listeria*-contaminated foods without becoming ill; however, people who are immunosuppressed can develop listeriosis after ingesting much lower doses.

In ruminants, listeriosis is most often linked to eating silage with pH > 5-5.5. This can occur in poorly fermented silage or, more often, in areas of aerobic deterioration in otherwise good silage. Clinical cases are described occasionally in animals at pasture or eating other feed, such as moist brewers' grains or hay bales that spoiled after becoming wet. Hay or commercial pellets contaminated with feces from ruminants or rodents, as well as silage, were thought to have caused some outbreaks in chinchillas. Carnivores can be infected from contaminated animal products or by predation on an infected animal. Cases in reptiles have occurred after feeding contaminated pork or frozen mice. Many different foods have been implicated in human outbreaks. While unpasteurized dairy products (e.g., soft cheeses) and various ready-to-eat refrigerated foods (e.g., pates, deli meats) are often involved, listeriosis has also been acquired from many other sources including raw meat and fish and uncooked vegetables or fruits. Contamination is sometimes traced to food products entering processing facilities; however, organisms can also become established in these facilities, sometimes persisting for many years. *L. monocytogenes* can grow at temperatures from 0.5°C (33°F) to 45°C (113°F), although growth is slower in the cold. Many strains can tolerate high salt or acid conditions in food. This organism can also undergo an adaptive response which increases its tolerance to adverse conditions. While it does not ordinarily proliferate in foods

< pH 4.4, it can tolerate pH as low as 3.5 if it is first exposed to moderate acidity.

Listeria can be shed in the feces of sick or subclinically infected vertebrates, including humans, and in the feces of invertebrates. Animals and humans can shed these organisms in milk and/or vaginal secretions with or without clinical signs, and sick individuals may occasionally excrete them in other secretions and excretions including nasal discharges and urine. The fetus can be infected *in utero*, and some neonates may acquire *Listeria* from the vagina at birth. Listeriosis has been transmitted between human newborns in the hospital via direct contact or on fomites, although person-to-person transmission otherwise seems to be absent or insignificant. *L. monocytogenes* has been isolated from human semen, and the possibility of venereal transmission was suggested in goats after an outbreak where breeding bucks seemed to be the only link between herds.

Disinfection

L. monocytogenes is susceptible to many common disinfectants including sodium hypochlorite, povidone iodine, chlorhexidine, 70% ethanol, glutaraldehyde and quaternary ammonium agents, though efficacy can be influenced by the presence of organic matter and adherence of the organism to surfaces. *L. monocytogenes* can be difficult to eliminate from some equipment in food processing facilities, probably because it is protected in biofilms or niches such as scratched surfaces. Some organisms in these facilities are known to be resistant to quaternary ammonium disinfectants.

Listeria can be killed by heat, including HTST pasteurization of milk. These organisms can also be destroyed by autoclaving (i.e., moist heat of 121°C/ 250°F for a minimum of 15 minutes or dry heat of 160-170°C/ 320-338°F for 1 hour).

Infections in Animals

Incubation Period

The incubation period for encephalitis in ruminants is often around 3-4 weeks, with a range of 1-7 weeks. Abortions can occur a week or more after exposure, while septicemia or gastroenteritis often develops shortly after exposure to contaminated food, sometimes as soon as 1-2 days. There is little information about the incubation period for listeriosis in other animals, but it was reported to range from 16 hours to nearly 2 months in turkeys.

Clinical Signs

Asymptomatic carriage of *Listeria* is much more common than disease. Clinical cases occur most often in cattle, sheep and goats, and the most complete descriptions of clinical signs are in these species. *L. monocytogenes* has been found in all syndromes, while *L. ivanovii* has been associated most often with reproductive losses in ruminants.

Ruminants

Reproductive losses are one of the most common syndromes in cattle and small ruminants. Animals may abort, typically late in gestation, or give birth to stillborn offspring, and some live neonates may develop septicemia. Reproductive losses can occur sporadically or in outbreaks; the latter are more likely to be seen in sheep and goats. The dam usually has few or no signs of illness except when the placenta is retained, which may result in metritis and septicemia. An uncommon syndrome reported in 3-7 day old calves is characterized by dyspnea, corneal opacity and meningitis, with nystagmus and mild opisthotonos and death within 12 hours.

Listeria can also cause CNS disease, often in adult ruminants. Neurological syndromes tend not to affect a herd at the same time as reproductive losses, although there are exceptions. Rhombencephalitis, which mainly affects the brainstem, is the most common form of CNS disease. It is thought to result from organisms reaching the brain via an ascending infection in nerves. Clinical cases typically occur in a single animal in the herd or develop in a few animals over the course of a few weeks. Depression and partial to complete anorexia are usually the initial signs, but some animals may appear unusually excitable. Sheep that are approached may attempt to flee but appear incoordinated and fall easily. A fever may also be apparent in the early stages, but it often disappears after a few days and is usually absent by the time the neurological signs appear. Other signs vary depending on the cranial nerves and other regions affected. Cranial nerve deficits tend to be unilateral, especially early. Common neurological signs include facial paralysis (e.g., a drooping ear or eyelid, decreased lip tone, dropped jaw or poor jaw tone), dysphagia, excessive salivation, nystagmus, torticollis, strabismus, incoordination and compulsive circling or turning of the head to one side. Inability to swallow may lead to dehydration. Animals become recumbent during the final stages, and may make involuntary running movements or characteristic chewing motions. The course of the disease is usually short in sheep and goats, typically lasting a few days before death, but it tends to progress more slowly in cattle, which often survive for 1-2 weeks. Animals that recover may have persistent neurological deficits.

CNS syndromes reported infrequently in ruminants include meningitis and diffuse meningoencephalitis, which are thought to result from bloodborne infections, and myelitis. Meningitis usually develops suddenly, with fever, rigidity of the neck muscles, muscle tremors and/or spasms, and cutaneous hyperesthesia of varying degrees, and progresses to drowsiness and coma in the final stages. Spinal myelitis is characterized by fever, ataxia and progressive paresis or paralysis of one or more limbs, but no cranial nerve signs and no apparent effect on mentation. Animals with listerial myelitis usually deteriorate quickly and must often be euthanized.

Septicemia is mainly seen in young ruminants or adults with metritis. Outbreaks of gastroenteritis with diarrhea have been described occasionally in sheep and cattle. Some of these animals can have extensive gastrointestinal hemorrhages, and sudden death is possible. Gastroenteritis may also precede or accompany septicemia. Keratoconjunctivitis can result from cranial nerve deficits that expose the cornea in rhombencephalitis, but it also occurs in animals with no other signs of listeriosis. The latter syndrome is known as silage eye, and usually results from direct inoculation of organisms into the eye. Ocular involvement can be unilateral or bilateral, and ranges from mild epiphora and conjunctivitis to severe keratitis, corneal edema and intrastromal abscesses, with or without uveitis. Milder cases of silage eye may be self-limited. Uncommonly seen syndromes include clinical mastitis (although organisms can be shed subclinically in the milk), and rarely reported forms such as *Listeria*-associated mesenteric lymphadenitis.

Other mammals

Septicemia, with or without concurrent encephalitis, is the most commonly described syndrome in animals other than ruminants. It has been seen in adults as well as young animals in some species including cats, dogs, horses, rabbits and chinchillas. In swine, septicemia usually affects nursing piglets; however, one report described listerial septicemia, hemorrhagic diarrhea and elevated mortality in fattening pigs associated with poor quality silage that also contained mycotoxins. Gastroenteritis sometimes precedes or accompanies septicemia in some species, including horses or chinchillas. Complications of intestinal intussusception and rectal prolapse have been seen in some chinchillas with enteritis.

Cases of isolated meningitis, meningoencephalitis or rhombencephalitis have also been reported in some species. Rhombencephalitis seems to progress rapidly in South American camelids, which often present in an advanced stage of the illness. Severe depression is the most common presentation in horses with listerial encephalitis, but normal mentation with circling is possible.

Abortions and stillbirths have been reported occasionally. Abortions tend to be late-term in rhesus macaques (*Macaca mulatta*). Although meningoencephalitis occurred in one pregnant animal, reproductive losses are not usually accompanied by systemic illness in this species. However, metritis and fatal septicemia are relatively common sequelae after reproductive losses in rabbits and hares.

Listeria keratoconjunctivitis has been seen in horses, rabbits, guinea pigs and other animals. Recurrent cases were reported in some horses fed haylage or silage. Unusual syndromes have been reported mainly in dogs. They included a case of localized pustular dermatitis, probably acquired after rolling in a contaminated carcass or placenta; osteomyelitis in a healthy adult dog; and a urinary tract

infection in a diabetic dog. *L. monocytogenes* was isolated in high numbers from two cases of tonsillitis in dogs, although a causative role was not proven.

Birds

Septicemia is the most common syndrome in birds. The signs are nonspecific and may include listlessness, diarrhea and weight loss or emaciation, but peracute deaths can also be seen. In birds, CNS disease can occur with or without involvement of other body systems. The neurological signs can include paresis or paralysis of the wings or legs, in addition to signs such as depression, torticollis, stupor, tremors and incoordination.

Reptiles

Septicemia, with nonspecific signs (e.g., lethargy, anorexia, dehydration, obtundation) has been reported in a few pet inland bearded dragons. Gas-filled intestines were common in these animals. Clinical cases also occurred in one group of alligators, but no description of these illnesses is available. All cases in reptiles have been fatal to date, including those in treated animals.

Post Mortem Lesions [Click to view images](#)

The lesions vary with the syndrome. Gross lesions are absent or minimal in animals with *Listeria* encephalitis and are usually limited to turbid CSF, congested meningeal vessels, mild discoloration of the brainstem, and occasionally, areas of softening in the medulla oblongata and/ or abscesses. Animals with septicemia usually have small necrotic foci in the internal organs, particularly the liver. Peritonitis is also common in some species such as rabbits. Ulcerative and hemorrhagic abomasitis, as well as enteritis and colitis, can be seen in listerial gastroenteritis in ruminants. Extensive hemorrhages were reported in some cases.

Aborted fetuses may be slightly to significantly autolyzed and edematous. The villi of the placental cotyledons are usually necrotic, and the chorion may be covered with brownish-red exudate. Pinpoint foci of necrosis are common in the liver and sometimes the lung, spleen, myocardium or other organs of fetuses infected with *L. monocytogenes*. There may also be clear or blood-tinged fluid in the serous cavities, and shallow erosions in the abomasal mucosa. Some fetuses have few gross lesions. Suppurative bronchopneumonia rather than multifocal hepatocellular necrosis is reported to be common in fetuses infected with *L. ivanovii*.

Birds

Areas of myocardial necrosis and degeneration and serofibrinous pericarditis are common in birds with septicemia. The spleen and liver are often enlarged, and foci of necrosis may be found in the internal organs, especially the liver. Granulomatous and caseous hepatic lesions and catarrhal enteritis have been seen in some cases. There are few or no gross lesions in the brain of birds with

encephalitis; however, some birds with encephalitis have concurrent lesions from septicemia.

Diagnostic Tests

L. monocytogenes, its nucleic acids and antigens may be detected in the placenta, fetus (e.g., fetal stomach contents) or uterine discharges after an abortion; in the blood of septicemic animals; in samples from sites of localization, such as cerebrospinal fluid (CSF) or ocular swabs; and in postmortem tissue samples such as the liver, kidneys, spleen and brain. Feed or other environmental samples may be tested in some investigations. Organisms are often undetectable in the CSF of animals with rhombencephalitis, and, in this syndrome, a definitive diagnosis may only be available at necropsy.

Listeria spp. can be isolated from many clinical samples on non-selective media. However, specialized enrichment techniques are needed to recover organisms from the brain, where they occur in low numbers, or from contaminated samples such as feces or food. At one time, it was common to use a cold enrichment technique simultaneously with standard bacteriological isolation in these cases. However, cold enrichment can take up to 3 months, and immunohistochemistry or PCR on tissue samples may provide a more rapid diagnosis. Enrichment techniques, including selective media and chromogenic media, have been developed for environmental samples and food, and might also be used with clinical samples from animals. Organisms are identified to the species level with biochemical tests. *L. monocytogenes*, *L. ivanovii* and *L. seeligeri* are the only beta-hemolytic species of *Listeria* on blood agar, though the zone of hemolysis for *L. monocytogenes* and *L. seeligeri* is narrow.

Nucleic acids may be identified in tissues and secretions by PCR. Loop-mediated isothermal amplification (LAMP) assays have also been published for *L. monocytogenes* and *L. ivanovii*. Immunohistochemistry or immunofluorescence can detect antigens in tissues. A number of commercial rapid identification methods have been developed to identify *L. monocytogenes* in food. In epidemiological investigations, *L. monocytogenes* can be subtyped with genetic techniques such as pulsed field gel electrophoresis (PFGE), whole genome sequencing, multivirulence-locus sequence typing (MVLST) and multilocus sequence typing (MLST). *Listeria* can be serotyped by agglutination, PCR or ELISAs; however, this is not very useful for tracing outbreaks, as most clinical cases are caused by a few common serotypes, and each serotype can contain more than one species of *Listeria*.

Serology is not used routinely for diagnosis. Many healthy animals have high *Listeria* titers, and cross-reactions can occur with enterococci, *Staphylococcus aureus* and other organisms in some tests. An anti-listeriolysin ELISAs for IgG is more specific than other assays, but rising titers would need to be seen, and this test is often negative or inconsistent in cases of encephalitis.

Treatment

L. monocytogenes is susceptible to many antibiotics *in vitro*, but some of these agents may not be effective *in vivo*. Penicillins are considered to be the drugs of choice, but other antibiotics including tetracyclines have sometimes been used. High doses and early treatment are required for animals with rhombencephalitis, and supportive treatment may also be required. Animals with severe or advanced neurological signs usually die despite treatment. Spinal myelitis is also reported to be poorly responsive to treatment. Antibiotic resistant organisms have been reported.

Control

Disease reporting

Veterinarians should check their national and/or local guidelines for any disease reporting requirements. Clinical cases must be reported in some U.S. states, but listeriosis in animals is not currently reportable at the federal level.

Prevention

Feeding good quality silage is important in preventing listeriosis in herbivores. Although silage with *Listeria* growth can appear normal, the superficial few inches exposed to air and any spoiled or moldy silage should not be fed, as they indicate areas where conditions may have allowed *Listeria* to grow. Any leftover silage should be removed after feeding and silage handling tools cleaned to prevent cross-contamination. Animals should also be kept away from rotting vegetation, which may contain high levels of organisms, and opportunities for fecal contamination of food should be minimized. Feed suspected to be the source of an outbreak should be removed while the cases are investigated.

Although *Listeria* is common in the environment, the number of organisms can differ between locations, and *L. monocytogenes* is readily recovered on some farms but not others. Sick animals should be isolated, and sources of contamination, such as the placenta and fetus, should be removed and destroyed. Thorough cleaning is reported to remove *Listeria* from fomites such as water tanks on some farms. It may also be helpful to control rodents, which can shed organisms in the feces, and to minimize stressors and concurrent diseases, which are suspected to increase susceptibility to listeriosis. Live attenuated vaccines have been used in ruminants in a few European countries, but no vaccine is available in North America.

Morbidity and Mortality

While listeriosis can occur in animals eating other feed, most cases in ruminants are linked to feeding silage. Clinical cases can occur year-round in some warm-climate countries, but in northern temperate climates they are most common in winter and early spring, and tend to be seen in feedlot or housed animals. Gastroenteritis in sheep often occurs in the winter after weaning, although outbreaks have

also been reported in animals on poor quality pastures at high stocking densities. Subclinical shedding of *L. monocytogenes* in feces is much more common than disease. There is little information about the factors that predispose nonpregnant animals to listeriosis, but some authors speculate that stressors including concurrent diseases, poor condition or immunosuppression may play a role. However, many cases of listeriosis occur in seemingly healthy animals.

Listerial encephalitis and reproductive losses tend to be sporadic in cattle, and encephalitis rarely affects more than 2-10% of the herd. Small ruminants seem to be more susceptible to listeriosis than cattle, and outbreaks are more common in these species. Abortions can affect up to 10-20% of a sheep flock, and higher rates are occasionally reported. The case fatality rate for encephalitis is estimated to be around 30-50% in cattle, but it is higher in sheep and goats, as treatment must be started early for success and the disease tends to progress more quickly in these species. The case fatality rate for untreated encephalitis can approach 100%.

Listeriosis is infrequently reported in animals other than ruminants, and while outbreaks can be seen, clinical cases are often sporadic. However, septicemia is reported to be common in farmed chinchillas, and clinical cases were seen in a number of horses fed silage in the winter in Iceland. Listeriosis is rare in nonhuman primates housed indoors, but reproductive losses occur regularly in one group of rhesus macaques kept in an outdoor enclosure. One study found that *L. monocytogenes* accounted for 2% of the isolates from blood cultures in severely ill neonatal foals. Variable morbidity and mortality rates have been reported in poultry: losses may not rise about normal background levels on some farms, but high morbidity and mortality rates have been reported on others.

Infections in Humans

Incubation Period

Although longer incubation periods are possible, current estimates suggest that most cases in nonpregnant humans, including encephalitis, become apparent within 2 weeks of exposure, and the incubation period is rarely over a month. Cutaneous rashes usually appear in 1-7 days, and gastroenteritis often within a few days. The incubation period for pregnancy losses ranges from 2 weeks to approximately 2 months.

Clinical Signs

Clinical syndromes in humans include reproductive losses, septicemia, CNS disease, febrile gastroenteritis, skin rashes and occasional localized conditions affecting other organs and tissues. Most serious illnesses occur in people who are immunocompromised, debilitated and/or elderly, but rashes, gastroenteritis and pregnancy losses often affect healthy people.

Common symptoms in febrile gastroenteritis, which usually occurs after eating heavily contaminated food, include fever, flu-like signs (e.g., nausea, headache, myalgia), diarrhea and abdominal pain. Vomiting may occur, especially in children. This condition is usually self-limiting within a few days. Life-threatening cases have been reported, but are rare.

Most skin rashes develop after direct contact with a heavily contaminated source such as an infected fetus. They are typically papular or pustular, localized and nonpruritic, and may sometimes be accompanied by fever, chills, localized lymphadenopathy or generalized pain. These rashes are usually self-limited. In a few cases, dissemination to the skin has been reported in immunosuppressed patients with systemic illnesses. Localized rashes and/or abscesses were seen in some of these cases, but at least one patient had a widespread papular rash. The skin can also be involved in some infants with septicemia (described below).

Healthy pregnant women typically remain asymptomatic or experience a mild flu-like illness and/or gastrointestinal signs, but may later abort or give birth to a stillborn or premature infant. Although abortions can be seen at other times, they are usually reported during the second half of pregnancy, and are most frequent in the third trimester. Live infants are sometimes ill at birth or become ill within the first few weeks. Neonatal illnesses are divided into early onset disease, which develops within the first week after birth and often affects premature infants, and late onset disease. Infants with early onset disease usually have septicemia, sometimes with disseminated granulomas, pustular skin lesions and/or abscesses in severe cases. Pneumonia and meningitis are less commonly reported syndromes. A significant number of early onset cases are fatal, and complications, including severe developmental and neurological defects, are common in infants that survive. Meningitis is the most common syndrome in late onset disease, although septicemia or colitis are seen occasionally. The onset of meningitis can be insidious in young infants. Most infants with late onset disease survive if they receive appropriate treatment, and while long-term neurological sequelae are possible, many recover fully. Septicemia can also be seen in adults who are immunosuppressed and/or debilitated.

In humans, CNS involvement may appear as meningitis, meningoencephalitis, rhombencephalitis or brain abscesses. Meningitis, the most common form, and meningoencephalitis usually occur in people who are immunosuppressed or elderly. Meningitis may appear with subtle and gradual signs in these populations, and some characteristic signs (e.g., fever, neck stiffness) may be absent. Localized brain abscesses are uncommon, and result in focal neurological signs that vary depending on the part of the brain affected. Listerial rhombencephalitis is an uncommon condition that occurs most often in healthy people. Its signs can include unilateral or bilateral cranial

nerve deficits, ataxia and other signs of cerebellar dysfunction, hemiparesis and impaired consciousness. Rhombencephalitis can be difficult to diagnose and deaths are common, often as the result of respiratory or cardiac failure. Survivors may have permanent sequelae.

Bone and joint infections (osteomyelitis, septic arthritis) tend to be reported mainly in people who have implants or other foreign material, and usually affect one site. Immunosuppression appears to be a predisposing factor in some but not all cases. Conjunctivitis, keratoconjunctivitis, chorioretinitis and endophthalmitis can also be seen in healthy or immunosuppressed individuals. Endophthalmitis is rare, often occurs without other signs of listeriosis, and usually affects only one eye. It can be difficult to treat, and residual visual defects are common. In rare instances, *L. monocytogenes* has also caused biliary tract infections (cholecystitis, cholangitis, biliary cyst), hepatitis and/or single or multiple liver abscesses, urinary tract infections (prostatitis, rarely pyelonephritis), endocarditis, peritonitis, respiratory disease (pneumonia, pleuritis) and other syndromes.

Diagnostic Tests

As in animals, listeriosis is usually diagnosed by isolating *L. monocytogenes* or detecting its nucleic acids and antigens in clinical samples such as blood, CSF, joint fluid, amniotic fluid, uterine swabs, postmortem tissue samples, and the placenta and other birth or abortion products. Cultures are often negative in cases of rhombencephalitis. Several serological tests are available, including an ELISA that detects IgG to listeriolysin. However, serology is difficult to interpret and rarely used, as antibodies are common in healthy people and previous exposure does not seem to be protective. Genetic analyses such as whole genome sequencing, PFGE and DNA hybridization are often used to trace outbreaks of listeriosis in humans, and food is commonly tested to determine the source of an outbreak.

Treatment

Penicillins are the most frequently used drugs in humans, although other agents, especially trimethoprim-sulfamethoxazole or macrolides, are sometimes employed. Adding gentamicin in serious cases is proposed to have a synergistic effect but this is controversial. Surgery (e.g., prosthesis replacement, debridement) may be required in some cases, especially those involving bones or joints. Treatment of pregnant women known to be infected reduces the risk of fetal complications.

Prevention

Listeriosis prevention is targeted mainly at high risk individuals, including pregnant women. Measures to reduce the risk of foodborne listeriosis, the most common source of infection, include cooking animal products, washing raw vegetables well, and avoiding uncooked high risk foods.

Some high risk foods are ready-to-eat deli meats, refrigerated pâtés and other meat spreads, refrigerated smoked seafood (e.g., lox), unpasteurized milk and various types of soft cheese (e.g., feta, Brie, bleu cheese, Camembert, and Mexican cheeses such as queso fresco and Panela) made from unpasteurized milk. People at elevated risk for listeriosis can eat foods such as deli meats if they are reheated to a high temperature (“steaming hot”). *Listeria* can grow in refrigerated foods, and leftovers should also be reheated. People should also remain aware of outbreak reports, as some recent cases were linked to foods not usually associated with listeriosis, such as cantaloupes, pre-cut celery and caramel apples.

Controlling *Listeria* in food processing establishments can be challenging. While some organisms occur only transiently after being introduced on foods, others can become established and persist for many years. Most countries use risk-based methodology for food safety, where a level of *L. monocytogenes* that poses a negligible risk to healthy people (e.g., < 100 organisms/gram) is allowed in most foods at consumption, with more stringent levels for some products such as baby foods. Environmental monitoring, product testing, and cleaning and sanitation are important in meeting these standards. In the U.S., the presence of any level of *L. monocytogenes* in any food prompts a recall, and additional measures may be needed. For instance, growth inhibitors may be added to some products or packaging may be designed to inhibit *Listeria*. Once a package is opened, these measures may no longer be effective, and refrigerated ready-to-eat products should be consumed within a few days after opening.

Barrier precautions (e.g., gloves), sanitation and hygiene decrease the risk of contact exposure while assisting at births or performing necropsies. Hand hygiene and other infection control measures are important when handling newborns, as nosocomial transmission has been reported in human nurseries. Recommendations have been published for treating or monitoring pregnant women exposed to contaminated foods. They vary with the symptoms and likelihood of exposure.

Morbidity and Mortality

Listeriosis is important mainly as a cause of reproductive losses in pregnant women and serious illnesses in people predisposed by various risk factors. Healthy people rarely become ill, although an estimated 1-15% of the population sheds *L. monocytogenes* without clinical signs. Gastroenteritis in healthy individuals normally occurs only after eating heavily contaminated foods. Skin rashes are usually an occupational disease and typically occur after handling infected newborns, birth or abortion products, aborted animals, or tissues from septicemic animals at necropsy, although one unusual case appeared to be related to gardening.

An estimated 15-30% of maternal infections are thought to result in abortions, stillbirths or fatal neonatal

illnesses. However, pregnancy alone does not seem to increase the risk of other serious forms of listeriosis. Known risk factors for serious disease include cancer, transplantation, liver disease/ cirrhosis, kidney disease/ dialysis, diabetes, uncontrolled HIV-1 infections (AIDS), and other diseases that are either immunosuppressive or are treated with immunosuppressive drugs. Gastrointestinal acid inhibitors also seem to increase the risk of illness. Most authors include being elderly as a risk factor for listeriosis; however, one study suggested that advanced age is not as important as the illnesses that affect this population.

Clinical cases can occur sporadically or in outbreaks of varying size, usually associated with food. In 2013, the reported incidence of listeriosis was 3 cases per million population in the U.S., 4 per million in Germany and 6 per million in Austria. The incidence seems to be rising in some areas, possibly due to changes in eating habits, food storage practices and/or an increased prevalence of susceptible individuals. The overall case fatality rate is estimated to be 20-30%, but it varies with the form of the disease. Gastroenteritis is usually self-limited and deaths are rare, while septicemia and CNS disease are life-threatening. Case fatality rates can be as high as 70% in untreated meningitis. Rhombencephalitis is often fatal, as it is uncommon and can be difficult to diagnose, and patients may not initially receive antibiotics appropriate for *L. monocytogenes*. Estimates of the case fatality rate in sick newborns vary, but some sources suggest that it is currently 20-30% or less in early onset disease and 10% or less in late onset cases.

Internet Resources

Centers for Disease Control and Prevention (CDC).

Listeriosis

<https://www.cdc.gov/listeria/>

European Centre for Disease Prevention and Control.

Listeriosis

<https://ecdc.europa.eu/en/listeriosis>

Public Health Agency of Canada. Pathogen Safety

Data Sheets

<https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html>

The Merck Manual

<http://www.merckmanuals.com/professional>

The Merck Veterinary Manual

<http://www.merckvetmanual.com/>

World Health Organization (WHO). Listeriosis

<https://www.who.int/mediacentre/factsheets/listeriosis/en/>

World Organization for Animal Health (OIE)

<http://www.oie.int>

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

<http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/>

OIE Terrestrial Animal Health Code

<http://www.oie.int/international-standard-setting/terrestrial-code/access-online/>

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