

MOLECULAR PATHOGENICITY AND CLINICAL MANIFESTATIONS OF LISTERIOSIS IN SMALL RUMINANTS: A REVIEW

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ABSTRACT

Listeriosis is an important infectious disease of goats, sheep, and other ruminants, caused mainly by *Listeria monocytogenes* and occasionally by *Listeria ivanovii* in small ruminants. In goats and sheep, the major clinical manifestations include rhombencephalitis or meningoencephalitis, abortion, stillbirth, neonatal septicemia, mastitis, and, rarely, ocular or gastrointestinal disease. The pathogenic potential of listeriosis-associated isolates depends on the interaction between bacterial genotype, conserved virulence genes, environmental adaptability, and infectious dose, route of infection, pregnancy status, mucosal damage, and host immunity. *Listeria monocytogenes* is a facultative intracellular pathogen that binds to and invades host cells, escapes from the phagosome through listeriolysin O and phospholipases, replicates within the cytosol, and spreads from cell to cell through ActA-mediated actin-based motility. These mechanisms enable the bacterium to evade the host immune response, invade the placenta and fetus, cause septicemia, and reach the nervous system. Studying naturally isolated strains from the brainstem, fetal-placental tissues, milk, feces, silage, farms, and farm environments is essential for understanding the relationship between molecular virulence and the ecology of host-pathogen interactions.

1. INTRODUCTION

Listeriosis is a high-consequence bacterial disease that is at the interface of veterinary medicine, food safety and public health. In farmed ruminants, and specifically in sheep and goats, it is best known as neurological disease, reproductive failure or newborn septicemia, although other localized manifestations exist (Sepahvand *et al.*, 2022; Bagatella *et al.*, 2022). The disease is of special significance to small-ruminant production because cases of the disease occur in the form of neurological or reproductive. nuclei of cranial nerves (Oevermann *et al.*, 2010; Precht *et al.*, 2020).

The pathology of the classical clinical syndrome, known as circling disease, corresponds to rhombencephalitis, with lesions in the medulla oblongata, the pons and *Listeria monocytogenes* is a Gram-positive, non-spore, facultatively anaerobic bacterium that is the principal etiological agent. This dual life is the reason why the organism can survive in soil, vegetation, silage, feces, water, milk and farm equipment, as well as cause severe invasive disease in susceptible hosts (Vazquez-Boland *et al.*, 2001; Orsi *et al.*, 2011; Radoshevich and Cossart, 2018). *L. monocytogenes* is also a major foodborne pathogen in humans, which makes small ruminants relevant as diseased hosts as well as potential sources of contamination in raw milk, dairy products, meat,

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manure-amended environments and mixed crop livestock systems (Pinto et al., 2023).

Here, the term listeriosis-associated isolated strains are used to embrace *Listeria* isolates recovered in clinical lesions, aborted materials, milk, feces, feed and farm environments, in epidemiology association with disease. The difference is important since the environmental isolation alone is not sufficient to demonstrate the pathogenic causation. The highly pathogenic strains are strongly evidenced by the recovery of the same or closely related strain in compatible lesions in clinically affected animals and in plausible exposure sources as in the outbreak investigations of small-ruminant listerial encephalitis (Wiedmann et al., 1994). This interpretation has been reinforced by modern genomic approaches that have made clonal-complex assignment, profiling of virulence and epidemiologically relevant genes and high-resolution linkage of animal, feed and environmental isolates possible (Cardenas-Alvarez et al., 2022).

Etiology and Taxonomy of *Listeria* Species

The genus *Listeria* includes small Gram-positive rods whose pathogenic potential may vary. The predominant cause of listeriosis in humans and animals is *L. monocytogenes*, whereas *L. ivanovii* is identified as the primary cause of ruminant disease, especially abortion in goats and sheep (Pizarro-Cerdá & Cossart, 2018). Other species, such as *L. innocua*, *L. welshimeri*, *L. seeligeri* and *L. grayi*, are generally considered non-pathogenic or even rarely pathogenic, although expanded taxonomy and whole-genome sequencing has made the older distinction between pathogenic and non-pathogenic species more complicated (Orsi et al., 2011; Radoshevich and Cossart, 2018).

L. monocytogenes can be further distinguished into serotypes and evolutionary lineages. Most commonly involved in human and animal disease are serotypes 1/2a, 1/2b and 4b, with most clinical and food-associated studies showing a preponderance of the molecular lineages I and II (Orsi et al., 2011). Some of the clonal complexes involved in invasive disease are found in lineage I, including clones that cause central-nervous-system and maternal-neonatal listeriosis in humans; lineage II is common in foods and

environmental niches but also causes disease (Maury et al., 2016). A genomic study of 73 ruminant listeriosis isolates conducted in the U.S. found all 1, 2 and 3 lineages among neurologic and fetal cases (Schoder et al., 2023).

Taxonomic identification has practical diagnostic value. The isolation of *L. monocytogenes* in brainstem lesions, fetal tissues, placenta or septicemic organs is of great importance when the lesions are compatible with listeriosis. The isolation of *L. ivanovii* in fetoplacental tissues is also significant in the small-ruminant abortion studies, although this species is not often associated with neuroinvasive disease compared to *L. monocytogenes* (Lianou et al., 2022).

Epidemiology of Listeriosis in Goats and Small Ruminants

Listeriosis is spread globally and is sporadically or epidemically spread. In goats and sheep, outbreaks are frequently associated with winter housing and feeding of conserved forage, particularly poorly fermented silage (Wiedmann et al., 1994; Low & Donachie, 1997). The organism is cold-tolerant, moderate salt-tolerant, and wide-range environmentally-stressed, which is supportive of its persistence in silage, bedding, feces, water and milking environment (Vazquez-Boland et al., 2001; Orsi et al., 2011).

Small ruminants are in an epidemiological niche, in that they can be both clinically affected and serve as a reservoir of *L. monocytogenes* in the farm environment. Asymptomatic shedding of feces can contaminate feed, soil and water, and infected dairy animals may contaminate milk (Sotohy et al., 2024). *L. monocytogenes* is known to be a reservoir in ruminants, and genomic analyses of clinical ruminant isolates have shown that strains that cause animal disease also include genotypes that are relevant to human listeriosis (Končurat and Sukalić, 2024).

Field epidemiology must be able to differentiate between exposure and disease. Most animals might consume *Listeria*-contaminated material, although only a subset may become clinically ill. The result is based on infectious dose, strain virulence, route of entry, pregnancy, age, oral mucosal injury, rumen functionality, nutritional stress and immune competence (Hong et al., 2024).

Sources of Infection and Transmission Pathways

The main sources of infection are infected silage, haylage, pasture, soil, decaying vegetation, water, feces, bedding, milk, uterine discharge, aborted fetuses and placentas (Schöb *et al.*, 2024). Silage has a special place as *L. monocytogenes* may proliferate in the case of inadequate fermentation, high pH, contaminated forage with soil, or when the silo face is not covered with soil. Wiedmann *et al.* (1994) examined one sheep and one goat outbreak of *Listeria* encephalitis, and recovered *L. monocytogenes* in both clinical material and silage, which supports the transmission of *Listeria* encephalitis between feed and water sources and small ruminants.

The primary route of exposure is by the oral route. Bacteria can stay in the gastrointestinal tract after ingestion, or be shed in feces, invade the intestinal mucosa, or disseminate through blood and mononuclear phagocytes (Vazquez-Boland *et al.*, 2001). Systemic dissemination may result in the occurrence of septicemia, hepatic and splenic lesions, or localization in the pregnant uterus and placenta. Following placental invasion, fetal infection, fetal death, abortion, stillbirth or weak newborns (López-Almela *et al.*, 2025).

Adult ruminants have a unique neuroinvasion. Entry into the body via oral mucosal abrasions or periodontal lesions is often followed by centripetal spread through cranial nerves, especially the trigeminal nerve (Oevermann *et al.*, 2010; Disson and Lecuit, 2012). This pathway is in line with asymmetric cranial lesions of the brainstem, as well as unilateral cranial nerve loss. It also discusses why rough feed, poor dentition, erupting teeth, oral trauma and abrasive silage can contribute to risk in adult goats and sheep (López-Almela *et al.*, 2025).

Virulence Factors and Molecular Pathogenicity

L. monocytogenes pathogenicity rests upon a multi-coordinated intracellular life cycle. It adheres to host cells, invades phagocytic and non-phagocytic cells, escapes the internalization vacuole, replicates in the cytosol, uses host actin to move about and disperses directly between adjacent cells (Palacios-Gorba *et al.*, 2021). This cell-to-cell life allows the immune to evade in that the bacteria can spread without any

extended extracellular exposure to antibodies, complement or neutrophil killing.

Adhesion and invasion

Important invasion-related proteins are internalins. InlA adenosylates E-cadherin and facilitates entry into epithelial cells, whereas InlB interacts with host receptors such as Met and promotes entry into several cell types (Moura *et al.*, 2021). Other internalins play a role in tissue tropism, intracellular survival or modulation of virulence. In the case of field isolates of goats and sheep, the presence of intact internalin genes supports invasive potential but pathogenicity must be interpreted with host species, tissue source and disease phenotype because some environmental isolates also carry virulence genes (Orsi *et al.*, 2011).

Phagosomal escape and intracellular survival

After internalization, *L. monocytogenes* escapes the phagosome through listeriolysin O, encoded by *hly*, and phospholipases PlcA and PlcB. Foundational experimental work showed that hemolysin-defective mutants were unable to replicate effectively intracellularly and were markedly attenuated, establishing listeriolysin O as a critical virulence determinant (Portnoy *et al.*, 1988). Cytosolic survival also requires nutrient acquisition, stress resistance, metabolic adaptation and regulation by PrfA, which activates key virulence genes during host infection (de las Heras *et al.*, 2011; Radoshevich and Cossart, 2018).

Actin-based motility and immune evasion

ActA is a protein on its surface that enlists host actin-polymerization machinery. Kocks *et al.* (1992) showed that *L. monocytogenes* induces actin assembly, which is dependent on the presence of ActA. The formation of actin comet-tails propels the bacteria through the cytoplasm and into the protrusions that are surrounded by other cells. This process is key to cell-to-cell spreading, tissue persistence, and immune evasion (Vazquez-Boland *et al.*, 2001; Cossart and Toledo-Arana, 2008).

Placental invasion

The pathogenic basis of abortion is the placental invasion. Following maternal bacteremia, organisms invade fetoplacental tissues and may induce necrotizing placentitis, fetal septicemia and fetal death

(Low and Donachie, 1997; Bagatella et al., 2022). InlA and InlB-related pathways play crucial roles in crossing epithelial barriers by experimental systems, although the contribution of each pathway to ruminant placenta remains unclear (Vazquez-Boland et al., 2001; Radoshevich and Cossart, 2018).

Neurotropism

A single virulence factor does not fully explain neurotropism of ruminants. Natural cases support the notion of an ascending neural route, with bacteria and lesions working their way outward along the peripheral cranial nerves up towards the brainstem (Oevermann et al., 2010). Disson and Lecuit (2012) pointed out that *L. monocytogenes* has been shown to target the central nervous system via a number of possible pathways, including an invasion of the blood-brain barrier and neural dissemination. However, in goats and sheep, the pattern of lesions of rhombencephalitis strongly supports cranial-nerve-related infection in many adults (Oevermann et al., 2010; Precht et al., 2020).

Host Susceptibility and Risk Factors in Goats and Small Ruminants

Host susceptibility is expressed in terms of age, pregnancy, nutritional status, immune competence, rumen activity, oral mucosal integrity and environmental exposure. The presence of neurological disease is especially common in adult sheep and goats, whereas pregnant animals are susceptible to placental infection and neonates to septicemia (Obaidat, 2024). Pregnancy is a significant risk factor since transient bacteremia have the potential to inoculate the placenta, causing fetoplacental infection and reproductive loss. The farm environment risk factors include feeding spoiled silage, poor forage fermentation, sudden dietary changes, overcrowding, poor bedding hygiene, contaminated water, inadequate disposal of aborted materials and poor milking sanitation. Mucosal injury of the oral cavity induced by coarse forage, periodontal disease or harsh silage may contribute to the invasion of the cranial nerves in adult ruminants (Oevermann et al., 2010; Precht et al., 2020). Asymptomatic faecal shedding and high stocking density and shared feed bunks may enhance exposure, and the depth of the fecal bed contributes to persistence within pens and pastures (Obaidat, 2024).

Host risk is altered by strain factors. Ruminant isolates associated with disease may be part of multiple lineages and clonal complexes and contain virulence, stress-tolerance and mobile genetic elements (Cardenas-Alvarez et al., 2022). The background of strains identified as hypervirulent in human listeriosis has been associated with central-nervous-system or maternal-neonatal disease, which supports the idea of strain background as the factor that can influence tissue tropism, and severity (Maury et al., 2016).

Clinical Manifestations of Listeriosis

The most common syndrome in adult goats and sheep, is the encephalitic variant. The clinical manifestations are depression, anorexia, fever in the early stages of the disease, head tilt, circling, unilateral facial paralysis, drooping ear, salivation, dysphagia, nystagmus, ataxia, recumbency and death (Low and Donachie, 1997; Precht et al., 2020). The signs are related to inflammation of the brainstem, cranial nerve nuclei. Clinical course can be fast and prognosis deteriorates with recumbency or severe dysphagia.

The reproductive manifestation in the form of abortion, stillbirth, weak neonates, placentitis, retained fetal membranes or metritis. Abortions are typical in late gestation but timing depends on the dynamic of infection and vulnerability of the fetus (Low and Donachie, 1997; Bagatella et al., 2022). The *L. monocytogenes* and *L. ivanovii* should both be included in the small-ruminant abort workups. Most frequent listeriosis is septicemic and is most common in neonates or compromised animals and may cause fever, weakness, diarrhea, respiratory distress or sudden death (Low and Donachie, 1997).

Other less frequent manifestations are mastitis, keratoconjunctivitis, uveitis and gastrointestinal disease. The epidemiological importance of such presentations is that they may lead to milk contamination, environmental persistence and zoonotic exposures (Obaidat, 2024).

Pathological Lesions and Disease Progression

Neurological listeriosis can cause gross lesions that are minimal. Histologically, typical changes include asymmetry of brainstem inflammation, microabscesses, perivascular cuffing, gliosis, neuronal degeneration, axonal damage and inflammatory infiltrates in the cranial nerve nuclei and tracts

(Oevermann *et al.*, 2010). Precht *et al.* (2020) compared magnetic resonance imaging with histopathology of naturally infected small ruminants and found that magnetic resonance imaging lesions identified in the brainstem were consistent with listerial rhombencephalitis inflammatory lesions.

The symptoms of reproductive listeriosis include necrotizing placental necrosis, fetal septicemia and fetal death. Fetuses can have multifocal necrosis of liver, spleen or other organs; fetal stomach contents can contain a large number of bacteria (Moura *et al.*, 2021). Septicemic disease can cause multifocal necrotic lesions in liver, spleen, lung and other viscera, particularly in neonates. Progression of disease should be then interpreted with regard to route: intestinal invasion and bacteremia favor septicemia or abortion, whereas oral mucosal entry and cranial-nerve spread favor rhombencephalitis (Oevermann *et al.*, 2010; Disson *et al.*, 2012).

Isolation, Identification, and Characterization of *Listeria* Strains

Isolation and characterization are best directed by lesions distribution, and clinical syndrome. In neurological cases, brainstem tissue is preferred whereas in abortions, placenta, fetal stomach contents and fetal viscera should be sampled (Moura *et al.*, 2021). Milk, feces, silage, water, and residues of bedding and feed are useful in investigations of outbreaks but these materials should be interpreted with caution since environmental isolation does not necessarily mean that a disease was caused.

Classical identification encompasses culture on selective media, Gram staining, beta-hemolysis, catalase positivity, tumbling motility, biochemical characterization and species-level differentiation. Molecular confirmation can be directed against *hly*, *iap*, *prfA*, *inlA* or other species-related genes. The subtyping techniques have since developed to include multilocus sequence typing, core-genome MLST and whole-genome sequencing (Orsi *et al.*, 2011; Cardenas-Alvarez *et al.*, 2022). To achieve high impact interpretation of the isolates associated with listeriosis, characterization must not be limited to species identification. A well-developed workup must include tissue source, lesion compatibility, presence of virulence-gene, lineage/clonal-complex assignment,

antimicrobial susceptibility and epidemiological comparison with feed or environmental isolates. Whole-genome sequencing is especially helpful to attribute disease-afflicted animals to contaminated silage or farm sources and to determine whether clinical isolates belong to any genotype associated with invasive disease in humans (Maury *et al.*, 2016).

Experimental and Field Evidence of Pathogenicity

The pathogenicity of *L. monocytogenes* is based on mechanistic principles, which have been determined by experimental studies. Portnoy *et al.* (1988) demonstrated that listeriolysin O is essential in the intracellular growth and virulence. Mengaud *et al.* (1996) found out that the receptor in InlA-mediated entry was E-cadherin. The study by Kocks *et al.* (1992) proved that bacterial actin assembly involves ActA. These papers describe the entry of pathogenic isolates, their survival within the cell and their spread in the tissues of the host.

Field evidence is also significant as it indicates pathogenicity in the host of nature. Wiedmann *et al.* (1994) reported two outbreaks of listerial encephalitis, one in sheep and one in goats and used pathology, microbiology and molecular methods to implicate clinical cases to contaminated silage. Oevermann *et al.* (2010) examined over 200 natural ruminant encephalitis cases and elucidated the lesion distribution and the pathogenesis of the disease. Precht *et al.* (2020) offered further evidence by using imaging and histopathology correlations to provide additional evidence on naturally infected goats and sheep.

The best field evidence of pathogenicity is obtained when the isolates are recovered on the basis of a purported source of exposure, and when the isolate is genetically related to a plausible source of exposure. Only feces isolates should be considered epidemiologically relevant but not necessarily causal unless supported by strain matching, clinical clustering or compatible lesions (Schöb *et al.*, 2024).

Antimicrobial Resistance and Therapeutic Considerations

It is imperative to treat at an early stage. Penicillin, ampicillin and oxytetracycline have been utilized in veterinary practice although treatment success has been inconsistent in advanced neurological disease

since lesions are often established before treatment begins (Hong et al., 2024). Supportive care needs to be combined with treatment and includes fluid therapy, nursing, correction of dehydration, assisted feeding and management of dysphagia or recumbency.

Listeria antimicrobial resistance has often been historically less common compared to many Gram-negative pathogens, but can develop through plasmid and conjugative element mechanisms (Charpentier and Courvalin 1999). Thus, clinical isolates should be subjected to susceptibility testing particularly in recurrent farm outbreaks, treatment failure, dairy herd with food-safety implications or a region with a high rate of antimicrobial use. The choice of antimicrobials should also include the national regulations, extra-label use, meat and milk withdrawal periods and pregnancy status.

The therapeutic choices ought to be taken at both the individual and flock level. Exposure will not be prevented by treating affected animals without the removal of contaminated silage or abortive materials. On the other hand, new infections can be reduced even in situations where individual treatment results are poor by rapid elimination of contaminated feed, isolation of sick or aborting animals and cleaning of contaminated areas (Low and Donachie, 1997; Wiedmann et al., 1994).

Prevention, Control, and Biosecurity Measures

Key areas of prevention are concerned with the sanitary procedures regarding the feed, the management of the environment, and the reproductive biosecurity measures. Silage should be harvested when the moisture content is optimum, firmly compressed, rapidly sealed, prevented from aerobic deterioration and discarded when moldy, rancid or contaminated with soil. The feed troughs and water nipples should be cleaned at regular intervals and the animal should be prevented from consuming any moldy silage edges, spoiled feeds or any visible contaminated fodder (Wiedmann et al., 1994).

During an abortion, the fetal membranes, the placenta, the littering materials, and the uterine discharges should be treated as if they were pathogens. Abortion infected animals should be separated and the contaminated littering material disposed of properly.

Personal protective equipment, including hand washing procedures, is necessary as *L. monocytogenes* is zoonotic and as the pregnant and immunosuppressed animal populations are more susceptible (Bagatella et al., 2022). Milk from sick animals should never enter the market and raw milk products should be handled properly.

Biosecurity procedures include the quarantine of animals entering the herd, prevention of feed contamination by fecal matter, consistent cleaning of the lambing pens, rat and bird control, sound waste management of manure, and prompt detection of neurologic symptoms and abortions. During an outbreak, an analysis of strains isolated from livestock, feeds, and the environment using molecular techniques could determine the persistent source and effective remedy action (Cardenas-Alvarez et al., 2022).

Public Health and Zoonotic Significance

L. monocytogenes is an important zoonotic foodborne pathogen, which in humans can cause febrile gastroenteritis, septicemia, meningitis, meningoencephalitis, miscarriage, stillbirth and neonatal disease. The susceptibility of women of childbearing age, neonates, elderly and immunocompromised people is more common to illness caused by this organism. Sheep and goats may contribute to the human health risk through fecal excretion, environment contamination and milk contamination where raw milk and/or raw milk cheese are produced (Shaaban et al., 2025).

The necessity for a One Health perspective in these cases is because the particular strains associated with disease in ruminants might carry attributes relevant to the causation of invasive human disease. Genomic investigations indicate that ruminant listeriosis isolates can carry clonal complexes and virulence factors of importance to invasive disease suggesting that veterinary surveillance supports food safety and public health information, and highlights farm workers, vets and laboratory personnel's risk of zoonotic exposure in abortion investigation, post mortems and in contact with raw milk or infected tissues (Alharbi et al., 2025).

Research Gaps and Future Perspectives

There is numerous research questions left unaddressed. Firstly, there is little goat-specific data available. Many research studies have included goats along with sheep and ruminant populations but goats are distinct with regard to their browsing habit, dairy management system, breeding cycle and production system and should therefore be studied separately. Studies specific to goats would help elucidate the strain distribution, tissue tropism, chance of abortion, milk shedding and the effectiveness of therapies.

Secondly, neurotropism in natural ruminant hosts is not fully characterized. While spread via the cranial nerves is well supported by the pattern of lesions, the molecular mechanisms of nerve entry, axon transport, immune modulation, and lesion tropism need to be thoroughly investigated (Oevermann *et al.*, 2010; Disson and Lecuit, 2012; Bagatella *et al.*, 2022). Third, genomic data should be coupled with phenotypic assessment and clinical data, as the presence of virulence genes alone may not fully represent pathogenicity, and a clear characterisation of pathogenicity needs to be based on strain and host interactions, as well as the environment.

High impact studies should in the future combine whole genome sequencing with strain identification, antimicrobial susceptibility, histopathological evaluation, farm management information, and surveillance under the One Health framework. Ideally, prospective studies on the outbreaks should involve sampling of affected animals, unaffected animals from the same pen, silage and water and the farm environment to identify genuine pathogenic strains in the field from potential environmental contamination and establish intervention strategies.

2. CONCLUSION

Listeriosis in goats and small ruminants is a biologically complex and economically important disease caused mainly by *L. monocytogenes* and, less commonly, by *L. ivanovii*. The pathogenicity of disease associated isolates is driven by conserved intracellular virulence mechanisms, strain lineage, environmental fitness and host susceptibility. In small ruminants, these mechanisms manifest as rhombencephalitis, abortion, neonatal septicemia, mastitis and environmental shedding. Naturally

isolated strains from brainstem lesions, fetoplacental tissues, milk and implicated feed are central to understanding pathogenicity because they connect molecular determinants to clinical disease in natural hosts.

3. CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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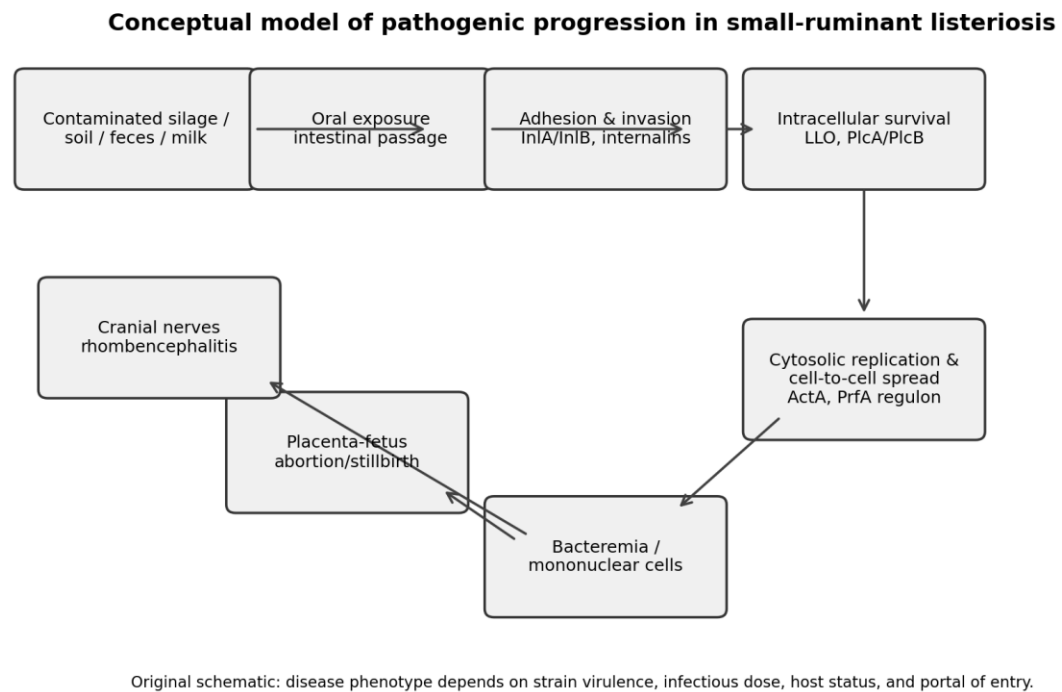


Figure 1. Conceptual pathogenesis model for listeriosis-associated strains in goats and small ruminants.
Original schematic prepared for this review.

Table 1. Major *Listeria* virulence determinants and relevance to small ruminant disease.

Virulence determinant	Primary function	Relevance in goats and sheep	Key sources
Internalins, especially InlA and InlB	Adhesion and invasion of host cells through receptor-mediated entry	Supports intestinal invasion, tissue tropism and invasive potential of clinical isolates	Mengaud <i>et al.</i> , 1996; Bierne <i>et al.</i> , 2007
Listeriolysin O, hly	Pore-forming cytolysin required for phagosomal escape	Essential for intracellular survival and systemic, placental and neural infection	Portnoy <i>et al.</i> , 1988; Vazquez-Boland <i>et al.</i> , 2001
PlcA, PlcB and Mpl	Membrane disruption and escape from primary or secondary vacuoles	Facilitates cell-to-cell spread and persistence in lesions	Vazquez-Boland <i>et al.</i> , 2001; de las Heras <i>et al.</i> , 2011
ActA	Actin polymerization and intracellular movement	Allows direct cell-to-cell spread and immune evasion in placenta, liver and neural tissues	Kocks <i>et al.</i> , 1992; Cossart & Toledo-Arana, 2008
PrfA regulon	Master transcriptional regulation of virulence genes	Coordinates the environmental-to-host transition and activation of pathogenicity	de las Heras <i>et al.</i> , 2011
Stress-response and survival loci	Tolerance of cold, acid, osmotic and farm environmental stress	Promotes persistence in silage, feces, milk and farm environments	Orsi <i>et al.</i> , 2011; Cardenas-Alvarez <i>et al.</i> , 2022

Table 2. Clinical syndromes, dominant pathogenesis and preferred diagnostic samples.

Syndrome	Dominant pathogenesis	Typical field signs	Preferred samples
Rhombencephalitis / meningoencephalitis	Cranial-nerve-associated ascent and brainstem infection	Circling, head tilt, unilateral facial paralysis, dysphagia, recumbency	Fresh and fixed brainstem, especially medulla and pons; CSF when available
Abortion / stillbirth	Maternal bacteremia with placental and fetal invasion	Late-term abortion, stillborn or weak neonates, metritis	Placenta, fetal stomach contents, fetal liver and spleen, vaginal discharge
Neonatal septicemia	Systemic dissemination after ingestion or in utero infection	Weakness, fever, diarrhea, respiratory distress, sudden death	Blood if ante-mortem; liver, spleen, lung and intestinal contents postmortem
Mastitis / milk shedding	Localized mammary infection or shedding from systemic infection	Abnormal milk, udder inflammation or subclinical shedding	Aseptic milk samples and bulk-tank milk
Environmental/farm contamination	Fecal shedding and survival in silage, soil, water and bedding	Often no individual signs; outbreak context	Silage, water, bedding, feces, feed-bunk residues and manure

Table 3. Evidence hierarchy for interpreting pathogenicity of *Listeria* isolates from small-ruminant farms.

Evidence level	Example finding	Interpretation
High	Same <i>L. monocytogenes</i> strain recovered from brainstem lesion and implicated silage in a neurological outbreak	Strong support for pathogenic field isolate and source linkage
High	Isolation from placenta/fetal organs with necrotizing placentitis or fetal septicemia	Strong support for reproductive listeriosis
Moderate	Clinical signs compatible with listeriosis and PCR/culture from relevant tissue, but no environmental comparison	Etiology likely if pathology is supportive
Moderate	Virulent lineage or complete virulence loci found in milk or fecal isolate during a flock outbreak	Epidemiologically important; causality requires lesion or strain-link evidence
Low	Isolation from silage or soil without disease or tissue confirmation	Exposure or contamination evidence only
Low	Single fecal isolate from apparently healthy animal without clinical context	Potential reservoir/shedding evidence; not proof of disease

Table 4. Practical prevention and control measures with expected impact.

Control point	Action	Expected impact
Silage quality	Ensure rapid anaerobic fermentation, low pH, clean harvest and discard spoiled portions	Reduces primary exposure dose
Feed-bunk hygiene	Remove old feed and avoid soil-contaminated forage	Limits oral exposure and fecal amplification
Reproductive biosecurity	Isolate aborting animals; dispose of fetus, placenta and bedding safely	Reduces environmental contamination and zoonotic exposure
Milk hygiene	Exclude milk from sick animals; pasteurize milk used for human consumption	Reduces foodborne risk
Early diagnosis	Sample brainstem, placenta or fetal tissues promptly	Improves etiological confirmation and outbreak response
Molecular surveillance	Use MLST/cgMLST/WGS where available	Links animal cases with feed, farm and public-health isolates
Antimicrobial stewardship	Treat early and use susceptibility data when possible	Improves responsible therapy and detects resistance