Epizootic bovine abortion (foothill abortion): the disease, diagnosis and control strategies
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Historical perspective
Epizootic bovine abortion (EBA) was recognized as a disease entity of beef cattle in the 1950’s in California. The disease, referred to regionally as foothill abortion, is believed to have existed in California as early as the 1920’s. The name, foothill abortion, was appropriately coined as the disease was noted to occur exclusively in pregnant cattle that were grazed in foothill and mountainous regions in California. The economic impact of foothill abortion was of such significance that it contributed to the establishment of the University of California’s School of Veterinary Medicine in Davis and research funds to study it were established as a permanent line-item in the state’s legislative budget.

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The disease
Foothill abortion is now recognized to occur in California, Southern Oregon and Nevada; occurrence in Southern Idaho is suspected, but not confirmed. The disease is expressed as a term abortion in beef cattle with gross and microscopic pathology sufficiently unique that it is typically diagnostic. A “foothill fetus” can present grossly in many different forms; gestational age at the time of infection and the associated fetal immune response contribute to the variation. The most typical presentation is that of a near-term haired-fetus with a pot-bellied appearance due to excessive accumulation of ascites, mucosal petechial hemorrhages in the eyelids, tongue and oral cavity, and enlarged, easily palpable prescapular lymph nodes. Occasionally, small denuded raised skin lesions may be seen. Fetuses can be aborted dead or delivered live, the latter typically dying within hours. A subset of infected calves born alive may survive for variable periods and would be considered weak calves. A smaller number of aborted affected fetuses will present without hair, with or without the pot-belly, and resemble the appearance of a pig. These latter fetuses are typically of a younger age and have undergone substantial autolysis. Upon revealing the abdominal cavity, via incision through the right side of the fetus, a variety of gross anomalies can be noted including excessive ascites and fibrin deposition, an enlarged mottled liver with rounded edges; the spleen can be sufficiently enlarged such that it is visible without manipulating the intestines. The mesenteric lymph nodes are typically enlarged and numerous, resembling grape clusters running the length of the small intestine. Extensive and enlarged visible lymph nodes are often present throughout the tissues. Grossly, the thymus presents with either distinct petechial hemorrhages on the white background or as a darkened tissue mass with extensive hemorrhage and necrosis and firm texture due to fibrin deposition. Microscopic examination of necropsy tissues reveals an extensive and acute vasculitis, focal-necrotizing lesions often resembling pyogranulomas in lymph nodes and spleen and a thymus characterized by atrophy of cortical thymocytes and infiltration by macrophages; these thymic lesions are pathognomonic for foothill abortion.

As a final note on the disease, recent studies testing the safety and efficacy of a live-virulent vaccine (see “Control” section below) have identified new and unexpected characteristics associated with infection by the causative bacterial pathogen, Pajaroelllobacter abortibovis. Experimental infection of cattle within 3-4 weeks of breeding can result in embryonic mortalities approaching 10%. Affected animals can successfully breed-back if the bulls are maintained in the herd over the summer months but short breeding periods of 30 to 45 days can result in increased numbers of non-pregnant animals. The basis of this anomaly is assumed to be due to recent evidence suggesting the bacterial pathogen can remain active in an infected animal for upwards of 60 days post-infection.

Foothill abortion has never been described in any species other than the bovine. Attempts to experimentally infect pregnant sheep, resulting in abortion or birth of weak lambs, were unsuccessful.
The slow intracellular replication of the causative agent (~1 day) requires that a long gestational period be available for it to become disseminated throughout the body prior to development of a vigorous fetal immune response that ultimately contributes to lesion development and death. The gestational period in sheep, goats and deer is sufficiently short that the complex bacterial pathogenesis cannot unfold prior to birth.

The etiologic agent
The search for the etiologic agent of foothill abortion spanned 50 years and began in the 1950’s with a focus on chlamydia and development of an associated vaccine that never caught traction. Upon identification that a unique tick, *Ornithodoros coriaceus*, (see “Disease transmission” section below) was the vector of foothill abortion, efforts were reinitiated to identify the causative agent, resulting in a focus on incriminating a retrovirus. These efforts were replaced in the 1980’s with a focus on *Borrelia coriaciae* and unidentified spirochetes as potential causes of foothill abortion. All of these studies were hampered by an inability to experimentally transmit the disease with any consistency; feeding 100’s of field-trapped *O. coriaceus* ticks on susceptible pregnant heifers was the only known way to transmit the disease and this was only successful approximately 50 percent of the time. Development of a reliable mechanism for transmission of foothill abortion in the 1990’s using cryopreserved thymus from select aborted fetuses facilitated studies that ultimately demonstrated the causative agent to be antibiotic susceptible. This advance, associated with the application of modern molecular biology techniques, culminated in 2005 with identification of a unique bacterium within the Myxococcales order, as being the etiologic agent. This unique bacteria has tentatively been coined *Pajaroellobacter abortibovis*, based upon a combination of the name of the tick vector, type of microbe, the disease and the susceptible host.

Disease transmission
Foothill abortion is an arthropod-borne bacterial disease that is transmitted by *O. coriaceus*; commonly referred to as the Pajaroello tick, initially coined by native American Indians residing in the coastal regions of Central California. The tick was feared more than rattlesnakes due to a severe hypersensitivity that could be established following a first bite. The unique distribution of the Pajaroello tick in foothill and mountainous regions of California contributed to its’ identification as being the vector of foothill abortion; the geographic distribution of the tick closely resembled the distribution of foothill abortion. While the geographic distribution of the tick extends down through Mexico and into Central America, the disease has never been reported south of the U.S border. The tick lives in the duff under trees and/or brush in arid environments, typically in mammalian bedding areas where they have somewhat reliable access to an occasional blood meal. The tick is attracted to CO₂ emitted by a warm-blooded host. Nymphs and adults obtain a blood meal within 20 to 30 minutes, then detach and fall back into the duff; larvae can remain on the host for up to a week and are believed to be responsible for slowly extending the distribution of the tick and the disease in an eastward direction. The tick undergoes multiple stages of development from the hatched larvae through nymph stages, ultimately becoming an adult. The tick appears to have the capacity to live in excess of ten years and larger ticks can survive for several years without a blood meal. Development of molecular diagnostic probes (see “Diagnosis” section) has permitted researchers to identify the presence of *P. abortibovis* in the salivary gland of field-collected ticks. Approximately 10 to 20% of ticks are infected, but only a small percentage (probably in the range of 1-2%) harbor sufficient bacteria to transmit the disease. No associations have been identified between presence of the bacteria with tick age, size or sex; transovarial transmission of the bacteria in ticks has not been demonstrated. The reservoir of the bacterial pathogen is currently unknown and could include the soil/duff in which the ticks live and/or unidentified mammalian and avian hosts.

Diagnosis
Diagnosis of foothill abortion has classically been based upon a combination of gross and microscopic anatomy, elevated levels of fetal immunoglobulin (Ig) and knowledge of dam exposure to areas inhabited by the Pajaroello tick vector during the window in which the fetus is susceptible to
infection (~60-150 days gestation). While a “classical” presentation of foothill abortion lends itself to a definitive diagnosis based upon pathognomonic lesions in the thymus, not all cases are straightforward. An immunohistochemistry assay is now routinely used as an adjunct to diagnosis by facilitating microscopic visualization of the causative bacteria in thin sections derived from formalin fixed necropsy tissues. A molecular diagnostic, based upon a polymerase chain reaction (PCR) applied to fetal necropsy tissues, has also proven to be a valuable tool in supporting diagnosis of foothill abortion, especially when the fetus has been badly scavenged by predators. A serologic assay for identification of *P. abortibovis* -specific antibodies in fetal serum or other body fluid has successfully been developed. This serologic assay is proving to be useful in identifying *P. abortibovis*-associated abortions, including aborted fetuses and weak calves that have largely cleared the bacterial infection. Serologic diagnosis requires that the subject has not ingested colostrum. The identification of antibodies specific for *P. abortibovis* have recently been identified in a few term abortions and apparent dystocias that did not present as foothill abortion based upon gross and microscopic pathology. The significance of such infections on near-term losses is currently unknown. Lastly, the serologic assay is being applied to identify past exposure of mature cattle to *P. abortibovis* to better define the geographic distribution of the pathogen in a manner that is not dependent upon collection of the Pajaroello tick or diagnosis of the disease.

**Control**

Control of foothill abortion has classically been limited to alteration of management practices that can sometimes reduce, though not eliminate, foothill abortion-associated losses. Two often-used techniques include: i) minimizing exposure of naïve replacement heifers to tick habitat during the gestational period in which the fetus is susceptible (currently considered to be about 60 to 150 days gestation) or ii) attempting to expose naïve replacements to the tick vector prior to breeding. Some producers have reported success in controlling foothill abortion by running feeder steers on a tick habitat in the spring in an attempt to “feed up” the ticks prior to introduction of susceptible pregnant heifers into that same habitat. The logic behind this approach is to reduce the number of hungry ticks in the area for several months, allowing the heifer’s developing fetus to sufficiently mature beyond 150 days gestation. A well-established approach to managing foothill abortion is breeding in the winter months when the ticks are at minimal activity and calving in the fall. This is more practical in moderate climates with winter grass range such as California’s coastal range and low-elevation foothill regions of the Sierra Nevada mountains bordering the Central Valley. The greatest losses to foothill abortion typically occur when naïve pregnant cattle are introduced from non-endemic areas into Pajaroello tick habitat. Such practices should be avoided at all costs as losses can approach 90%.

Development of a vaccine for foothill abortion became a priority upon identification of the causative bacterial agent of foothill abortion, *P. abortibovis*. Efforts to propagate the bacteria in a variety of synthetic media and primary and secondary cell culture systems were met with limited success. The successful infection of mice with severe-combined immunodeficiency (SCID) provided a potential way forward for vaccine production. Infection of SCID mice with *P. abortibovis*, derived from fetal bovine necropsy tissues, results in development of a wasting disease at 60-70 days post-inoculation. While lesions typical of foothill abortion are absent in necropsied mice, spleens are enlarged and contain viable intracellular bacteria. Spleens can be converted into single-cell suspensions by pressing the macerated organ through sterile screen meshes; such cells can be successfully rate-frozen and cryopreserved in liquid nitrogen with long-term maintenance of cell and bacterial viability. A flow-cytometric technique has been developed to determine the percentage of splenocytes harboring bacteria. The ability to quantitate the number of infected cells in a given population of murine splenocytes provided the necessary quality control (ability to control the dose of bacteria) to proceed with development of an experimental live virulent vaccine for foothill abortion. Naïve heifers that were vaccinated, then bred and challenged at the peak of fetal susceptibility (90-100 days gestation) produced healthy calves while the majority of negative controls had term abortions. Preliminary field studies with the experimental foothill vaccine have been conducted in multiple herds in California and Nevada with no systemic reactions, minor reactions at the vaccine injection site and no documented cases of foothill abortion. To date, the
vaccine has enjoyed 100% success in preventing foothill abortion under both experimental and field conditions. Efforts are currently underway at the University of California-Davis to license and commercialize the cryopreserved vaccine.

**Economic impact**

Foothill abortion has, and continues to be, the #1 disease in California negatively impacting calf production by beef producers; the relative impact in Oregon and Nevada is unknown. The economic impact of “foothill” is exaggerated due to the heifer/cow’s production being lost for an entire year since the abortion occurs at term. Additional impacts of the term abortion, typically in replacement heifers, are associated with impaired clearance of the placenta that is often associated with compromised subsequent conception and irreparable damage to the distended udder in animals grazed in brushy country. Altering management practices to reduce foothill abortion losses in endemic areas by fall-calving (discussed in the “Control” section) can result in reduced feed efficiency on summer range, especially on ranches east of the Sierra Nevada and Cascade Mountains where cattle must be fed hay over the winter months.