Review Article

Journal of Advanced Veterinary Research
(2025) Volume 15, Issue 4, 514-519

Epizootic bovine abortion: A devastating disease for cattle

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ARTICLE INFO

Recieved: 02 July 2025

Accepted: 21 July 2025

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Keywords:

Abortion, Cattle, Disease, EBA, *Pajaroellobacter abortibovis*

ABSTRACT

Foothill abortion, also known as Epizootic Bovine Abortion (EBA), is a condition that causes abortion in cattle. EBA is caused by the bacterium *Pajaroellobacter abortibovis*, which is transported by the Pajaroello tick (*Ornithodoros coriaceus*). EBA is thought to have existed in California since the 1920s, and in the early 1950s it was identified as a major factor limiting the state's maximum calf output. Since 1954, California cow ranches have seen significant calf losses of up to 65% in the early stages of pregnancy due to EBA. It seems that *P. abortibovis* enters the growing fetus through the placenta of infected cows. The immune system's reaction to EBA includes the return of immune cells to eradicate bacteria and bacterial multiplication. Chronic prenatal infections caused by EBA agents result in extensive gross and histologic lesions. Abortion frequently happens in the last trimester, and lesions progress over three months or longer. Historically, fetal pathology, higher fetal serum immunoglobulin levels, and a history of the dam grazing in an area thought to be endemic for the disease during pregnancy have been used to diagnose EBA. Cows six months or less pregnant, the availability of hungry Pajaroello ticks in the cows' grazing area, cows who have not been exposed before and lack immunity, and warm, dry weather that speeds up the tick's metabolism are risk factors for EBA. Controlling EBA has classically involved only making adjustments to management techniques that can occasionally lessen, but not always completely eradicate, the losses brought on by EBA.

Introduction

Foothill abortion, also known as Epizootic Bovine Abortion (EBA), is a condition that causes abortion in cattle (Blanchard *et al.*, 2022). This illness is confined to the hilly or mountainous regions of California, northern Nevada, and southern Oregon, and it causes significant economic harm (Stott *et al.*, 2002). EBA is caused by the bacterium *Pajaroellobacter abortibovis*, which is transported by the Pajaroello tick (*Ornithodoros coriaceus*) (Brooks *et al.*, 2016). EBA is thought to have existed in California since the 1920s, and in the early 1950s it started to be acknowledged as a major barrier to the state's optimum calf production (Blanchard *et al.*, 2022). This condition has been and still is a leading cause of abortion in Californian beef cattle; estimates for Oregon and Nevada are unavailable; cases in Southern Idaho are suspected but not substantiated (Hall *et al.*, 2002).

The extended abortion storm caused by EBA typically affects heifers or cows who have just been introduced to the area, though abortions can happen three to five months after leaving the endemic area (Kendrick, 1976). The rate of miscarriage can approach 60% and typically happens in the last trimester. The fetuses hardly ever experience autolysis, and the animals miscarry without illness (Givens and Marley, 2008). Pregnant beef cattle that graze in hilly and mountainous regions for the first time during the summer months are generally at risk of experiencing late-stage abortions or giving birth to frail calves that die from infection.

A miscarried fetus may have generalized lymphomegaly, splenomegaly, and hepatomegaly. Pathologically, affected fetuses frequently exhibit enlarged organized lymphoid tissue (including the spleen and lymph nodes), petechial hemorrhages (small, round, red-purple) in the mucous membranes (nose, gums, and nose), an enlarged liver, and extensive ascites (abnormal accumulation of serous fluid in the abdominal cavity, resulting in a markedly enlarged abdomen) (Kimsey *et al.*, 1983). The level of fetal IgG is high. Cows are frequently exposed to endemic regions prior to reaching breeding age, and they hardly ever terminate future pregnancies (Blanchard *et al.*, 2022).

This condition is defined as an abortion in beef cattle with pathology that is distinct enough to be diagnostic both in terms of gross and microscopic examination. The distinctive gross and microscopic presentation of the fetus, the mother's medical history (including whether she had been grazed in the foothills or infested mountain areas during the summer and during pregnancy), and extremely high blood immunoglobulin levels are generally the basis for the traditional and primary diagnosis of EBA (Kennedy *et al.*, 1983). Under a microscope, the illness is typified by focal necrotic lesions that may manifest as pyogranulomas in the lymph nodes and spleen, acute vasculitis, and proliferation of lymphocytes and mononuclear phagocytes (Kennedy *et al.*, 1983). EBA is pathognomonic for distinct diseases in the thymus that are marked by macrophage infiltration and cortical thymocyte atrophy.

The beef cattle business has been the main source of significant reproductive losses linked to this disease since these animals typically graze in environments that harbor tick vectors, though losses can also happen in dairy breeds. The purpose of this article was to provide a comprehensive review of EBA or Foothill abortion. This article examines some possible methods for controlling disease.

Etiology

Before *Pajaroellobacter abortibovis*, a novel Deltaproteobacteria closely linked to the Myxococcales, was discovered as the etiologic agent in 2005, the causative agent of EBA had been elusive for more than 50 years (Brooks *et al.*, 2016). Prior to that time, several attempts to use tra-

ISSN: 2090-6277/2090-6269/

ditional staining methods, such as Gram staining, to visualize bacteria had failed. Gram staining and electron microscopy techniques were used to approach the morphological characterisation of *P. abortibovis* (Haddad *et al*., 2021). Bacteria are difficult to identify with typical Gram stain techniques, although they can be easily detected by sliver staining and immunohistology. Using the McDonald Gram Stain and the modified Sandiford Gram Stain, the bacteria are poorly visible as pink rods, suggesting that they are gram-negative or, maybe more precisely, gram-indeterminate (Brooks *et al*., 2016).

An effective diagnostic method for assessing microbial structures is transmission electron microscopy (TEM) (Golding *et al*., 2016). In contrast to Gram-positive bacteria, which have a visible cell membrane with a homogeneous outer peptidoglycan layer up to 50 nm, Gram-negative bacteria are described in previously published research as having an outer membrane, a periplasmic space with a thin peptidoglycan layer, and an inner membrane (cytoplasm) (Silhavy *et al*., 2010). *P. abortibovis* was evaluated under an electron microscope, revealing a cell envelope structure typical of Gram-negative bacteria and an approximate dimension of 1.7x0.46 mm (Brooks *et al*., 2016).

Furthermore, the agent was finally identified as deltaproteobacterium using molecular biology techniques on necropsy tissue from ill fetuses (King *et al*., 2005). The pathogen's 16S rRNA sequence showed 89.4% similarity with *Polyangium cellulosum*, also known as *Sporangium cellulosum*, a Myxococcales member (Lim and Sears, 1989). In this family of prokaryotes, *Lawsonia intracellularis* is the only other known mammalian pathogen. It is a deltaproteobacterium that is mostly linked to pig enteritis (Vannucci and Gebhart, 2014). Recently, the EBA bacterial agent was further characterized and given the name *P. abortibovis* (Brooks *et al*., 2016). Together with the fact that *P. abortibovis* is a mammalian pathogen and infects arachnids, the revised 16S rRNA phylogenetic study between *P. abortibovis* and *S. cellulosum* indicates that *P. abortibovis* belongs to a different genus than Sorangium (Brooks *et al*., 2016).

History

EBA is thought to have existed in California since the 1920s, and in the early 1950s it was identified as a major factor limiting the state's maximum calf output (Blanchard *et al*., 2022). Beginning in the 1950s with an emphasis on chlamydia and the creation of a related vaccine that never gained traction, the 50-year hunt for the causative agent of EBA began. After it was determined that a particular tick, *Ornithodoros coriaceus*, was the cause of foothill abortion, research into the cause was resumed, and the retrovirus was eradicated (Lane *et al*., 1985). The emphasis on unidentified spirochetes and Borrelia coriaciae as possible causes of EBA took the place of these initiatives in the 1980s (McDowell *et al*., 2003). The inability to consistently spread the disease experimentally hindered all these studies; the only known method of spreading the disease was to feed susceptible pregnant cows hundreds of *O. coriaceus* ticks that had been trapped in the field, and this method only worked roughly half the time (Teglas *et al*., 2006). Cryopreserved thymus glands from certain aborted fetuses were used in the 1990s to build a dependable method for abortion transmission in hilly regions, which aided research that eventually showed the causal pathogen is antibiotic-susceptible (Anderson *et al*., 2006). The identification of a distinct bacterium in the order Myxococcales as the causative agent in 2005 marked the culmination of this advancement, which was linked to the use of contemporary molecular biology techniques (Yen *et al*., 2023). Based on the combination of the tick vector's name, the microbe type, the ailment, and the vulnerable host, this bacterium is tentatively known as *P. abortibovis* (Brooks *et al*., 2016).

Epidemiology

Little is known about the epidemiology of EBA. Some have suggested that pregnant cows may contract the disease when on foothill pastures, which explains why the condition is more common in beef cattle than dairy cattle (Blanchard *et al*., 2022). Since 1954, California cow ranches have seen significant calf losses of up to 65% in the early stages of pregnancy due to EBA (Givens and Marley, 2008). Since the majority of California's beef cattle, if not all of them, spend at least some of their gestation in the foothills and mountains, some experts believe that the purported association between abortion and foothill grazing is entirely accidental (Hall *et al*., 2002). However, determining the causative agent's identity would be crucial to answering this contentious and significant subject.

Pathogenesis

It seems that *P. abortibovis* enters the growing fetus through the placenta of infected cows (Brooks *et al*., 2016). There were no overt clinical symptoms in the broodstock, regardless of whether it was infected by experimental inoculation or tick bite. Historical communications documenting reactions to experimental flea bites most likely reflected reactions to flea saliva and/or infected microorganisms (de la Fuente *et al*., 2023). A "window" in the fetus's development makes it vulnerable to infections that could eventually result in fetal illness (Romero *et al*., 2007). Vulnerability is widely thought to occur from conception through the second trimester of pregnancy, though this window is not clearly defined. There is no documented susceptibility in the first 60 days of pregnancy.

Despite the pathogen's apparent lack of effect on fertilization, research is being done to see whether it could cause early embryonic death in a tiny percentage of infected animals (Givens and Marley, 2008). Fetal infection is a gradual process, and it takes two to three months for identifiable lesions to appear. According to immunohistochemistry, the bacteria seem to multiply intracellularly in histiocytes; in short-term cultures of macrophages obtained from fetal necropsy tissue, replication is extremely slow (about one day) (Brooks *et al*., 2016). The arterial orientation of the lesions throughout the fetus, the intracellular nature of the infection, and the disease's gradual but steady course all support the theory that the lesions are immunologically mediated. The sluggish spread throughout the body and the formation of lesions that occur at the same time as the fetal immune system matures immunologically are definitely caused by delayed bacterial growth (Blanchard *et al*., 2022).

In mountainous regions, pregnant ewes do not seem to be at risk for abortion; in one unpublished investigation, pregnant ewes infected during the first trimester gave birth to healthy lambs (Studdert and McKercher, 1968). According to these latter investigations, the bacteria reproduce and spread slowly, and the gestation time in sheep is too short for the development of immunologically mediated lesions and miscarriages. Although mule deer (*Odocoileus hemionus*) are significant tick vector hosts, there is no proof that EBA is present in this species (Yabsley *et al*., 2005). Their six to seven-month gestation cycle, which is in between that of sheep and cattle, may be too brief to permit the onset of disease. On the other hand, frequent exposure to the organism through tick bites may provide immunity, and in an abortion, the fetus is promptly destroyed, leaving no trace (Fogaça *et al*., 2021). There have been several unsuccessful attempts to infect immunocompetent lab animals, including mice and rabbits, with illness.

Mice suffering from severe combined immunodeficiency disease (SCID) are vulnerable to infection by *P. abortibovis* (Blanchard *et al*., 2014). It took two to three weeks for C3H-scid animals to be put down after exhibiting signs of wasting seven to eight weeks after infection. An enlarged spleen with many pathogenic germs is the sole visible gross lesion. Pregnant cows can be reliably infected with bacteria from cryopreserved spleen cells from SCID mice infected with *P. abortibovis* (Blanchard *et al*., 2014). The recovered organisms showed great vitality and were not opsonized, in contrast to bacteria taken from bovine fetuses. The aforementioned theory that the fetal bovine lesions are immunologically mediated would be supported by the absence of EBA-like lesions in infected immunodeficient mice.

Immune response

The immune system's reaction to EBA includes the return of immune cells to eradicate bacteria and bacterial multiplication. Replication of the *P. abortibovis* bacterium starts when the cow mounts an immunological response. After then, immune cells go back to where the infected cells were and eliminate any bacteria that may still be there (Blanchard *et al.*, 2022). This procedure, which takes five to eight weeks, is thought to function similarly to a second "booster" shot. It has been demonstrated that immunity lasts for at least three years. Cattle are expected to develop a stronger immune response over the course of three years due to natural exposure through tick bites as long as they are grazing in the Pajaroello tick habitat (Chen *et al.*, 2007). Fetuses that are not yet immune have a robust immune response, while cows typically react to the bacteria very little (Jawor *et al.*, 2017). This results in abortion approximately four months after the cow becomes infected and seriously damages the cow's own tissues and organs.

Pathology

Chronic prenatal infections caused by EBA agents result in extensive gross and histologic lesions. Abortion frequently happens in the last trimester, and lesions progress over three months or longer (Kimsey *et al.*, 1983). Fetal death happens either before or shortly after delivery, and as previously stated, the fetus is nearly always fresh. Petechial hemorrhages are frequently seen on the oral cavity and conjunctival mucosa, and they are especially noticeable along the tongue's ventral side (Hall *et al.*, 2002). In general, enlarged lymph nodes are prevalent. Certain superficial nodes are easily palpable through the skin, such as the prescapular lymph nodes. An EBA fetus may have prescapular lymph nodes measuring 16 g or more, whereas the prescapular lymph nodes of a typical term fetus weigh between 3.5 and 7.0 g (Hall *et al.*, 2002).

Severe ascites-induced abdominal distension is a variable trait, while fibrin clots and some degree of ascites are typically present (Delano *et al.*, 2002). An enlarged and blocked liver with a nodular capsule is a striking but erratic gross pathology in EBA. An enlarged spleen along with expanded internal lymph nodes is a more regular gross alteration (Anderson *et al.*, 2006). There may be cervical edema, diffuse interlobular bleeding, and a shrinkage of the thymus. The lungs could have some expansion. Small gray inflammatory foci in the kidneys, heart, or other organs could be among the other gross abnormalities (Constable *et al.*, 2017).

The diagnosis of EBA must be confirmed by histological analysis of fetal tissue, particularly lymphoid organs. Despite not always being present, thymic lesions that occur late in the course of the disease seem to be specific to EBA (Anderson *et al.*, 2006). Additional characteristics include the infiltration of macrophages into the medulla and the loss of cortical thymocytes. The interlobular septa are frequently enlarged by hemorrhage and fibrin, and macrophages have penetrated them (Hall *et al.*, 2002). The lymphoid follicles' hyperplasia and the widespread macrophage infiltration in the sinuses and medulla are the causes of the lymph nodes' noticeable expansion (Boes and Durham, 2017). The spleen's white pulp also exhibits lymphoid hyperplasia and macrophage infiltration. Abortion may result from acute necrosis of the lymphoid organs, which is frequently observed late in the course of the disease, following a proliferative response (Reichel *et al.*, 2018). In most organs, including the liver, lungs, and brain, widespread inflammatory lesions are also observed; these lesions typically have a vascular aspect.

Anomalies in the brain include vasculitis and granulomatous meningitis with localized gliosis (Underwood *et al.*, 2015). There is focal granulomatous infiltration in the interlobular septa and mononuclear cell infiltration in the thickened pulmonary alveolar septa (Wang *et al.*, 2024). Granulomatous portal hepatitis with varying centrilobular congestion and hepatic cord atrophy is a constant, albeit less specific, characteristic (Howarth *et al.*, 1956).

Clinical symptoms

Neither naturally nor experimentally treated cows displayed any symptoms of illness at any point after exposure to EBA. Approximately one week following tick feeding, there has been a little increase in the total leukocyte count (Coker *et al.*, 2012). Since practically all abortions take place in the third trimester, the time between exposure to abortion is abnormally long, typically ranging from three to four months (Givens and Marley, 2008). The fetuses are typically in a relatively fresh state (i.e., nonautolytic) when they are ejected. Aborted EBA fetuses' serum contains extremely high levels of immunoglobulins, particularly immunoglobulin G (IgG) (150–800 mg/dl; geometric mean, roughly 300 mg/dl). In certain situations, immunoglobulin levels can even approach that of neonates fed colostrum (>1 g/dl) (Spezialetti and Osebold, 1991). No other disease entity is known to regularly cause such elevated levels of fetal bovine immunoglobulin.

Some calves may survive parturition but die during the neonatal period, and the chronic nature of the disease process in the fetus and late stages of pregnancy implies that the extremely stressed fetus protects its own birth through cortisol secretion (Jawor *et al.*, 2021). Aborted cows or heifers frequently start nursing; in any event, they usually exhibit little long-term consequences of the illness and can conceive in the following breeding season, assuming the aborted birth went smoothly (Blanchard *et al.*, 2022).

Diagnosis

Historically, fetal pathology, higher fetal serum immunoglobulin levels, and a history of dam grazing in an area thought to be endemic for the disease during pregnancy have been used to diagnose EBA (Chen *et al.*, 2007). EBA is typically associated with significant microscopic and gross abnormalities. Aborted fetuses are typically in excellent condition (not autolyzed) and exhibit several gross abnormalities, such as petechial hemorrhages in the thymus and mucous membranes (oral cavity, tongue, and eyelids), skin lesions, an enlarged liver, an enlarged spleen, and an enlarged abdomen due to extensive ascites with excessive fibrin (Anderson, 2007). Under a microscope, the lesions are extensive and exhibit a vascular orientation with lymphocyte and mononuclear phagocyte infiltration (Kennedy *et al.*, 1983). The organized lymphatic tissue may develop focal necrotic lesions, whereas the thymus may develop pathognomonic lesions, which are typified by macrophage infiltration and cortical thymocyte loss (Reichel *et al.*, 2018).

The inability to grow the causal agent continues to be a barrier to microbiological diagnosis of EBA. All attempts to cultivate *P. abortibovis* on synthetic media have failed, and although some limited short-term replication of the bacteria has been seen in primary cultures of macrophages derived from fetal lymphoid necropsy tissue, substantive propagation of the bacteria in either primary or established cell lines has not been possible (Blanchard *et al.*, 2010). Both conventional and TaqMan-based polymerase chain reaction (PCR) techniques have been created to target the bacterial 16S ribosomal gene (Chakravorty *et al.*, 2007). The presence of *P. abortibovis* in necropsy tissue of infected fetuses exhibiting classic EBA disease can be determined using either technique. TaqMan is the preferred assay for detecting low bacterial concentrations in necropsy tissue taken from fetuses suspected of being infected, such as weak calves that might or might not be nursing and fetuses exhibiting dubious or nonclassical EBA pathology (Richter *et al.*, 2010). Since only infrequently infected ticks will have enough bacteria to be detected by conventional PCR, the TaqMan assay is also recommended for detecting *P. abortibovis* in vectors (Blanchard *et al.*, 2014).

P. abortibovis was not visible in fetal tissue using standard bacterial histological staining. Therefore, *P. abortibovis* was visualized under a microscope in formalin-fixed necropsy tissue sections using a modified Steiner silver staining technique that was applied to the distantly related deltaproteobacterium *Lawsonia intracellularis* (Brooks *et al*., 2016). The current preferred techniques for the microscopic diagnosis of EBA include immunofluorescence applied to printed smears and/or fresh tissue homogenates, and Steiner staining and immunohistochemistry performed to thin sections of formalin-fixed necropsy tissue.

Recently, a serological test based on fluorescent antibodies was validated for the diagnosis of EBA. Setting a titer of 1000 as the cutoff criterion for a positive test resulted in 100% specificity and 95% sensitivity (Blanchard *et al*., 2014). This test has been very helpful in making a prompt diagnosis, particularly when the fetal immune system had eradicated most of the *P. abortibovis*. Veterinary professionals and beef producers in rural areas who lack simple access to diagnostic labs can also benefit from this serological test, which allows them to detect the condition by providing a sample of bodily fluids, like blood or ascites, rather than the entire fetus.

Transmission

"Pajaroello" is pronounced "pa-har-wayo" and is derived from the Spanish terms "paja," which means straw, and "huello," which means hoof-bottom. There have been a lot of legends about the Pajaroello louse throughout history. Native Mexicans in Central California's coastal mountains around the beginning of the 20th century tended to think that three tick bites would be fatal (Parola *et al*., 2013). They were more afraid of the Pajaroello tick than the rattlesnake, and there were frequent reports of individuals who had been bitten by the bug and lost arms or legs. Human flea bites can cause severe local reactions (showing hypersensitivity), including considerable swelling of the affected appendix, even though the folklore seems to be grossly exaggerated (Youssefi *et al*., 2014).

Carl L. Koch originally described *Ornithodoros coriaceus* in Mexico in 1844 (Nava *et al*., 2014). The fact that this tick is the only Ornithodoros species with two sets of eyes in the Western Hemisphere makes it simple to recognize. Apart from one record of ticks in Paraguay, most of the early samples came from Mexico and California (Nava *et al*., 2007). In contrast to the hard-bodied ticks, the Pajaroello tick does not cling to its host. At elevations between 180 and 2,440 meters (590 and 8,000 feet), it mostly inhabits the bedding of large animals, such as cattle and deer, in tough soil that has been mingled with tree litter (Failing *et al*., 1972). Ticks are drawn to warm-bodied creatures that "lie down" by releasing carbon dioxide (CO2) and tearing the skin with their mouthparts (Carr and Salgado, 2019). Ticks can stay attached to their host for seven to nine days as larvae, but within five to fifty minutes, adult ticks (males, females, and nymphs) enlarge with gathered blood and depart. The Pajaroello tick has been gradually expanding eastward from California due to human relocation, domestication, and livestock management, as well as perhaps preying on migratory mammals (Failing *et al*., 1972). As a result, the steep regions of Nevada and Oregon that were previously thought to be endemic for neither the disease nor the tick were recognized to have abortion.

Larger fleas can live for several years without feeding on blood, and fleas seem to have a lifespan of over ten years. The advent of molecular diagnostic assays has made it possible for scientists to determine whether *P. abortibovis* is present in the salivary glands of ticks that were collected in the field. Only a small fraction of ticks (about 1-2%) carry enough bacteria to spread the disease, despite the fact that between 10 and 20% of ticks are afflicted. Transovarial transmission of the bacteria in ticks has not been proven, and there is no correlation between the presence of bacteria and the tick's age, size, or sex. Currently unknown, the bacterial pathogen's reservoir may consist of the soil or husks in which ticks reside, as well as unnamed mammalian and avian hosts. EBA transmission can be seen in Figure 1.

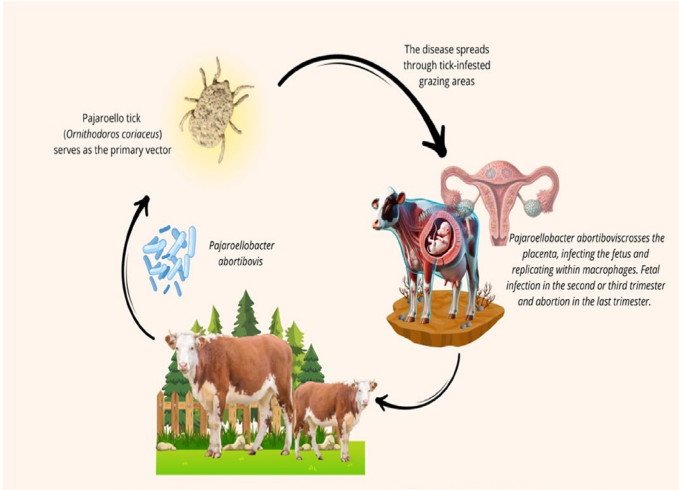

Figure 1. Transmission of *Pajaroellobacter abortibovis* through Pajaroello tick (*Ornithodoros coriaceus*) in cattle.

Risk factors

Cows six months or less pregnant, the availability of hungry Pajaroello ticks in the cows' grazing area, cows who have not been exposed before and lack immunity, and warm, dry weather that speeds up the tick's metabolism are risk factors for EBA (McKercher *et al*., 1976). This illness is found in high deserts, mountains, and arid hilly regions in Nevada, Oregon, and California (Blanchard *et al*., 2022). Grazing in slopes, mountains, or high desert regions makes cows prone to sickness (Teglas *et al*., 2006). Since Pajaroello ticks do not fare well in damp or submerged environments, it is not an issue for the cattle to graze in irrigated pastures or flood-prone areas (Chen *et al*., 2007). Compared to dairy cattle, beef cattle are more susceptible to this illness. Milking cows three times a day increases their risk of miscarriage (Albuja *et al*., 2017).

Economic impact

EBA-related losses can range from 10% to 90% when pregnant, uncalved cows graze in endemic areas (Blanchard *et al*., 2022). Frequent grazing in enzootic settings results in significant immunity development in the animals, which lowers (though not completely eliminates) fetal losses as cows get older (L'Huissier *et al*., 2022). In endemic areas, abortion-related losses remain the biggest obstacle to successful calf production in the foothills. In order to reduce pregnant cows' exposure to foothill and mountain regions during the sweltering summer months, herd management might be modified to change the breeding cycle (Blanchard *et al*., 2024). This method necessitates fall calving, which frequently means that many farmers must forgo effective feed utilization.

Treatment

There is presently no cure or vaccination for EBA since the etiologic agent has not been identified with certainty and cannot be replicated in vitro. It is wise to suggest antimicrobial medication to the heifer at or prior to exposure due to the suspected agent's apparent antibiotic susceptibility (Blanchard *et al*., 2022). However, any treatment must be administered over an extended period because exposure can happen over very lengthy intervals. Although older anecdotal evidence indicates that giving chlortetracycline during tick season offers some benefit, there is currently no data to support this strategy (Hromníková *et al*., 2022). Before such tactics can be suggested, well-controlled clinical trials are required. In an effort to create particular immunogens and possibly build logical treatment plans, scientists are currently putting a lot of effort into separating and purifying the fetal thymus's causal agent.

Vaccination

The discovery of *P. abortibovis*, the bacterial agent responsible for EBA, made the creation of a vaccination for the condition a top priority. There has been little success in trying to grow bacteria in primary and secondary cell culture methods and other synthetic media. A possible route for the development of vaccines is provided by the successful inoculation of mice with severe combined immunodeficiency (SCID). Debilitating disease developed 60–70 days after SCID mice were infected with *P. abortibovis*, which was isolated from fetal bovine necropsy tissue (Welly *et al*., 2017). Sementara lesi khas aborsi kaki bukit tidak ada pada tikus yang dinekropsi, limpa membesar dan mengandung bakteri intraseluler yang hidup. The macerated spleen can be pressed through sterile gauze to create a single-cell suspension, which can then be successfully frozen and cryopreserved in liquid nitrogen while maintaining bacterial and cell viability over an extended period (Grégoire *et al*., 2020).

Flow-cytometric techniques have been developed to measure the percentage of splenocytes carrying bacteria. The quality control (ability to regulate the bacterial dose) required to proceed with the development of an experimental live virulent vaccination for abortion in hilly regions is provided by the capacity to quantify the number of infected cells in a particular mouse splenocyte population (Brooks *et al*., 2016). Vaccinated young heifers that were mated and challenged between 90 and 100 days of gestation, when fetal susceptibility was at its highest, produced healthy calves, but the majority of negative controls had full-term miscarriages (Blanchard *et al*., 2022).

Several herds in California and Nevada have participated in preliminary field experiments using experimental vaccines in the hill region; no documented incidences of abortions have been reported, and there have been no systemic reactions or minor reactions at the injection site (Blanchard *et al*., 2022). The vaccination has so far been 100% effective in preventing abortion in hilly regions in both field and experimental settings. The University of California-Davis is now working on licensing and commercializing cryopreserved vaccines.

Control

Controlling EBA has classically involved only making adjustments to management techniques that can occasionally lessen, but not always completely eradicate, the losses brought on by EBA. Two popular methods are as follows: first, reducing the amount of time that naive replacement heifers are exposed to tick habitat while the fetus is at its most vulnerable (now estimated to be between 60 and 150 days of gestation). In contrast, the second one aims to replace the tick vector naively before it breeds (Lane *et al*., 2010). In order to "feed" the ticks before reintroducing vulnerable pregnant heifers into the same area, some producers have reported effectiveness in reducing EBA by putting feeder bulls into tick habitat in the spring (Brites-Neto *et al*., 2015). According to the reasoning behind this strategy, the developing heifer fetus will be able to mature adequately after 150 days of gestation if there are less hungry ticks in the vicinity for a few months.

Breeding throughout the winter, when tick populations are at their lowest, and giving birth in the fall is the conventional method of controlling EBA (Chen *et al*., 2007). Low-lying regions of the Sierra Nevada mountains that border the Central Valley and coastal California are examples of temperate climates with cool-season grasses where this is more feasible. The biggest abortion losses in the hills typically happen when pregnant, non-endemic cattle are introduced into the Pajaroello tick's habitat (Barr and Anderson, 1993). Since the losses can amount to 90%, such activities should be avoided at all costs.

Conclusion

Epizootic Bovine Abortion significantly impacts cattle in California, Nevada, and Oregon, caused by *P. abortibovis* transmitted by ticks. Characterized by late-term abortions and specific pathological findings, it poses serious economic challenges for the beef cattle industry, necessitating effective disease management strategies.

Acknowledgments

The authors would like to acknowledge the Kementerian Pendidikan, Kebudayaan, Riset dan Teknologi that has funded this research. This review article is funded by the Airlangga Research Fund 2024 with grant number: 672/UN3/2024.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Albuja, C., Ortiz, O., López, C., Hernández-Cerón, J., 2019. Economic impact of pregnancy loss in an intensive dairy farming system. Vet. Mex. OA 6, 1–8. doi: 10.22201/fmvz.24486760e.2019.1.572.

Anderson, M.L., 2007. Infectious causes of bovine abortion during mid- to late-gestation. Theriogenology 68, 474–486. doi: 10.1016/j.theriogenology.2007.04.001.

Anderson, M.L., Kennedy, P.C., Blanchard, M.T., Barbano, L., Chiu, P., Walker, R.L., Manzer, M., Hall, M.R., King, D.P., Stott, J.L., 2006. Histochemical and immunohistochemical evidence of a bacterium associated with lesions of epizootic bovine abortion. J. Vet. Diagn. Invest. 18, 76–80. doi: 10.1177/104063870601800110.

Barr, B.C., Anderson, M.L., 1993. Infectious diseases causing bovine abortion and fetal loss. Vet. Clin. North Am. Food Anim. Pract. 9, 343–368. doi: 10.1016/S0749-0720(15)30650-2.

Blanchard, M.T., Anderson, M.L., Hoar, B.R., Pires, A.F., Blanchard, P.C., Yeargan, B.V., Teglas, M.B., Belshaw, M., Stott, J.L., 2014. Assessment of a fluorescent antibody test for the detection of antibodies against epizootic bovine abortion. J. Vet. Diagn. Invest. 26, 622–630. doi: 10.1177/1040638714545506.

Blanchard, M.T., Chen, C.I., Anderson, M., Hall, M.R., Barthold, S.W., Stott, J.L., 2010. Serial passage of the etiologic agent of epizootic bovine abortion in immunodeficient mice. Vet. Microbiol. 144, 177–182. doi: 10.1016/j.vetmic.2010.01.002.

Blanchard, M.T., Teglas, M.B., Anderson, M.L., Moore, P.F., McNabb, B.R., Collins, K.M., Yeargan, B.V., Stott, J.L., 2022. Protection of Cattle against Epizootic Bovine Abortion (EBA) Using a Live *Pajaroellobacter abortibovis* Vaccine. Vaccines (Basel) 10, 335. doi: 10.3390/vaccines10020335.

Blanchard, M.T., Teglas, M.B., Collins, K.M., Anderson, M.L., McNabb, B.R., Stott, J.L., 2024. Protective immunity induced through two calving seasons following administration of live epizootic bovine abortion agent (EBAA) vaccine. Vet. Immunol. Immunopathol. 272, 110772. doi: 10.1016/j.vetimm.2024.110772.

Boes, K.M., Durham, A.C., 2017. Bone Marrow, Blood Cells, and the Lymphoid/Lymphatic System. Pathol. Basis Vet. Dis. 1, 724–804.e2. doi: 10.1016/B978-0-323-35775-3.00013-8.

Brites-Neto, J., Duarte, K.M., Martins, T.F., 2015. Tick-borne infections in human and animal population worldwide. Vet. World 8, 301–315. doi: 10.14202/vetworld.2015.301-315.

Brooks, R.S., Blanchard, M.T., Clothier, K.A., Fish, S., Anderson, M.L., Stott, J.L., 2016. Characterization of *Pajaroellobacter abortibovis*, the etiologic agent of epizootic bovine abortion. Vet. Microbiol. 192, 73–80. doi: 10.1016/j.vetmic.2016.07.001.

Carr, A.L., Salgado, V.L., 2019. Ticks home in on body heat: A new understanding of Haller's organ and repellent action. PLoS One 14, e0221659. doi: 10.1371/journal.pone.0221659.

Chakravorty, S., Helb, D., Burday, M., Connell, N., Alland, D., 2007. A detailed analysis of 16S ribosomal RNA gene segments for the diagnosis of pathogenic bacteria. J. Microbiol. Methods 69, 330–339. doi: 10.1016/j.mimet.2007.02.005.

Chen, C.I., King, D.P., Blanchard, M.T., Hall, M.R., Aldridge, B.M., Bowen, L., Stott, J.L., 2007. Identification of the etiologic agent of epizootic bovine abortion in field-collected *Ornithodoros coriaceus* Koch ticks. Vet. Microbiol. 120, 320–327. doi: 10.1016/j.vetmic.2006.10.036.

Coker, M.R., Rauw, W.M., Nieto, N.C., Thain, D., Teglas, M.B., 2012. Hematologic and IgG responses of heifers experimentally infected with the agent of epizootic bovine abortion. Vet. Clin. Pathol. 41, 344–352. doi: 10.1111/j.1939-165X.2012.00446.x.

Constable, P.D., Hinchcliff, K.W., Done, S.H., Grünberg, W., 2017. Diseases Primarily Affecting the Reproductive System. Vet. Med. 1, 1758–829.

de la Fuente, J., Estrada-Peña, A., Rafael, M., Almazán, C., Bermúdez, S., Abdelbaset, A.E., Kasaija, P.D., Kabi, F., Akande, F.A., Ajagbe, D.O., Bamgbose, T., Ghosh, S., Palavesam, A., Hamid, P.H., Oskam, C.L., Egan, S.L., Duarte-Barbosa, A., Hekimoğlu, O., Szabó, M.P.J., Labruna, M.B., Dahal, A., 2023. Perception of Ticks and Tick-Borne Diseases Worldwide. Pathogens 12, 1258. doi: 10.3390/pathogens12101258.

Delano, M.L., Mischler, S.A., Underwood, W.J., 2002. Biology and Diseases of Ruminants: Sheep, Goats, and Cattle. Lab. Anim. Med. 1, 519–614. doi: 10.1016/B978-012263951-7/50017-X.

Failing, R.M., Lyon, C.B., McKittrick, J.E., 1972. The pajaroello tick bite. The frightening folklore and the mild disease. Calif. Med. 116, 16–19.

Fogaça, A.C., Sousa, G., Pavanelo, D.B., Esteves, E., Martins, L.A., Urbanová, V., Kopáček, P., Daffre, S., 2021. Tick Immune System: What Is Known, the Interconnections, the Gaps, and the Challenges. Front. Immunol. 12, 628054. doi: 10.3389/fimmu.2021.628054.

Givens, M.D., Marley, M.S., 2008. Infectious causes of embryonic and fetal mortality. Theriogenology 70, 270–285. doi: doi.org/10.1016/j.theriogenology.2008.04.018.

Golding, C.G., Lamboo, L.L., Beniac, D.R., Booth, T.F., 2016. The scanning electron microscope in microbiology and diagnosis of infectious disease. Sci. Rep. 6, 26516. doi: 10.1038/srep26516.

Grégoire, F., Bakinahe, R., Petitjean, T., Boarbi, S., Delooz, L., Fretin, D., Saulmont, M., Mori, M., 2020. Laboratory Diagnosis of Bovine Abortions Caused by Non-Maintenance Pathogenic Leptospira spp.: Necropsy, Serology and Molecular Study Out of a Belgian Experience. Pathogens 9, 413. doi: 10.3390/pathogens9060413.

Haddad, G., Bellali, S., Takakura, T., Fontanini, A., Ominami, Y., Khalil, J.B., Raoult, D., 2021. Scanning Electron Microscope: A New Potential Tool to Replace Gram Staining for Microbe Identification in Blood Cultures. Microorganisms 9, 1170. doi: 10.3390/microorganisms9061170.

Hall, M.R., Hanks, D., Kvasnicka, W., Bosomworth, A., Smith, H., Stott, J.L., Blanchard, M.T., Anderson, M.L., 2002. Diagnosis of epizootic bovine abortion in Nevada and identification of the vector. J. Vet. Diagn. Invest. 14, 205–210. doi: 10.1177/104063870201400303

Howarth, J.A., Moulton, J.E., Frazier, L.M., 1956. Epizootic bovine abortion characterized by fetal hepatopathy. J. Am. Vet. Med. Assoc. 128, 441–449.

Hromníková, D., Furka, D., Furka, S., Santana, J.A.D., Ravingerová, T., Klöcklerová, V., Žitňan, D., 2022. Prevention of tick-borne diseases: challenge to recent medicine. Biologia (Bratisl) 77, 1533–1554. doi: 10.1007/s11756-021-00966-9.

Jawor, P., Mee, J.F., Stefaniak, T., 2021. Role of Infection and Immunity in Bovine Perinatal Mortality: Part 2. Fetomaternal Response to Infection and Novel Diagnostic Perspectives. Animals 11, 2102. doi: 10.3390/ani11072102.

Jawor, P., Stefaniak, T., Mee, J.F., 2017. Immune and inflammatory biomarkers in cases of bovine

perinatal mortality with and without infection in utero. J. Dairy Sci. 100, 1408–14416. doi: 10.3168/jds.2016-11825.
Kendrick, J.W., 1976. Epizootic bovine abortion. Theriogenology 5, 99–101. doi: 10.1016/0093-691X(76)90030-3
Kennedy, P.C., Casaro, A.P., Kimsey, P.B., Durant, R.H.B., Bushnell, R.B., Mitchell, G.M., 1983. Epizootic bovine abortion: histogenesis of the fetal lesions. Am. J. Vet. Res. 44, 1040–1048.
Kimsey, P.B., Kennedy, P.C., Bushnell, R.B., Casaro, A.P., BonDurant, R.H., Oliver, M.N., Kendrick, J.W., 1983. Studies on the pathogenesis of epizootic bovine abortion. Am. J. Vet. Res. 44, 1266–1271.
King, D.P., Chen, C.I., Blanchard, M.T., Aldridge, B.M., Anderson, M., Walker, R., Maas, J., Hanks, D., Hall, M., Stott, J.L., 2005. Molecular identification of a novel deltaproteobacterium as the etiologic agent of epizootic bovine abortion (foothill abortion). J. Clin. Microbiol. 43, 604–609. doi: 10.1128/jcm.43.2.604-609.2005.
L'Huissier, P.G., Chihuailaf, R., Letelier, R., Allende, R., Ruiz, A., Junod, T., 2022. Monitoring different causal patterns of bovine abortion syndrome. Vet. Mex. OA 9, 1–22. doi: 10.22201/fmvz.24486760e.2022.652.
Lane, R.S., Burgdorfer, W., Hayes, S.F., Barbour, A.G., 1985. Isolation of a spirochete from the soft tick, *Ornithodoros coriaceus*: a possible agent of epizootic bovine abortion. Science 230, 85–87. doi: 10.1126/science.3898367.
Lane, R.S., Mun, J., Peribáñez, M.A., Fedorova, N., 2010. Differences in prevalence of Borrelia burgdorferi and Anaplasma spp. infection among host-seeking Dermacentor occidentalis, Ixodes pacificus, and *Ornithodoros coriaceus* ticks in northwestern California. Ticks Tick-borne Dis. 1, 159–167. doi: 10.1016/j.ttbdis.2010.09.004.
Lim, P.O., Sears, B.B., 1989. 16S rRNA sequence indicates that plant-pathogenic mycoplasmalike organisms are evolutionarily distinct from animal mycoplasmas. J. Bacteriol. 171, 5901–5906. doi: 10.1128/jb.171.11.5901-5906.1989.
McKercher, D.G., Theis, J.H., Wada, E.M., Loomis, E.C., Bolton, V., Ito, H., 1976. Recent studies on epizootic bovine abortion. Theriogenology 6, 251–262. doi: 10.1016/0093-691X(76)90018-2.
McDowell, J.V., Tran, E., Hamilton, D., Wolfgang, J., Miller, K., Marconi, R.T., 2003. Analysis of the ability of spirochete species associated with relapsing fever, avian borreliosis, and epizootic bovine abortion to bind factor H and cleave c3b. J. Clin. Microbiol. 41, 3905–3910. doi: 10.1128/jcm.41.8.3905-3910.2003
Nava, S., Beati, L., Dunlop, J., Guglielmone, A.A., 2014. Reestablishment of Amblyomma tenellum Koch, 1844 (Acari: Ixodidae). Ticks Tick Borne Dis. 5, 620–623. doi: 10.1016/j.ttbdis.2014.04.012.
Nava, S., Lareschi, M., Rebollo, C., Usher, C.B., Beati, L., Robbins, R.G., Durden, L.A., Mangold, A.J., Guglielmone, A.A., 2007. The ticks (Acari: Ixodida: Argasidae, Ixodidae) of Paraguay. Ann. Trop. Med. Parasitol. 101, 255–270. doi: 10.1179/136485907X176319.
Parola, P., Paddock, C.D., Socolovschi, C., Labruna, M.B., Mediannikov, O., Kernif, T., Abdad, M.Y., Stenos, J., Bitam, I., Fournier, P.E., Raoult, D., 2013. Update on tick-borne rickettsioses around the world: a geographic approach. Clin. Microbiol. Rev. 26, 657–702. doi: 10.1128/cmr.00032-13.
Reichel, M.P., Wahl, L.C., Hill, F.I., 2018. Review of Diagnostic Procedures and Approaches to Infectious Causes of Reproductive Failures of Cattle in Australia and New Zealand. Front. Vet. Sci. 5, 222. doi: 10.3389/fvets.2018.00222.
Richter, B., Ladinig, A., Nedorost, N., Weissenböck, H., 2010. A TaqMan quantitative polymerase chain reaction assay for the detection of *Lawsonia intracellularis* in fecal and tissue samples from pigs. J. Vet. Diagn. Invest. 22, 70–73. doi: 10.1177/104063871002200112.
Romero, R., Espinoza, J., Gonçalves, L.F., Kusanovic, J.P., Friel, L., Hassan, S., 2007. The role of inflammation and infection in preterm birth. Semin. Reprod. Med. 25, 21–39. doi: 10.1055/s-2006-956773.
Silhavy, T.J., Kahne, D., Walker, S., 2010. The bacterial cell envelope. Cold Spring Harb. Perspect. Biol. 2, a000414. doi: 10.1101/cshperspect.a000414.
Spezialetti, R., Osebold, J.W., 1991. Surface markers on bovine fetal lymphocytes and immunoglobulin synthesis in a congenital infection related to epizootic bovine abortion. Res. Vet. Sci. 51, 239–245. doi: 10.1016/0034-5288(91)90070-5.
Stott, J.L., Blanchard, M.T., Anderson, M., Maas, J., Walker, R.L., Kennedy, P.C., Norman, B.B., BonDurant, R.H., Oliver, M.N., Hanks, D., Hall, M.R., 2002. Experimental transmission of epizootic bovine abortion (foothill abortion). Vet. Microbiol. 88, 161–173. doi: 10.1016/S0378-1135(02)00109-8.
Studdert, M.H., McKercher, D.G., 1968. Bedsonia abortion of sheep. I. Aetiological studies. Res. Vet. Sci. 9, 48–56. doi: 10.1016/S0034-5288(18)34590-9.
Teglas, M.B., Drazenovich, N.L., Stott, J., Foley, J.E., 2006. The geographic distribution of the putative agent of epizootic bovine abortion in the tick vector, *Ornithodoros coriaceus*. Vet. Parasitol. 140, 327–333. doi: 10.1016/j.vetpar.2006.03.027.
Underwood, W.J., Blauwiekel, R., Delano, M.L., Gillesby, R., Mischler, S.A., Schoell, A., 2015. Biology and Diseases of Ruminants (Sheep, Goats, and Cattle). Lab. Anim. Med. 1, 623–694. doi: 10.1016/B978-0-12-409527-4.00015-8.
Vannucci, F.A., Gebhart, C.J. 2014. Recent Advances in Understanding the Pathogenesis of *Lawsonia intracellularis* Infections. Vet. Pathol. 51, 465–477. doi: 10.1177/0300985813520249.
Wang, S., Li, W., Wang, Z., Yang, W., Li, E., Xia, X., Yan, F., Chiu, S., 2024. Emerging and reemerging infectious diseases: global trends and new strategies for their prevention and control. Signal Transduct. Target Ther. 9, 223. doi: 10.1038/s41392-024-01917-x.
Welly, B.T., Miller, M.R., Stott, J.L., Blanchard, M.T., Islas-Trejo, A.D., O'Rourke, S.M., Young, A.E., Medrano, J.F., Van Eenennaam, A.L., 2017. Genome Report: Identification and Validation of Antigenic Proteins from *Pajaroellobacter abortibovis* Using De Novo Genome Sequence Assembly and Reverse Vaccinology. G3 (Bethesda) 7, 321–331. doi: 10.1534/g3.116.036673.
Yabsley, M.J., Davidson, W.R., Stallknecht, D.E., Varela, A.S., Swift, P.K., Devos, J.C. Jr, Dubay, S.A., 2005. Evidence of tick-borne organisms in mule deer (*Odocoileus hemionus*) from the western United States. Vector Borne Zoonotic Dis. 5, 351–362. doi: 10.1089/vbz.2005.5.351.
Yen, N.T.N., Chung, D.D., Hong, N.T.K., Cham, N.P., Nhan, V.T., Linh, D.T.L., Ngoc, N.L.B., Thai, N.M., Nga, N.D., Anh, N.T., 2023. Isolation, phylogenetic analysis and bioprospection of myxobacteria from Vietnam. Biodiversitas 24, 5653–5663. doi: 10.13057/biodiv/d241047.
Youssefi, M.R., Ebrahimpour, S., Rezaei, M., Ahmadpour, E., Rakhshanpour, A., Rahimi, M.T., 2014. Dermatitis caused by Ctenocephalides felis (cat flea) in human. Caspian J. Intern. Med. 5, 248–250.