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Primer

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# Listeriosis

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## Abstract

Listeriosis is a serious food-borne bacterial infection caused by *Listeria monocytogenes*. *L. monocytogenes* is a facultative intracellular bacterial species that can replicate inside human cells, as well as thrive in a variety of environments, including soil, decaying vegetation, animal intestines and foods such as unpasteurized dairy products, soft cheese, raw meat, fish, seafood, vegetables and fruits. Clinically, *L. monocytogenes* can cause gastroenteritis in healthy individuals or serious invasive infections in at-risk populations. For example, maternal–fetal infections during pregnancy can lead to adverse pregnancy outcomes. In the elderly and immunosuppressed, listeriosis can cause septicaemia and central nervous system infections (also known as neurolisteriosis) with high mortality and risk of long-term sequelae. Genomic studies have identified four lineages of *L. monocytogenes*, with lineage I comprising the most virulent strains. The pathogenicity of *L. monocytogenes* reflects its ability to resist gastric and bile acids, colonize the intestinal lumen, cross the intestinal barrier, survive intracellularly in the bloodstream, evade immune responses, and cross the placental and blood–brain barriers. Diagnosis of listeriosis (septicaemia, neurolisteriosis, maternal–neonatal listeriosis or focal listeriosis) involves clinical observations and microbiological testing based on bacterial culture or DNA detection in individuals with prior antimicrobial therapy. Treatment typically involves aminopenicillins and aminoglycosides, with no evidence of clinically meaningful acquired antimicrobial resistance. Although listeriosis is a well-studied infection, a clearer picture of its global burden, its pathophysiology, the dynamics of the *L. monocytogenes* population and transmission routes is needed. On the host side, new risk factors, including genetics, and new treatment regimens to improve patient outcomes need to be identified.

## Sections



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## Introduction

Listeriosis is a food-borne infectious disease caused by *Listeria monocytogenes*, a ubiquitous Gram-positive bacterial species that can grow in a wide range of temperatures and tolerate a variety of environmental stressors, including acidity and osmolarity, allowing it to survive, persist and grow in soil, decaying plants, water, animal intestinal lumen, food and animal feed[1–3]. *L. monocytogenes* is a facultative intracellular bacterium, meaning that it can replicate inside and outside host cells. In healthy individuals, *L. monocytogenes* causes a self-limiting gastroenteritis. However, in at-risk populations, *L. monocytogenes* infection can cause invasive listeriosis, the four main presentations of which are septicaemia, neurolisteriosis, maternal–neonatal listeriosis and rare forms of focal infections. Invasive listeriosis results from the ability of *L. monocytogenes* to cross the intestinal barrier, leading to bacteraemia, and the blood–brain and placental barriers, leading to central nervous system (CNS) and fetal–placental infections, respectively[4,5]. These severe manifestations are associated with specific conditions, such as pregnancy and immunodeficiencies caused by haematological malignancies, immunosuppressive medications, including after organ transplantation, HIV infection without co-trimoxazole prophylaxis and/or ageing[5–7]. In fact, the emergence and increasing incidence of listeriosis is associated with an increasingly ageing and/or immunosuppressed population[8].

Listeriosis is primarily caused by eating contaminated food, including unpasteurized dairy products, deli meats, raw or under-cooked meat and fish, fruits and vegetables, or food that has been contaminated during processing or by contaminated water[9]. The incidence of human listeriosis has increased in the twentieth century with animal farming practices, food-processing industrialization, refrigeration and trade[10,11]. Indeed, *L. monocytogenes* can colonize both wildlife and livestock, persist in artisanal and industrial food-processing facilities and equipment, and grow at refrigeration temperatures, where it can cross-contaminate products[12]. Listeriosis is rare compared to other food-borne infections such as campylobacteriosis and salmonellosis[8]. However, listeriosis has the highest rate of hospitalization of all food-borne infections in industrialized countries, with a case fatality rate around 30% for neurolisteriosis and as high as 45% for non-maternal septicaemia even with appropriate antibiotic treatment, partly due to associated comorbidities[6,8,13,14]. It is the third leading cause of death from food-borne infections in the USA[14]. It is also associated with major pregnancy complications in more than 80% of maternal–fetal infection cases[6]. In addition to being a public health issue and an economic threat to the agri-food industry, *L. monocytogenes* is a well-established model facultative intracellular pathogen, which has contributed to fundamental discoveries in microbiology, cell biology and immunology[4,15–18].

In this Primer, we review the epidemiology of listeriosis, from both a bacterial perspective (reservoirs, global distribution and population structure including hypovirulent and hypervirulent strains) and a host perspective (risk factors and disease outcomes), its pathophysiology, its clinical and microbiological diagnosis and management, and strategies for its treatment and prevention.

## Epidemiology

### Reservoir, sources and modes of transmission

The ability of *L. monocytogenes* to grow at temperatures ranging from 0 °C to 45 °C, as well as to tolerate a wide range of pH (3.0–9.0) and osmolarity levels (up to 10% salt concentration[19]), explains its ubiquitousness in the environment[3]. Livestock, especially cattle, can be contaminated, either as asymptomatic carriers or by developing listeriosis[20], and contribute to the persistence, amplification and spread of *L. monocytogenes* in dairy products and the farm environment[21]. Additionally, domestic and wild mammals and birds can spread *L. monocytogenes* in their faeces, contaminating the environment or animal feed[1,8,22,23]. *L. monocytogenes* enters the food chain through contaminated raw materials, animal products such as raw milk[24] and environmental surfaces in food-processing environments[3,25,26]. Cross-contamination during food processing, inadequate sanitation and poor temperature control also facilitate its spread. As *L. monocytogenes* can grow slowly at refrigeration temperatures and at a wide range of pH and salt concentrations, it can persist in food production chains and be found in many types of food[27], particularly ready-to-eat (RTE) products such as deli meats, dairy products including soft cheeses, pâtés and smoked fish[28–34]. Fruits and vegetables can also be contaminated during food processing and distribution, or in domestic refrigerators, as can vegan substitutes for milk and cheese[35,36].

The consumption of contaminated food is almost the only source of human infection with *L. monocytogenes*[37]. The only known cases of inter-host transmission of *L. monocytogenes* include: vertical from pregnant women to their fetus via the placenta[38]; very rare cases of contamination in farmers and veterinarians through direct contact with tissues of infected animals, leading to cutaneous infection[39]; and horizontal faecal–oral transmission in hospitals, which has been reported in neonates, due to their immature microbiota[40,41].

### Global burden

In the European Union (EU) and the USA, reported positive samples ranged from 0% to 3% across most food products[8,42]. A 2019 meta-analysis of international data indicated a prevalence of 2.9% in deli meat, 2.4% in soft cheese and 2.0% in packaged salad, with 2% (salad) to 25% (soft cheese) of positive samples above the regulatory food safety limit criterion of 100 colony-forming units (CFU) per gram[43]. Although transient faecal or asymptomatic carriage of *L. monocytogenes* in humans is not uncommon, with *L. monocytogenes* prevalence in faecal culture-based studies ranging between 0.2% and 5%[44], and *L. monocytogenes* nucleic acids detectable in faeces in up to 10% of the general population[45], human cases of listeriosis are rare and associated with predisposing conditions[6]. Indeed, despite the relatively high number of contaminated food portions (mass of RTE food ingested per meal, estimated at 55 million above 100 CFU/g consumed by the population of those over 75 years of age in the EU each year[46]), the incidence of confirmed cases remains low. Listeriosis is thought to occur worldwide[47] (Fig. 1) but its prevalence and incidence are only reliably known in countries with mandatory reporting systems. In 2023, there were 0.66 cases of listeriosis per 100,000 people across the EU (2,952 cases, of which 96.5% resulted in hospitalization)[8] and 0.31 cases per 100,000 people in the USA[14], and the worldwide incidence was estimated at 0.337 per 100,000 people in 2010 (ref. 47). In countries with mandatory reporting systems, most cases of listeriosis are sporadic. Indeed, epidemiological surveillance and whole-genome sequencing-based microbiological surveillance allow clusters of cases to be detected, contamination sources to be identified, and large listeriosis outbreaks to be prevented[48–51]. Studies aimed at providing a global view of *L. monocytogenes* clonal diversity have shown its worldwide distribution and the existence of a few predominant and globally distributed clones. For example, lineage I clonal complexes (CC) CC1, CC4 and CC6 strains are the most frequently associated with clinical isolates in Western countries[52–54]. Sequence type (ST) 87 (ST87) is the most common *L. monocytogenes*

clinical ST in East Asia[34,55] and ST328 is the most common in India, with these strains rarely reported in Europe and North America. These epidemiological findings highlight the need for high-quality surveillance systems for listeriosis, especially in parts of the world where little is currently known about *L. monocytogenes* prevalence and listeriosis incidence.

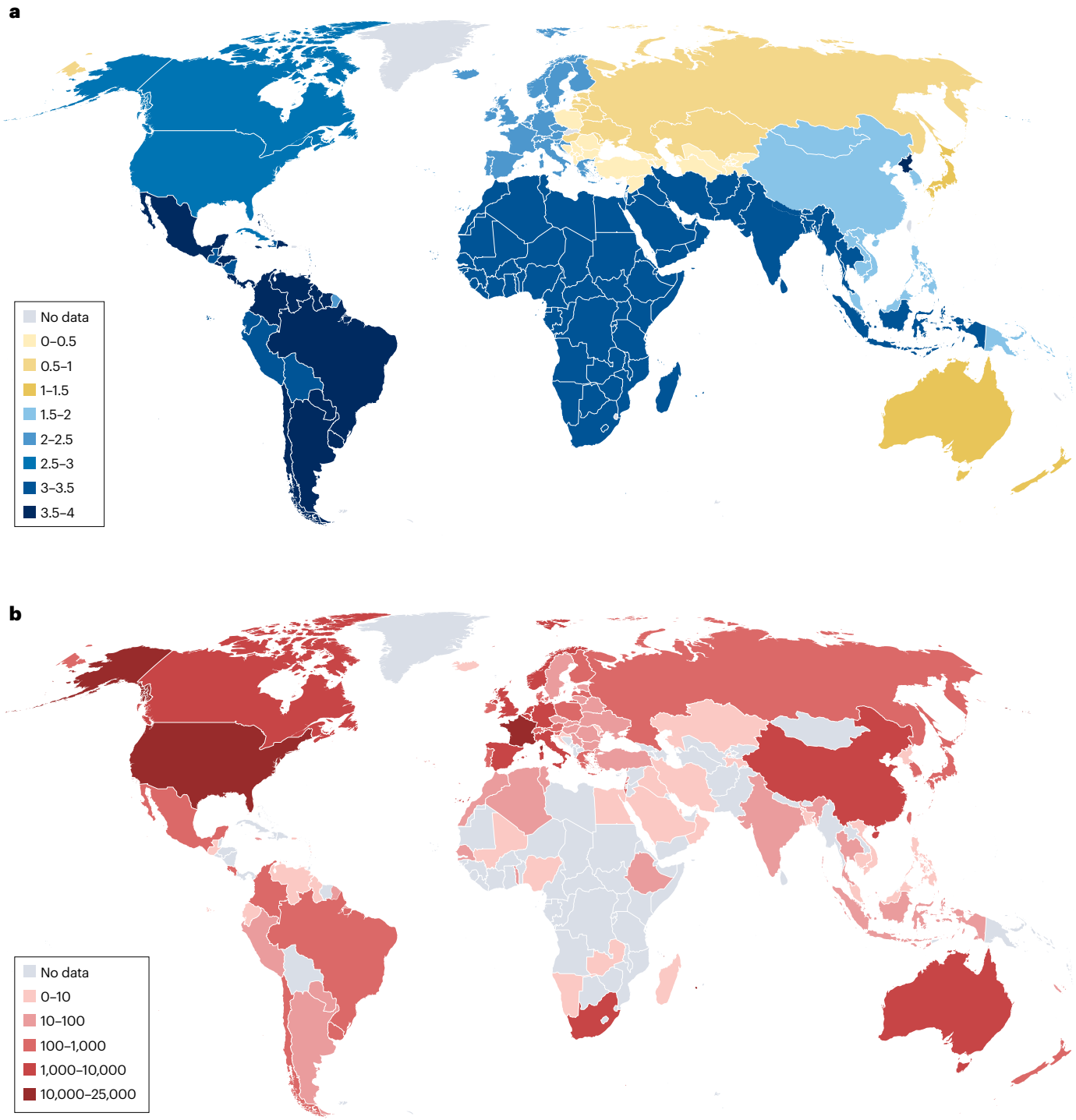



**Fig. 1 | Estimation of the global burden of listeriosis and of the number of isolates sequenced. a**, Burden of human listeriosis estimated by disability-adjusted life-years per 100,000 people (including stillbirths) by WHO subregion[47]. **b**, Number of sequenced *Listeria monocytogenes* isolates per country in the BIGSdb-Lm genome database from 1921 to 2025 (total 85,145 clinical, food and environmental strains). Part **a** reprinted with permission from ref. 47, Elsevier. Part **b** adapted with permission from https://bigsdb.pasteur.fr/listeria/, Institut Pasteur.

## Box 1 | Active surveillance of listeriosis cluster and outbreak management

Listeriosis surveillance relies on the integration of microbiological and epidemiological investigations to detect clusters, identify sources of contamination and prevent and control outbreaks. The effectiveness of surveillance is ensured by comprehensive mandatory reporting of clinical cases and genomic typing of clinical and food or food-processing environment isolates collected through surveillance.

**Microbiological surveillance**

- Isolation and phenotypic characterization of the isolates: agar plating, matrix-assisted laser desorption ionization–time-of-flight analysis and serogenogrouping.
- Genomic typing: core genome multilocus sequence typing (cgMLST), whole-genome MLST (wgMLST) or single-nucleotide polymorphism typing.
- Querying a genomic database (such as BIGSdb-Lm).

**Definition of clusters and outbreaks**

- Sporadic case: an isolated clinical case with or without identification of the source of contamination.
- Cluster of cases: two or more clinical isolates of the same genotype (such as the cgMLST type) with or without an identified food source.
- Nosocomial cluster: food-borne transmission within a health-care setting in patients hospitalized for more than 15 days without external food consumption or cross-contamination (observed in adults served with contaminated food in the hospital and in neonates upon horizontal transmission[40]).
- Outbreak: a substantial cluster of clinical cases linked to an identified food source.
- Food or environmental cluster: isolates of the same genotype (such as the cgMLST type) from food or food environment without associated clinical cases.

**Epidemiological surveillance**

- Enhanced epidemiological and microbiological surveillance to detect additional cases and sources of contamination (such as through analysis of food questionnaires, patient loyalty cards and identification of contaminated batches).
- Investigation of the origin of food contamination (involving identification of production and distribution chains).
- Inspection to identify sources of contamination (including production and/or distribution sites).
- Investigation of care practices, inspection of hospital kitchens and contamination of surfaces and equipment in the event of a nosocomial case.
- Product recalls, management and control of food contamination.

**Cluster and outbreak management**

- Alert phase: initiated in response to a public health threat (for example, when several cases linked to the same strain have been reported, contamination source hypothesis).
  - Screening and querying or notification of international or regional genomic databases and food alert systems.
  - Public communication.
- End of cluster or outbreak: joint decision-making by public health and food safety authorities, and reference laboratories, followed by:
  - Monitoring of cluster or outbreak clones.
  - Possible reassessment of control measures, improvement of surveillance protocols, and new recommendations for at-risk individuals.

### Surveillance

It is essential to implement mandatory reporting of all invasive listeriosis cases (septicaemia, CNS infection and maternal–fetal infection), along with submitting the isolate to a reference laboratory. Microbiological surveillance of at-risk food production and distribution sites is also essential[56]. The public health cornerstone of listeriosis surveillance is the early detection of clusters of cases associated with an isolate, and the identification of the source of contamination using genomic typing, in order to avoid large outbreaks (see below)[48,51] (Box 1).

### Risk factors

Listeriosis occurs mainly in older adults and/or immunocompromised patients. Pregnancy is also a major risk factor for listeriosis (relative risk 30–110 (refs. 7,57)), with newborns being a population at increased risk of infection. Newborns are infected prenatally, via the transplacental route, but in rare cases can become infected in the first days of life, due to their immature microbiota which leads to low neonatal gut resistance to *L. monocytogenes* colonization[40]. A higher prevalence has been reported in pregnant women in England and Wales in those with low socioeconomic status than in those with high socioeconomic status[58], as well as among groups with specific dietary preferences, such as Hispanic women in the USA who frequently consume unpasteurized Mexican-style cheese[59].

Other common risk factors for listeriosis include: male sex; older age (over 65 years of age, with much increased prevalence in those over 80 years of age), which may reflect immunosenescence and a higher frequency of comorbidities compared with younger individuals; acquired cellular and/or innate immunodeficiency; solid organ or bone marrow transplantation; HIV infection; haematological malignancies (especially lymphoproliferative haemopathies, such as chronic lymphocytic leukaemia, lymphoma or multiple myeloma); solid organ cancer; diabetes; chronic renal failure or dialysis; or cirrhosis[6]. The use of immunosuppressive drugs such as corticosteroids, chemotherapeutic agents and other immunosuppressive biotherapies, such as anti-TNF monoclonal antibodies, are also associated with increased risk of listeriosis[6,7,60,61]. The most common immunosuppressive comorbidities in the French MONALISA national prospective cohort study (818 total patients between 2009 and 2013) were solid organ cancer (in 31%) and diabetes (in 22%)[6]. A French retrospective cohort study including 1,959 patients between 2001 and 2008 demonstrated a 1,139-fold increase in listeriosis in patients with chronic lymphocytic leukaemia and a 350-fold increase in patients with multiple myeloma[7]. This study also suggested that the risk of listeriosis, compared with a control population under 65 years of age, was 361 times higher in patients undergoing dialysis, 356 times higher in patients with giant cell arteritis and an oral corticosteroids dose above 0.5 mg/kg/day, 78 times higher

in patients with a solid tumour, and 20 times higher in patients over 74 years of age[7]. Finally, the existence of a subset of patients (4–10%) who develop neurolisteriosis without any known risk factor[6] raises questions about the possibility of yet-unidentified host susceptibility factors, which are currently being investigated (NCT03357536).

### Mortality and morbidity

Invasive listeriosis is associated with poor outcomes. A meta-analysis estimated that listeriosis caused 23,150 illnesses (95% credible interval 6,061–91,247), 5,463 deaths (1,401–21,497) and 172,823 disability-adjusted life-years (DALYs) (44,079–676,465) worldwide in 2010 (ref. 47) (Fig. 1a). Isolated septicaemia (with no other clinically apparent infection location) is associated with a 3-month mortality of up to 46%, despite appropriate antibiotic therapy, and neurolisteriosis with a 3-month mortality of 13% to 40% depending on the absence or presence of concomitant bacteraemia, respectively[6]. This might also reflect, at least in part, the severity of patient comorbidities including malignancy and immunosuppression. If left untreated, neurolisteriosis is fatal[6]. Importantly, the mortality associated with other focal invasive *L. monocytogenes* infections is also very high, as exemplified by the 3-month mortality of *L. monocytogenes*-associated spontaneous bacterial ascites (52%)[62] or *L. monocytogenes*-associated endocarditis (41%)[63]. Parameters independently associated with increased 3-month mortality include monocytopenia, ongoing neoplasia, concomitant multi-organ failure or worsening of a pre-existing condition[6]. In addition, persistent neurological impairment is reported in 44% of patients recovering from neurolisteriosis[6]. Such impairments include (1) persistent focal motor deficits, sensory loss, seizures, altered consciousness or memory loss[64] and (2) the number of neurological signs at baseline, which are two parameters that are independently associated with persistent neurological impairment (OR 21.65 (95% CI 2.58–181.59) and 1.37 (95% CI 1.11–1.69), respectively)[6].

In a 2022 prospective study of the outcomes of neonatal listeriosis, in-hospital mortality was 5%[65], which is much lower than previously reported in the 1990s and 2000s[66,67]. Improved survival rates are likely to reflect major improvements in neonatal intensive care, particularly for premature infants. A study of long-term neurological outcomes showed that 66% of children that survived neonatal listeriosis had persistent neurological impairment at a median age of 5 years, with 18% having severe impairment[68]. Impairments include cognitive deficiencies, reduced executive function, and sensory or motor impairments. Rather than listeriosis itself, gestational age at birth (that is, prematurity due to infection), seemed to be the main determinant of neurological impairment. Indeed, the neurological and neurodevelopmental outcomes of children with neonatal listeriosis did not differ from those of gestational age-matched control children without infection from a contemporary national cohort[68]. These data support the implementation of systematic long-term screening for this vulnerable population, and the provision of tailored education and support.

### *L. monocytogenes* population structure

*L. monocytogenes* strains were first subdivided into 14 serovars by serotyping based on *Listeria* somatic and flagellar antigens[69]. The *L. monocytogenes* species was next divided into four evolutionary lineages based on multilocus enzyme electrophoresis (lineages I and II) and multilocus genotyping (lineages III and IV)[70]. A multilocus sequence typing (MLST) approach based on the allelic variation of seven housekeeping genes allowed identification of sequence types and the definition of CCs that have at least six alleles in common[71]. A core genome MLST (cgMLST) scheme, based on the sequencing of 1,748 core loci, is now widely used internationally to group strains into sublineages (with up to 150 allelic differences) and cgMLST type (CT) (with up to seven allelic differences)[54]. An alternative cgMLST scheme based on 1,701 core loci with a CT threshold of up to ten allelic differences is used for surveillance in Germany and Austria[72].

Lineage I (primarily serotypes 1/2b and 4b) and lineage II (primarily serotypes 1/2a and 1/2c) account for most isolates, but there is an uneven distribution at the level of CCs and sublineages. Most human listeriosis cases and outbreaks worldwide are associated with lineage I isolates[48,53,70]. A study based on 6,633 strains prospectively collected in France, where listeriosis is a notifiable disease, showed that lineage I, in particular CC1, CC4 and CC6, was strongly associated with a clinical origin (isolated in human samples), whereas lineage II, in particular CC9 and CC121, was the most common lineage isolated from food[53,73] (Fig. 2). In the USA, CC1, CC4 and CC6 are also the most common in clinical samples[74], whereas the lineage I CC87 is the most frequent clonal complex in clinical samples from China and Taiwan[34]. Analyses of clinical and biological data collected at the National Reference Centre in France from 818 patients with listeriosis enrolled in the MONALISA prospective cohort study on *Listeria* and listeriosis further showed that food-associated clones CC9 and CC121 were more frequently isolated from highly immunocompromised patients, whereas CC1, CC4 and CC6 were more common in patients with few or no immunosuppressive comorbidities[53]. These findings led to the hypothesis that CC1, CC4 and CC6 might be hypervirulent, and that CC9 and CC121 might be hypovirulent, which was confirmed in a humanized mouse model of *L. monocytogenes* infection[53]. Lineage III and IV strains are rare and tend to be associated with listeriosis in animals[75–77].

## Mechanisms/pathophysiology

*L. monocytogenes* is a facultative intracellular pathogen that can invade non-phagocytic cells, such as epithelial cells, and survive in professional phagocytes. The pathogenicity of *L. monocytogenes* arises from its ability to cross the intestinal, blood–brain and placental barriers, leading to bacteraemia, CNS infection and maternal–neonatal infection, respectively[17,78] (Fig. 3). Various animal models and bacterial strains have been used to gain mechanistic insights into the pathogenesis of *L. monocytogenes* and its interaction with the host (Box 2).

### In vitro studies of host–*L. monocytogenes* interactions

As a facultative intracellular pathogen, *L. monocytogenes* has been a powerful model to study host–pathogen interactions at the cellular level[4,16,17]. In vitro studies using reference strains have identified the core genes and corresponding gene products involved in the intracellular lifestyle of *L. monocytogenes* (Fig. 3a). Transposon-based mutagenesis has revealed that two genes organized in an operon (the *inlAB* operon) encoding InlA and InlB proteins mediate entry into non-phagocytic cells[79]. Further analysis showed that InlA allows *L. monocytogenes* to enter epithelial cells by interacting with the host receptor E-cadherin (Ecad)[80], whereas InlB interacts with c-Met, the ubiquitously expressed receptor for hepatocyte growth factor[81]. Interestingly, these interactions are species-specific: InlA interacts with human Ecad but not with rat or mouse Ecad, due to a single amino acid difference at position 16 of the Ecad EC1 domain[82], and InlB does not interact with rabbit or guinea pig c-Met[83].

Once internalized into host cells, *L. monocytogenes* mediates vacuolar escape via the pore-forming activity of listeriolysin O (LLO),

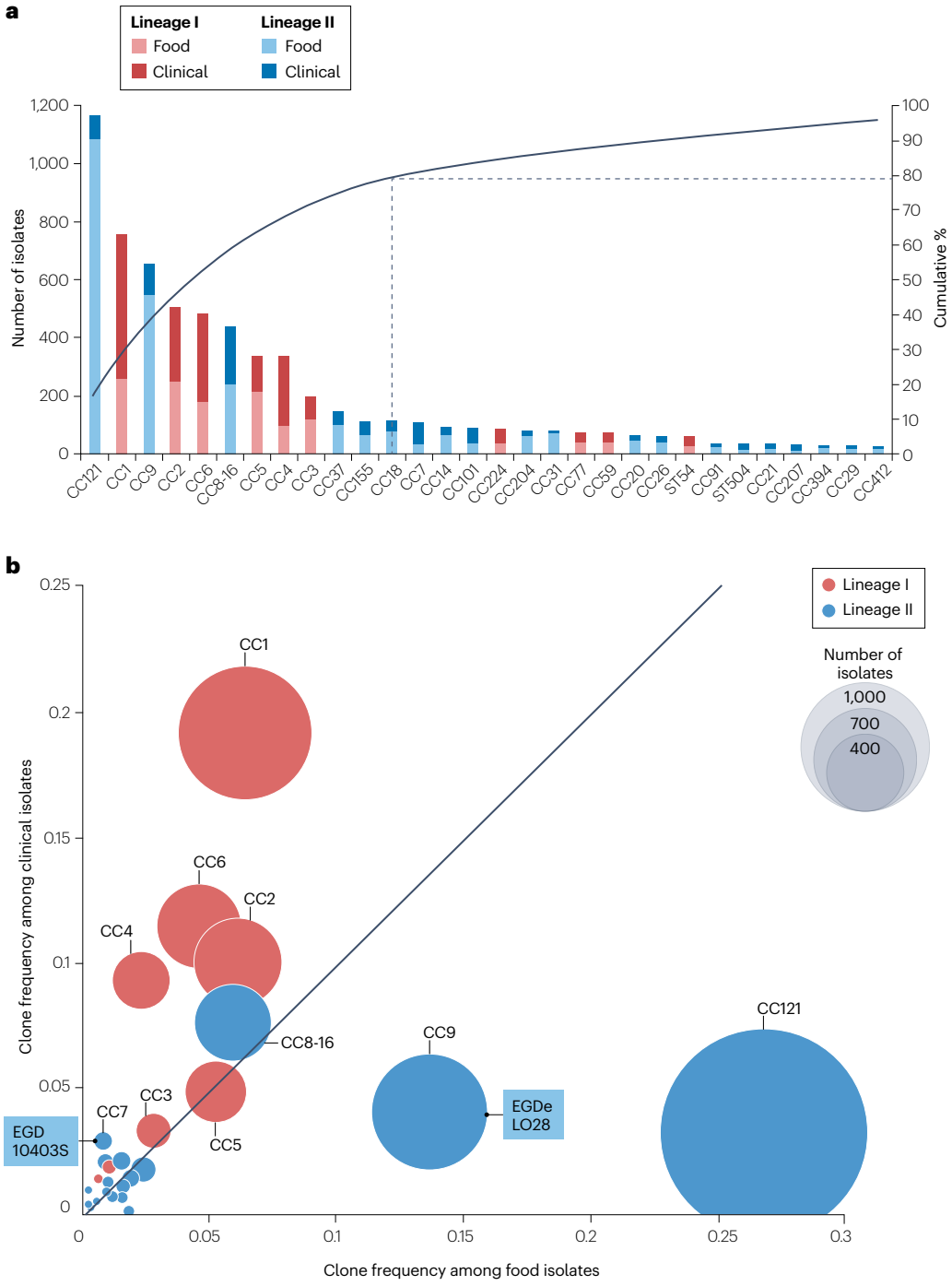



**Fig. 2 | Prevalence of the main clonal complexes among clinical and food isolates in France. a**, The 30 most prevalent clonal complexes (CC) (representing 80% of all isolates), ordered by the total number of isolates. The curve represents the cumulative percentage of isolates pertaining to clones, ordered by the total number of isolates. Only clones with more than ten isolates are shown. **b**, Frequencies of clonal complexes among food and clinical isolates. Circle size is proportional to the number of isolates per clonal complex. Data are based on 6,633 genome sequences. Adapted from ref. 53, Springer Nature Limited.

encoded by *hly*, which was discovered by transposon mutagenesis to identify non-haemolytic mutants on blood agar plates[84–86]. Once inside the cytoplasm, *L. monocytogenes* can propel itself by forming actin comet tails through the action of ActA, a protein that polymerizes host cell actin[87,88]. This actin polymerization phenotype has been observed in other unrelated intracellular bacterial pathogens, such as *Shigella* and *Rickettsia*, as well as the vaccinia virus. Actin-based intracellular motility allows *L. monocytogenes* to escape autophagy[89] and, together with InlC that modifies cell junctions, spread to neighbouring cells[87,90]. Both *hly* and *actA* are located on LIPI-1, together with the virulence genes *plcA* and *plcB*, which encode phospholipases involved in vacuolar escape that are activated by the metalloproteinase Mpl[91,92]. The nucleomodulin OrfX in LIPI-1 dampens the oxidative response of infected macrophages, contributing to intracellular bacterial survival[93].

Both the *inlAB* operon and the LIPI-1 genes are regulated by the major transcription factor positive regulatory factor A (PrfA).

The *prfA* gene is also located in LIPI-1 and is transcriptionally regulated by itself and σB, the major stress response transcription factor of *L. monocytogenes*[94]. *prfA* is further regulated post-transcriptionally by its 5′UTR, in a temperature-dependent manner, and can be inhibited by the *trans*-acting ribosomal proteins SreA and SreB[95,96]. Finally, PrfA is activated post-translationally by glutathione, which is both imported from the host and produced by the *L. monocytogenes* glutathione synthase (GshF), and is required for its full activation[97]. The activity of GshF and PrfA are tightly regulated by the bacterial environment (such as temperature, glutathione and peptide composition specific to eukaryotic cells), allowing *L. monocytogenes* to coordinate the expression of its virulence factors in the host[98–102]. The complete sequencing of the genome of *L. monocytogenes* (reference strain EGDe) and of the closely related avirulent species *L. innocua* enabled new virulence factors to be identified through comparative genomics[103].

## Survival in the gut lumen

As a food-borne pathogen, *L. monocytogenes* first survives in the stomach and the gut lumen.

**Stomach.** The stomach is characterized by high acidity (pH 1.5–3.5) and *L. monocytogenes* has been shown to tolerate acidic conditions (pH 3.0) through an adaptive tolerance response[104,105]. This adaptive tolerance response is mediated by glutamate decarboxylases from the *gadT2D2* operon that maintain intracellular pH and are transcriptionally regulated by both σB[106] and GadR upon mild acid induction upstream of the stomach (pH 4.0–6.0)[107]. Activation of σB by a low pH also allows *L. monocytogenes* to adapt to subsequent phases of infection, via transcription of genes involved in bile resistance, the *inlAB* operon, and the central virulence regulator PrfA[108].

**Bile.** Bile salts help digest food and also have antimicrobial activity. They are synthesized in hepatocytes, stored in the gallbladder and released via the bile duct into the duodenum. Bsh is a bile salt hydrolase produced by *L. monocytogenes* that promotes the survival of *L. monocytogenes* in the intestinal and hepatic phases of listeriosis[109]. The operon *bilE* encodes a two-component bile exclusion system, consisting of the ATPase BilEA and the transmembrane BilEB protein that binds to bile. BilE allows *L. monocytogenes* to tolerate otherwise lethal concentrations of bile[110]. Both *bsh* and *bilE* are regulated by σB and PrfA. *L. monocytogenes* can also sense bile through the bile-regulated transcription factor A (BrtA), which induces the expression of *mdrT*, encoding a bile cholic acid efflux pump[111].

**Microbiota.** Once in the gut, *L. monocytogenes* interacts with the resident microbiota, which can either help or hinder its maintenance in the lumen. The microbiota consists of bacteria, archaea, bacteriophages, fungi and eukaryotic viruses that confer resistance to colonization by pathogens, including *L. monocytogenes*[112]. In humans and mice, a specific microbiota signature is associated with asymptomatic faecal carriage of *L. monocytogenes*, although the exact causative species and underlying mechanisms remain unknown[45]. Similarly, immature microbiota in neonates sensitizes them to *L. monocytogenes* infection, with the potential to lead to listeriosis even with low oral inoculum[40]. Transfer of certain members of the microbiota to germ-free mice shows that some species, including lactobacilli[113] and clostridial species[112], can limit *L. monocytogenes* intestinal colonization, and the bacterium *Akkermansia muciniphila* reduces *L. monocytogenes* infection in specific pathogen-free mice[114,115]. Whether such interactions between certain bacterial species and *L. monocytogenes* occur in mice or humans with native complex microbiota remains to be determined.

Conversely, *L. monocytogenes* can affect the microbiota. Certain strains of the hypervirulent lineage I produce a bacteriocin, listeriolysin S, encoded in the LIPI-3, which targets Gram-positive *Lactococcus lactis*, *Staphylococcus aureus* and *L. monocytogenes* lineage II in vitro[116]. Listeriolysin S activity leads to a modification of the microbiota in vivo that favours infection[116,117]. Mechanistic analysis in vitro showed that listeriolysin S permeabilizes the membrane of the target bacteria in a contact-dependent manner[118]. Another bacteriocin, Lmo2776, expressed mostly by lineage I strains, specifically targets the intestinal commensal *Segatella copri* (formerly *Prevotella copri*)[119]. Paradoxically, *S. copri* favours *L. monocytogenes* infection, and the precise role of Lmo2776 during infection in humans remains to be characterized[119].

**Motility.** *L. monocytogenes* expresses flagellin, encoded by the *flaA* gene, which enables flagellum-mediated motility in vitro[120]. However, the role of *flaA* in vivo remains unclear. A study based on in vivo two-photon microscopy suggested that flagellin allows motile *L. monocytogenes* to target epithelial cells during the first 3 h of infection[121], and that *flaA* is then downregulated at 37 °C via the transcriptional repressor MogR[122,123]. This downregulation inhibits the host pro-inflammatory response induced by interaction of flagellin with the Toll-like receptor TLR5 (ref. 124). The expression of FliF, a protein similar to the flagellar basal body component, and FliI, a protein similar to the cognate ATPase that energizes the flagellar export apparatus, is also downregulated at 37 °C[125].

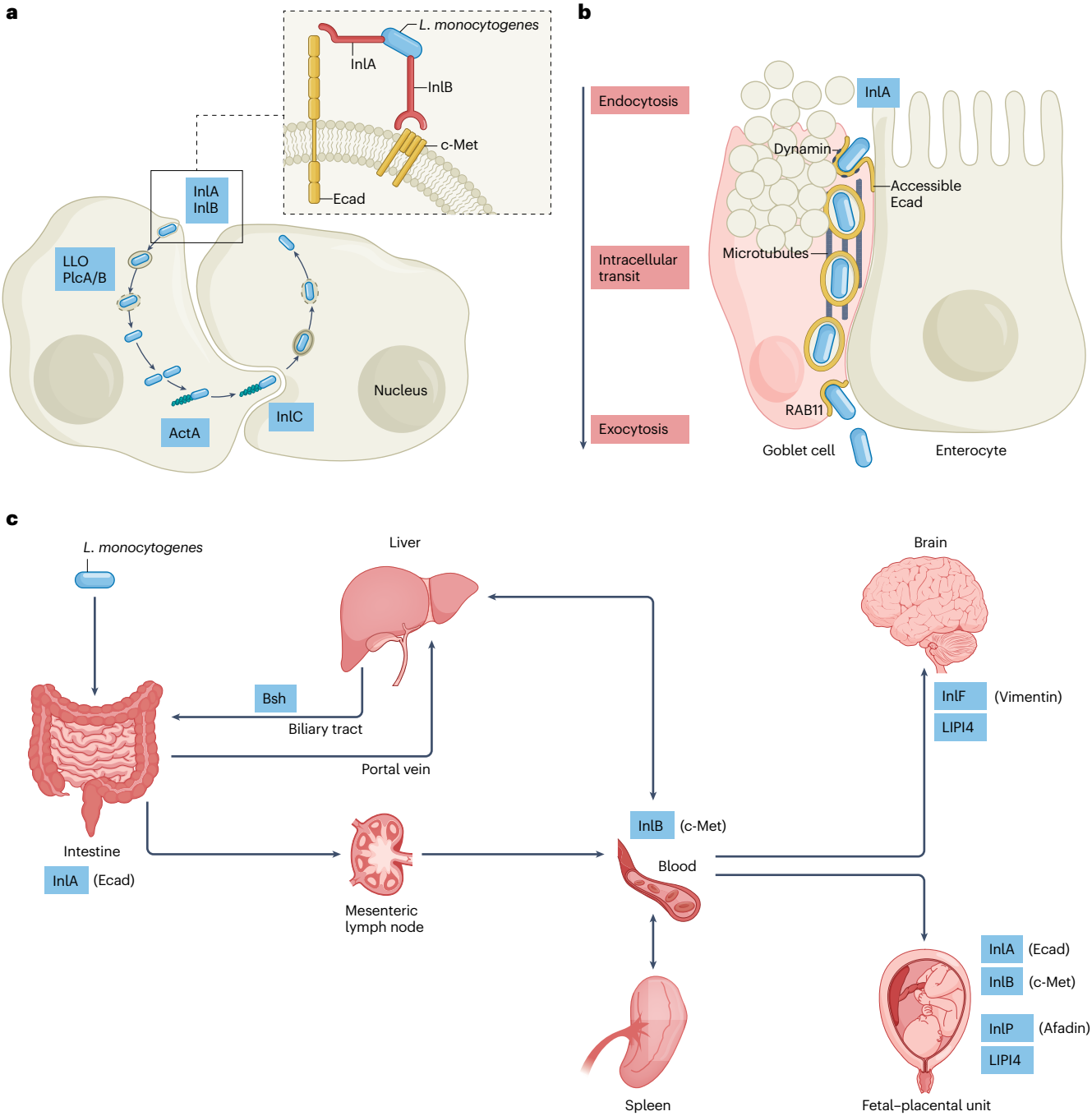
**Mucus interaction.** Mucus synthesized by goblet cells protects the epithelial barrier from luminal bacteria. *L. monocytogenes* InlB, InlC, InlJ and InlL have been shown in vitro to interact with Muc2, the major component of intestinal mucus, via their leucine-rich repeat domain[126,127]. This interaction may help *L. monocytogenes* to adhere to goblet cells (see below).

## Crossing the intestinal barrier

*L. monocytogenes* can cross the intestinal epithelial barrier in an InlA-dependent or InlA-independent manner (Fig. 4a). At the villus level, *L. monocytogenes* targets goblet cells via interaction of InlA with the luminally accessible Ecad, and accesses the lamina propria by transcytosis, hijacking the Ecad recycling pathway[128–130] (Fig. 5a). Luminally accessible Ecad is also present at the epithelial folds and at the tips of villi where epithelial cells extrude[130,131], enabling *L. monocytogenes* to target these sites, although at a much lower frequency than goblet cells[130,131]. At the Peyer's patch level, *L. monocytogenes* crosses the intestinal barrier via the epithelial microfold (M) cells in an InlA-independent manner, whereas InlB has been reported to be involved in Peyer's patch infection[132–134]. InlA-dependent crossing at the intestinal, caecal and colonic levels leads to systemic dissemination and is associated with little to no host local intestinal response[129,135–137]. By contrast, Peyer's patch infection induces a local response that contains infection[136] and a decrease in mature goblet cell numbers, which impairs subsequent InlA-dependent entry at the villus level[138].

## Systemic dissemination

The mechanisms by which *L. monocytogenes* spreads from intestinal tissue to internal organs via the lymphatic and vascular blood circulation remain mostly unknown (Fig. 3c). In vivo studies have shown that bacteria that reach the brain are located in monocytes in the blood[139],




suggesting that extracellular bacteria are dispensable for *L. monocytogenes* dissemination to the CNS. The main mechanism of systemic dissemination is *L. monocytogenes* infection of monocytes[139,140]. Experiments in mice conducted with an *L. monocytogenes* strain expressing a murinized version of InlA indicated that extracellular bacteria and dendritic cells might also be involved[141]. However, as this strain artefactually interacts with villous M cells in the gut[137], this finding remains to be confirmed in more relevant experimental systems. Once in the lymphatic and blood circulation, *L. monocytogenes* infects the spleen and the liver[129].

**Spleen.** In the spleen, marginal zone macrophages rapidly take up *L. monocytogenes* from the blood and transfer them to CD8α$^+$ dendritic cells[142–144]. Marginal zone B cells produce the anti-inflammatory interleukin IL-10, which allows bacteria to proliferate in CD8α$^+$ dendritic cells[143]. After migrating to the white pulp of the spleen, CD8α$^+$ dendritic cells induce the recruitment of natural killer cells that produce interferon-γ (IFNγ), leading to the differentiation of dendritic cells into TipDCs that secrete TNF and nitric oxide, limiting bacterial replication[145]. White pulp TipDCs then promote activation of CD8$^+$ T cells, which can kill circulating infected monocytes[146–148].

**Fig. 3 | Mechanisms of *L. monocytogenes* infection. a**, Infection steps of *Listeria monocytogenes*, occurring in epithelial cells in vitro and in phagocytes in vivo. The figure shows the entry, growth and spread of *L. monocytogenes* between cells. The magnified region shows cellular entry through E-cadherin (Ecad) and c-Met receptors through interaction with InlA and InlB in non-phagocytic cells only. Once *L. monocytogenes* enters the cell, it can escape from the vacuole in a listeriolysin O (LLO)-dependent and PlcA/B-dependent manner and propel itself in the cytoplasm by polymerizing actin via ActA. *L. monocytogenes* can then spread from cell to cell in an InlC-dependent manner[90]. **b**, Mechanism of transcytosis across goblet cell in vivo. *L. monocytogenes* InlA interacts with the luminal-accessible epithelial Ecad of intestinal goblet cells. *L. monocytogenes* hijacks the Ecad recycling pathway: the bacterium is endocytosed in a dynamin-dependent manner, transcytosed in a microtubule-dependent manner within a vacuole, and released at the basolateral side of the goblet cell in a Rab11-dependent manner. **c**, Successive steps of listeriosis. *L. monocytogenes* virulence factors are indicated in blue and their host receptor are indicated in parentheses. Once ingested, *L. monocytogenes* crosses the intestinal barrier and disseminates systemically via the lymphatic circulation (top arrow) and portal vein (bottom arrow) and induces bacteraemia. *L. monocytogenes* then infects the spleen and liver, where it can replicate. Infected monocytes can transport *L. monocytogenes* to the brain and cause central nervous system infections, most commonly meningoencephalitis. In pregnant women, *L. monocytogenes* crosses the placental barrier and infects the fetus, leading to abortion or neonatal infection. LIPI4, *Listeria* pathogenicity island 4. Part **a** adapted from ref. 87, CC BY-NC-SA 4.0. Part **b** reprinted with permission from ref. 128, Elsevier. Part **c** reprinted with permission from ref. 78, Elsevier.

**Liver.** As indicated by one of its former names, *Listerella hepatolytica*[149], *L. monocytogenes* also infects the liver. In experimentally infected mice, *L. monocytogenes* induces the death of Kupffer cells, the resident macrophages of the liver, by necroptosis[150]. A consequence of Kupffer cell necroptosis is the recruitment of microbicidal type 1 inflammatory monocytes and a subsequent type 2 response that allows tissue repair[150]. *L. monocytogenes* can also survive extracellularly in the bile of infected mice and humans[151], leading to the release of bacteria into the intestine via the gallbladder and biliary duct[152,153].

### Crossing the placental barrier

A key virulence property of *L. monocytogenes* is its ability to actively cross the placental barrier and infect the fetus (Fig. 4b). InlA has a critical role in this infection step, by interacting with Ecad expressed on the epithelial cells that form a syncytial barrier between the maternal blood and the fetus called the syncytiotrophoblast[154]. However, InlA alone is not sufficient to mediate *L. monocytogenes* internalization in the syncytiotrophoblast, and InlB, by activating PI3-kinase PI3Kα via its receptor c-Met, is required for the InlA-dependent crossing of the placental barrier[133,135] (Fig. 5b). The internalin family InlP protein, by interacting with afadin, a cytoplasmic protein associated with cell junctions, has also been reported to allow *L. monocytogenes* entry into the placenta, as well as into the liver and spleen[155,156]. Vacuolar escape and cell-to-cell spreading mediated by LLO and ActA are required for *L. monocytogenes* to spread within the placenta[157,158]. It remains to be determined whether *L. monocytogenes* reaches the placenta only extracellularly, or also intracellularly via circulating infected cells. Once infecting the placenta, *L. monocytogenes* can be shed back into the systemic maternal circulation and disseminate to maternal organs[159]. On the maternal side, fetal–placental infection is associated with only mild, flu-like symptoms and neurolisteriosis is not a classic complication of maternal listeriosis in non-immunosuppressed pregnant women, suggesting that *L. monocytogenes* is more successful in crossing the placental barrier than the blood–brain barrier.

### Crossing the blood–brain barrier

The first known isolate of *L. monocytogenes* was obtained from the cerebrospinal fluid of a soldier who died of meningitis in 1918 (ref. 160). A decade later, circling disease was observed in sheep as a result of a lateral infection of the brainstem by *L. monocytogenes*[161]. It is now well documented that *L. monocytogenes* commonly infects the hindbrain (rhombencephalon) of cattle, probably by retrograde axonal migration through mucosal injury in the oropharyngeal cavity during chewing (rumination)[162]. In humans, *L. monocytogenes* mostly causes meningoencephalitis, and rhombencephalitis is not the most common presentation, suggesting that it crosses the blood–brain barrier, consistent with the bacteraemia being frequently associated with neurolisteriosis in humans, unlike in cattle. Indeed, *L. monocytogenes* can infect the endothelial cells of the blood–brain barrier in an ActA-dependent manner by cell-to-cell spread from circulating infected monocytes[139,163,164] (Fig. 4c). It has been shown in a mouse model of infection that brain infection is clonal, suggesting that only a few bacteria actually invade the brain to induce neurolisteriosis[165]. Importantly, hypervirulent *L. monocytogenes* strains, which most commonly cause neurolisteriosis, overexpress InlB, in a σB-dependent manner[166], leading to the upregulation of c-FLIP via c-Met and the activation of PI3Kα, inhibiting the caspase 8-dependent apoptosis of infected monocytes induced by $CD8^+$ T cells. The resulting increased number of circulating infected monocytes increases their likelihood of transferring their infectious content to the brain upon adhesion to endothelial cells[139] (Fig. 5c). InlF, which is expressed by lineage II *L. monocytogenes* strains, has been experimentally demonstrated to play a role in brain infection in mice by interacting with vimentin on endothelial cell surfaces[167]. A putative *inlF* gene is present in lineage I, with 74% identity to lineage II *inlF*[168]. As lineage I strains are more prevalent in clinical samples and in particular in neurolisteriosis cases[6,53], it remains to be determined whether this homologue also enables brain infection, questioning the relevance of *inlF* as a major determinant of *L. monocytogenes* neurotropism. The fate of bacteria, the types of infected cells in the brain, and the consequences on brain functions remain to be investigated.

### Host response to *L. monocytogenes*

*L. monocytogenes* is a widely used model pathogen to study the innate and adaptive immune responses to intracellular pathogens[18]. The inoculation of *L. monocytogenes* in mice allowed the characterization of the $CD8^+$ T cell-mediated immune response[169], which has a major role in the clearance of *L. monocytogenes* infection and protective immunity[170], and revealed that the B cell-mediated humoral response does not provide protection[171]. These observations are in line with *L. monocytogenes* intracellular location in vivo and might also be linked to the induction of anti-inflammatory IL-10 in B cells during *L. monocytogenes* infection[172]. Using severe combined immunodeficient (SCID) mice, which lack both T and B cells, it has been shown that the innate immune response, and in particular the production of IFNγ by natural killer cells, allows the host to limit bacterial proliferation and survive the infection[173], even though *L. monocytogenes* can persist in macrophage vacuoles in the liver[174], further demonstrating the crucial role of T cells in clearing intracellular infection. Both IFNγ and TNF are crucial in the innate immune response to *L. monocytogenes* infection, as mice lacking these cytokines are highly susceptible to *L. monocytogenes* infection[175,176]. By contrast, type I

## Box 2 | Relevant host and bacterial models

### Animal models

The larvae of the invertebrate greater wax moth *Galleria mellonella*, which can survive at 37 °C and in which listeriolysin O and ActA are expressed and active[252–254], can be used as a simple model to assess *Listeria* virulence[255]. However, two major differences from vertebrates hamper the study of human listeriosis in this model: the absence of the InlA receptor E-cadherin (Ecad) and the absence of an adaptive immune response. Owing to the species specificities described above, mice, rats (InlA–Ecad), guinea pigs and rabbits (InB–c-Met) present challenges in the study of certain aspects of listeriosis. Gerbils, from which *Listeria monocytogenes* was first isolated in the wild[149], express Ecad and c-Met receptors that are permissive for interaction with InlA and InlB[135], respectively, but until recently[256] the genetic and molecular tools to study the host response to infection were lacking. In addition to gerbils, genetically modified mouse models have been generated. Transgenic mice expressing human Ecad in the intestine demonstrated the critical role of the InlA–Ecad interaction in crossing the intestinal barrier (see the section 'Crossing the intestinal barrier'[129]). Knock-in mice in which the glutamic acid in the 16th position of Ecad EC1 is replaced by a proline ('humanized' E16P knock-in mice) were used to study the InlA–Ecad interaction in the whole organism and showed the interdependent role of InlA and InlB in *L. monocytogenes* crossing the placental barrier (see the section 'Crossing the placental barrier'[135]).

### *L. monocytogenes* strains

In vitro studies have mostly been carried out with lineage II strains — the reference strains EGD and 10403S belonging to CC7, and the LO28 (with a premature stop codon in *inlA*) and EGDe[71] strains belonging to CC9 — or with F2365, a lineage I strain with a premature stop codon mutation in *inlB*[257]. As explained in the section '*L. monocytogenes* population structure', lineage I strains are strongly associated with clinical cases and are more virulent in vivo than lineage II reference strains[53], highlighting the need to use clinically relevant strains to study listeriosis in vivo. Such an approach enabled the discovery of virulence factors present only in hypervirulent strains, such as listeriolysin S in certain lineage I strains[258] or *Listeria* pathogenicity island 4 (LIPI4) in CC4 strains[53]. Furthermore, a thorough analysis of strains representative of *L. monocytogenes* genetic diversity revealed that the responsiveness of the general stress response regulator σB is a critical regulator of *L. monocytogenes* virulence, as it leads to increased transcription of both *inlA* and *inlB* in hypervirulent strains, including those belonging to CC1, CC4 and CC6 (ref. 166). These findings highlight that, in addition to accessory genes, differential transcriptional regulation of virulence genes, rather than the presence or absence of accessory virulence genes, is a critical determinant of virulence heterogeneity in *L. monocytogenes* species[166].

IFN, expressed upon STING activation by cyclic di-AMP secreted by *L. monocytogenes*[177], paradoxically promotes *L. monocytogenes* infection after intravenous mouse inoculation[178,179]. The host response to *L. monocytogenes* is tissue-specific, depending on the resident phagocytic cells. In the gut, infected myeloid cells from the Peyer's patches induce a pro-inflammatory response via IL-12, whereas myeloid cells from the villus do not[138], through a mechanism that remains to be elucidated. In the blood, *L. monocytogenes* is mainly found in circulating monocytes, which survive $CD8^+$ T cell killing in an InlB-dependent manner[139].

At the placental level, infected syncytiotrophoblasts secrete the chemokines CSF1 and MCP1, leading to the recruitment of neutrophils and macrophages[180,181]. Neutrophils and macrophages secrete TNF and IL-12, thereby activating decidual natural killer cells to produce IFNγ, which enhances the bactericidal activity of decidual macrophages[182]. Decidual macrophages also secrete perforin 2, which is protective against *L. monocytogenes* but harmful to the fetus at high doses[183]. Inflammasomes are also induced in infected syncytiotrophoblasts, leading to the secretion of IL-1β, which induces inflammasomes in recruited monocytes and protect against *L. monocytogenes* infection[184]. Decidual natural killer cells can also directly kill *L. monocytogenes* in trophoblasts by injecting granulysin via nanotubes, without killing the host cells[185]. Interestingly, although immunoglobulins are not able to protect against *L. monocytogenes* in non-pregnant individuals, maternal IgGs are transferred to the newborn and can protect against *L. monocytogenes* due to a deacetylation of immunoglobulins during pregnancy that inhibits IL-10 expression in B cells[186].

Innate and adaptive immunity are critical to control *L. monocytogenes* and mediate long-lasting immunity[18,187]. However, *L. monocytogenes* can evade innate and adaptive immune responses by virtue of several of its features, including its intracellular location, its intracellular motility that evades autophagy, the structure of its peptidoglycan that restricts its detection by the cytosolic sensors and lyzozyme[188,189], and the immunosuppressive activity of *L. monocytogenes* gene products such as InlB[139], InlC[190] and InlH[191].

## Diagnosis, screening and prevention

### Clinical diagnosis

*L. monocytogenes* infection presents either as a benign gastroenteritis that usually goes undetected, or as listeriosis, a systemic infection with overt symptoms. Gastroenteritis typically occurs 20–24 h after ingestion of food that is highly contaminated ($10^6$–$10^9$ CFU/g) with *L. monocytogenes*[192–194]. It presents as a self-limited, possibly febrile, spontaneously resolving infection with diarrhoea and flu-like symptoms that occurs in otherwise healthy individuals[192,194]. Listeriosis, by contrast, is a severe infection that falls into four categories: septicaemia, neurolisteriosis, maternal–neonatal listeriosis and rare forms of focal infection[6] (Fig. 6). Data from Europe and the USA indicate that the incubation period of listeriosis differs based on its clinical form, with a median incubation time of 5 days for septicaemia (range 0–29 days), 10 days for neurolisteriosis (range 0–21 days) and 23 days for maternal–neonatal listeriosis (range 0–67 days)[195,196].

**Septicaemia.** Septicaemia is the most common invasive form of listeriosis. It accounts for 60% of listeriosis cases and occurs primarily in patients with compromised immunity and comorbidities. The median age of patients with septicaemia, and the number of comorbidities and immunosuppressive treatments, are higher than in those with neurolisteriosis[6]. Septicaemia presents as a non-specific combination of fever (87%), influenza-like illness (20%), diarrhoea (20%),

worsening or decompensation of an underlying comorbidity (43%), and/or multivisceral failure (18%)[6]. Septic shock is reported in less than 2% of patients with invasive listeriosis.

**Neurolisteriosis.** Neurolisteriosis presents as a meningoencephalitis in 84% of patients, and as an isolated meningitis in 13%. Symptoms of brainstem involvement (rhombencephalitis) are reported in 17% of patients[6,197,198]. Half of all patients with neurolisteriosis present with altered consciousness (median Glasgow Coma Scale score of 12 out of 15). Single or multiple brain abscesses are observed in 3% of patients[6,199]. In some patients, cerebrospinal fluid analysis reveals decreased glucose levels, increased protein levels and increased cellularity, with lymphocytes, neutrophils or mixed cell counts[6]. Neuroradiological features are neither sensitive nor specific, and consist of a combination of infection-related lesions such as abscesses, nodular lesions, leptomeningitis or ventriculitis, age-related lesions such as non-specific white matter lesions or dilated Virchow–Robin spaces and vascular lesions, either ischaemic and/or haemorrhagic[200]. The detection of parenchymal lesions is associated with a poor prognosis (OR 5.60 for in-hospital mortality, 95% CI 1.42–29.6; $P = 0.02$)[200].

**Maternal–fetal listeriosis.** Maternal infection is thought to occur at any stage of pregnancy, although most infections are reported during the third trimester (70% in the French cohort[6]). Low rates of infection detection in the first trimester might reflect under-reporting, as women do not yet receive obstetric care during this period[6,201,202]. The clinical presentation in pregnant women is non-specific and includes obstetric signs such as uterine contractions, labour or acute fetal distress (75% of the French MONALISA cohort), fever (25–85% of infected women according to case series[6,203]) or fetal loss on admission (21%). In 5% of infected mothers, listeriosis presents as undifferentiated fever (that is, fever without other signs)[6]. Maternal infection characterized by bacteraemia, which can be asymptomatic, is almost never complicated by neurolisteriosis during pregnancy, highlighting the preferential tropism of *L. monocytogenes* for the fetal–placental unit compared to the CNS in the absence of concomitant immunosuppression[48]. However, maternal listeriosis almost always has a negative impact on pregnancy outcome (95%), causing fetal loss (24%), preterm delivery (45%), acute fetal distress (21%) and neonatal infection (76%, early onset 70%, late onset 6%)[6,65]. In the French MONALISA cohort, 83% of infected mothers experienced major complications (miscarriage, extreme prematurity at <32 weeks of pregnancy or neonatal infection[6]), although *L. monocytogenes* is not teratogenic, in contrast to *Toxoplasma* and rubella virus, for example[6,65,67].

**Neonatal listeriosis.** Neonatal infection presents as either early-onset listeriosis (within the first 7 days of life) or as a late-onset listeriosis (between 7 and 28 days of life). Of the 189 live births in the maternal–fetal infection section of the MONALISA cohort, 70% presented with early-onset listeriosis, 6% with late-onset listeriosis and only 14% were considered healthy (uninfected and without complications related to prematurity)[65]. Early-onset infection presents as non-specific sepsis, with haemodynamic, respiratory and neurological failure that are worsened by prematurity. Granulomatosis infantiseptica, characterized by pustular and granulomatous cutaneous and visceral lesions reflecting disseminated infection of *L. monocytogenes*, has been reported in rare cases[65,204]. Late-onset neonatal listeriosis presents as septicaemia associated with meningitis[65].

**Focal infections.** Focal (that is, localized) *L. monocytogenes* infections are rare (Fig. 6). In decreasing order of incidence, focal infections can manifest as peritoneal fluid infections, endocarditis or vascular infections, pleuropulmonary infections, biliary tract listeriosis, skin, lymphatic and urinary tract infections, and endophthalmitis[62,63,151,205–209]. For all these types of *L. monocytogenes*-associated infections, the symptoms and signs do not differ from those associated with other bacterial species. Peritoneal fluid infections (also known as spontaneous bacterial peritonitis) constitute the fourth most common presentation of invasive listeriosis, after septicaemia, neurolisteriosis and maternal–fetal infection[62]; peritoneal fluid infections occur in patients with immunosuppression, cirrhosis, end-stage heart failure, peritoneal carcinoma or peritoneal dialysis. Skin infections develop by direct inoculation, from farm animals in the case of farmers or veterinarians, and via unidentified routes in immunosuppressed patients. It is not associated with bacteraemia, ruling out haematogenous seeding (spreading of infection through the bloodstream), as in granulomatosis infantiseptica[39,208].

## Microbiological diagnosis

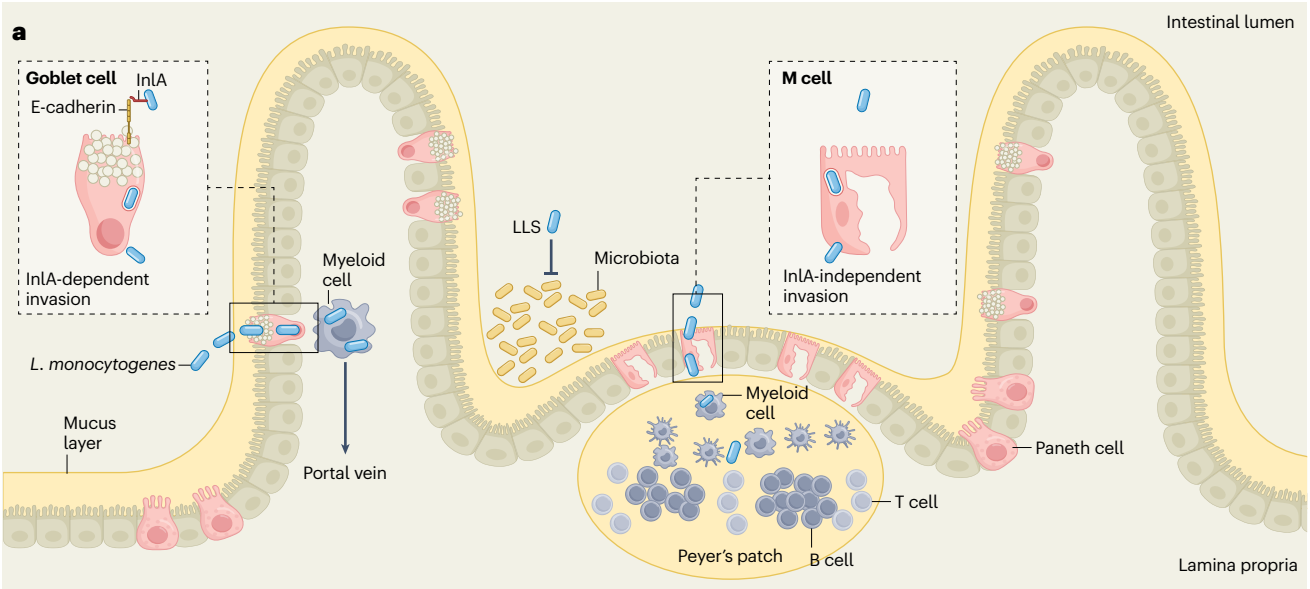
Diagnosis of listeriosis is based on isolation of *L. monocytogenes* or DNA detection (by PCR) in an otherwise sterile body site, including specimens of maternal, fetal or neonatal origin, blood and cerebrospinal fluid. *L. monocytogenes* can also be isolated from faeces, although given the high frequency of asymptomatic faecal carriage, its presence has little diagnostic value[45], and faecal isolation is not routinely performed. Microscopic examination after Gram staining reveals small Gram-positive bacilli that can be mistaken for corynebacteria. Additional analyses enable identification. *L. monocytogenes* grows on conventional media incubated at 37°C for 24-48 h. Cultivation on horse blood agar reveals a characteristic β-haemolysis (complete haemolysis). At 25 °C, *L. monocytogenes* is mobile with a characteristic tumbling motility mediated by peritrichous flagella. Proteomic analysis by matrix-assisted laser desorption ionization–time-of-flight mass spectrometry allows rapid identification of *L. monocytogenes* and other species of the *Listeria* genus of interest for public health and food safety[210].

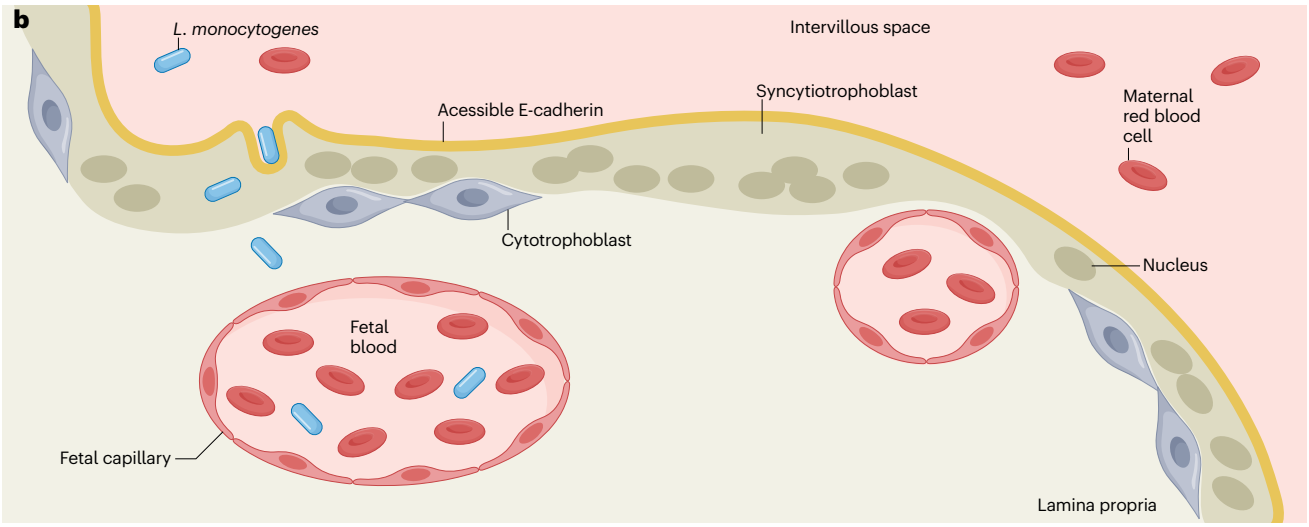
Stool culture on chromogenic selective media is not routinely performed but can be useful to identify the origin of *L. monocytogenes*-associated gastroenteritis outbreaks[192–194]. Cerebrospinal fluid culture is positive in 84% of patients with neurolisteriosis; blood culture is positive in 63% of patients with neurolisteriosis, and in 55% of pregnant women with neurolisteriosis[6]. The placenta is the most useful source of tissue for the microbiological diagnosis of maternal–neonatal listeriosis, with 78% of sample cultures positive for infection[6].

PCR-based assays that amplify the *hly* gene for LLO are useful for diagnosis from cerebrospinal fluid, given their high specificity, and particularly when previous antibiotic therapy prevents *L. monocytogenes* culture[211]. These assays have a low negative predictive value but a high positive predictive value. Multiplex PCR used in panels detecting pathogens involved in meningitis and encephalitis, including *L. monocytogenes*, have an expected sensitivity and specificity with regard to *L. monocytogenes* that is comparable to simplex PCR[212]. Serological tests have no diagnostic value and should not be used, as they lack both sensitivity and specificity[213].

## Serogrouping

*L. monocytogenes* surveillance was initially based on serotyping. *L. monocytogenes* can be divided into 14 serotypes[214,215], with serotypes 1/2a, 1/2b or 4b accounting for 95% of listeriosis infections[12,53]. However,


a
Intestinal lumen
Goblet cell
InlA
E-cadherin
InlA-dependent invasion
Myeloid cell
L. monocytogenes
Mucus layer
Portal vein
LLS
Microbiota
M cell
InlA-independent invasion
Myeloid cell
Paneth cell
T cell
Peyer's patch
B cell
Lamina propria


b
L. monocytogenes
Intervillous space
Acessible E-cadherin
Syncytiotrophoblast
Maternal red blood cell
Cytotrophoblast
Nucleus
Fetal blood
Fetal capillary
Lamina propria

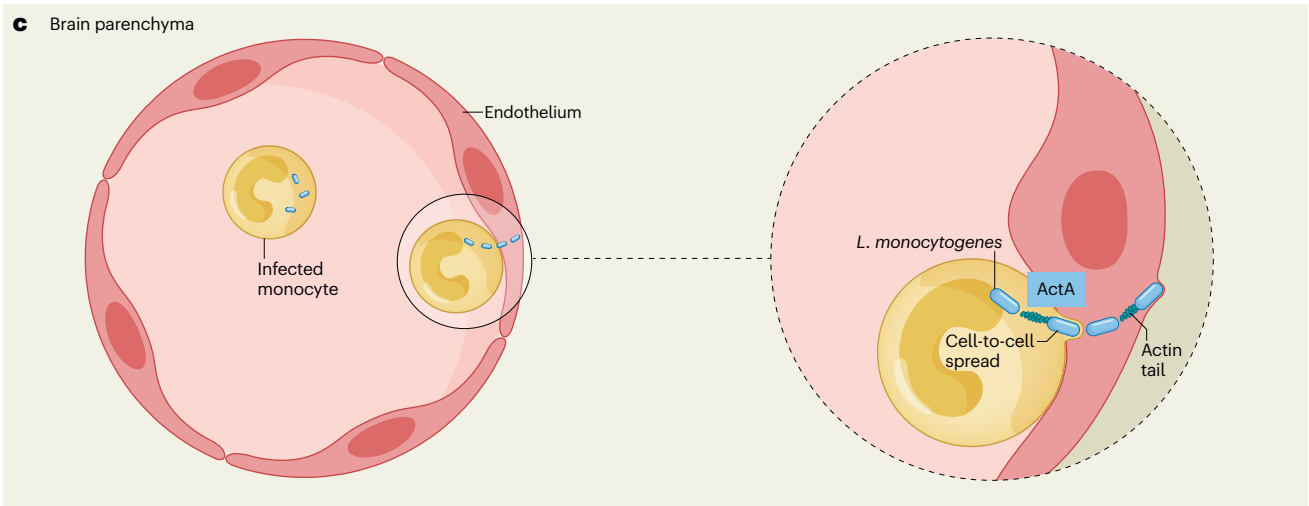

c
Brain parenchyma
Endothelium
Infected monocyte
L. monocytogenes
ActA
Cell-to-cell spread
Actin tail

**Fig. 4 | Mechanisms by which *L. monocytogenes* crosses host barriers.** **a**, *Listeria monocytogenes* crosses the intestinal barrier through the interaction of InlA with luminally accessible E-cadherin on goblet cells at the villus level and in an InlA-independent manner via microfold (M) cells at the Peyer's patch level. **b**, *L. monocytogenes* crosses the placental barrier through the interaction of InlA with accessible E-cadherin on the surface of syncytiotrophoblasts, the epithelium that forms the placental barrier. **c**, *L. monocytogenes* crosses the blood–brain barrier by cell-to-cell spread from circulating infected monocytes to brain endothelial cells in a listeriolysin O-dependent and ActA-dependent manner. LLS, listeriolysin S. Part **a** reprinted with permission from ref. 78, Elsevier. Part **b** adapted with permission from ref. 250, Elsevier. Part **c** reprinted from ref. 139, Springer Nature Limited.

serotyping is time consuming, requires specific reagents, and its results can be difficult to interpret[216]. To overcome these limitations, a multiplex PCR assay has been developed that identifies four major groups within *L. monocytogenes*: group IIa (serotypes 1/2a and 3a), group IIb (1/2b, 3b and 7), group IIc (1/2c and 3c) and group IVb (4b, 4 d and 4e), with an additional group L (rare serotypes 4a, 4ab, 4c)[214]. This internationally validated serogrouping method is used as a first-line typing method in routine *L. monocytogenes* surveillance and has been adapted to real-time PCR typing[217]. Of note, even if the assay lacks discriminatory power, as unrelated strains can share the same serotype, its results are useful as a first-line tool to identify putative clusters of cases and food sources in the context of listeriosis surveillance.

## Genomic typing

Advances in sequencing technologies have fundamentally changed the standards for bacterial typing, with a shift towards genomic typing. One of the first genomic typing techniques used to detect *L. monocytogenes* was pulsed-field gel electrophoresis (PFGE), which uses restriction enzymes to generate genomic DNA fragments of different sizes followed by separation by electrophoresis[218]. Later, MLST was the first typing method to provide phylogenetic information. The MLST scheme used to characterize *L. monocytogenes* is based on seven genes and identified CCs, most of which are geographically and temporally widespread[52,53,71,219]. Although *L. monocytogenes* MLST has helped to harmonize nomenclature internationally, its discriminative power is insufficient to define clusters of cases and identify contamination sources[54]. Based on the allelic encoding of 1,748 core genes, cgMLST has dramatically improved the discrimination of *L. monocytogenes* isolates compared with PFGE and MLST, and allows for detailed phylogenetic analysis. Determining cgMLST types allows for simple and efficient communication between laboratories and health authorities in the face of outbreaks or emerging strains[57].

To standardize and facilitate the genomic typing of *L. monocytogenes* internationally, the Institut Pasteur has created and curates a bacterial isolate genome sequence database (BIGSdb) dedicated to *Listeria* (BIGSdb-Lm). This web platform, which welcomes international contributions, hosts collections of curated, open or private databases of *Listeria* isolates, genomes and genotypes based on MLST, cgMLST and databases of antimicrobial resistance, biocide tolerance and virulence genes (Fig. 1b).

A single-nucleotide polymorphism (SNP)-based genomic typing method for *L. monocytogenes* surveillance involves identifying high-quality SNPs across the whole genome[220,221]. This method enables precise strain differentiation, shows high concordance with other genomic approaches, such as cgMLST and whole-genome MLST (wgMLST)[222–224], and is complementary to these typing methods for epidemiological investigations and outbreak detection[220]. However, the choice of reference genomes and SNP calling algorithms can influence the results, emphasizing the need for standardized protocols[225]. Moreover, SNP-based genotyping is computationally and analytically more complex and resource-consuming than cgMLST[226].

## Prevention

Prevention of listeriosis is based on four complementary approaches: avoidance of at-risk food products, pre-emptive treatment of maternal fever, antibiotic prophylaxis in specific settings, and contact precautions for affected neonates to prevent horizontal transmission.

**Food choices and handling.** Preventive strategies for pregnant women, older adults and immunosuppressed individuals centre on dietary caution and hygienic food practices. Key guidelines include the avoidance of unpasteurized dairy products — particularly soft cheeses such as Brie, Camembert, blue-veined varieties and queso fresco — any cheese crust, as well as refrigerated smoked seafood, pâtés, RTE deli meats, and pre-packaged salads unless reheated or freshly prepared[227]. The Centers for Disease Control and Prevention, WHO and the European Food Safety Authority all emphasize the importance on ensuring that at-risk populations consume only pasteurized dairy products and guaranteeing that high-risk foods are heated to ≥74 °C before consumption[46,228,229].

Safe food handling practices are equally critical. Hands should be washed after handling raw produce or meat, kitchen surfaces sanitized regularly, and raw and cooked foods stored separately to prevent cross-contamination. Cold storage should be maintained at or below 4 °C, and leftovers should be consumed within 24–48 h and only after thorough reheating[46]. Public health efforts increasingly focus on integrating food safety education into prenatal care, particularly for populations with elevated vulnerability due to socioeconomic disadvantage or culturally rooted dietary preferences, such as women of Mexican origin consuming Mexican-style cheese, which can be a source of listeriosis[59].

**Antimicrobial prophylaxis and pre-emptive treatment.** Aminopenicillin should be prescribed to any pregnant woman with undifferentiated fever, especially after consuming foods at high risk of *L. monocytogenes* contamination or foods that have been recalled because of *L. monocytogenes* contamination[230]. Indeed, aminopenicillin is associated with a significant reduction in the severity of illness in infants when given antenatally in the setting of suspected listeriosis[65]. Asymptomatic pregnant women exposed to contaminated food (that is, food recalled for *L. monocytogenes* contamination) should be treated prophylactically[230]. Negative blood cultures cannot exclude maternal listeriosis due to their low sensitivity (55% in the French MONALISA cohort); therefore, the decision to discontinue prophylactic antibiotic therapy should be discussed in a multidisciplinary setting, and be based on evidence of an alternative cause of the maternal fever. Co-trimoxazole-based regimens developed for pneumocystosis and toxoplasmosis prophylaxis in immunosuppressed individuals have also been shown to be effective in preventing listeriosis (OR 0.07, 95% CI 0.006–0.76; $P = 0.029$)[231]. Finally, neonates represent a specific population at risk of horizontal nosocomial transmission due to their low resistance to *L. monocytogenes* intestinal colonization[40]. Contact precautions for infected infants must be

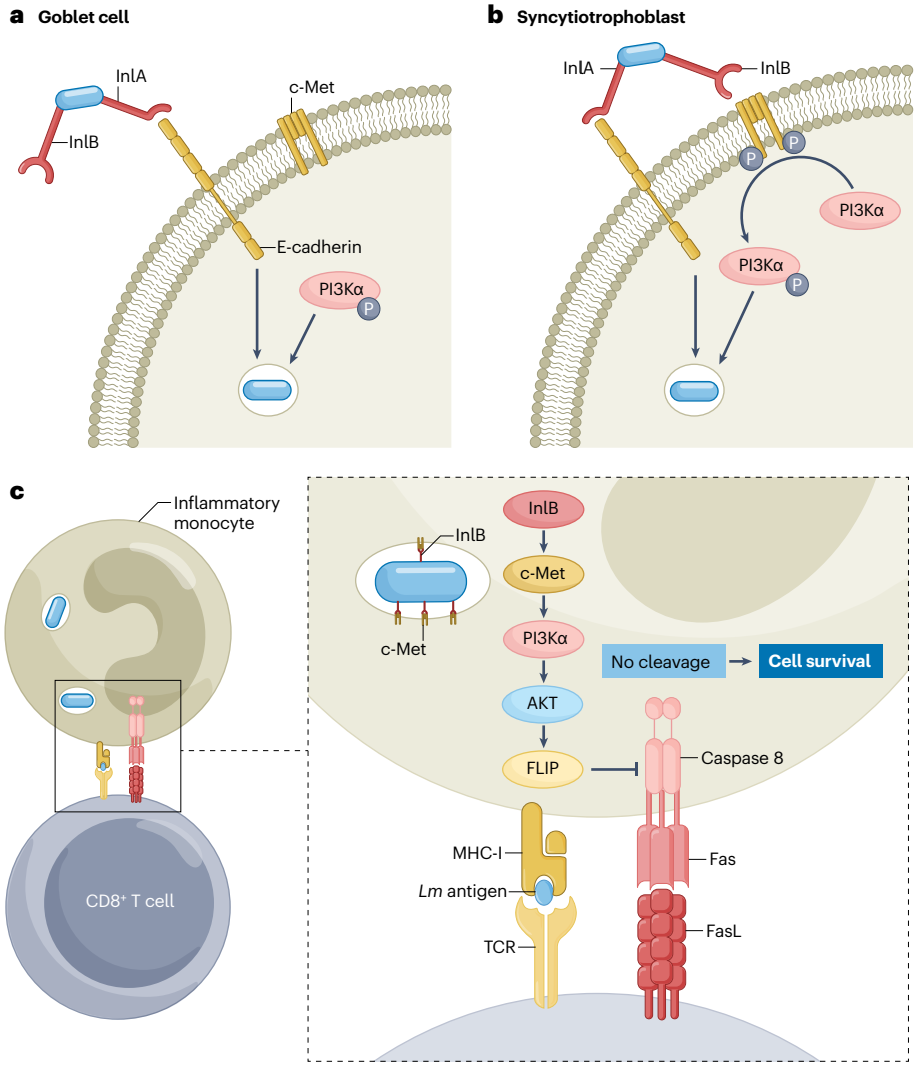



**Fig. 5 | Molecular mechanisms involved in *L. monocytogenes* cell invasion and survival. a**, In goblet cells, c-Met-dependent activation of PI3Kα by InlB is dispensable for entry, because PI3Kα activity, which is required for InlA-dependent entry, is constitutive[129,130,133,251]. **b**, In the syncytiotrophoblast, PI3Kα is not constitutively activated, and PI3Kα activation by InlB–c-Met interaction is needed for InlA-dependent entry[133,135,154]. **c**, In inflammatory monocytes, c-Met activation by InlB leads to the activation of PI3Kα and the ensuing upregulation of FLIP, which in turn blocks caspase 8 activation and inhibits Fas-dependent apoptosis induced by anti-*Listeria monocytogenes* $CD8^+$ T cells. Cell survival of infected monocytes promotes persistence of *L. monocytogenes* in the host, dissemination to the central nervous system and transmission[139]. *Lm* antigen, *L. monocytogenes* antigen; MHC-I, major histocompatibility complex class I; TCR, T cell receptor. Part **c** adapted from ref. 139, Springer Nature Limited.

followed to reduce the risk of cross-contamination with potentially fatal consequences.

## Management

### Food safety management

The effective control of food-borne biological hazards requires a comprehensive approach to hygiene and process management[232]. Central to such an approach is maintaining a high level of environmental hygiene within production facilities and designing equipment that enables thorough and efficient cleaning. Sanitation procedures, including disinfection and drying, must be scientifically grounded and consistently applied to prevent microbial persistence and cross-contamination.

Monitoring the production environment is also essential for the early detection of contamination. Strict control of the cold chain is also crucial, as temperature fluctuations can substantially affect the growth of pathogens, especially for RTE and chilled products. Product safety also hinges on the application of validated inactivation treatments that are tailored to the specific risks associated with each product category. Furthermore, it is crucial to determine a scientifically justified shelf life beyond processing, achieved by predictive microbiology, product challenge testing and growth studies, and taking into account the company's historical data and process parameters. Finally, additional safeguards must be applied when producing food intended for vulnerable populations, for whom even low levels of contamination can have serious health consequences. Overall, a proactive, science-based approach to food safety management is essential to ensure compliance and protect public health.

### Antimicrobial therapy

Several antibiotics have in vitro bactericidal activity against *L. monocytogenes*, including aminopenicillin and carbapenems, glycopeptides, moxifloxacin, aminoglycosides and co-trimoxazole[233–236]. Among the β-lactams, oxacillin and cephalosporins (including third-generation cephalosporins) are ineffective in killing *L. monocytogenes* in vitro and in vivo due to poor binding to their target penicillin-binding proteins[234,237]. Effective β-lactams (such as amoxicillin or ampicillin) and aminoglycosides act synergistically in combination, and the

combination is highly bactericidal. Due to the rarity of listeriosis and its non-specific presentation, which can result in a delayed diagnosis, no clinical trials have determined the optimal antibiotic treatment for each form of the disease. Management guidelines are therefore largely based on expert opinion, data from animal models of neurolisteriosis, and the results of observational studies (Table 1). Antimicrobial therapy is used to treat invasive listeriosis, but not gastroenteritis, as it is self-limited and resolves spontaneously.

**Antimicrobial resistance.** Although acquired antimicrobial resistance is a major general concern[238], it is not currently a threat with respect to *L. monocytogenes*. In a study based on all *L. monocytogenes* isolates collected in France between 2012 and 2019, antimicrobial resistance was analysed both phenotypically and genotypically[236]. In line with the findings of previous studies[239,240], all *L. monocytogenes* strains tested were found to be naturally resistant to at least three different classes of antimicrobials, including cephalosporins, monobactams and oxacillin, and to first-generation quinolones (nalidixic acid), fosfomycin and sulfonamides. Of note, despite natural sulfonamide resistance, *L. monocytogenes* is more sensitive to co-trimoxazole than to trimethoprim, highlighting its incomplete natural resistance to sulfamides. Acquired antimicrobial resistance was observed in only 2.23% of isolates and was more common in food than in clinical isolates. Of these isolates, acquired antimicrobial resistance could be inferred from their sequenced genomes, except for ciprofloxacin, and they had acquired resistance to tetracyclines (due to *tetM*), trimethoprim (*dfrD*), lincosamides (*lnuG*), macrolides (*ermB*, *mphB*) and phenicols (*fexA*). Importantly, all strains tested were sensitive to the drug of choice for the treatment of listeriosis (aminopenicillins and aminoglycosides)[236], as previously reported[239].

As with other bacteria, *L. monocytogenes* antimicrobial resistance is routinely tested in vitro, although it is important to consider that the in vivo context might modify the resistance phenotype. Indeed, *L. monocytogenes* is resistant to fosfomycin in vitro but sensitive to this antibiotic in a mouse model of infection[241], an effect explained by in vivo upregulation of the sugar phosphate permease Hpt, which transports fosfomycin into the bacterial cell[242]. Moreover, studies suggest that the microbiota may modify the efficacy of antibiotics. Indeed, *Escherichia coli* producing β-lactamase enzymes impaired the efficacy of ampicillin treatment against *L. monocytogenes* in a mouse model, leading to systemic dissemination[243]. Furthermore, exposure of *L. monocytogenes* to biocides used by the food industry resulted in the overexpression of specific *L. monocytogenes* efflux pumps that could affect the efficacy of antibiotics such as ciprofloxacin[240].

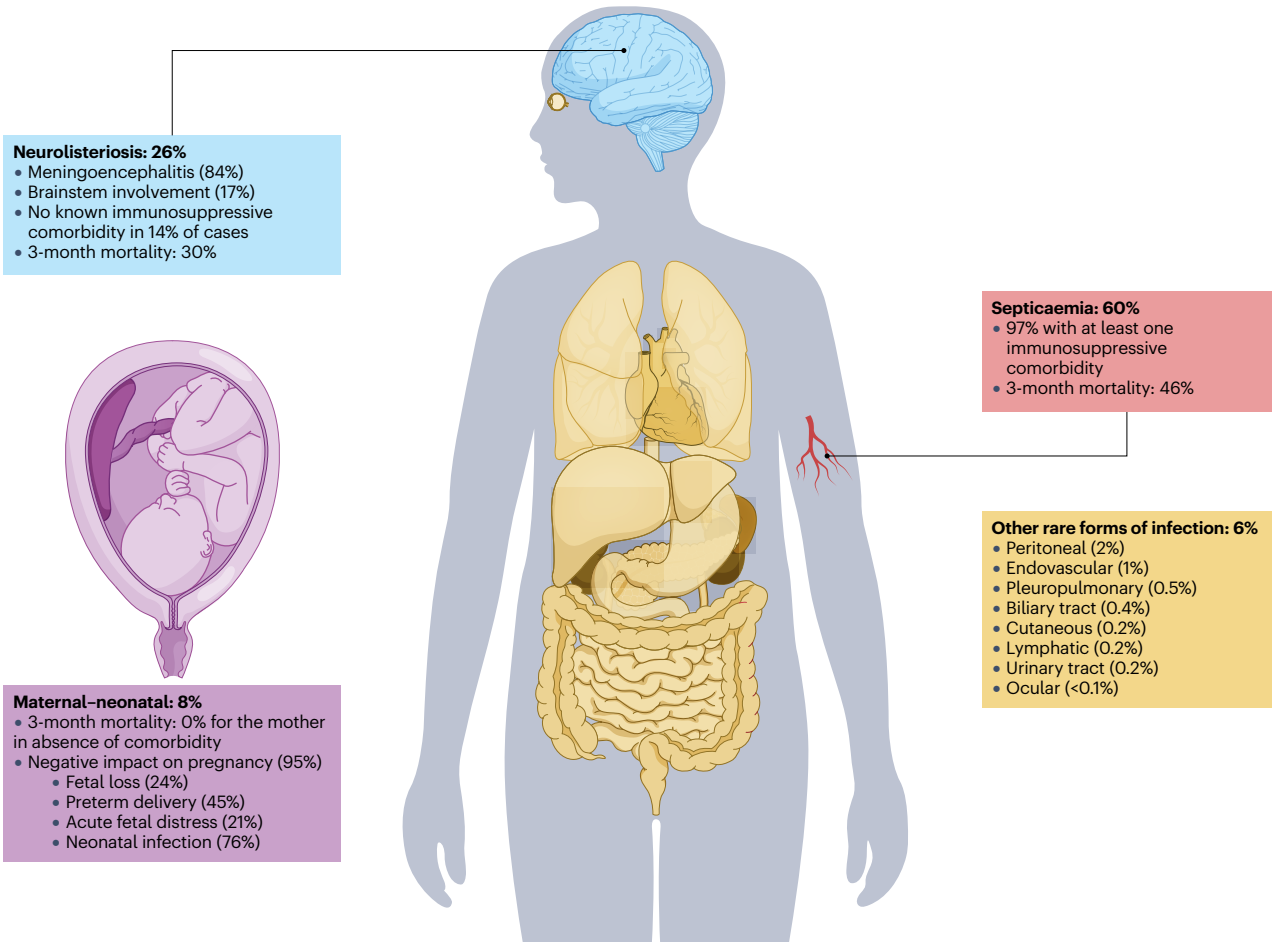



**Fig. 6 | Clinical presentation and features of listeriosis.** The most common clinical forms of invasive listeriosis are septicaemia, neurolisteriosis and maternal–neonatal complications. Percentages are those from French surveillance data and indicate the percentage of patients affected by each manifestation of listeriosis. Other, rare forms of infections can also occur in ~6% of cases[62,63,151,205–209].

**Table 1 | Available antimicrobial therapies for invasive listeriosis**

| Clinical feature | First-line | Second-line | Third-line |
|---|---|---|---|
| Septicaemia | Amoxicillin 21 days + gentamicin 3–5 days | Co-trimoxazole 21 days + gentamicin 3–5 days or meropenem 21 days + gentamicin 3–5 days | Vancomycin 21 days + gentamicin 3–5 days or moxifloxacin + gentamicin 3–5 days |
| Neurolisteriosis | | | |
| Maternal listeriosis | Amoxicillin 21 days +/− gentamicin 3–5 days | Co-trimoxazole 21 days +/− gentamicin 3–5 days or meropenem 21 days +/− gentamicin 3–5 days | Vancomycin 21 days +/− gentamicin 3–5 days |
| Neonatal listeriosis | Amoxicillin 21 days +/− gentamicin 3–5 days | Meropenem 21 days +/− gentamicin 3–5 days | Vancomycin 21 days +/− gentamicin 3–5 days |
| Maternal fever without additional clinical symptoms[a] | Amoxicillin 7–10 days | Co-trimoxazole 7–10 days | Erythromycin 7–10 days or azithromycin 7–10 days |

+, with; +/−, with or without. [a]Antimicrobials used for pre-emptive treatment.

**Maternal–neonatal listeriosis.** Treatment of maternal listeriosis is based on ampicillin or amoxicillin for 14–21 days, which can be combined with gentamicin for 3 days. In the case of allergy to β-lactams, the second-line therapy is based on co-trimoxazole, after testing for resistance to trimethoprim, as long as the mother is not in the first trimester of pregnancy due to potential teratogenic effects. Third-line therapies include vancomycin, to which *L. monocytogenes* rarely exhibits resistance[244].

Treatment of neonatal listeriosis is based on the same combination of ampicillin or amoxicillin and gentamicin. Co-trimoxazole is contraindicated in neonates. Vancomycin and meropenem can be safely used in newborns as alternative therapies, but do not constitute the treatment of choice. Antimicrobial therapy duration varies according to the type of neonatal presentation and ranges from 7 to 21 days in newborns with neonatal meningitis.

**Neurolisteriosis and septicaemia.** The efficacy of ampicillin or amoxicillin, gentamicin, trimethoprim or sulfamethoxazole and moxifloxacin in treating neurolisteriosis have been confirmed in rat, mouse and rabbit models[233,235]. The combination of amoxicillin and gentamicin has been shown to be more effective than amoxicillin alone both in vitro and in vivo[245]. In the MONALISA study, effective β-lactams, aminoglycosides and co-trimoxazole were all independently associated with increased survival in patients with neurolisteriosis or septicaemia. Patients treated with effective β-lactams had a higher survival rate than those not treated with β-lactams (66% versus 11%; $P < 0.0001$), and those treated with aminoglycosides also had an increased survival rate compared with those not treated with aminoglycosides (69% versus 46%; $P = 0.0001$)[6]. Patients who received a combination of an effective β-lactam and an aminoglycoside for more than 3 days had a higher survival rate than those who received this combination for a shorter duration (OR 0.35). The recommended total duration of treatment is 21 days for any antibiotic therapy, although this could be extended to 4–6 weeks in patients with concomitant brain abscesses. Treatment of other types of listeriosis, such as focal infections, is not standardized but is usually based on the same combination of ampicillin or amoxicillin and gentamicin, with amoxicillin alone or co-trimoxazole as follow-up treatment. For neurolisteriosis and septicaemia, second-line therapy in patients with documented severe β-lactam allergy includes co-trimoxazole and meropenem in combination with gentamicin.

### Additional measures

The role of adjuvant corticosteroids in the treatment of neurolisteriosis remains a matter of debate. In the French MONALISA cohort, adjunctive dexamethasone was independently associated with increased mortality: among 32 patients who received dexamethasone, survival was 53%, compared with 73% in the 220 patients who did not receive dexamethasone in addition to antibiotic treatment (OR 4.58, 95% CI 1.50–13.98)[6]. Similarly, a Dutch observational study (1998–2012) suggested a trend towards worse outcomes in patients receiving adjuvant dexamethasone[198]. By contrast, a more recent nationwide Dutch cohort study (2006–2022) found a beneficial effect of dexamethasone when administered for at least 4 days. Among 83 eligible patients, those receiving adjunctive corticosteroids had significantly better outcomes on a composite end point of mortality and severe long-term disability compared with 79 untreated patients (OR 0.40, 95% CI 0.19–0.81)[246]. However, indication bias and immortal time bias could not be fully accounted for in these observational analyses, and the clinical usefulness of adjunctive corticosteroids in neurolisteriosis thus remains to be fully elucidated.

## Quality of life

Data on the long-term quality of life of patients who survive listeriosis are lacking, with a paucity of information on its long-term physical and psychosocial effects. Nonetheless, the morbidity and mortality of severe listeriosis, in both adult and neonatal patients, implies a substantial impact on quality of life[68,247]. As an example, it has been shown for neonates that term is the major determinant of neurological impairments[68]. A high number of DALYs associated with listeriosis further suggests that the illness has a substantial negative effect on productivity losses and quality of life of patients[47].

## Outlook

Although listeriosis is a well-studied infection, several key questions remain. These include defining the global burden of the infection, understanding the dynamics of the *L. monocytogenes* population, identifying the transmission routes, determining the host risk factors that are independent of immunosuppressive treatment or age, and defining new treatment regimens that could improve patient outcomes.

### Global disease burden

To limit the risk of outbreaks caused by contaminated food, listeriosis is a notifiable disease in most European countries, as well as in North America, Asia (Hong Kong and Taiwan), Africa (South Africa) and Oceania (Australia). Surveillance also involves strain characterization and genome sequencing[51]. These surveillance approaches have provided an accurate picture of the incidence of *L. monocytogenes* in these countries. However, the incidence of listeriosis remains unknown in many countries in which *L. monocytogenes* is present but listeriosis is not a notifiable disease, particularly in Asia, Africa and Latin America. A more comprehensive study of listeriosis on a global scale would make it possible to better define the extent of the disease burden and monitor the emergence of new clones or antibiotic-resistant strains.

### *L. monocytogenes* population dynamics and transmission routes

The spread of *L. monocytogenes* CC1 strains has been shown to be linked to the trade of cattle and dairy products[11]. However, other current and past spreading mechanisms cannot be excluded. In fact, the most recent common ancestor of lineages I and II is estimated to have appeared between 30 and 67 million years ago[248]. Although this dating can be refined, it suggests that *L. monocytogenes* spread and diversified long before humans existed. Expanding the collection of *L. monocytogenes* from different regions of the world and sample types other than those from food, food-processing environments and clinical settings and cattle, such as wild animal and diverse environments would improve our understanding of population dynamics and transmission routes.

### Identifying new risk factors for listeriosis

Although predisposing factors responsible for the onset of human listeriosis can be identified in most cases[6], a subset of patients (4–10%) develop neurolisteriosis without any identified risk factor. This suggests that host factors, which may be of (epi)genomic and/or microbiota origin, might be involved in susceptibility or resistance to infection. With regard to host genetics, the ongoing genome-wide association study for listeriosis (NCT03357536) will enable the discovery of genes associated with listeriosis in patients with no known predisposing factors, especially patients with neurolisteriosis[6,200].

Gut microbiota composition has been shown to be involved in the colonization resistance to *L. monocytogenes*[112] and, conversely, associated with *L. monocytogenes* faecal carriage[45]. Studies based on mouse models of infection, combined with bovine and human samples would help identify components of the microbiota that might either promote or prevent *L. monocytogenes* intestinal carriage and/or the onset of listeriosis.

### Defining the best therapeutic regimen to improve survival

The continuing high morbidity and mortality of listeriosis, which has not improved over the past 40 years, highlights the urgent need for a more evidence-based assessment of the best therapeutic regimens[6,199,201]. This includes the use of aminosides and corticosteroids in neurolisteriosis, the optimal duration of treatment, and whether the combination of effective β-lactam and co-trimoxazole can prove clinically synergistic, particularly in the subset of patients with brain abscesses, given the excellent diffusion of the latter in the cerebral parenchyma[249]. Preventive therapy should also be optimized for maternal listeriosis; the benefit of gentamicin needs to be confirmed, as does the duration of maternal treatment after delivery.

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### References


1. Fenlon, D. R. Wild birds and silage as reservoirs of *Listeria* in the agricultural environment. *J. Appl. Bacteriol.* **59**, 537–543 (1985).
2. Weis, J. & Seeliger, H. P. Incidence of *Listeria monocytogenes* in nature. *Appl. Microbiol.* **30**, 29–32 (1975).
3. Gandhi, M. & Chikindas, M. L. Listeria: a foodborne pathogen that knows how to survive. *Int. J. Food Microbiol.* **113**, 1–15 (2007).
4. Radoshevich, L. & Cossart, P. *Listeria monocytogenes*: towards a complete picture of its physiology and pathogenesis. *Nat. Rev. Microbiol.* **16**, 32–46 (2018).
5. Koopmans, M. M., Brouwer, M. C., Vazquez-Boland, J. A. & van de Beek, D. Human listeriosis. *Clin. Microbiol. Rev.* **36**, e0006019 (2023).
6. Charlier, C. et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. *Lancet Infect. Dis.* **17**, 510–519 (2017).
**This unique prospective clinical study of listeriosis presents a detailed analysis of the clinical features and prognostic factors associated with invasive listeriosis, alongside an evaluation of the effectiveness of its treatments.**
7. Goulet, V. et al. Incidence of listeriosis and related mortality among groups at risk of acquiring listeriosis. *Clin. Infect. Dis.* **54**, 652–660 (2012).
8. European Food Safety Authority (EFSA); European Centre for Disease Prevention and Control (ECDC) The European Union One health 2023 Zoonoses report. *EFSA J.* **22**, e9106 (2024).
9. Ferreira, V., Wiedmann, M., Teixeira, P. & Stasiewicz, M. J. *Listeria monocytogenes* persistence in food-associated environments: epidemiology, strain characteristics, and implications for public health. *J. Food Prot.* **77**, 150–170 (2014).
10. Marget, W. & Seeliger, H. P. *Listeria monocytogenes* infections — therapeutic possibilities and problems. *Infection* **16**, S175–S177 (1988).
11. Moura, A. et al. Emergence and global spread of *Listeria monocytogenes* main clinical clonal complex. *Sci. Adv.* **7**, eabj9805 (2021).
**This study demonstrates the global spread of the major clinical clonal complex CC1 of *L. monocytogenes* and highlights its biogeography and its probable origin in cattle.**
12. Swaminathan, B. & Gerner-Smidt, P. The epidemiology of human listeriosis. *Microbes Infect.* **9**, 1236–1243 (2007).
13. Dewey-Mattia, D., Manikonda, K., Hall, A. J., Wise, M. E. & Crowe, S. J. Surveillance for foodborne disease outbreaks — United States, 2009-2015. *MMWR Surveill. Summ.* **67**, 1–11 (2018).
14. Shah, H. J. et al. Reported incidence of infections caused by pathogens transmitted commonly through food: impact of increased use of culture-independent diagnostic tests — Foodborne Diseases Active Surveillance Network, 1996-2023. *MMWR Morb. Mortal. Wkly. Rep.* **73**, 584–593 (2024).
15. Cossart, P. & Lecuit, M. Interactions of *Listeria monocytogenes* with mammalian cells during entry and actin-based movement: bacterial factors, cellular ligands and signaling. *EMBO J.* **17**, 3797–3806 (1998).
16. Cossart, P. Raising a bacterium to the rank of a model system: the *Listeria* paradigm. *Annu. Rev. Microbiol.* **77**, 1–22 (2023).
17. Lecuit, M. *Listeria monocytogenes*, a model in infection biology. *Cell Microbiol.* **22**, e13186 (2020).
18. Pamer, E. G. Immune responses to *Listeria monocytogenes*. *Nat. Rev. Immunol.* **4**, 812–823 (2004).
**This publication provides an extensive and detailed overview of the immune response to *L. monocytogenes*.**
19. Mcclure, P. J., Roberts, T. A. & Oguru, P. O. Comparison of the effects of sodium chloride, pH and temperature on the growth of *Listeria monocytogenes* on gradient plates and in liquid medium. *Lett. Appl. Microbiol.* **9**, 95–99 (1989).
20. Fenlon, D. R., Wilson, J. & Donachie, W. The incidence and level of *Listeria monocytogenes* contamination of food sources at primary production and initial processing. *J. Appl. Bacteriol.* **81**, 641–650 (1996).
21. Nightingale, K. K. et al. Ecology and transmission of *Listeria monocytogenes* infecting ruminants and in the farm environment. *Appl. Env. Microbiol.* **70**, 4458–4467 (2004).
22. Oswaldi, V. et al. Distribution and characteristics of *Listeria* spp. in pigs and pork production chains in Germany. *Microorganisms* **10**, 512 (2022).
23. Yoshida, T., Sugimoto, T., Sato, M. & Hirai, K. Incidence of *Listeria monocytogenes* in wild animals in Japan. *J. Vet. Med. Sci.* **62**, 673–675 (2000).
24. Maury, M. M. et al. Hypervirulent *Listeria monocytogenes* clones' adaption to mammalian gut accounts for their association with dairy products. *Nat. Commun.* **10**, 2488 (2019).
25. Carpentier, B. & Cerf, O. Review — persistence of *Listeria monocytogenes* in food industry equipment and premises. *Int. J. Food Microbiol.* **145**, 1–8 (2011).
26. Kathariou, S. Listeria monocytogenes virulence and pathogenicity, a food safety perspective. *J. Food Prot.* **65**, 1811–1829 (2002).
27. FAO/WHO. *Joint FAO/WHO Expert Meeting on Microbiological Risk Assessment of* Listeria monocytogenes *in Foods. Part 2: Risk Assessment Models: Summary and Conclusions* (WHO, 2023).
28. Belias, A., Bolten, S. & Wiedmann, M. Challenges and opportunities for risk- and systems-based control of *Listeria monocytogenes* transmission through food. *Compr. Rev. Food Sci. Food Saf.* **23**, e70071 (2024).
29. Desai, A. N., Anyoha, A., Madoff, L. C. & Lassmann, B. Changing epidemiology of *Listeria monocytogenes* outbreaks, sporadic cases, and recalls globally: a review of ProMED reports from 1996 to 2018. *Int. J. Infect. Dis.* **84**, 48–53 (2019).
30. Garner, D. & Kathariou, S. Fresh produce-associated listeriosis outbreaks, sources of concern, teachable moments, and insights. *J. Food Prot.* **79**, 337–344 (2016).
31. Je, H. J., Kim, U. I. & Koo, O. K. A comprehensive systematic review and meta-analysis of *Listeria monocytogenes* prevalence in food products in South Korea. *Int. J. Food Microbiol.* **415**, 110655 (2024).
32. Lambrechts, K. & Rip, D. *Listeria monocytogenes* in the seafood industry: exploring contamination sources, outbreaks, antibiotic susceptibility and genetic diversity. *Microbiologyopen* **13**, e70003 (2024).
33. Liu, Y. et al. The prevalence of *Listeria monocytogenes* in meat products in China: a systematic literature review and novel meta-analysis approach. *Int. J. Food Microbiol.* **312**, 108358 (2020).
34. Tsai, Y. H. et al. Genomic surveillance of *Listeria monocytogenes* in Taiwan, 2014 to 2019. *Microbiol. Spectr.* **10**, e0182522 (2022).
35. Bartula, K., Begley, M., Latour, N. & Callanan, M. Growth of food-borne pathogens *Listeria* and *Salmonella* and spore-forming paenibacillus and bacillus in commercial plant-based milk alternatives. *Food Microbiol.* **109**, 104143 (2023).
36. Leclercq, A. et al. Outbreak of listeriosis associated with consumption of vegan cheese. *N. Engl. J. Med.* **390**, 1439–1440 (2024).

37. Schlech, W. F. 3rd et al. Epidemic listeriosis — evidence for transmission by food. *N. Engl. J. Med.* **308**, 203–206 (1983).
**This seminal study demonstrates the role of food as a source of contamination in a listeriosis outbreak.**
38. Driscoll, S. G., Gorbach, A. & Feldman, D. Congenital listeriosis: diagnosis from placental studies. *Oncologia* **20**, 216–220 (1962).
39. McLauchlin, J. & Low, J. C. Primary cutaneous listeriosis in adults: an occupational disease of veterinarians and farmers. *Vet. Rec.* **135**, 615–617 (1994).
40. Charlier, C. et al. Fatal neonatal listeriosis following *L. monocytogenes* horizontal transmission highlights neonatal susceptibility to orally acquired listeriosis. *Cell Rep. Med.* **4**, 101094 (2023).
41. Colodner, R. et al. *Listeria monocytogenes* cross-contamination in a nursery. *Am. J. Infect. Control.* **31**, 322–324 (2003).
42. Luchansky, J. B. et al. Survey for *Listeria monocytogenes* in and on ready-to-eat foods from retail establishments in the United States (2010 through 2013): assessing potential changes of pathogen prevalence and levels in a decade. *J. Food Prot.* **80**, 903–921 (2017).
43. Churchill, K. J., Sargeant, J. M., Farber, J. M. & O'Connor, A. M. Prevalence of *Listeria monocytogenes* in select ready-to-eat foods — deli meat, soft cheese, and packaged salad: a systematic review and meta-analysis. *J. Food Prot.* **82**, 344–357 (2019).
44. Schoder, D., Guldimann, C. & Martlbauer, E. Asymptomatic carriage of *Listeria monocytogenes* by animals and humans and its impact on the food chain. *Foods* **11**, 3472 (2022).
45. Hafner, L. et al. *Listeria monocytogenes* faecal carriage is common and depends on the gut microbiota. *Nat. Commun.* **12**, 6826 (2021).
46. EFSA Panel on Biological Hazards (BIOHAZ) *Listeria monocytogenes* contamination of ready-to-eat foods and the risk for human health in the EU. *EFSA J.* **16**, e05134 (2018).
47. de Noordhout, C. M. et al. The global burden of listeriosis: a systematic review and meta-analysis. *Lancet Infect. Dis.* **14**, 1073–1082 (2014).
**This study estimated the global burden of listeriosis and was a critical first step towards the efficient worldwide control of this deadly infection.**
48. Thomas, J. et al. Outbreak of listeriosis in South Africa associated with processed meat. *N. Engl. J. Med.* **382**, 632–643 (2020).
49. Jacquet, C. et al. Investigations related to the epidemic strain involved in the French listeriosis outbreak in 1992. *Appl. Env. Microbiol.* **61**, 2242–2246 (1995).
50. Goulet, V. et al. Listeriosis outbreak associated with the consumption of rillettes in France in 1993. *J. Infect. Dis.* **177**, 155–160 (1998).
51. Moura, A. et al. Real-time whole-genome sequencing for surveillance of *Listeria monocytogenes*, France. *Emerg. Infect. Dis.* **23**, 1462–1470 (2017).
52. Chenal-Francisque, V. et al. Worldwide distribution of major clones of *Listeria monocytogenes*. *Emerg. Infect. Dis.* **17**, 1110–1112 (2011).
53. Maury, M. M. et al. Uncovering *Listeria monocytogenes* hypervirulence by harnessing its biodiversity. *Nat. Genet.* **48**, 308–313 (2016).
**This study demonstrates the uneven distribution of clonal complexes, and that clinically associated clonal complexes are hypervirulent.**
54. Moura, A. et al. Whole genome-based population biology and epidemiological surveillance of *Listeria monocytogenes*. *Nat. Microbiol.* **2**, 16185 (2016).
**This study provides a detailed analysis of the population structure of *L. monocytogenes* and describes core genome multi-locus sequence typing as a new reference methodology for genotyping *L. monocytogenes*.**
55. Wang, Y. et al. Genomic dissection of the most prevalent *Listeria monocytogenes* clone, sequence type ST87, in China. *BMC Genom.* **20**, 1014 (2019).
56. de Valk, H. et al. Surveillance of listeria infections in Europe. *Eur. Surveill.* **10**, 251–255 (2005).
57. Pouillot, R., Hoelzer, K., Jackson, K. A., Henao, O. L. & Silk, B. J. Relative risk of listeriosis in Foodborne Diseases Active Surveillance Network (FoodNet) sites according to age, pregnancy, and ethnicity. *Clin. Infect. Dis.* **54**, S405–S410 (2012).
58. Mook, P., Grant, K. A., Little, C. L., Kafatos, G. & Gillespie, I. A. Emergence of pregnancy-related listeriosis amongst ethnic minorities in England and Wales. *Eur. Surveill.* **15**, 17–23 (2010).
59. Silk, B. J. et al. Invasive listeriosis in the Foodborne Diseases Active Surveillance Network (FoodNet), 2004-2009: further targeted prevention needed for higher-risk groups. *Clin. Infect. Dis.* **54**, S396–S404 (2012).
60. Hooper, D. C., Pruitt, A. A. & Rubin, R. H. Central nervous system infection in the chronically immunosuppressed. *Medicine* **61**, 166–188 (1982).
61. Slifman, N. R., Gershon, S. K., Lee, J. H., Edwards, E. T. & Braun, M. M. *Listeria monocytogenes* infection as a complication of treatment with tumor necrosis factor alpha-neutralizing agents. *Arthritis Rheum.* **48**, 319–324 (2003).
62. Blanchard, F. et al. *Listeria monocytogenes*-associated spontaneous bacterial peritonitis in France: a nationwide observational study of 208 cases. *Lancet Infect. Dis.* **24**, 783–792 (2024).
63. Shoai-Tehrani, M. et al. *Listeria monocytogenes*-associated endovascular infections: a study of 71 consecutive cases. *J. Infect.* **79**, 322–331 (2019).
64. Venkatesan, A. et al. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the International Encephalitis Consortium. *Clin. Infect. Dis.* **57**, 1114–1128 (2013).
65. Charlier, C. et al. Neonatal listeriosis presentation and outcome: a prospective study of 189 cases. *Clin. Infect. Dis.* **74**, 8–16 (2022).
66. McLauchlin, J. Human listeriosis in Britain, 1967-85, a summary of 722 cases. 1. Listeriosis during pregnancy and in the newborn. *Epidemiol. Infect.* **104**, 181–189 (1990).
67. Mylonakis, E., Paliou, M., Hohmann, E. L., Calderwood, S. B. & Wing, E. J. Listeriosis during pregnancy: a case series and review of 222 cases. *Medicine* **81**, 260–269 (2002).
68. Charlier, C. et al. Long-term neurological and neurodevelopmental outcome of neonatal listeriosis in France: a prospective, matched, observational cohort study. *Lancet Child. Adolesc. Health* **7**, 875–885 (2023).
69. Seeliger, H. P. R. & Höhne, K. in *Methods in Microbiology* Vol. 13 Ch. II (eds Bergan, T. & Norris, J. R.) 31–49 (Academic, 1979).
70. Orsi, R. H., den Bakker, H. C. & Wiedmann, M. *Listeria monocytogenes* lineages: genomics, evolution, ecology, and phenotypic characteristics. *Int. J. Med. Microbiol.* **301**, 79–96 (2011).
71. Ragon, M. et al. A new perspective on *Listeria monocytogenes* evolution. *PLoS Pathog.* **4**, e1000146 (2008).
72. Ruppitsch, W. et al. Defining and evaluating a core genome multilocus sequence typing scheme for whole-genome sequence-based typing of *Listeria monocytogenes*. *J. Clin. Microbiol.* **53**, 2869–2876 (2015).
73. Felix, B. et al. A European-wide dataset to uncover adaptive traits of *Listeria monocytogenes* to diverse ecological niches. *Sci. Data* **9**, 190 (2022).
74. Lee, S. et al. *Listeria monocytogenes* source distribution analysis indicates regional heterogeneity and ecological niche preference among serotype 4b clones. *mBio* **9**, e00396-18 (2018).
75. Rasmussen, O. F., Skouboe, P., Dons, L., Rossen, L. & Olsen, J. E. *Listeria monocytogenes* exists in at least three evolutionary lines: evidence from flagellin, invasive associated protein and listeriolysin O genes. *Microbiology* **141**, 2053–2061 (1995).
76. Ward, T. J., Ducey, T. F., Usgaard, T., Dunn, K. A. & Bielawski, J. P. Multilocus genotyping assays for single nucleotide polymorphism-based subtyping of *Listeria monocytogenes* isolates. *Appl. Env. Microbiol.* **74**, 7629–7642 (2008).
77. Senay, T. E. et al. Neurotropic lineage III strains of *Listeria monocytogenes* disseminate to the brain without reaching high titer in the blood. *mSphere* **5**, e00871-20 (2020).
78. Kammoun, H. et al. Listeriosis, a model infection to study host–pathogen interactions in vivo. *Curr. Opin. Microbiol.* **66**, 11–20 (2022).
79. Gaillard, J. L., Berche, P., Frehel, C., Gouin, E. & Cossart, P. Entry of *L. monocytogenes* into cells is mediated by internalin, a repeat protein reminiscent of surface antigens from gram-positive cocci. *Cell* **65**, 1127–1141 (1991).
**This study uses transposon mutagenesis to identify *inlA*, which encodes an internalin, an *L. monocytogenes* surface protein that mediates its internalization into epithelial cells.**
80. Mengaud, J., Ohayon, H., Gounon, P., Mege, R. M. & Cossart, P. E-cadherin is the receptor for internalin, a surface protein required for entry of *L. monocytogenes* into epithelial cells. *Cell* **84**, 923–932 (1996).
**This study uncovers E-cadherin as the epithelial host receptor of the major virulence factor InlA.**
81. Shen, Y., Naujokas, M., Park, M. & Ireton, K. InlB-dependent internalization of Listeria is mediated by the Met receptor tyrosine kinase. *Cell* **103**, 501–510 (2000).
**This study demonstrates that c-Met is the host receptor of InlB.**
82. Lecuit, M. et al. A single amino acid in E-cadherin responsible for host specificity towards the human pathogen *Listeria monocytogenes*. *EMBO J.* **18**, 3956–3963 (1999).
**This study demonstrates the species specificity of internalin interaction with E-cadherin.**
83. Khelef, N., Lecuit, M., Bierne, H. & Cossart, P. Species specificity of the *Listeria monocytogenes* InlB protein. *Cell Microbiol.* **8**, 457–470 (2006).
84. Gaillard, J. L., Berche, P. & Sansonetti, P. Transposon mutagenesis as a tool to study the role of hemolysin in the virulence of *Listeria monocytogenes*. *Infect. Immun.* **52**, 50–55 (1986).
85. Portnoy, D. A., Jacks, P. S. & Hinrichs, D. J. Role of hemolysin for the intracellular growth of *Listeria monocytogenes*. *J. Exp. Med.* **167**, 1459–1471 (1988).
86. Kathariou, S., Metz, P., Hof, H. & Goebel, W. Tn916-induced mutations in the hemolysin determinant affecting virulence of *Listeria monocytogenes*. *J. Bacteriol.* **169**, 1291–1297 (1987).
87. Tilney, L. G. & Portnoy, D. A. Actin filaments and the growth, movement, and spread of the intracellular bacterial parasite, *Listeria monocytogenes*. *J. Cell Biol.* **109**, 1597–1608 (1989).
**This study uses electron microscopy to show the entire intracellular cycle of *L. monocytogenes*, including cell entry, vacuolar escape, the formation of actin comet tails and cell-to-cell spread.**
88. Kocks, C. et al. *L. monocytogenes*-induced actin assembly requires the actA gene product, a surface protein. *Cell* **68**, 521–531 (1992).
**This study uses transposon mutagenesis to identify *actA*, whose gene product mediates the formation of actin tails that propel *L. monocytogenes* in the cytoplasm and from cell to cell.**
89. Yoshikawa, Y. et al. *Listeria monocytogenes* ActA-mediated escape from autophagic recognition. *Nat. Cell Biol.* **11**, 1233–1240 (2009).
90. Rajabian, T. et al. The bacterial virulence factor InlC perturbs apical cell junctions and promotes cell-to-cell spread of Listeria. *Nat. Cell Biol.* **11**, 1212–1218 (2009).
91. Camilli, A., Tilney, L. G. & Portnoy, D. A. Dual roles of plcA in *Listeria monocytogenes* pathogenesis. *Mol. Microbiol.* **8**, 143–157 (1993).
92. Domann, E., Leimeister-Wachter, M., Goebel, W. & Chakraborty, T. Molecular cloning, sequencing, and identification of a metalloprotease gene from *Listeria monocytogenes* that is species specific and physically linked to the listeriolysin gene. *Infect. Immun.* **59**, 65–72 (1991).
93. Prokop, A. et al. OrfX, a nucleomodulin required for *Listeria monocytogenes* virulence. *mBio* **8**, e01550-17 (2017).

94. Gaballa, A., Guariglia-Oropeza, V., Wiedmann, M. & Boor, K. J. Cross talk between SigB and PrfA in *Listeria monocytogenes* facilitates transitions between extra- and intracellular environments. *Microbiol. Mol. Biol. Rev.* **83**, e00034-19 (2019).
95. Johansson, J. et al. An RNA thermosensor controls expression of virulence genes in *Listeria monocytogenes*. *Cell* **110**, 551–561 (2002).
96. Loh, E. et al. A trans-acting riboswitch controls expression of the virulence regulator PrfA in *Listeria monocytogenes*. *Cell* **139**, 770–779 (2009).
97. Reniere, M. L. et al. Glutathione activates virulence gene expression of an intracellular pathogen. *Nature* **517**, 170–173 (2015).
98. Anaya-Sanchez, A., Feng, Y., Berude, J. C. & Portnoy, D. A. Detoxification of methylglyoxal by the glyoxalase system is required for glutathione availability and virulence activation in *Listeria monocytogenes*. *PLoS Pathog.* **17**, e1009819 (2021).
99. Berude, J. C., Kennouche, P., Reniere, M. L. & Portnoy, D. A. *Listeria monocytogenes* utilizes glutathione and limited inorganic sulfur compounds as sources of essential cysteine. *Infect. Immun.* **92**, e0042223 (2024).
100. Brenner, M. et al. Listeria monocytogenes TcyKLMN cystine/cysteine transporter facilitates glutathione synthesis and virulence gene expression. *mBio* **13**, e0044822 (2022).
101. Krypotou, E. et al. Control of bacterial virulence through the peptide signature of the habitat. *Cell Rep.* **26**, 1815–1827.e5 (2019).
102. Siletti, C. et al. C-di-AMP accumulation disrupts glutathione metabolism in *Listeria monocytogenes*. *Infect. Immun.* **92**, e0044024 (2024).
103. Glaser, P. et al. Comparative genomics of *Listeria* species. *Science* **294**, 849–852 (2001).
**This study determines and compares the genome sequence of a reference strain of *L. monocytogenes* to that of the closely related, avirulent species *L. innocua*.**
104. Davis, M. J., Coote, P. J. & O'Byrne, C. P. Acid tolerance in *Listeria monocytogenes*: the adaptive acid tolerance response (ATR) and growth-phase-dependent acid resistance. *Microbiology* **142**, 2975–2982 (1996).
105. O'Driscoll, B., Gahan, C. G. & Hill, C. Adaptive acid tolerance response in *Listeria monocytogenes*: isolation of an acid-tolerant mutant which demonstrates increased virulence. *Appl. Env. Microbiol.* **62**, 1693–1698 (1996).
106. Guerreiro, D. N. et al. Acid stress signals are integrated into the σB-dependent general stress response pathway via the stressosome in the food-borne pathogen *Listeria monocytogenes*. *PLoS Pathog.* **18**, e1010213 (2022).
107. Wu, J., McAuliffe, O. & O'Byrne, C. P. A novel RofA-family transcriptional regulator, GadR, controls the development of acid resistance in *Listeria monocytogenes*. *mBio* **14**, e0171623 (2023).
108. Dorey, A., Marinho, C., Piveteau, P. & O'Byrne, C. Role and regulation of the stress activated sigma factor sigma B ($\sigma^B$) in the saprophytic and host-associated life stages of *Listeria monocytogenes*. *Adv. Appl. Microbiol.* **106**, 1–48 (2019).
109. Dussurget, O. et al. *Listeria monocytogenes* bile salt hydrolase is a PrfA-regulated virulence factor involved in the intestinal and hepatic phases of listeriosis. *Mol. Microbiol.* **45**, 1095–1106 (2002).
110. Sleator, R. D., Wemekamp-Kamphuis, H. H., Gahan, C. G., Abee, T. & Hill, C. A PrfA-regulated bile exclusion system (BilE) is a novel virulence factor in *Listeria monocytogenes*. *Mol. Microbiol.* **55**, 1183–1195 (2005).
111. Quillin, S. J., Schwartz, K. T. & Leber, J. H. The novel *Listeria monocytogenes* bile sensor BrtA controls expression of the cholic acid efflux pump MdrT. *Mol. Microbiol.* **81**, 129–142 (2011).
112. Becattini, S. et al. Commensal microbes provide first line defense against *Listeria monocytogenes* infection. *J. Exp. Med.* **214**, 1973–1989 (2017).
113. Archambaud, C. et al. Impact of lactobacilli on orally acquired listeriosis. *Proc. Natl Acad. Sci. USA* **109**, 16684–16689 (2012).
114. Jin, T. et al. Intestinal linoleic acid contributes to the protective effects of *Akkermansia muciniphila* against *Listeria monocytogenes* infection in mice. *Imeta* **3**, e196 (2024).
115. Keane, J. M. et al. *Akkermansia muciniphila* reduces susceptibility to *Listeria monocytogenes* infection in mice fed a high-fat diet. *Gut Microbes* **15**, 2229948 (2023).
116. Quereda, J. J. et al. Bacteriocin from epidemic *Listeria* strains alters the host intestinal microbiota to favor infection. *Proc. Natl Acad. Sci. USA* **113**, 5706–5711 (2016).
117. Quereda, J. J., Meza-Torres, J., Cossart, P. & Pizarro-Cerda, J. Listeriolysin S: a bacteriocin from epidemic *Listeria monocytogenes* strains that targets the gut microbiota. *Gut Microbes* **8**, 384–391 (2017).
118. Meza-Torres, J. et al. Listeriolysin S: a bacteriocin from *Listeria monocytogenes* that induces membrane permeabilization in a contact-dependent manner. *Proc. Natl Acad. Sci. USA* **118**, e2108155118 (2021).
119. Rolhion, N. et al. A *Listeria monocytogenes* bacteriocin can target the commensal *Prevotella copri* and modulate intestinal infection. *Cell Host Microbe* **26**, 691–701.e5 (2019).
120. Dons, L., Rasmussen, O. F. & Olsen, J. E. Cloning and characterization of a gene encoding flagellin of *Listeria monocytogenes*. *Mol. Microbiol.* **6**, 2919–2929 (1992).
121. Wortel, I. M. N., Kim, S., Liu, A. Y., Ibarra, E. C. & Miller, M. J. Listeria motility increases the efficiency of epithelial invasion during intestinal infection. *PLoS Pathog.* **18**, e1011028 (2022).
122. Grundling, A., Burrack, L. S., Bouwer, H. G. & Higgins, D. E. *Listeria monocytogenes* regulates flagellar motility gene expression through MogR, a transcriptional repressor required for virulence. *Proc. Natl Acad. Sci. USA* **101**, 12318–12323 (2004).
123. Shen, A. & Higgins, D. E. The MogR transcriptional repressor regulates nonhierarchal expression of flagellar motility genes and virulence in *Listeria monocytogenes*. *PLoS Pathog.* **2**, e30 (2006).
124. Hayashi, F. et al. The innate immune response to bacterial flagellin is mediated by Toll-like receptor 5. *Nature* **410**, 1099–1103 (2001).
125. Bigot, A. et al. Role of FliF and Flil of *Listeria monocytogenes* in flagellar assembly and pathogenicity. *Infect. Immun.* **73**, 5530–5539 (2005).
126. Linden, S. K. et al. *Listeria monocytogenes* internalins bind to the human intestinal mucin MUC2. *Arch. Microbiol.* **190**, 101–104 (2008).
127. Popowska, M., Krawczyk-Balska, A., Ostrowski, R. & Desvaux, M. InlL from *Listeria monocytogenes* is involved in biofilm formation and adhesion to mucin. *Front. Microbiol.* **8**, 660 (2017).
128. Kim, M., Fevre, C., Lavina, M., Disson, O. & Lecuit, M. Live imaging reveals *Listeria* hijacking of E-cadherin recycling as it crosses the intestinal barrier. *Curr. Biol.* **31**, 1037–1047 e1034 (2021).
129. Lecuit, M. et al. A transgenic model for listeriosis: role of internalin in crossing the intestinal barrier. *Science* **292**, 1722–1725 (2001).
**This study reports on the generation of a humanized transgenic mouse model expressing human E-cadherin in intestinal epithelial cells, revealing that the interaction between InlA and E-cadherin mediates *L. monocytogenes* crossing of the intestinal barrier.**
130. Nikitas, G. et al. Transcytosis of *Listeria monocytogenes* across the intestinal barrier upon specific targeting of goblet cell accessible E-cadherin. *J. Exp. Med.* **208**, 2263–2277 (2011).
131. Pentecost, M., Otto, G., Theriot, J. A. & Amieva, M. R. *Listeria monocytogenes* invades the epithelial junctions at sites of cell extrusion. *PLoS Pathog.* **2**, e3 (2006).
132. Chiba, S. et al. Listerial invasion protein internalin B promotes entry into ileal Peyer's patches in vivo. *Microbiol. Immunol.* **55**, 123–129 (2011).
133. Gessain, G. et al. PI3-kinase activation is critical for host barrier permissiveness to *Listeria monocytogenes*. *J. Exp. Med.* **212**, 165–183 (2015).
134. Pron, B. et al. Comprehensive study of the intestinal stage of listeriosis in a rat ligated ileal loop system. *Infect. Immun.* **66**, 747–755 (1998).
135. Disson, O. et al. Conjugated action of two species-specific invasion proteins for fetoplacental listeriosis. *Nature* **455**, 1114–1118 (2008).
**This study shows that InlA–E-cadherin and InlB–c-Met interactions are necessary and act together for *L. monocytogenes* to cross the placental barrier in Ecad E16P knock-in humanized mice, as well as in gerbil, a natural host for *L. monocytogenes*.**
136. Lecuit, M., Sonnenburg, J. L., Cossart, P. & Gordon, J. I. Functional genomic studies of the intestinal response to a foodborne enteropathogen in a humanized gnotobiotic mouse model. *J. Biol. Chem.* **282**, 15065–15072 (2007).
137. Tsai, Y. H., Disson, O., Bierne, H. & Lecuit, M. Murinization of internalin extends its receptor repertoire, altering *Listeria monocytogenes* cell tropism and host responses. *PLoS Pathog.* **9**, e1003381 (2013).
138. Disson, O. et al. Peyer's patch myeloid cells infection by *Listeria* signals through gp38$^+$ stromal cells and locks intestinal villus invasion. *J. Exp. Med.* **215**, 2936–2954 (2018).
139. Maudet, C. et al. Bacterial inhibition of Fas-mediated killing promotes neuroinvasion and persistence. *Nature* **603**, 900–906 (2022).
140. Jones, G. S. & D'Orazio, S. E. Monocytes are the predominant cell type associated with *Listeria monocytogenes* in the gut, but they do not serve as an intracellular growth niche. *J. Immunol.* **198**, 2796–2804 (2017).
141. Nowacki, J. S., Jones, G. S. & D'Orazio, S. E. F. *Listeria monocytogenes* use multiple mechanisms to disseminate from the intestinal lamina propria to the mesenteric lymph nodes. *Microbiol. Spectr.* **13**, e0259524 (2025).
142. Aichele, P. et al. Macrophages of the splenic marginal zone are essential for trapping of blood-borne particulate antigen but dispensable for induction of specific T cell responses. *J. Immunol.* **171**, 1148–1155 (2003).
143. Liu, D. et al. IL-10-dependent crosstalk between murine marginal zone B cells, macrophages, and CD8α$^+$ dendritic cells promotes *Listeria monocytogenes* infection. *Immunity* **51**, 64–76.e7 (2019).
144. Neuenhahn, M. et al. CD8α$^+$ dendritic cells are required for efficient entry of *Listeria monocytogenes* into the spleen. *Immunity* **25**, 619–630 (2006).
145. Kang, S. J., Liang, H. E., Reizis, B. & Locksley, R. M. Regulation of hierarchical clustering and activation of innate immune cells by dendritic cells. *Immunity* **29**, 819–833 (2008).
146. Aoshi, T. et al. Bacterial entry to the splenic white pulp initiates antigen presentation to CD8$^+$ T cells. *Immunity* **29**, 476–486 (2008).
147. Jung, S. et al. In vivo depletion of CD11c$^+$ dendritic cells abrogates priming of CD8$^+$ T cells by exogenous cell-associated antigens. *Immunity* **17**, 211–220 (2002).
148. Zammit, D. J., Cauley, L. S., Pham, Q. M. & Lefrancois, L. Dendritic cells maximize the memory CD8 T cell response to infection. *Immunity* **22**, 561–570 (2005).
149. Pirie, J. H. H. A new disease of veld rodents, "Tiger river disease.". *Pub South. Afr. Inst. Med. Res.* **62**, 163–186 (1927).
150. Bleriot, C. et al. Liver-resident macrophage necroptosis orchestrates type 1 microbicidal inflammation and type-2-mediated tissue repair during bacterial infection. *Immunity* **42**, 145–158 (2015).
151. Charlier, C. et al. *Listeria monocytogenes*-associated biliary tract infections: a study of 12 consecutive cases and review. *Medicine* **93**, e105 (2014).
152. Hardy, J. et al. Extracellular replication of *Listeria monocytogenes* in the murine gall bladder. *Science* **303**, 851–853 (2004).
153. Louie, A., Zhang, T., Becattini, S., Waldor, M. K. & Portnoy, D. A. A multiorgan trafficking circuit provides purifying selection of *Listeria monocytogenes* virulence genes. *mBio* **10**, e02948-19 (2019).
154. Lecuit, M. et al. Targeting and crossing of the human maternofetal barrier by *Listeria monocytogenes*: role of internalin interaction with trophoblast E-cadherin. *Proc. Natl Acad. Sci. USA* **101**, 6152–6157 (2004).
155. Faralla, C. et al. *Listeria monocytogenes* InlP interacts with afadin and facilitates basement membrane crossing. *PLoS Pathog.* **14**, e1007094 (2018).

156. Faralla, C. et al. InlP, a new virulence factor with strong placental tropism. *Infect. Immun.* **84**, 3584–3596 (2016).
157. Bakardjiev, A. I., Stacy, B. A. & Portnoy, D. A. Growth of *Listeria monocytogenes* in the guinea pig placenta and role of cell-to-cell spread in fetal infection. *J. Infect. Dis.* **191**, 1889–1897 (2005).
158. Le Monnier, A. et al. ActA is required for crossing of the fetoplacental barrier by *Listeria monocytogenes*. *Infect. Immun.* **75**, 950–957 (2007).
159. Bakardjiev, A. I., Theriot, J. A. & Portnoy, D. A. *Listeria monocytogenes* traffics from maternal organs to the placenta and back. *PLoS Pathog.* **2**, e66 (2006).
160. Dumont, J. & Cotoni, L. Bacille semblable au bacille du rouget du porc rencontré dans le liquide céphalo-rachidien d'un méningitique. *Ann. Inst. Pasteur* **35**, 625–633 (1921).
161. Gill, D. A. "Circling" disease: a meningoencephalitis of sheep in New Zealand. *Vet. J.* **89**, 258–270 (1933).
162. Oevermann, A. et al. Neuropathogenesis of naturally occurring encephalitis caused by *Listeria monocytogenes* in ruminants. *Brain Pathol.* **20**, 378–390 (2010).
163. Drevets, D. A., Jelinek, T. A. & Freitag, N. E. *Listeria monocytogenes*-infected phagocytes can initiate central nervous system infection in mice. *Infect. Immun.* **69**, 1344–1350 (2001).
164. Join-Lambert, O. F. et al. *Listeria monocytogenes*-infected bone marrow myeloid cells promote bacterial invasion of the central nervous system. *Cell Microbiol.* **7**, 167–180 (2005).
165. Chevee, V. et al. Temporal and spatial dynamics of *Listeria monocytogenes* central nervous system infection in mice. *Proc. Natl Acad. Sci. USA* **121**, e2320311121 (2024).
166. Hafner, L. et al. Differential stress responsiveness determines intraspecies virulence heterogeneity and host adaptation in *Listeria monocytogenes*. *Nat. Microbiol.* **9**, 3345–3361 (2024).
167. Ghosh, P. et al. Invasion of the brain by *Listeria monocytogenes* is mediated by InlF and host cell vimentin. *mBio* **9**, e00160-18 (2018).
168. Tsai, Y. H., Orsi, R. H., Nightingale, K. K. & Wiedmann, M. *Listeria monocytogenes* internalins are highly diverse and evolved by recombination and positive selection. *Infect. Genet. Evol.* **6**, 378–389 (2006).
169. Mackaness, G. B. Cellular resistance to infection. *J. Exp. Med.* **116**, 381–406 (1962).
170. McGregor, D. D., Koster, F. T. & Mackaness, G. B. The short lived small lymphocyte as a mediator of cellular immunity. *Nature* **228**, 855–856 (1970).
171. Edelson, B. T. & Unanue, E. R. Intracellular antibody neutralizes *Listeria* growth. *Immunity* **14**, 503–512 (2001).
172. Lee, C. C. & Kung, J. T. Marginal zone B cell is a major source of Il-10 in *Listeria monocytogenes* susceptibility. *J. Immunol.* **189**, 3319–3327 (2012).
173. Tripp, C. S., Wolf, S. F. & Unanue, E. R. Interleukin 12 and tumor necrosis factor alpha are costimulators of interferon gamma production by natural killer cells in severe combined immunodeficiency mice with listeriosis, and interleukin 10 is a physiologic antagonist. *Proc. Natl Acad. Sci. USA* **90**, 3725–3729 (1993).
174. Birmingham, C. L. et al. Listeriolysin O allows *Listeria monocytogenes* replication in macrophage vacuoles. *Nature* **451**, 350–354 (2008).
175. Harty, J. T. & Bevan, M. J. Specific immunity to *Listeria monocytogenes* in the absence of IFNγ. *Immunity* **3**, 109–117 (1995).
**This study shows the major role of IFNγ against *L. monocytogenes* infection.**
176. Rothe, J. et al. Mice lacking the tumour necrosis factor receptor 1 are resistant to TNF-mediated toxicity but highly susceptible to infection by *Listeria monocytogenes*. *Nature* **364**, 798–802 (1993).
**This study shows the major role of TNF against *L. monocytogenes* infection.**
177. Woodward, J. J., Iavarone, A. T. & Portnoy, D. A. c-di-AMP secreted by intracellular *Listeria monocytogenes* activates a host type I interferon response. *Science* **328**, 1703–1705 (2010).
178. Auerbuch, V., Brockstedt, D. G., Meyer-Morse, N., O'Riordan, M. & Portnoy, D. A. Mice lacking the type I interferon receptor are resistant to *Listeria monocytogenes*. *J. Exp. Med.* **200**, 527–533 (2004).
179. Carrero, J. A., Calderon, B. & Unanue, E. R. Type I interferon sensitizes lymphocytes to apoptosis and reduces resistance to *Listeria* infection. *J. Exp. Med.* **200**, 535–540 (2004).
180. Guleria, I. & Pollard, J. W. The trophoblast is a component of the innate immune system during pregnancy. *Nat. Med.* **6**, 589–593 (2000).
181. Qiu, X., Zhu, L. & Pollard, J. W. Colony-stimulating factor-1-dependent macrophage functions regulate the maternal decidua immune responses against *Listeria monocytogenes* infections during early gestation in mice. *Infect. Immun.* **77**, 85–97 (2009).
182. Barber, E. M., Fazzari, M. & Pollard, J. W. Th1 cytokines are essential for placental immunity to *Listeria monocytogenes*. *Infect. Immun.* **73**, 6322–6331 (2005).
183. Gayle, P. et al. Maternal- and fetal-encoded perforin-2 limits placental infection by a bloodborne pathogen. *J. Immunol.* **205**, 1878–1885 (2020).
184. Megli, C., Morosky, S., Rajasundaram, D. & Coyne, C. B. Inflammasome signaling in human placental trophoblasts regulates immune defense against *Listeria monocytogenes* infection. *J. Exp. Med.* **218**, e20200649 (2021).
185. Crespo, A. C. et al. Decidual NK cells transfer granulysin to selectively kill bacteria in trophoblasts. *Cell* **182**, 1125–1139.e18 (2020).
186. Erickson, J. J. et al. Pregnancy enables antibody protection against intracellular infection. *Nature* **606**, 769–775 (2022).
187. Maudet, C., Levallois, S., Disson, O. & Lecuit, M. Innate immune responses to *Listeria* in vivo. *Curr. Opin. Microbiol.* **59**, 95–101 (2021).
188. Boneca, I. G. et al. A critical role for peptidoglycan N-deacetylation in *Listeria* evasion from the host innate immune system. *Proc. Natl Acad. Sci. USA* **104**, 997–1002 (2007).
189. Aubry, C. et al. OatA, a peptidoglycan O-acetyltransferase involved in *Listeria monocytogenes* immune escape, is critical for virulence. *J. Infect. Dis.* **204**, 731–740 (2011).
190. Gouin, E. et al. The *Listeria monocytogenes* InlC protein interferes with innate immune responses by targeting the IκB kinase subunit IKKα. *Proc. Natl Acad. Sci. USA* **107**, 17333–17338 (2010).
191. Personnic, N. et al. The stress-induced virulence protein InlH controls interleukin-6 production during murine listeriosis. *Infect. Immun.* **78**, 1979–1989 (2010).
192. Aureli, P. et al. An outbreak of febrile gastroenteritis associated with corn contaminated by *Listeria monocytogenes*. *N. Engl. J. Med.* **342**, 1236–1241 (2000).
193. Dalton, C. B. et al. An outbreak of gastroenteritis and fever due to *Listeria monocytogenes* in milk. *N. Engl. J. Med.* **336**, 100–105 (1997).
194. Ooi, S. T. & Lorber, B. Gastroenteritis due to *Listeria monocytogenes*. *Clin. Infect. Dis.* **40**, 1327–1332 (2005).
195. Goulet, V., King, L. A., Vaillant, V. & de Valk, H. What is the incubation period for listeriosis? *BMC Infect. Dis.* **13**, 11 (2013).
196. Angelo, K. M., Jackson, K. A., Wong, K. K., Hoekstra, R. M. & Jackson, B. R. Assessment of the incubation period for invasive listeriosis. *Clin. Infect. Dis.* **63**, 1487–1489 (2016).
197. Koopmans, M. M., Bijlsma, M. W., Brouwer, M. C., van de Beek, D. & van der Ende, A. *Listeria monocytogenes* meningitis in the Netherlands, 1985-2014: a nationwide surveillance study. *J. Infect.* **75**, 12–19 (2017).
198. Koopmans, M. M. et al. *Listeria monocytogenes* sequence type 6 and increased rate of unfavorable outcome in meningitis: epidemiologic cohort study. *Clin. Infect. Dis.* **57**, 247–253 (2013).
199. Mylonakis, E., Hohmann, E. L. & Calderwood, S. B. Central nervous system infection with *Listeria monocytogenes*. 33 years' experience at a general hospital and review of 776 episodes from the literature. *Medicine* **77**, 313–336 (1998).
200. Charlier, C. et al. Imaging of human neurolisteriosis: a prospective study of 71 cases. *Clin. Infect. Dis.* **67**, 1419–1426 (2018).
201. Elinav, H. et al. Pregnancy-associated listeriosis: clinical characteristics and geospatial analysis of a 10-year period in Israel. *Clin. Infect. Dis.* **59**, 953–961 (2014).
202. Charlier, C., Disson, O. & Lecuit, M. Maternal-neonatal listeriosis. *Virulence* **11**, 391–397 (2020).
203. Elinav, H., Hershko-Klement, A., Solt, I., Glikman, D. & Nir-Paz, R. Pregnancy-associated listeriosis: many beliefs, few facts. *Lancet Infect. Dis.* **15**, 1128–1130 (2015).
204. Klatt, E. C., Pavlova, Z., Teberg, A. J. & Yonekura, M. L. Epidemic perinatal listeriosis at autopsy. *Hum. Pathol.* **17**, 1278–1281 (1986).
205. Blot, M. et al. Listeria-associated lymphadenitis: a series of 11 consecutive cases and review of the literature. *Open. Forum Infect. Dis.* **9**, ofab598 (2022).
206. Chersich, M. F. et al. Diagnosis and treatment of *Listeria monocytogenes* endophthalmitis: a systematic review. *Ocul. Immunol. Inflamm.* **26**, 508–517 (2018).
207. Morgand, M. et al. *Listeria monocytogenes*-associated respiratory infections: a study of 38 consecutive cases. *Clin. Microbiol. Infect.* **24**, 1339.e1–1339.e5 (2018).
208. Pilmis, B. et al. Cutaneous listeriosis, a case series of 16 consecutive patients over 25 years. *J. Infect.* **80**, 232–254 (2020).
209. Danion, F. et al. *Listeria monocytogenes* isolation from urine: a series of 15 cases and review. *Clin. Microbiol. Infect.* **23**, 583–585 (2017).
210. Thouvenot, P. et al. MALDI-TOF mass spectrometry-based identification of *Listeria* species in surveillance: a prospective study. *J. Microbiol. Methods* **144**, 29–32 (2018).
211. Le Monnier, A., Abachin, E., Beretti, J. L., Berche, P. & Kayal, S. Diagnosis of *Listeria monocytogenes* meningoencephalitis by real-time PCR for the *hly* gene. *J. Clin. Microbiol.* **49**, 3917–3923 (2011).
212. Schnuriger, A. et al. Differential performance of the FilmArray meningitis/encephalitis assay to detect bacterial and viral pathogens in both pediatric and adult populations. *Microbiol. Spectr.* **10**, e0277421 (2022).
213. Seeliger, H. P. & Langer, B. Serological analysis of the genus *Listeria*. Its values and limitations. *Int. J. Food Microbiol.* **8**, 245–248 (1989).
214. Doumith, M., Buchrieser, C., Glaser, P., Jacquet, C. & Martin, P. Differentiation of the major *Listeria monocytogenes* serovars by multiplex PCR. *J. Clin. Microbiol.* **42**, 3819–3822 (2004).
215. Yin, Y. et al. A hybrid sub-lineage of *Listeria monocytogenes* comprising hypervirulent isolates. *Nat. Commun.* **10**, 4283 (2019).
216. Schonberg, A. et al. Serotyping of 80 strains from the WHO multicentre international typing study of *Listeria monocytogenes*. *Int. J. Food Microbiol.* **32**, 279–287 (1996).
217. Burall, L. S. et al. Development and validation of a quantitative PCR method for species verification and serogroup determination of *Listeria monocytogenes* isolates. *J. Food Prot.* **84**, 333–344 (2021).
218. Buchrieser, C., Brosch, R. & Rocourt, J. Use of pulsed field gel electrophoresis to compare large DNA-restriction fragments of *Listeria monocytogenes* strains belonging to serogroups 1/2 and 3. *Int. J. Food Microbiol.* **14**, 297–304 (1991).
219. Haase, J. K. et al. The ubiquitous nature of *Listeria monocytogenes* clones: a large-scale multilocus sequence typing study. *Env. Microbiol.* **16**, 405–416 (2014).
220. Chen, Y. et al. Whole genome and core genome multilocus sequence typing and single nucleotide polymorphism analyses of *Listeria monocytogenes* isolates associated with an outbreak linked to cheese, United States, 2013. *Appl. Env. Microbiol.* **83**, e00633-17 (2017).
221. Jagadeesan, B., Baert, L., Wiedmann, M. & Orsi, R. H. Comparative analysis of tools and approaches for source tracking *Listeria monocytogenes* in a food facility using whole-genome sequence data. *Front. Microbiol.* **10**, 947 (2019).

222. Halbedel, S. et al. Whole-genome sequencing of recent *Listeria monocytogenes* isolates from Germany reveals population structure and disease clusters. *J. Clin. Microbiol.* **56**, e00119-18 (2018).
223. Henri, C. et al. An assessment of different genomic approaches for inferring phylogeny of *Listeria monocytogenes*. *Front. Microbiol.* **8**, 2351 (2017).
224. Mixao, V. et al. Multi-country and intersectoral assessment of cluster congruence between pipelines for genomics surveillance of foodborne pathogens. *Nat. Commun.* **16**, 3961 (2025).
225. Lüth, S., Kleta, S. & Al Dahouk, S. Whole genome sequencing as a typing tool for foodborne pathogens like *Listeria monocytogenes* — the way towards global harmonisation and data exchange. *Trends Food Sci. Tech.* **73**, 67–75 (2018).
226. Luth, S., Deneke, C., Kleta, S. & Al Dahouk, S. Translatability of WGS typing results can simplify data exchange for surveillance and control of *Listeria monocytogenes*. *Microb. Genom.* **7**, mgen000491 (2021).
227. Lamont, R. F. et al. Listeriosis in human pregnancy: a systematic review. *J. Perinat. Med.* **39**, 227–236 (2011).
228. *Risk Assessment of* Listeria monocytogenes *in Foods: Part 1: Formal Models – Meeting Report* (FAO & WHO, 2024).
229. Safe2Eat: food poisoning. *European Food Safety Authority* https://www.efsa.europa.eu/en/safe2eat/food-poisoning (2025).
230. Committee ppinion no 614: management of pregnant women with presumptive exposure to *Listeria monocytogenes*. *Obstet. Gynecol.* **124**, 1241–1244 (2014).
231. Fernandez-Sabe, N. et al. Risk factors, clinical features, and outcomes of listeriosis in solid-organ transplant recipients: a matched case-control study. *Clin. Infect. Dis.* **49**, 1153–1159 (2009).
232. Tuytschaever, T., Raes, K. & Sampers, I. *Listeria monocytogenes* in food businesses: from persistence strategies to intervention/prevention strategies — a review. *Compr. Rev. Food Sci. Food Saf.* **22**, 3910–3950 (2023).
233. Grayo, S., Join-Lambert, O., Desroches, M. C. & Le Monnier, A. Comparison of the in vitro efficacies of moxifloxacin and amoxicillin against *Listeria monocytogenes*. *Antimicrob. Agents Chemother.* **52**, 1697–1702 (2008).
234. Hof, H., Nichterlein, T. & Kretschmar, M. Management of listeriosis. *Clin. Microbiol. Rev.* **10**, 345–357 (1997).
235. Penn, R. L., Ward, T. T. & Steigbigel, R. T. Effects of erythromycin in combination with penicillin, ampicillin, or gentamicin on the growth of *Listeria monocytogenes*. *Antimicrob. Agents Chemother.* **22**, 289–294 (1982).
236. Moura, A. et al. Phenotypic and genotypic antimicrobial resistance of *Listeria monocytogenes*: an observational study in France. *Lancet Reg. Health Eur.* **37**, 100800 (2024).
237. Vicente, M. F., Perez-Daz, J. C., Baquero, F., Angel de Pedro, M. & Berenguer, J. Penicillin-binding protein 3 of *Listeria monocytogenes* as the primary lethal target for β-lactams. *Antimicrob. Agents Chemother.* **34**, 539–542 (1990).
238. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. *Lancet* **404**, 1199–1226 (2024).
239. Baquero, F., V, F. L., Duval, M. & Coque, T. M. Ecogenetics of antibiotic resistance in *Listeria monocytogenes*. *Mol. Microbiol.* **113**, 570–579 (2020).
240. Luque-Sastre, L. et al. Antimicrobial resistance in *Listeria* species. *Microbiol. Spectr.* https://doi.org/10.1128/microbiolspec.ARBA-0031-2017 (2018).
241. Scortti, M. et al. Coexpression of virulence and fosfomycin susceptibility in *Listeria*: molecular basis of an antimicrobial in vitro–in vivo paradox. *Nat. Med.* **12**, 515–517 (2006).
242. Scortti, M. et al. Epistatic control of intrinsic resistance by virulence genes in Listeria. *PLoS Genet.* **14**, e1007525 (2018).
243. Gjonbalaj, M. et al. Antibiotic degradation by commensal microbes shields pathogens. *Infect. Immun.* **88**, e00012-20 (2020).
244. Janakiraman, V. Listeriosis in pregnancy: diagnosis, treatment, and prevention. *Rev. Obstet. Gynecol.* **1**, 179–185 (2008).
245. Michelet, C., Leib, S. L., Bentue-Ferrer, D. & Tauber, M. G. Comparative efficacies of antibiotics in a rat model of meningoencephalitis due to *Listeria monocytogenes*. *Antimicrob. Agents Chemother.* **43**, 1651–1656 (1999).
246. Brouwer, M. C. & van de Beek, D. Adjunctive dexamethasone treatment in adults with *Listeria monocytogenes* meningitis: a prospective nationwide cohort study. *eClinicalMedicine* **58**, 101922 (2023).
247. Pogreba-Brown, K. et al. Complications associated with foodborne listeriosis: a scoping review. *Foodborne Pathog. Dis.* **19**, 725–743 (2022).
248. Meinersmann, R. J., Phillips, R. W., Wiedmann, M. & Berrang, M. E. Multilocus sequence typing of *Listeria monocytogenes* by use of hypervariable genes reveals clonal and recombination histories of three lineages. *Appl. Env. Microbiol.* **70**, 2193–2203 (2004).
249. Nau, R., Sorgel, F. & Eiffert, H. Penetration of drugs through the blood–cerebrospinal fluid/blood–brain barrier for treatment of central nervous system infections. *Clin. Microbiol. Rev.* **23**, 858–883 (2010).
250. Lecuit, M. Understanding how *Listeria monocytogenes* targets and crosses host barriers. *Clin. Microbiol. Infect.* **11**, 430–436 (2005).
251. Kim, S. H., Cho, B. H., Kim, K. S. & Jang, Y. S. Complement C5a promotes antigen cross-presentation by Peyer's patch monocyte-derived dendritic cells and drives a protective $CD8^+$ T cell response. *Cell Rep.* **35**, 108995 (2021).
252. Joyce, S. A. & Gahan, C. G. M. Molecular pathogenesis of *Listeria monocytogenes* in the alternative model host *Galleria mellonella*. *Microbiology* **156**, 3456–3468 (2010).
253. Mukherjee, K. et al. *Galleria mellonella* as a model system for studying *Listeria* pathogenesis. *Appl. Env. Microbiol.* **76**, 310–317 (2010).
254. Mukherjee, K., Hain, T., Fischer, R., Chakraborty, T. & Vilcinskas, A. Brain infection and activation of neuronal repair mechanisms by the human pathogen *Listeria monocytogenes* in the lepidopteran model host *Galleria mellonella*. *Virulence* **4**, 324–332 (2013).
255. Asai, M., Li, Y., Newton, S. M., Robertson, B. D. & Langford, P. R. *Galleria mellonella*-intracellular bacteria pathogen infection models: the ins and outs. *FEMS Microbiol. Rev.* **47**, fuad011 (2023).
256. Wang, Y. et al. Generation of gene-knockout Mongolian gerbils via CRISPR/Cas9 system. *Front. Bioeng. Biotechnol.* **8**, 780 (2020).
257. Nightingale, K. K. et al. *Listeria monocytogenes* F2365 carries several authentic mutations potentially leading to truncated gene products, including inlB, and demonstrates atypical phenotypic characteristics. *J. Food Prot.* **70**, 482–488 (2007).
258. Cotter, P. D. et al. Listeriolysin S, a novel peptide haemolysin associated with a subset of lineage I *Listeria monocytogenes*. *PLoS Pathog.* **4**, e1000144 (2008).



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