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REVIEW

A Comprehensive Review of the Common Bacterial Infections in Dairy Calves and Advanced Strategies for Health Management

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Abstract: Dairy farming faces a significant challenge of bacterial infections in dairy calves, which can have detrimental effects on their health and productivity. This review offers a comprehensive overview of the most prevalent bacterial infections in dairy calves, including *Escherichia coli, Salmonella typhimurium, Salmonella dublin, Salmonella enterica, Clostridium perfringens, Pasteurella multocida, Listeria monocytogenes, Mycoplasma bovis*, and *Haemophilus somnus*. These pathogens can cause various clinical signs and symptoms, leading to diarrhea, respiratory distress, septicemia, and even mortality. Factors such as management practices, environmental conditions, and herd health influence the incidence and severity of the infections. Efficient management and prevention strategies include good colostrum and nutrient feeding, early detection, appropriate treatment, hygiene practices, and supportive care. Regular health monitoring and diagnostic tests facilitate early detection and intervention. The use of antibiotics should be judicious to prevent antimicrobial resistance and supportive care such as fluid therapy and nutritional support promotes recovery. Diagnostic methods, including immunological tests, culture, polymerase chain reaction (PCR), and serology, aid in the identification of specific pathogens. This review also explores recent advancements in the diagnosis, treatment, and prevention of bacterial infections in dairy calves, providing valuable insights for dairy farmers, veterinarians, and researchers. By synthesizing pertinent scientific literature, this review contributes to the development of effective strategies aimed at mitigating the impact of bacterial infections on the health, welfare, and productivity of young calves. Moreover, more research is required to enhance the understanding of the epidemiology and characterization of bacterial infections in dairy calves.

Keywords: bacteria, diarrhea, pneumonia, septicemia, vaccination, dairy calve

Introduction

Dairy farming plays a crucial role in meeting the growing global demand for milk and dairy products.[1] However, one of the major challenges faced by dairy farmers is the prevalence of bacterial infections in dairy calves.[2] Bacterial infections can have severe effects on the respiratory, digestive, and immune systems of animals that reduce the growth rates, and increase morbidity and mortality of dairy calves. This results in significant economic losses for the dairy industry, attributable to treatment costs and mortality.[2] Therefore, understanding the common pathogenic bacterial infections affecting dairy calves, their effects, and effective management strategies is essential for ensuring the well-being and performance of the dairy industry.[3]

To comprehensively address this issue, it is necessary to explore the most prevalent bacterial infections encountered in dairy calves. Studies have identified several primary bacterial pathogens responsible for infections in calves, including *Escherichia coli, Salmonella spp., Clostridium spp*., and various species of *Pasteurella* and *Mycoplasma*.[4,5] These pathogens can cause a range of clinical signs and symptoms, such as diarrhea, respiratory distress, septicemia, and even mortality in severe cases. The incidence and severity of bacterial infections in dairy calves are influenced by various factors, including management practices, environmental conditions, and the general health status of the herd.[6]

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An efficient management and prevention strategy for bacterial infections in dairy calves requires a multifaceted approach. These include good colostrum feeding, proper nutrition, and optimal hygienic practices that can significantly reduce the risk of infections.[7] Early detection of infections through regular health monitoring and diagnostic tests also allows for timely intervention and treatment of emerging, reemerging, and novel infectious diseases.[8] Antibiotics are commonly employed to treat bacterial infections in dairy calves, but their use should be judicious to prevent the development of antimicrobial resistance and ensure animal welfare.[9] Furthermore, supportive care, including fluid therapy and nutritional support, plays a vital role in managing infected calves and promoting their recovery. This review aims to provide a comprehensive overview of the most common bacterial infections observed in dairy calves, their effects on calf health and productivity, and current management practices. To explore recent advancements in the diagnosis, treatment, and prevention of bacterial infections in dairy calves, we conducted a comprehensive review of the latest research findings and emerging technologies. The information discussed here serves as a valuable resource for dairy farmers, veterinarians, and researchers, aiding in the development of effective strategies to mitigate the impact of bacterial infections on calf health and welfare.

Common Causes of Bacterial Infections in Dairy Calves

Escherichia coli (*E. coli*)

Escherichia coli is a gram-negative, rod-shaped, motile or non-motile, non-spore-forming, facultative anaerobic bacterium that commonly inhabits the gastrointestinal tract of calves (Table 1). *E. coli* is a type species that belongs to *Enterobacteriaceae* family and *Escherichia* genus. It can be pathogenic and non-pathogenic.[10] Non-pathogenic strains are part of the normal flora of the gut, aiding the hosts by producing vitamin K2 and preventing the establishment of pathogenic bacteria in the intestine *E. coli* can be differentiated into 190 serotypes (serogroups) based on somatic (O), capsular (K), and flagellar (H) antigens. About 80 different capsular polysaccharide (K) antigens are present. There are about 174 O antigens and 56 H antigens. It is serotyped depending on the combination of O, H, and K antigens (eg, O157: H7). Serotyping of *E. coli* with molecular and phage typing is a useful epidemiological tool.[6]

Escherichia coli can be grouped into six pathotypes depending on virulence factors. These are enterotoxigenic *E. coli* (ETEC), shigatoxin-producing *E. coli* (STEC), enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enteroaggressive *E. coli* (EAEC), and enterohaemorrhagic *E. coli* (EHEC).[11] ETEC, EPEC, and EHEC are the diarrheagenic pathotypes occurring in young farm animals. ETEC strains are the most common cause of neonatal diarrhea because they produce the K99 (F5) adhesion antigen and heat-stable enterotoxin.[12,13] The virulence factor facilitates sticking of bacteria to the villous epithelial cells in the intestine to prevent elimination by peristalsis and production of heat-stable and heat-labile enterotoxin. During the first four days after birth, newborn calves are especially vulnerable to ETEC infection and have "watery" diarrhea if infected.[14]

Table 1 Common Bacterial Species in Dairy Calves with Their Type, Management Practices, Effects, and Diagnostic Methods

Bacteria	Type	Management	Effects	Sample	Diagnostic Methods
Escherichia coli	Gram-negative	Good hygiene practices, vaccination	Diarrhea, sepsis, Colisepticemia,	Feces, blood	Bacterial culture, PCR
Salmonella	Gram-negative	Good hygiene practices, vaccination	Diarrhea, sepsis, pneumonia	Feces, blood, tissue	Bacterial culture, PCR
Clostridium perfringens	Gram-positive	Good hygiene practices, vaccination, feeding management	Diarrhea	Feces, intestine content	Toxin detection, PCR
Mycoplasma bovis	Gram-negative	Good hygiene practices, antibiotic treatment	Pneumonia, otitis media, arthritis	Nasal swabs, ear swabs	PCR, serology
Pasteurella multocida	Gram-negative	Good hygiene practices, antibiotic treatment	Pneumonia, septicemia	Nasal swabs, blood	Bacterial culture, PCR
Haemophilus somnus	Gram-negative	Good hygiene practices, antibiotic treatment	Respiratory disease, septicemia, arthritis	Nasal swabs, blood, synovial fluid	Bacterial culture, PCR
Listeria monocytogenes	Gram-positive	Good hygiene practices, feeding management	Meningitis, septicemia, abortion	Brain tissue, blood, feces	Bacterial culture, PCR

The prevalence of enterotoxigenic *E. coli* in diarrheic calves exhibits considerable variation geographically and across different herds, depending on the age of the animals. Consequently, enterotoxigenic colibacillosis is a leading cause of diarrhea in calves below 3 days of age, but it does not trigger diarrhea outbreaks in older calves[12,15] suggests that the presence of *E. coli* in dairy calves can be associated with age groups, environmental and management conditions of the farms, and inadequate intake of colostrum by calves. Poor hygiene practices can also lead to the accumulation of pathogenic strains in the surroundings of young animals.[15,16] Furthermore, according to[17] a significant amount of pathogenic *E. coli* may surpass the colostrum immunity. In severe cases of *E. coli* outbreaks, even calves as young as 16 to 24 hours can be affected, with younger calves having a higher risk of dying from severe dehydration that progressively sets in.[18]

The transmission of the organism in a herd occurs through fecal-oral route from contaminated objects such as bedding, pails, boots, tools, clothing, feed, and water supplies. Poor sanitation increases the likelihood of newborn calves contracting *E. coli* scours infections from their environment.[19,20] *E. coli* strains that cause diarrhea initially colonize the gut of the calf by attaching to the intestinal wall using pili or fimbriae, which are fine, fuzz-like protrusions. The $K99^{+}$ antigen designates these pili, and the strains that possess them are called enterotoxigenic *E. coli* (ETEC).[21] Good hygiene practices and vaccination can help prevent the infection caused by *E. coli*. However, if infected, calves may suffer from diarrhea, and sepsis. Feces and blood are the preferred sample types for diagnosis.[22,23]

Cultural isolation, serological test, and molecular diagnostic approaches can be used to diagnose *E. coli*. Serological diagnosis of the bacteria is carried out using latex agglutination, fluorescent antibody technique, and an ELISA test to detect fimbrial antigens (K99) or enterotoxin directly from fecal samples or isolated colonies.[24,25] ELISA using monoclonal antibodies is the most sensitive diagnosis method.[17] Conventional diagnostic procedures such as cultural isolation, serological tests, and pathotyping methods are time consuming, expensive, and cannot distinguish definitively strains of *E. coli* infection. Therefore, rapid nucleic-based tests have been developed around the world to detect circulating bacterial strains based on amplification and detection of nucleic acid.[26] Sensitive and specific molecular diagnostic techniques like PCR and sequencing play a significant role in the detection and differentiation of strains compared to conventional diagnostic tools. The most commonly used molecular diagnostic technique for the detection of *E. coli* strains is PCR. The assays are more sensitive, specific, and less labor-intensive compared to conventional diagnostic methods. The development of biosensor devices has the potential to become indispensable in detecting low colony-forming units of pathogenic *E. coli* in environmental samples (Table 1).[27]

Salmonella

Members of the genus *Salmonella* are gram-negative, facultative, and rod-shaped short-bacilli bacteria belonging to the family *Enterobacteriaceae*[28] (Table 1). There are three central species of *Salmonella: Salmonella enterica, Salmonella bongori,* and *Salmonella subterranean* (*S. subterranean)* based on differences in their 16S rRNA sequence analysis. The type species *of Salmonella enterica* is again subdivided into six subdivisions of *Salmonella enterica* subspecies based on their genomic relatedness and biochemical properties the type species.[29] *Salmonella enterica* subspecies enterica is the dominant subspecies affecting humans and domestic animals.[30] Currently, there are more than 2700 *Salmonella* serovars that are serologically identified by antigenic variation in O (lipopolysaccharide), H (flagella), and VI (capsular) antigens in accordance with the Kauffmann-White scheme.[30] A *Salmonella* infection is a common problem in captive animals like dairy calves that cause enteritis. The issue is particularly severe in calves younger than one month old.[31] The infected calves develop fibrin purulent necrotizing enteritis, which is characterized by a severe diffuse infiltrate mainly composed of neutrophils.[32] The genus *Salmonella* is motile except *S. enterica ser. Pullorum* and *S. enterica ser. Gallinarum*, which lacks flagella.[33]

The most common isolated *Salmonella* serotypes in cattle are *Salmonella typhimurium* and *Salmonella dublin*. These serotypes exhibit multiple resistances to commonly used antibiotics.[34] *Salmonella dublin* and *S. typhimurium* are host-specific and non-host-specific, respectively, that affect calves severely between six and twelve weeks of age. *Salmonella* infection has a wide range of clinical manifestations, from asymptomatic to clinical salmonellosis. Acute diarrheal disease is most common with *S. typhimurium* and systematic disease with *S. dublin* in cattle. The disease is mainly found in dairy cattle rather than beef cattle and is associated with management practices. The infective dose, predisposing

factors, and immunity status of the hosts determine the outcome of the infection. *Salmonella* infection has per acute (diarrhea and septicemia), acute (fever), and chronic (unthrifty scruffy hair) forms.[5,35,36]

The pathogenicity of *Salmonella* serotypes differs depending upon the difference in virulence potential of serovars and susceptibility of an infected host. The pathogenesis of *Salmonella* infection is governed by many virulence factors including type three secretion systems (T3SS), virulent plasmids, flagella, capsule, and other adhesion systems. Parts of the adhesion system produced by most serovars of *Salmonella enterica* include adhesins, invasins, toxins, fimbriae, and hemagglutinins. These virulence factors enable *Salmonella* to colonize the host cell, bypassing the defense mechanisms of the host. Genes contained on a wide range of genetic elements, including bacterial chromosomes, plasmids, prophages, and other SPIs, encode these bacterial virulence factors.[37]

The persistence of *Salmonella* in the environment plays a significant role in the epidemiology of calf salmonellosis. They are commonly found in farm effluents and human sewage. Salmonellosis is most prevalent in intensive animal husbandry, especially dairy, poultry, and swine production.[38] This makes the epidemiology of salmonellosis complex. The fecal wastes of infected animals and humans are potential sources of contamination of the environment and the food chain.[39] Sick animals shed organisms through their saliva, nasal secretions, colostrum, and milk, which can lead to oral transmission of the disease in the dairy.[40,41] Fecal-oral transmission is the primary mode of direct animal-to-animal transmission.[42] Furthermore, indirect transmission of *Salmonella* can occur via contaminated feed and water supplies, pasture contaminated by slurry or sewage, and wildlife vectors like small mammals and birds.[12]

Different approaches to *Salmonella* diagnosis, including cultural isolation, immunology-based assays, nucleic acid-based assays, miniaturized biochemical assays, and biosensors, are present. Conventional cultural isolation protocols are laborious and time-consuming.[43] Immunology-based assays that use specific mono- or polyclonal antibodies binding to somatic or flagellar antigens are widely used for the detection of *Salmonella* species from representative specimens. The assays include ELISA, latex agglutination tests, immunodiffusion, and immunochromatography (dipstick). The assays are a valuable option for detecting non-cultural *Salmonella* cells (Table 1). The studies showed immunology-based assays are more rapid and specific than cultural methods to isolate *Salmonella* species in conjunction with immune-magnetic separation techniques. The shortcomings of the assays are cross-reactions with closely related antigens, a longer enrichment time to get a number of cells, and a high cost for automation. The methods handle large samples and are readily automated to reduce time and labor. ELISA test is used to determine the infection status of individual animals and the entire herd. The test can distinguish between recently infected (increased Ab. titer) and convalescent (decreased Ab. titer) calves. Constant titers are recognized in carrier hosts.[31,44]

The nucleic acid-based assays utilize a specific nucleic acid target sequence to detect the organisms directly from samples or colonies. The assays are more sensitive, specific, and inclusive than other methods.[43] Direct hybridization (DNA probe) and amplification of genetic materials (PCR) methods are the two main diagnostic techniques.[45,46] The PCR test is a primer mediated enzymatic amplification of specific segments of DNA for the detection of *Salmonella* pathogens.[47] *Salmonella* invasion gene (invA) is highly conserved among *Salmonella* species and could serve as a reliable and accurate target gene for molecular detection of the genus *Salmonella*.[48] The amplified products are detected using either gel-based systems or real-time PCR. The assays detect a very low number of organisms in the sample. This capability shortens the enrichment time to reach the *Salmonella* concentration needed for reliable detection by PCR compared to other methods.

A biosensor is an integrated receptor-transducer device made up of a detector and a biological recognition system (receptor). Without any additional processing stages or reagents in between signal sampling and output, it converts the biochemical (biological) response into a quantifiable output signal.[49] When a particular analyte attaches to the biological recognition element, a recognition signal is generated. According to,[43] the signal can take the form of changes in mass, oxygen consumption, potential difference, refractive index, pH, and other parameters. Current immunology and nucleic acid-based diagnostics are replaced by the biosensor diagnostic approach. A biosensor device can identify biological components such as enzymes, nucleic acids, entire cells, tissue, and biomimetic materials.[50] *Salmonella* prevention and control can be achieved by adopting the principles of Hazard Analysis Critical Control Point (HACCP). Strict biosecurity measures, appropriate disinfection, avoiding stressful conditions, and frequent immunization play a significant role in *Salmonella* prevention and control programs.[51]

Clostridium perfringens

The genus *Clostridium* contains a diverse group of gram-positive anaerobic rods that form heat-resistant endospores.[52] It is widespread in the environment and is normally found in soil and feces. The genus causes different types of *Clostridium* bacterial diseases through one or more of the several species of *Clostridium* and their potent toxins.[53] The diseases include tetanus, botulism, blackleg, malignant edema, and bacillary hemoglobinuria in humans and animals (Table 2). *Clostridium* diseases can be neurotoxic, histotoxic, and enteric diseases. The genus *Clostridium* contains about 200 species of spore-forming anaerobic rods. However, most of the species are non-pathogenic bacteria living in the environment. The clostridial species that have veterinary and medical importance are *Clostridium perfringens, Clostridium tetani, Clostridium difficile, Clostridium chauvoei, Clostridium novyi* type A, *Clostridium haemolyticum*, and *Clostridium septicum*.[53] Among these, *Clostridium perfringens* and *Clostridium difficile* species are the most important pathogens in dairy calves.

Members of the species *Clostridium perfringens* (*C. perfringens*) are gram-positive, rod-shaped, non-motile, spore forming, and anaerobic bacterium belonging to the genus *Clostridium* and the family *Clostridiaceae* (Table 1). The species is commonly found in the intestines of calves. The bacteria are the most widespread with a ubiquitous environmental distribution in soil, sewage, water, preserved feeds, contaminated colostrum or milk, and calf housing environments.[54,55] Although these bacteria are typically not harmful in small quantities in the intestine, they can multiply and thrive under certain circumstances, leading to enterotoxaemia. This condition occurs when the bacteria produce specific toxins in the small intestine, resulting in both localized and systemic effects.[56] The pathogen proliferates during warm weather after heavy rainfall.[57] *Clostridium* infections are common in young animals, particularly in calves under the age of two weeks. However, they have also been observed in calves up to two months old.[3]

The virulence of *C. perfringens* is mediated by toxins and degradative enzymes. Five different types of toxinotypes (A, B, C, D, and E) depend on the production of four major toxins, namely alpha (CPA), beta (CPB), epsilon (ETX), and iota (ITX)[54] (Table 3). Besides the major toxins, *C. perfringens* can produce other toxins such as enterotoxin, necrotic enteritis like B toxin (NetB), and beta-2 toxins that play a significant role in the pathogenesis of *C. perfringens*-associated diseases in animals and humans.[58] Among *Clostridium* species, *C. perfringens* is the major toxin producer. Type C is

Table 2 Pathogenic *Clostridium* Species and Diseases

Toxin-Based Disease Categories	*Clostridium species*	Diseases
Histotoxic Clostridia	*Clostridium (C.) chauvoei*	Blackleg
	C. septicum	Malignant edema
	C. novyi type B	Black disease
	C. haemolyticum	Bacillary haemoglobinuria
Neurotoxic Clostridia	*C. tetani*	Lockjaw
	C. botulism	Botulism
Enteric Clostridia	Perfringens type A	Haemorrhagic enteritis
	C. difficile	–
	C. perfringens type D	Pulpy kidney

Table 3 Types of *C. Perfringens* and Major Toxins Produced

C. perfringens Type	Major toxins				
	Alpha (plc)	Beta (cpb)	Epsilon (etx)	Iota (iap)	Enterotoxin (cpe)
A	+	–	–	–	+/–
B	+	+	–	–	+/–
C	+	+	–	–	+/–
D	+	–	+	–	+/–
E	+	–	–	+	+/–

frequently encountered and highly virulent in calves under 10 days old, usually under five days old.[54] It is responsible for inducing hemorrhagic enteritis and sudden death in newborn calves. The epsilon toxin may spread through contaminated food, water, or aerosol transmission. The organism enters the body through ingestion from the soil or fecal contamination on the surface of the dam's udder since the organism is ubiquitous. This makes it easy for calves to be exposed to and ingest varying amounts of the pathogen.[59] It then attaches to the epithelial cells of the intestinal villus, although toxin production and mucosal damage may occur before attachment.[54]

The affected calves display sudden symptoms of depression, weakness, abdominal pain, and bloating.[55] If diarrhea does develop, it might contain streaks of blood and tissue. Typically, *Clostridia* bacteria inhabit the gastrointestinal tract of cattle as part of their natural microbiota. However, under conditions such as dietary stress, injury, management changes, parasitism, or other unusual circumstances that create conducive growth environment, they can produce potent toxins that cause problems.[23]

Immunological and molecular biological tests are the main detection methods for *C. perfringens* from representative samples. Toxins or antigens secreted by different *C. perfringens* can be detected using immunological assays.[57] The main immunological detection methods are the serum neutralization test, Nagler's test, and the ELISA test. SDS-PAGE electrophoresis technology was used to identify the type of *C. perfringens*. The detection of major toxin in *C. perfringens* can also be done using PCR and multiplex PCR[60.] PCR detects alpha toxins of the species via amplification of alpha toxin gene.[61] Good hygiene practices, feeding management, and vaccination can prevent the infection caused by *C. perfringens*.[4,62] Preventive strategies for pathogens depend on good farm management practices, limiting their susceptibility to infection through vaccination, high hygienic levels of tools and structures for handling of the animal can avoid risk of infections (Table 1). Good management practices in harvesting, storing, and feeding the animals prevent diseases associated with enterotoxic clostridia.[63,64]

Mycoplasma bovis

The genus *Mycoplasma* is a gram-negative bacterium that belongs to the *Mycoplasmataceae* family (Table 1). The genus *Mycoplasma* is characterized by a small genome size, a lack of a cell wall, and a low G+C content. Currently, the genus *Mycoplasma* contains at least 130 species, and *Mycoplasma bovis* (*M. bovis*) is considered one of the important causes of bovine mycoplasmosis. The classification is based on 16S rRNA gene sequencing for differentiation between closely related species.[65]

Mycoplasma bovis is a significant worldwide opportunistic pathogen of intensively reared beef and dairy calves. It is a significant cause of pneumonia, otitis media, and arthritis in young dairy calves less than three months of age.[66] The disease caused by *M. bovis* is chronic, debilitating, and unresponsive to antimicrobial therapy. The disease can persist for a very long period in a herd, with the possibility of the infected animals shedding microorganisms for a few weeks to several months.[67] The virulence factors of *M. bovis* are adhesion, host cell invasion, host immune system modulation, production of secondary metabolites, biofilm formation, and synergistic infections with other viral and/or bacterial microorganisms that enable evading the host immune system.[68] *Actinomyces pyogenes, Haemophilus somnus*, and *Pasteurella* species may synergistically act with *M. bovis* to cause bovine pneumonic pasteurellosis, bovine enzootic bronchopneumonia, or bovine respiratory disease (BRD). The disease is also significant from an animal welfare point of view, as it often results in calves that are subject to severe, chronic disease for which veterinarians can only provide limited relief. It is a major concern in the dairy industry, as it can lead to economic losses due to decreased milk production and increased morbidity and mortality in calves. Therefore, improved preventive and therapy strategies are needed for the disease.[69]

Mycoplasma bovis infections in dairy calves can present with a range of clinical signs. Respiratory disease is the most common manifestation, which can range from mild to severe.[70] Affected calves may show signs of coughing, nasal discharge, fever, otitis media in young calves, polyarthritis in adult animals, and mastitis in dairy cows, arthritis, lameness, joint swelling, pain, and difficulty breathing. In severe cases, calves may develop pneumonia and require intensive care. In some cases, the infection can spread to the central nervous system, leading to neurological signs such as incoordination and seizures.[71] *Mycoplasma bovis* can be transmitted directly through nose-to-nose contact or aerosols, or indirectly through contaminated utensils and the respiratory secretions of infected animals. A major transmission route

for *M. bovis* from cows to calves is thought to be ingestion of contaminated milk.[72] Colonization of the respiratory tract occurs more often in calves fed milk infected with *M. bovis* compared to calves fed non-infected milk. It can survive for a long period of time in a protected environment, with the greatest survival in humid and cool conditions. Apparently healthy animals can harbor the organism in the upper respiratory tract for long periods of time, acting as a reservoir for infection in the herd.[66,73]

The diagnosis of *M. bovis* infection is challenging as the clinical signs are not specific. Cultural isolation, serological tests, and molecular diagnostic approaches can be used to diagnose *Mycoplasma bovis* infections from nasal swabs, joint fluid, and blood samples. PCR is a molecular technique that can detect the DNA of *Mycoplasma bovis* in samples. Serology involves testing for antibodies against the bacterium in the blood.[70,74]

Antibiotics are used for the treatment of *Mycoplasma bovis* infections in dairy calves, although they are difficult to treat. However, the choice of antibiotics can be challenging since *Mycoplasma bovis* is resistant to many commonly used antibiotics.[75] The bacteria are resistant to several antimicrobial classes, including fluoroquinolones, macrolides, tetracyclines, and β-lactams, because of the uncontrolled usage of antimicrobial agents in the animal industry. The cost of infection is primarily associated with the intensive treatment of affected calves coupled with the culling of animals that are unresponsive to treatments.[76] Antimicrobial susceptibility testing is recommended to guide antibiotic selection. Supportive care is also an important component of treatment. Calves with respiratory disease may require oxygen supplementation, nebulization, and bronchodilators. Those with arthritis may require pain management and joint support.[77] Preventing and controlling *Mycoplasma bovis* infections in dairy calves requires a comprehensive approach that includes biosecurity measures, vaccination, and appropriate antibiotic use. Good hygiene practices, such as cleaning and disinfecting equipment and surfaces, can reduce the risk of transmission. Vaccination against *Mycoplasma bovis* can also be effective in reducing the severity of infections in calves (Table 1). However, there is no single vaccine available that provides complete protection against all strains of the bacterium.[66,70]

Pasteurella multocida

The genus *Pasteurella* belongs to the family *Pasteurellaceae. Pasteurella* species are a short rod/coccobacilli-shaped bacterium that is capsulated, non-spore-forming, gram-negative, non-motile, facultative anaerobic. They are also sugar fermentative, oxidase and catalase positive, and bipolar in gram stain.[17] The species also exists as a commensal and opportunistic pathogen found in the upper respiratory and proximal gastrointestinal tracts of animals. They are responsible for major bacterial causative agents of bovine respiratory disease.[78] The most important members of the *Pasteurellaceae* family in the livestock industry include *M. haemolytica, P. multocida, and B. trehalosi*. These species are the most common cause of pneumonic and hemolytic septicemia in cattle and small ruminants that pose serious hazards to the livestock sector.[76] *Pasteurella* species are widespread and cause a wide range of economically significant endemic and epizootic diseases in ruminants all over the world. *Pasteurella species* cause respiratory, systemic, and local infections in various animal species, including dairy calves.[77] *P. multocida* and *M. haemolytica* are two primary bacterial pathogens causing pneumonia and hemorrhagic septicemia in calves that affect the health, welfare, and productivity of calves.[79]

Hemorrhagic septicemia (HS) is an acute, fatal, and septicemic disease of cattle and buffaloes in tropical regions of the world. Hemorrhagic septicemia is the most economical contagious bacterial disease caused by B2 and E2 serotypes of *P. multocida*,[80] and Serotype E2 is predominantly found in Africa. The disease is characterized by the sudden onset of fever, profuse salivation, severe dyspnea, and death in about 24 hours. Hemorrhagic septicemia is list B disease by OIE since it is a primary pasteurellosis with 100% mortality in infected animals in endemic areas of Africa and Asia. Thus, HS is the most economically important bacterial diseases.[81] The morbidity and mortality rates of the disease range between 50% and 100%, respectively. Morbidity depends on the immune status of the animal, either acquired naturally or induced by vaccination. The occurrence of the disease is often associated with wet humidity during the rainy season, transportation, and other stress factors. Pneumonic pasteurellosis is responsible for huge mortality in feedlot cattle. In general, pneumonic pasteurellosis and hemorrhagic septicemia diseases cause significant economic losses in the cattle sector due to high morbidity and mortality rates across the world.[82]

Virulence genes are significant in the pathogenesis of *P. multocida*. The virulent genes of *P. multocida* include fimbriae and adhesions (nanB and nanH), outer membrane proteins (OMP) and toxins (toxA).[83,84] These virulent factors promote *P. multocida* colonization and invasion by impairing host defense mechanisms, destroying host tissues, and inducing a lethal host inflammatory response.[85] The virulent determinants also keep organisms in the respiratory tract by preventing phagocytosis and increasing resistance to complement and bactericidal effects of the host defense mechanisms.[86]

Identifying the organisms' circulating serotypes is critical for effectively preventing and controlling pasteurellosis in domestic ruminants,[87] and also important for the selection of vaccine strains. *P. multocida* is divided into five serogroups based on capsular structure (A, B, D, E, and F) using indirect hemagglutination test and further subdivided into 16 serotypes based on lipopolysaccharide composition by Heddleston gel diffusion precipitation assay.[88,89] B2 and E2 cause hemorrhagic septicemia in addition to the possible pneumonia or septicemia caused by the remainder of the capsular serogroups and somatic serotypes.[90]

Mannheimia haemolytica is a major pathogen in ruminants of all age groups, and it is the main cause of bovine and ovine pneumonic pasteurellosis.[91,92] It has two biotypes (A and T) based on fermentation of arabinose and trehalose, respectively.[93] Based on their surface antigen, these biotypes are further subdivided into 17 serotypes. Thirteen of these are biotype A, while the remaining four are biotype T (3, 4, 10, and 15). The most prevalent serotypes of *M. haemolytica* are A1 and A2, which are found worldwide. Bovine serotype A1 is considered to be the most prevalent cause of bovine pasteurellosis. *M. haemolytica* serotype A2 typically causes pneumonic pasteurellosis in small ruminants of all age groups.[94] *M. haemolytica* uses capsules, adhesions, lipopolysaccharides (LPS), OMP, and various protease virulent determinant factors to colonize and infect the lungs.[95] The pathogenicity of *M. haemolytica* is associated with various virulence genes. These include leukotoxin (lkt), leukotoxin C (lktC), putative adhesion (ahs), and outer membrane lipoprotein (gs60). The identification of these genes reveals crucial information about *M. haemolytica's* pathogenicity.[96]

The diagnosis of pneumonic pasteurellosis is based on the history of patients, clinical signs, and conventional bacterial isolation. Recently advanced and more confirmatory diagnostic assays are PCR, RT-PCR, RFLP, real-time PCR, gene sequencing, and phylogenetic analysis.[97] The phenotypic and genetic characterization of *P. multocida* serotypes that are currently circulating in the field is critical for disease prevention and control strategy. It is also important to precisely distinguish the phylogeny of fastidious pathogens and virulence genes as a future step in vaccine development.[98] Calves infected with *P. multocida* may develop pneumonia and septicemia. Nasal swabs and blood are the preferred sample types for diagnosis. The transmission of *P. multocida* can occur through direct contact with infected animals, contaminated equipment, or aerosolization of the bacteria. The risk of infection is higher in calves that are stressed, malnourished, or have weakened immune systems.[99]

The major clinical signs in the infected dairy calves are fever, cough, nasal discharge, and difficulty breathing. The infection can also cause local infections including abscesses and septicemia, which can lead to significant economic loss in the dairy industry.[75] The risk factors that increase infection of dairy calves are stress (environmental and management problem), overcrowding, poor ventilation, and co-infection with other pathogens.[100] Good management practices, such as vaccination, proper nutrition, and hygiene, can help prevent *Pasteurella* infections and reduce the severity of BRD in dairy calves.[101] Treatment of *Pasteurella* infection in dairy calves typically involves the use of antibiotics. Supportive care, including fluid therapy and nutritional support, may also be necessary for severely affected calves.[102]

Listeria monocytogenes

The genus listeria is an intracellular gram-positive bacterium that belongs to the family *Listeriaceae*. The genus is characterized by non-capsulated, coccoid to rod shaped cells, facultative anaerobes, flagellated, and non-spore forming bacterium[103] (Table 1). The genus contains six species including *Listeria monocytogenes, L. ivanovii, L. innocua, L. welshimeri, L. seeligeri*, and *L. grayi. Listeria monocytogenes* and *L. ivanovii* are two main pathogenic species for animals and humans.[104,105] *Listeria monocytogenes* (*L. monocytogenes*) is ubiquitous and widely spread in the environment such as soil, mud, plant decaying vegetation, raw and treated sewages, water, food processing facilities.[106] The organism also possesses unique physiological characteristics that can grow at refrigerator temperatures. The species *L. monocytogenes* is the causative agent of listeriosis in humans and animals.[107] It is one of the most significant emerging

and opportunistic food-borne bacterial diseases in humans. The infection can result in septicemia, meningitis, uterine infection (abortion and still birth), subclinical mastitis, and sometimes death in dairy calves and cow. Listeriosis usually occurs in calves, pregnant cows and immunocompromised cattle.[108]

The virulence potential of *L. monocytogenes* is determined by several molecular determinants. Hemolysin (listeriolysin O), two phospholipase, protein (ActA), internalin A (InlA), ternalin B (InlB), and cytotoxins are the main virulence factors of *L. monocytogenes*.[109] The virulence factors are essential for intracellular motility of the pathogen. The hemolysin toxin lyses tissue and blood cells. The cytotonic toxin stimulates cyclic AMP production similar to cholera toxin. All serotypes of *L. monocytogenes* have the ability to provoke monocytosis. Host and environment-related risk factors that expose animals to infection are poor nutritional status, age, parity, sudden change in weather, late pregnancy, and parturition stress, transport, and overcrowding.[108]

Listeria monocytogenes is transmitted by ingestion, inhalation, or direct contact with infected animals. Ingestion of contaminated silage, feed, water, or bedding is the primary modes of transmission.[110] Calves that develop the septicemic *L. monocytogenes* disease may acquire infection from contamination of the cow teat from the ingestion of milk containing the organism or from a cow with subclinical bacteremia, through the navel from the environment, and also from congenital infection.[23] The clinical signs of listeriosis depend on pathogenic strains and immune status of the host. The clinical manifestation of listeriosis in dairy cows is neonatal septicemia, encephalitis, and abortion in late pregnancy.[111] *L. monocytogenes* can also cause depression, fever, diarrhea in some cases, anorexia, meningitis, and neurological signs in calves. These neurological signs include circling, head pressing, and ataxia.[112]

Listeria monocytogenes can be diagnosed via bacterial culture, animal inoculation, immunological assays, and molecular tests from brain tissue, blood, and feces specimens.[102] The most recommended drugs for the disease listeriosis include penicillin G, aminoglycosides, trimethoprim, sulfamethoxazole, and tetracycline in dairy calves.[113] Prevention of infection in dairy calves can be achieved through good management practices, such as maintaining clean and hygienic facilities and equipment, ensuring proper colostrum management, and minimizing stress on the calves (Table 1). Vaccination may also be effective in preventing infection in calves.[114]

Haemophilus somnus

Haemophilus somnus (*H. somnus*) is a gram-negative bacterium that causes respiratory and joint infections in calves[115] (Table 1). This bacterium is considered an opportunistic pathogen, which means it can cause disease when the immune system of the calf is compromised.[116] Good hygiene practices and antibiotic treatment can prevent *H. somnus* infection.[117] Calves infected with *H. somnus* may develop respiratory disease, septicemia, and arthritis. Nasal swabs, blood, and synovial fluid are the preferred sample types for diagnosis.[118] Bacterial culture and PCR are commonly used diagnostic methods for *H. somnus* infection[119].

Respiratory disease caused by *H. somnus* is characterized by fever, depression, coughing, and nasal discharge. In severe cases, the calf may develop pneumonia, which can be fatal. Furthermore, the bacterium can invade the nervous system of the calf, leading to septicemia, meningitis, and other neurological symptoms.[118] Several risk factors have been associated with *H. somnus* infection in dairy calves, including stress, transportation, overcrowding, and poor ventilation.[120] Diagnosis of *H. somnus* infections in dairy calves can be challenging, as the bacterium can be difficult to isolate and culture from clinical samples.[121] Molecular techniques such as PCR and DNA sequencing have been developed to aid in the diagnosis of *H. somnus* infections, but these methods can be expensive and require specialized equipment and expertise.[119]

Studies have shown that the use of antimicrobial agents can be effective in treating *H. somnus* infection in dairy calves. However, the emergence of antimicrobial resistance in this bacterium has raised concerns about the long-term effectiveness of treatments.[122] Prevention and control of *H. somnus* infections in dairy calves involve a multi-faceted approach, including vaccination, biosecurity measures, and appropriate management practices.[101] Vaccines against *H. somnus* are available and can be effective in reducing the incidence and severity of BRD and reproductive diseases.[123] Biosecurity measures, such as quarantine and disinfection protocols, can help to prevent the introduction and spread of *H. somnus* on dairy farms (Table 1). Management practices, such as minimizing stress and optimizing nutrition, can also help to maintain the health and immune function of dairy calves.[124]

Conclusion

The review highlights the significant challenges of bacterial infections in dairy calves, emphasizing common bacterial infections, clinical manifestations, and factors influencing their occurrence. Effective management strategies, including early detection, proper treatment, and preventive measures such as good colostrum feeding, are crucial. The review also underscores the importance of judicious antibiotic use, supportive care, and advancements in diagnostics. Furthermore, it explores recent advancements in diagnosis and prevention, providing valuable insights for dairy farmers, veterinarians, and researchers. Comprehending the common bacterial pathogens, their methods of transmission, and the factors that impact infection rates is essential for the successful implementation of management strategies. Further study is essential for a deeper understanding of the epidemiology and characterization of these infections in dairy calves.

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