

do occur. No epidemiologic or clinical evidence supports person-to-person transmission (other than vertical transmission from mother to fetus) or waterborne infection. In line with its survival and multiplication at refrigeration temperatures, *L. monocytogenes* is commonly found in processed and unprocessed foods of animal and plant origin, especially soft cheeses, delicatessen meats, hot dogs, milk, and cold salads; fresh fruits and vegetables can also transmit the organism. Because food supplies are increasingly centralized and normal hosts tolerate the organism well, outbreaks may not be immediately apparent. The U.S. Food and Drug Administration has a zero-tolerance policy for *L. monocytogenes* in ready-to-eat foods.

### DIAGNOSIS

Symptoms of listerial infection overlap greatly with those of other infectious diseases. Timely diagnosis requires that the illness be considered in groups at risk: pregnant women; elderly persons; neonates; individuals immunocompromised by organ transplantation, cancer, or treatment with tumor necrosis factor antagonists or glucocorticoids; and patients with a variety of chronic medical conditions, including alcoholism, diabetes, renal disease, and rheumatologic and hepatic illnesses. Meningitis in older adults (especially with parenchymal brain involvement or subcortical brain abscess) should trigger consideration of *L. monocytogenes* infection and treatment. Listeriosis occasionally affects healthy, young, nonpregnant individuals. HIV-infected patients are at risk; however, listeriosis seems to be prevented by trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis targeting other AIDS-related infections. The diagnosis is typically made by culture of blood, cerebrospinal fluid (CSF), or amniotic fluid. *L. monocytogenes* may be confused with “diphtheroids” or pneumococci in Gram-stained CSF or may be gram-variable and confused with *Haemophilus* species. Polymerase chain reaction diagnostics have been described but are not widely available, and serology is not clinically useful.

### CLINICAL MANIFESTATIONS

Listerial infections present as several clinical syndromes, of which meningitis and septicemia are most common. Monocytosis is seen in infected rabbits but is not a hallmark of human infection.

**Gastroenteritis** Appreciated only since the outbreaks of the late 1980s, listerial gastroenteritis typically develops within 48 h of ingestion of a large inoculum of bacteria in contaminated foods. Attack rates are high (50–100%). *L. monocytogenes* is neither sought nor found in routine fecal cultures, but its involvement should be considered in outbreaks when cultures for other likely pathogens are negative. Sporadic intestinal illness appears to be uncommon. Manifestations include fever, diarrhea, headache, and constitutional symptoms. The largest reported outbreak occurred in an Italian school system and included 1566 individuals; ~20% of patients were hospitalized, but only one person had a positive blood culture. Isolated gastrointestinal illness does not require antibiotic treatment. Surveillance studies show that 0.1–5% of healthy asymptomatic adults may have stool cultures positive for the organism.

**Bacteremia** *L. monocytogenes* septicemia presents with fever, chills, and myalgias/arthralgias and cannot be differentiated from septicemia involving other organisms. Meningeal symptoms, focal neurologic findings, or mental status changes may suggest the diagnosis. Bacteremia is documented in 70–90% of cancer patients with listeriosis. A nonspecific flulike illness with fever is a common presentation in pregnant women. Endocarditis of prosthetic and native valves is an uncommon complication, with reported fatality rates of 35–50% in case series. A lumbar puncture is often prudent, although not necessary, in pregnant women without central nervous system (CNS) symptoms.

**Meningitis** *L. monocytogenes* causes ~5–10% of all cases of community-acquired bacterial meningitis in adults in the United States. Case-fatality rates are reported to be 15–26% and do not appear to have changed over time. This diagnosis should be considered in all older

or chronically ill adults with “aseptic” meningitis. The presentation is more frequently subacute (with illness developing over several days) than in meningitis of other bacterial etiologies, and nuchal rigidity and meningeal signs are less common. Photophobia is infrequent. Focal findings and seizures are common in some but not all series. The CSF profile in listerial meningitis most often shows white blood cell counts in the range of 100–5000/μL (rarely higher); 75% of patients have counts below 1000/μL, usually with a neutrophil predominance more modest than that in other bacterial meningitides. Low glucose levels and positive results on Gram’s staining are found ~30–40% of the time. Hydrocephalus can occur.

**Meningoencephalitis and Focal CNS Infection** *L. monocytogenes* can directly invade the brain parenchyma, producing either cerebritis or focal abscess. Approximately 10% of cases of CNS infection are macroscopic abscesses resulting from bacteremic seeding; the affected patients often have positive blood cultures. Concurrent meningitis can exist, but the CSF may appear normal. Abscesses can be misdiagnosed as metastatic or primary tumors and, in rare instances, occur in the cerebellum and the spinal cord. Invasion of the brainstem results in a characteristic severe rhombencephalitis, usually in otherwise healthy older adults (although there are numerous other infectious and noninfectious causes of this syndrome). The presentation may be biphasic, with a prodrome of fever and headache followed by asymmetric cranial nerve deficits, cerebellar signs, and hemiparetic and hemisensory deficits. Respiratory failure can occur. The subacute course and the often minimally abnormal CSF findings may delay the diagnosis, which may be suggested by MRI showing ring-enhancing lesions after gadolinium contrast and hyperintense lesions on diffusion-weighted imaging. MRI is superior to CT for the diagnosis of these infections.

**Infection in Pregnant Women and Neonates** Listeriosis in pregnancy is a severe and important infection. The usual presentation is a nonspecific acute or subacute febrile illness with myalgias, arthralgias, backache, and headache. Pregnant women with listeriosis are usually bacteremic. This syndrome should prompt blood cultures, especially if there is no other reasonable explanation. Involvement of the CNS is rare in the absence of other risk factors. Preterm delivery is a common complication, and the diagnosis may be made only post-partum. As many as 70–90% of fetuses from infected women can become infected. Prepartum treatment of bacteremic women enhances the chances of delivery of a healthy infant. Women usually do well after delivery: maternal deaths are very rare, even when the diagnosis is made late in pregnancy or post-partum. Overall mortality rates for fetuses infected in utero approach 50% in some series; among live-born neonates treated with antibiotics, mortality rates are much lower (~20%). *Granulomatosis infantiseptica* is an overwhelming listerial fetal infection with miliary microabscesses and granulomas, most often in the skin, liver, and spleen. Less severe neonatal infection acquired in utero presents at birth. “Late-onset” neonatal illness typically develops ~10–30 days post-partum. Mothers of infants with late-onset disease are not ill.

### TREATMENT

## INFECTIONS CAUSED BY LISTERIA MONOCYTOGENES

### ANTIBIOTICS

No clinical trials have compared antimicrobial agents for the treatment of *L. monocytogenes* infections. Data from studies conducted in vitro and in animals as well as observational clinical data indicate that ampicillin is the drug of choice, although penicillin also is highly active. Adults should receive IV ampicillin at high doses (2 g every 6 h). Many experts recommend the addition of gentamicin for synergy (1.0–1.7 mg/kg every 8 h); retrospective uncontrolled trials are not conclusive, but one study suggests that gentamicin may not help. TMP-SMX, given IV, is the best alternative for the penicillin-allergic patient (15–20 mg of TMP/kg per day in divided doses every 6–8 h). The dosages recommended cover CNS infection and