Diagnosis of infectious abortion in domestic ruminants

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Abstract

Abortion problems in a client's herd will often prompt the veterinarian to seek the assistance of a veterinary diagnostic laboratory. The chances of obtaining an answer for the abortions are improved when there is good communication between the veterinarian and diagnostician which leads to appropriate sampling and test selection. A persistent effort in abortion diagnosis is warranted as many surveys find that a cause is determined in less than half of abortion submissions to diagnostic laboratories. The majority of diagnosed abortions are attributed to infections by a moderate number of bacterial, viral, fungal and protozoal agents. The pathology and other findings used in the laboratory diagnosis of the major infectious agents causing abortion in the cattle, sheep and goats will be discussed.

Keywords: Infectious abortion, diagnosis, domestic ruminants

Introduction

Veterinarians confronted by a herd abortion problem often seek assistance from a veterinary diagnostic laboratory that has the capacity to perform a variety of pathology, microbiology and immunology procedures to help identify the cause. Abortion diagnosis is challenging as indicated by the fact that an etiology, most attributed to infections, is identified in less than half of submissions. In the past several decades there has been improvement in the diagnostic success in abortion cases, likely due to improvements in procedures and new knowledge about significant causes. There are regional differences in the infectious agents identified in various geographic locations, presumably reflecting various factors such as climate, production type, feeds, management practices, vaccination programs, as well as sampling and laboratory procedures available.[1-5]

Abortion diagnosis protocol

Information provided with the submissions about the herd abortion problem may help suggest potential causes and exclude others. Some useful information would include an estimate of the abortion rate in the herd, the duration of the problem, and the gestational ages of the abortions. Other information to include with the submission would be whether the aborted fetuses are fresh or autolyzed, the age of the aborting dams, whether the placentas are retained, whether aborting animals appear sick, whether natural or artificial breeding is used, and the vaccination history.

Pathognomonic gross lesions are uncommon and may be obscured by autolysis. Gross lesions are often undependable guides by which to select specific diagnostic tests so most diagnostic laboratories use a standardized diagnostic protocol containing a panel of diagnostic procedures aimed at identifying the relevant abortifacients known to be associated with abortions in their region. There are differences in the procedures selected as part of the abortion protocol among veterinary diagnostic laboratories depending on many factors. Consult your diagnostic laboratory to determine the optimal samples and conditions to submit specimens in an abortion workup. The web sites that most laboratories maintain are an efficient way to obtain information on specific test and sample requirements.

The following example of an abortion protocol can be modified depending on the condition and type of samples submitted, or other circumstances. The intact aborted fetus, placenta and a serum sample from the dam are the optimal specimens. When available, samples from several abortions are recommended. The placenta is often critical to successful determination of the cause of abortion, particularly in the sheep and goats where the placenta may be the primary tissue affected. A complete necropsy examination is performed on the fetus to identify any gross lesions and to estimate the fetal age and degree of autolysis. If the entire fetus cannot be submitted the preferred samples would include

complete selection of formalin fixed tissues and fresh lung, liver, kidney, placenta, fetal thoracic fluid, and abomasal fluid. These samples should be submitted chilled in separate sterile containers and the fluids in sterile tubes (not syringes). It is important that both the veterinarian and client are aware that there are numerous zoonotic infections associated with ruminant abortion (brucellosis, leptospirosis, listeriosis, salmonellosis, Chlamydophila, Coxiella and others), so appropriate precautions should be employed in sampling and shipping specimens. Formalin fixed tissues for histopathology examination include brain, lung, heart, liver, kidney, adrenal, spleen, thymus, lymph node, skeletal muscle, abomasum, small intestine, eyelid and placenta.[6,7]

The routine microbiological diagnostic protocol includes an aerobic bacterial culture and *Brucella* culture on the lung, an aerobic culture and *Campylobacter* culture on the liver, and an aerobic culture, *Brucella* culture, and *Campylobacter* culture on the abomasal fluid. The abomasal fluid is also examined with a gram stain and a dark field examination for *Campylobacter* and trichomonads. The abomasal fluid may be cultured for *Tritrichomonas foetus* on appropriate media based on positive dark field examinations or other indications. A direct smear on the kidney is examined for leptospires by fluorescent antibody staining. Bacteria cultures of the placenta are dependent on condition and gross lesions. Fungal cultures are performed if there are suggestive placental or skin lesions.

Routine virology procedures vary among laboratories. Routine virus isolation in tissue culture on an organ pool of fetal tissues, usually including lung, liver, spleen, kidney, adrenal and placenta, is performed by some diagnostic laboratories. Other protocols may limit routine virology testing to bovine herpes virus (BHV-1) and bovine viral diarrhea virus (BVDV) fluorescent antibody stains in cattle and border disease virus (BDV) in sheep on frozen sections of fetal lung (or liver) and kidney. BHV-1 and BVDV virus immunohistochemistry procedures are relatively specific and sensitive with the advantage that the pathologist can retrospectively test for the presence of the virus based on the lesions observed the fetal tissues. Polymerase chain reaction (PCR) assays for the DNA of various bacterial, viral and protozoal agents are available for use in some diagnostic laboratories.

An abortion serology panel on a single serum sample from an aborting dam may help determine if there had been exposure to an agent but usually cannot differentiate between vaccination and natural exposure, or between recent versus incidental previous exposure. Paired acute and convalescent serum samples rarely can identify a significantly rising titer to a particular pathogen because maternal seroconversion often precedes abortion and paired serum samples collected at and following abortion may not demonstrate an increasing titer. Maternal serology is most useful when serum from non-vaccinated animals is examined, when several animals from the herd are tested, and when history on each animal is provided. Some advocate collecting and storing serum from select pregnant animals for use as a paired sample in the event of an abortion. Routine serology on the bovine dam includes BHV-1, BVDV types I and 2, leptospira serovars *canicola, grippotyphosa, hardjo, icterohamorrhagiae,* and *pomona , Neospora caninum,* and brucella serology. In sheep and goats usual dam serology tests may include BDV, leptospira serovars, bluetongue virus, brucella and *Toxoplasma gondii* serology.

Immunologic procedures on the fetus depend on the post mortem condition and fetal age. A quantitative immunoglobulin assay for bovine IgG can be performed on blood or thoracic fluid. If the fetal IgG is elevated (>20 mg/dl), this is an indication of an active immune response by the fetus to a foreign antigen which is usually an infectious agent.[8] If there is evidence of elevated IgG, serology for IBR, BVD, *Leptospira*, *Neospora*, *Brucella abortus*, bluetongue virus and parainfluenza 3 virus can be performed. When specific fetal titers are elevated, they suggest fetal exposure to that agent. On occasion, low titers to one or more of these agents may be present in a fetus without other evidence of infection so a cautious interpretation is warranted. The source of antibody in the fetal fluids, particularly when antibody to multiple agents is present, is not certain but possibly maternal antibodies may cross to the fetus due to placental lesions.

When available, the placenta should be examined and sampled. In a fresh normal placenta the cotyledons are red with a clear, translucent intercotyledonary placenta although with autolysis the cotyledons become dull brown and the intercotyledonary placenta less translucent. Intercotyledonary

opacity can be associated with edema, inflammation or fibrosis. Exudate on the surface or thickening of the chorioallantois is evidence of inflammation. Cotyledons whose surface is depressed relative to the surrounding intercotyledonary placenta ("cupping") can be an indication of inflammation in the surrounding stroma. Gross abnormalities in the cotyledons include adherent caruncular tissue, hemorrhage, necrosis and exudation.

An estimation of the gestational age of the fetus can be made from the crown to rump length and the extent and distribution of hair development.[9] Potentially useful external changes include evidence of meconium staining implying fetal distress and round raised skin plaques that can be associated with mycotic infection. With the fetus opened, an estimation of the degree of autolysis can be made. Evidence that the fetus may have been alive at the time of parturition such as lung inflation, hemorrhage surrounding the umbilical vessels or thrombosis of the umbilical arteries should be noted. A freshly aborted fetus will usually have clear amber colored fluid in the body cavities but within one to two days following death, serosanguinous fluid collects in the body cavities and subcutis. This process is followed by gradual dehydration of the tissues such that by a week following fetal death the fetus is dehydrated with no abomasal content.

The selection of fetal tissues for histopathology examination varies among laboratories due to a variety of factors. While autolytic changes are common and can be severe, unless the fetus is mummified, histopathology will usually provide some information concerning any evidence of infectious disease and therefore help to evaluate whether the microbiology or immunology results are relevant. Examination of a full selection of tissues is recommended whenever possible. Although autolysis may render the fetal brain to consist of liquefied fragments, collection of this material into formalin is still recommended because the histologic detail is surprisingly preserved. A complete histological examination of the fetal tissues provides information about the distribution of lesions which may also suggest the route of fetal infection and potential causes. Some infections proliferate in the placenta then enter the fetus through the umbilical vessels leading to hepatic and systemic changes. Examples of this pattern of fetal injury can include such agents as *Listeria*, *Salmonella*, BHV-1 and *Neospora.* In other bacterial and fungal infections which initiate a placental infection and then invade via the placental fluids surrounding the fetus the inflammatory lesions are usually associated with lungs, digestive tract or skin. Histologic examination of the eyelid having both conjunctiva mucosa and skin can be a useful and sensitive indicator of infection.[8] On occasion in situations with severe placentitis, there may not be any significant inflammatory lesions in the fetus.

Diagnostic features of infectious causes of abortion

The following sections discuss the presentation and diagnosis of commonly diagnosed infectious causes of abortion in cattle, sheep and goats.

Bacterial infections

Sporadic abortions associated with opportunistic bacterial infections. A diverse group of bacterial species are associated with opportunistic infections of the placenta and fetus resulting in abortion. These bacteria are not contagious pathogens but are commonly found in the environment or on mucosal surfaces. A maternal bacteremia is the presumed means by which they reach the gravid uterus and subsequently infect the placenta. The specific reasons for the susceptibility of the placenta to colonization by these bacteria is uncertain but factors such as local oxygen and nutrient levels, decreased inflammatory responses and isolation from maternal immunity are likely involved. Among the bacteria in this group *Arcanobacterium pyogenes* is the most commonly identified but *Bacillus* spp., *E. coli*, *Histophilus somni*, *Pasteurella* spp., *Pseudomonas* spp., *Serratia marcescens*, *Staphylococcus* spp., *Streptococcus* spp and many other bacteria species have been associated with sporadic placentitis and abortion.[1,10,11] While opportunistic bacterial infections are a significant proportion of diagnosed abortions their occurrence is sporadic. Abortion storms are not associated with this group of bacteria so if multiple abortions occur in a herd this might suggest maternal health issues that could enhance hematogenous

bacterial infections or there could be additional infectious agents involved in the abortion. A possible example is that up to a third of bovine abortions associated with *Arcanobacterium pyogenes*, *Bacillus* sp. or mycotic infections had concurrent BVDV virus infection in one large Midwest abortion survey.[12]

Sporadic bacterial abortions may occur at any stage of gestation, but most are identified in the second half of gestation. There are no specific signs in the dam although the placenta may be retained. The degree of fetal autolysis is variable. The placenta may have yellow to brown surface exudation. Gross fetal lesions may infrequently include fibrin exudation in body cavities. Histologic lesions include suppurative placentitis and neutrophilic fetal bronchopneumonia of varying severity. In *Arcanobacterium pyogenes* infection large clusters of bacterial colonies may be present in the lung with minimal inflammation. As the bacteria involved are common in the environment or mucosa, their presence in fetal tissues might be due to incidental contamination. Therefore in order to establish an etiologic diagnosis the bacteria should be isolated in pure or nearly pure culture from abomasal contents or tissues and there should be lesions consistent with a bacterial infection in the fetus or placenta.[7]

Brucellosis. Brucellosis in sheep, goats and cattle is caused by several brucella species, *Brucella ovis*, *Brucella melitensis* and *Brucella abortus*. *Brucella ovis* is a relatively newly recognized mutant that is predominately associated with epididymitis in the ram although the infection can be transmitted to the ewe at breeding resulting in infertility or on occasion, placentitis with abortion or premature live lambs. *Brucella melitensis* is the major cause of brucellosis in sheep and goats although the disease is not currently present in North America. *Brucella abortus* infection causes brucellosis in cattle worldwide. The infection is now rare in the United States and Canada due to eradication programs but pockets of infection persist primarily in wildlife populations. Infection is primarily through ingestion, the bacteria multiply in regional lymph nodes and then spread hematogenously to other organs, most importantly, the mammary gland, mammary lymph nodes and gravid uterus usually during the second trimester. Bacteria invade the placental trophoblasts and cause chronic placentitis and fetal infection resulting in fetal death due to placental disruption and endotoxemia. Fetuses abort 24 to 72 hours after *in utero* death and abortion usually occurs after the fifth month of pregnancy. Metritis and retained placenta are common. Grossly there is often a severe placentitis with edema, focal necrosis of cotyledons and thickened intercotyledonary areas with adherent yellowish exudate. The fetus is frequently autolyzed with no gross lesions. Histologically, there is severe placentitis with numerous bacteria visible in chorionic epithelial cells. Fetal lesions consist of bronchopneumonia which can vary in severity and character from acute neutrophilic bronchopneumonia to more chronic pleocellular bronchointerstital pneumonia with periairway infiltrate of mononuclear cells. Bacterial isolation is necessary to confirm the diagnosis. *B. abortus* can be isolated from various sources including fetal abomasal fluid, lung, placenta, uterine fluid and milk. Various serologic tests have been developed for governmental surveillance and detection of cattle exposed to *B. abortus.*[13]

Listeriosis. Listeria species are widespread in the environment and abortion due to *Listeria monocytogenes* and *L. ivanovii* infections occur throughout the United States. Most abortions have a sporadic occurrence but in some conditions abortion storms may occur. In some instances, there may be illness in aborting dams with fever and anorexia due to metritis. Listeriosis can cause encephalitis but this is not commonly seen in association with abortion. The infection can be spread by ingestion from environmental contamination of the feces of carrier animals and discharges from aborting animals. Outbreaks of listeria abortions have been associated with ingestion of poorly fermented silage which provides a favorable environment for the proliferation of the organism.

Fetuses are usually aborted in the third trimester and often markedly autolyzed. The placenta is usually retained at abortion. Gross lesions are often absent or obscured by autolysis but in some, pinpoint white to yellow foci are present in the liver. Additional gross findings may include small pale foci in placental cotyledons, and fibrin in body cavities. The histopathologic changes include suppurative placentitis and multifocal necrotizing or suppurative hepatitis. Focal necrotizing mucosal lesions with

bacterial colonization may be present in the intestine. In addition, meningitis and intravascular bacterial colonization in many organs with or without associated inflammatory lesions is sometimes encountered. In most aborted fetuses listeria species are present in multiple tissues and usually does not require cold enhancement for successful isolation. In fresh tissues, liver impression smears or abomasal fluid can be gram stained to identify gram-positive coccobacilli. In fixed tissues, gram staining is often useful in multiple tissues particularly liver sections. Immunohistochemistry stains for *Listeria monocytogenes* utilizing commercially available antibody can assist the diagnosis when a positive culture result is unavailable.

Salmonellosis. In the United States, abortions attributed to salmonella species infections are not common and usually present as sporadic occurrences. Although, in the United Kingdom and some other regions of the world salmonella abortion is a significant cause of both enzootic and epizootic abortion in cattle and sheep. Most cattle abortions are associated with *Salmonella dublin* infections but other serotypes can be involved. In sheep, occasional abortion outbreaks in densely populated flocks have been associated with *Salmonella abortus-ovis* and *S. brandenburg.* The infection is presumed to originate from the intestinal tract with bacteremic episodes leading to the localization and proliferation in the placentome. The abortions are usually in the second half of gestation and the placenta is often retained. The chorioallantois is thickened with fibrinous fluid with a diffusely grey to red chorionic surface. Portions of caruncular tissue may be adherent to the cotyledons. The fetus is usually quite autolyzed and may be emphysematous. Usually no remarkable gross lesions can be identified though indistinct pale foci may rarely be present in the liver. In the placenta there is neutrophilic placentitis and mineralization with bacterial proliferation in cotyledonary villi. In the liver there can be a multifocal suppurative hepatitis. Lung lesions may be minimal consisting of neutrophilic bronchial exudate. Salmonella and listeria abortions have similarities in that the bacterial infection proliferates in the placenta followed by massive infection of the fetal liver, septicemia and death, often without development of bronchopneumonia typical of some other bacterial infections of the placenta.[14]

Leptospirosis. Leptospirosis is likely an under-diagnosed cause of infertility and abortion. The most significant serovars of *Leptospira interrogans* associated with bovine abortion are *L. hardjo* and *L. pomona* though rarely *Leptospira interrogans* serovars *icterohemorrhagiae* and *grippotyphosa* have been associated with bovine abortion. In sheep, leptospirosis is not a common cause of late term abortion and stillbirth although outbreaks in intensively managed conditions may occur. The major serovar involved is *L. hardjo*. *Leptospira hardjo* serovars are adapted to cattle who serve as the maintenance host while other serovars of leptospira involved in bovine abortions are maintained in other domestic or wildlife species. Leptospires can be shed in urine for several weeks and more prolonged urine shedding can be observed with *L. hardjo* infections. Leptospires can survive in wet environments for up to 30 days and can penetrate intact mucous membranes or abraded skin. Abortion may be the only clinical sign observed although fever, hemolytic anemia, hemoglobinuria, icterus, and mortality can be seen in younger cattle. In lactating cattle, agalactia and mastitis can occur with flaccid udders and thick yellow to occasionally blood-tinged secretions.[15-16]

Reproductive disease can occur one to three months following initial infection with *L. hardjo* and is associated with infertility, abortions four months to term, and weak calves. Abortion due to *L. pomona* usually occurs in the last trimester. The herd abortion rate seldom exceeds 10% with *L. hardjo* infections but can be higher with herd infections of *L. pomona.* The aborted fetus is usually autolyzed. Icterus may be seen in late gestation fetuses infected with *L. pomona*. Histologic lesions may not be observed but in some cases renal tubular necrosis and interstitial nephritis is present. Bile retention within liver canaliculi may be present. Nonsuppurative meningitis has also been reported.

Because leptospires are labile and difficult to culture, bacterial isolation is impractical for routine diagnostics. Identification of leptospires by darkfield microscopy of fetal fluids or silver stains of fetal tissues is rarely successful. Fluorescent antibody examination of fetal kidney smears using multivalent

antisera is a convenient, rapid procedure although not highly sensitive and specific. The specific leptospira serovar involved cannot be determined with this procedure. Immunohistochemistry staining is sometimes useful in identifying leptospires in bovine fetal tissues but autolytic fragmentation of the spirochetes can make interpretation difficult. PCR assays are available and used by some diagnostic laboratories to identify leptospira in fetal tissues.

Maternal serology using the microscopic agglutination microtiter test may be useful in the diagnosis of leptospirosis, though caution must be used to distinguish between vaccination, previous exposure, and recent infection. Serology for *L. hardjo* is especially difficult to interpret since infected animals often have a low or negative titer at the time of abortion. Higher serologic titers are associated with *L. pomona* infection at the time of abortion but seroconversion usually precedes abortion and the titer may be declining. It can be difficult to distinguish between vaccination and field exposure titers although multivalent vaccines usually produce low and short-lived titers compared to recent field exposures. In addition, the multivalent bacterins usually exhibit a pattern of elevated titers to multiple serovars as contrasted with elevated titers to a single serovar following field exposure. Fetal titers of 1:40 or above would be supportive of a diagnosis but most infected fetuses have no detectable titer.

Chlamydophila abortus. *Chlamydophila (Chlamydia) abortus* is a significant cause of late term abortion in sheep and goats. Herd outbreaks may occur in pregnant animals which acquire the infection orally from contaminated fecal or placental sources. Intestinal colonization can be followed by blood borne infection of the placenta resulting in placentitis and abortion. The placental lesions are often grossly evident with cotyledonary necrosis and exudation with intercotyledonary opacity and thickening. The fetus is usually well preserved and only rarely there may be pinpoint necrotic foci visible in the liver. Histologically placentitis is the most consistent feature with chorionic epithelial necrosis and pleocellular exudation. Remaining trophoblasts may contain intracytoplasmic organisms. The stroma of the chorioallantois is expanded by edema and mixed inflammatory cells, frequently with fibrinoid vasculitis of major arteries. Gimenez stained impression smears of placenta can demonstrate elementary bodies suggestive of *Chlamydophila* although specific antibody utilizing either a fluorescent antibody stain on impressions smears or immunohistochemistry stains on histologic sections is needed for confirmation.[17]

Ureaplasma diversum. *Ureaplasma diversum*, in the Mycoplasma family, is a common mucosal inhabitant of the reproductive and respiratory tract of cattle. There is evidence of considerable genetic variation among *U. diversum* isolates which could be associated with more pathologic potential in some stains. *Ureaplasma diversum* has been associated with granular vulvitis, infertility, embryonic death, abortion, stillbirths and the birth of weak calves. In North America, the diagnosis of *Ureaplasma diversum* as a cause of abortion in cattle is regional. In some northern regions a substantial portion of abortions are attributed to this infection while in other regions it is rarely identified. The differences may reflect differences in infection rate or perhaps a lack of appropriate microbiologic procedures regionally available by diagnostic laboratories by which to identify this fastidious organism.[18]

Fetuses are usually aborted the last third of gestation and stillbirths or weak calves may occur. The aborted fetuses are often in fresh condition. Retained placenta is frequently reported. There is placentitis in which the amnion is often most affected portion of the placental membranes. The amnion is thick and opaque with multifocal to extensive areas of hemorrhage, fibrin exudation, necrosis and fibrosis. Similar changes may be present in the chorioallantois which are usually more severe on the allantoic surface. The cotyledons may be tan to dark red, cupped with adherent caruncular material. Histologic changes in the stroma of the chorioallantois and amnion include fibrosis, necrosis and mineralization with macrophage and plasma cell infiltrates and mononuclear vasculitis. In the fetus the lungs may be swollen and firm grossly. Histologically, the lung lesions consist of a nonsuppurative alveolitis and periairway mononuclear infiltrate. Erosive lymphoplasmocytic conjunctivitis has been reported.

Ureaplasma diversum is a common inhabitant of the upper respiratory tract and lower reproductive tract of cattle so contamination of placental and fetal tissues is a potential confounding factor in diagnosis. Diagnosis of *U. diversum* as the cause of abortion can be supported by the isolation of the organism from the fetus or placenta, or by demonstration of specific *U. diversum* DNA by PCR assay coupled with the presence of compatible lesions in the lung and placenta.[19]

Campylobacter species. In sheep and goats, *Campylobacter fetus* ss *fetus* and *C. jejuni* (ss *jejuni*) infections are a significant cause of late term abortion, stillbirths and weak lambs/kids. Campylobacter abortions can occur as a flock outbreak in which the intestinal infection can spread orally through the flock resulting in new intestinal infection and subsequent hematogenous infection of the placenta in pregnant naive animals. These campylobacter species also cause sporadic abortions in cattle through a similar mechanism of hematogenous spread of an intestinal infection. However, cattle have another clinically important campylobacter species, *Campylobacter fetus* ss *venerealis*, which is a venereal disease that causes infertility with early embryonic death and occasional abortions occurring at four to seven months gestation. In bovine campylobacter abortion it is important to identify the specific species involved as *C. fetus* ss. *venerealis* is venereally transmitted and must be differentiated from the other intestinal campylobacter species.

Gross lesions of campylobacter abortion are usually found in the placenta. The changes are not unique but usually consist of swelling, necrosis and yellow-brown discoloration of cotyledons with intercotyledonary thickening with variable exudation. Aborted fetuses can be in variable post mortem condition ranging from fresh to autolyzed. Serosanguinous to fibrinous exudation is often present in the pleural cavity, peritoneal cavity or pericardial sac. In small ruminants, a striking but inconsistent gross lesion can be present in the liver consisting of multiple white to brown circular to ring foci up to 4 cm in diameter. Occasionally sporadic sheep abortions similar lesions can be associated with an anaerobic bacterium, *Flexispira rappini*.[20] Splenomegaly is a variable feature and fetal serum immunoglobulin levels may be moderately elevated.

Histologic changes include fibrinous neutrophilic placentitis with chorionic necrosis, neutrophilic bronchopneumonia, fibrinous neutrophilic serositis and occasionally a lymphocytic abomasitis In small ruminants multifocal hepatic necrosis can be present depending on the post mortem condition and other factors. Silver stains of fetal tissues with inflammation may assist in the diagnosis by identification of curved silver stained bacteria. Immunohistochemistry has been used to detect *Campylobacter fetus* in fetal tissues and differentiate it from other campylobacter species.[21] In a fresh fetus, campylobacter may be identified in darkfield microscopic examination of abomasal fluid as small bacteria with darting motility. *Campylobacter fetus* ss. *venerealis* is fastidious, requiring careful sample collection and proper transport. The bacteria can be cultured from lung, placenta, and abomasal fluid. The bacteria can also be identified in preputial samples and vaginal secretions. Phenotypic characterization and molecular techniques have been used to differentiate campylobacter species.[22]

Epizootic bovine abortion. Epizootic bovine abortion (EBA, also known as foothill abortion) is a cause of abortion and premature calving in cattle grazing foothill rangelands in California, Nevada and Oregon. The infection is transmitted to susceptible pregnant cattle by an argasid tick (*Ornithodorus coriaceus),* that feeds on deer and cattle. The disease is seen in heifers or cows exposed to endemic areas for the first time while in the first trimester of pregnancy. Abortions, either sporadic or as an outbreak, usually occur in the last trimester and premature weak calves may also occur. Following an abortion affected cattle are resistant to repeat abortion.[23]

A currently unnamed and unculturable gram negative bacterium is presumed to be the etiology of EBA based on molecular techniques on extracted 16S bacterial ribosomal DNA fragments in infected fetal tissues and ticks. The DNA sequences suggest that the bacterium is a delta-proteobacteria in the Myxobacteria family. A modified Steiner silver stain and immunohistochemistry can stain the bacterium in the thymus, spleen, lymph node and in other tissues in the sites of inflammatory lesions.[24]

The diagnosis of EBA is based on the identification of characteristic gross and histologic lesions which are chronic, having developed over a period of three months or more. The fetus is usually fresh and may be born alive. Petechiae are common in the mucosa of the conjunctiva and oral cavity. There is enlargement of peripheral and internal lymph nodes. Enlarged superficial lymph nodes can be easily palpated through the skin. Abdominal distension due to ascites and liver enlargement is often present. Splenic enlargement and enlargement of internal lymph nodes is usual. The thymus may be reduced in size with interlobular or widespread hemorrhage and edema in the cranial portion. Histologic examination of fetal tissues, particularly the lymphoid organs, is required to confirm the diagnosis. Thymic lesions, which are unique in EBA, develop late in the course of the disease and consist of a loss of cortical thymocytes and infiltration of the medullary region with macrophages. The thymic interlobular septa are distended with edema, fibrin, hemorrhage and cellular infiltrates consisting of macrophages and other mixed inflammatory cells. The gross enlargement of the lymph nodes is associated with lymphoid hyperplasia and widespread macrophage infiltration in the sinuses and medulla. There is lymphoid hyperplasia and histiocytic infiltration in the spleen. Late in the course of disease, following the proliferative response, acute necrotic foci develop in lymphoid organs. There are widespread inflammatory lesions with a vascular orientation in most organs, including the brain, lung, heart, liver, kidney, skeletal muscle and other organs. Fetal serum immunoglobulin levels are usually markedly elevated from 100 to 1000 mg/dl.

Coxiella burnetii. *Coxiella burnetii* is an obligate intracellular coccobacilli in the Rickettsiaceae family associated with late term abortion in sheep, goats, rarely cattle and is a zoonotic disease causing of Q fever in humans. Animals can be persistently infected resulting in environmental contamination from milk, feces, uterine discharges and placenta. New infections are by oral transmission and dust inhalation. Problems of abortions, stillbirths or weak newborn animals tend to occur in newly infected animals. Aborted fetuses are in variable post mortem condition but usually fresh. Gross lesions are usually confined to the placenta where the intercotyledonary placenta is thick and covered with white to yellow exudate with variable circumferential infiltration of the cotyledons. Histologically there is suppurative inflammation of the chorion with necrosis of villi and chorionic epithelium. Remaining trophoblasts often have swollen foamy basophilic cytoplasm containing organisms. The chorioallantoic stroma is infiltrated with mononuclear cells and plasma cells. The organisms are usually plentiful and special stains on smears or histologic sections can help to visualized them but specific antibody stains either fluorescent antibody on smears or immunohistochemistry on sections, or PCR on placenta should be employed to differentiate *Coxiella* from other similar organisms, especially *Chlamydophila*.[25,26]

Fungal infections

Mycotic abortion is reported worldwide with an overall low incidence in North America. The majority of mycotic abortions in cattle in the United States are associated with *Aspergillus fumigatus* with other *Aspergillus* spp., *Absidia* spp., *Mucor* spp., *Rhizopus* spp., *Candida* spp. and other fungi less commonly reported.[27] The fungi responsible are ubiquitous saprophytes in the environment. The concentration of fungal conidia in the environment may increase the risk for fetal infection since more cases occur in the winter where cattle are housed and fed. Injury to the respiratory or digestive tract of the dam may also enhance the entry of fungi into the bloodstream. Localization in the uterus probably occurs by hematogenous spread from these sites of entry. Experimentally, intravenous injection of *A. fumigatus* causes abortion 23 to 35 days post-infection. *Mortierella wolfii*, a common abortifacient in the southern hemisphere, is rare in North America.

Mycotic abortions usually occur as sporadic third trimester abortions. Clinical signs in the dam are infrequent aside from retained placentas. Placentitis is the primary lesion so submission of the placenta is critical to the diagnosis. Grossly there is often a severe placentitis involving both the cotyledons and intercotyledonary placenta results in a diffusely thickened, leathery placenta. Cotyledons may have necrotic, hemorrhagic infarcts with adherent caruncular tissue. Histologically, the placenta may

have suppurative inflammation, necrosis, and vasculitis with thrombosis associated with fungal invasion. Fetal autolysis may be minimal, especially with *Aspergillus fumigatus* infections. In the fetus lesions are variable and may be absent. In a minority of affected fetuses there may be raised circumscribed plaques on the skin. Internally fetal lesions associated with mycotic infection may include bronchopneumonia or focal digestive tract inflammation associated with fungal invasion. A rapid presumptive diagnosis may be obtained by direct microscopic examinations of scrapings of placental or skin lesions after digestion with 10% potassium hydroxide (KOH) solution. Samples of the abomasal fluid can be examined in a similar manner. The fungi are not digested by the KOH solution and can be visualized microscopically in the wet mount. Histologic identification of fungi in tissue lesions utilizing histochemical stains is also effective. For isolation cultures of the placenta, abomasal fluid, or lung on fungal media with antibiotics to suppress bacterial growth can be employed. As fungi are ubiquitous in the environment their presence could be the result of contamination so the diagnosis of mycotic abortion requires compatible lesions in the placenta or fetus in addition to the microscopic demonstration or isolation of fungi.

Viral infections

Herpes virus infections. Bovine herpesvirus type I is found worldwide although there has been successful eradication in some European countries. In the United States, it remains a significant cause of abortion which is frequently epizootic. Infection at breeding can cause infertility and embryonic death may result from infections early in pregnancy. The virus may persist as a latent infection following acute infection. Infection occurs through contact with infected cattle shedding virus from respiratory, ocular, and reproductive secretions. Exposure of previously unexposed, non-vaccinated pregnant cattle can result in abortion storms with 25 to 60% of cows aborting. Experimentally, abortion occurs at any stage of gestation, but in field conditions abortions are usually seen in the second half of gestation. Most abortions occur several weeks (20 to 52 days) following initial infection of the dam that may not exhibit signs of illness other than abortion.[28]

Aborted fetuses are usually five months to term and are autolyzed with red tinged fluid in body cavities and fascia. There are usually no gross lesions other than placental edema though rarely indistinct pinpoint white foci may be appreciated in the liver. A presumptive diagnosis can be made from histopathology of the liver which despite considerable autolysis usually has striking multifocal necrosis, best appreciated at low magnification. Focal necrotizing lesions are usually present in other fetal tissues, especially lung, adrenal, spleen and lymph node. Eosinophilic intranuclear inclusions are often difficult to recognize but may be identified in the adrenal cortical lesions. Placentitis with necrosis and vasculitis in placenta villi is usually present associated with abundant viral antigen as detected with immunohistochemistry. Diagnosis is confirmed by viral isolation, by detection of viral antigen in fetal tissues by immunofluorescent staining on frozen tissue sections (especially kidney) or by immunohistochemistry on formalin fixed tissues (especially liver, lung, kidney, adrenal, placenta) using monoclonal antibodies. Caprine herpes virus is related to BHV-1 and in goats is associated with a similar array of diseases manifestations including late term abortion.[29]

Pestivirus infections. Bovine virus diarrhea virus (BVDV) and border disease virus (BDV) are common, closely related *Pestivirus* species and some cross species infection may occur between cattle and sheep.[30] BVDV virus infection is widespread in the cattle population and in susceptible pregnant animals fetal infection is likely to occur. Fetal infections have a variable outcome depending on the timing of the infection, the biotype and other properties of the virus. An important aspect of fetal BVD virus infection is that noncytopathic BVD virus infections in fetuses prior to four months gestation can result in persistently infected live calves which are a major source of infection for other cattle. Contact with infected animals shedding the virus and contaminated biologics are additional sources of infection.

There are often no obvious clinical signs seen in herds with fetal losses due to BVD virus and abortions occur a few days or several weeks following maternal infection. Fetal BVD virus infection can

have variable outcomes depending on the gestational age of the fetus infected and other factors. First trimester infections can cause infertility, embryonic death, fetal resorption, mummification, or abortion. However, infections with noncytopathic BVD virus between 18 to 125 days gestation may result in persistently infected live calves. Fetal infections beyond approximately four months gestation often result in transient fetal infections, with the development of a fetal immune response, specific fetal antibody production, and elimination of the virus. However, abortions can also occur during later gestational infections. Mid-gestational infections (from approximately 100 to 150 days gestation), can also result in the birth of term calves with congenital anomalies.[31] The fetal lesions associated with abortions attributed to BVD virus infection are quite variable. The fetuses can be fresh or autolyzed and mummification can occur. The aborted fetuses may be small for their gestational age or premature small calves may be born. Gross lesions that may suggest BVD virus infection in the nervous system includes microencephaly, cerebellar hypoplasia, hydranencephaly and hydrocephalus. Ocular lesions including microphthalmia, cataracts, retinal dysplasia and optic neuritis have been described. Alopecia may be present. Thymic hypoplasia with histologic evidence of thymic cortical atrophy is associated with BVD virus infection. Pulmonary and renal hypoplasia or dysplasia has been reported. BVD virus infection has been associated with a necrotizing myocarditis with nonsuppurative vasculitis in the heart and the affected fetuses may exhibit marked anasarca with a round dilated heart and chronic passive congestion of the liver.

Proof that BVD virus infection is the cause for an abortion is confounded by the fact that the virus may infect the fetus without causing abortion and there are diverse fetal lesions attributed to infection. To attribute BVD virus infection as the cause of abortion, evidence of infection needs to be combined with compatible fetal pathology and/or herd history. Fetal infection can be determined by detection of the virus in fetal tissues by various methods.[32] Virus isolation on a pool of fetal tissues (most often lung, liver, kidney and/or lymphoid organs) is widely used in diagnostic laboratories although it is a relatively expensive and time-consuming procedure. Virus isolation is specific but the sensitivity in diagnostic submissions is estimated to be reduced due to autolysis and other factors. Fluorescent antibody staining for BVDV on frozen sections of either lung or liver and kidney is often used as it is a convenient and rapid procedure. However, there are significant false positives and false negative results with this procedure compared to either virus isolation or immunohistochemistry. BVDV immunohistochemistry using monoclonal antibody appears to be a sensitive and specific procedure capable of detecting a variety of virus isolates.[33,34] Useful tissues for BVDV immunohistochemistry staining include kidney, lung and placenta. In fetuses with vasculitis and necrotizing myocarditis immunohistochemistry may demonstrate the presence of BVDV antigens in the vessel wall and/or muscle. A number of BVDV PCR procedures are available in diagnostic laboratories that have been evaluated and appear highly sensitive in detecting BVDV in a variety of samples.[35]

After four months gestation the fetus may respond immunologically to BVDV infection so a positive BVDV titer in the fetal fluids is an indication of fetal infection. However, if earlier infection by noncytopathic BVDV induces persistent infection, the fetus may be immunotolerant so a negative fetal serology does not rule out infection. Serology on the dam is of limited value in diagnosing BVDV abortion, particularly if animals are vaccinated.

An important outcome of fetal infection with noncytopathic BVD virus is the birth of persistently infected calves which are a significant source of infection to the herd. Virus isolation, serology, immunohistochemistry, polymerase chain reaction and antigen capture ELISA procedures have been used to screen for the presence of persistently infected animals as a means to control this infection. The choice of the optimal screening procedure for a specific herd will depend on a number of factors which have been reviewed.[36] Skin ear notch biopsy procedures utilizing BVDV immunohistochemistry or antigen capture ELISA to identify individual persistently infected animals have been evaluated.[32-35]

Reproductive disease associated with BDV infection in sheep and goats has many similarities to BVDV infection in cattle. The infection is common in sheep, less so in goats. Most BDV isolates are noncytopathogenic and the primary effects of the infection are seen in the fetus, influenced by the gestation age similar to BVDV infection in pregnant cattle. After about 90 days gestation the fetus is

immunocompetent to BDV infection and prior to this, infection may result in a variety of changes including fetal death, mummification, abortion, abnormal organ development, stillbirth or weak lambs/kids, or the birth of clinically normal, persistently infected offspring which are a major source of infection. A notable syndrome associated with BDV infection is the "hairy shaker syndrome" in which there is curly hair-like wool, frequently abnormally pigmented, with tremors or neurologic deficits in the affected live animal. Various central nervous system dysplastic or hypoplastic lesions can be observed but hypomyelination is the most consistent change. An oligodendrocytic dysfunction is thought to be responsible either from direct viral infection of oligodendrocytes or due to a hormonal effect from low thyroxine activity due to viral infection of thyroid follicular cells. Confirmation of BDV as the cause of reproductive problems in sheep and goats utilizes similar procedures as with BVDV in cattle.[30]

Cache Valley virus. Cache Valley virus is a bunya virus, endemic in North America and transmitted by arthropods including *Culicoides* spp., gnats and mosquitoes, that is known to cause disease in pregnant sheep. Depending on the stage of gestation at which the fetus is infected, fetal death, abortion or fetal abnormalities can occur. The most striking gross lesions associated with this teratogenic virus infection are arthrogryposis, vertebral abnormalities (scoliosis, torticollis) and various central nervous changes including hydranencephaly, porencephaly, hydrocephalus and micromyelia. Diagnosis is difficult as the virus is usually eliminated earlier in gestation. A serology test is available which is best utilized on affected pre-colostral lambs. Cases of congenital defects such as arthrogryposis/hydranencephaly suspected to be due to a teratogenic virus infection merit attention as similar lesions can be caused by another bunya virus, akabane, which is exotic to North America.[37]

Bluetongue virus. Bluetongue virus (BTV) infection is a worldwide, arthropod (*Culicoides* spp.) transmitted *Orbivirus* virus infection with a seasonal occurrence. There are multiple BTV serotypes which vary considerably in their virulence. The ability of the virus to cross the placenta and cause fetal infection is enhanced in egg or cell culture adapted vaccine strains. Reproductive disease associated with BTV is seen in sheep and cattle and is influenced by the stage of gestation that infection occurs and the serotype involved. In sheep, infection early in gestation can result in fetal death with resorption, mummification or abortion. Between approximately 50 to 80 days gestation, the viral infection can induce cavitating brain lesions resulting in hydranencephaly or porencephaly in fetuses that survive to birth. Nonsuppurative meningoencephalitis with cerebral cortical necrosis is present. Cattle are frequently infected with BTV and can maintain a prolonged viremia but reproductive disease associated with BTV has historically been uncommon and sporadic apparently limited to certain cell-adapted strains of BTV. However, recently BTV serotype 8 as emerged in Europe as a significant cause of both clinical disease in cattle and the infection has an enhanced ability to cause fetal infection. Reproductive disease in the bovine is similar to that in sheep. In early gestation, less than 70 days, death with absorption or abortion can occur. Between 70 and 130 days BTV targets neuronal and glial cells progenitor cells in the subepidermal region of the cerebrum resulting in hydranencephaly. Slightly later infections but prior to fetal immunocompetence at 150 days, can result in porencephaly and hydrocephalus. Later infection may result in encephalitis without brain malformations. The diagnosis of BTV infection can be difficult because the virus may longer be present in a term fetus presented with compatible brain lesions. Fetal or precolostral antibodies can indicate exposure. BTV PCR assays are available in many diagnostic laboratories.[38,39]

Protozoal infections

Tritrichomonas foetus. Trichomoniasis is a venereal disease that is primarily associated with early embryonic loss. However, occasional abortions may occur and submission of these may offer the first opportunity to identify this disease in some infected herds. Abortions can occur from two months to late gestation with variable autolysis. In most cases there are no gross lesions other than placental edema.

Histologic lesions consist of pleocellular placentitis and fetal bronchopneumonia occasionally with multinucleated giant cells in the lung airways.[40] In fresh samples, trichomonads may be identified in abomasal fluid samples by darkfield microscopy followed by confirmation by culture of the fluid utilizing appropriate media. The trichomonads may be visualized in the placenta, lung and other tissues in routine hematoxylin-eosin stained sections. Histochemical stains such as Giemsa and Bodian's silver protargol are useful in identifying trichomonads in tissue sections. Immunohistochemistry utilizing polyclonal and monoclonal antibodies is an effective method to detect *Tritrichomonas foetus* in fetal and placental sections.[41]

Neospora caninum. Neospora infection is a major cause of abortion and fetal infection worldwide in beef and dairy cattle with only rare incidences in sheep and goats.[42-43] This protozoan parasite has a complex life cycle utilizing both horizontal and vertical methods of transmission. In horizontal transmission the carnivore definitive host, identified as dogs and coyotes, can shed infective oocysts in their feces from which the intermediate ruminant host can acquire the infection. The other method of transmission, vertical transmission, is an important means of maintaining this infection. The protozoa can be maintained in the cow as a chronic infection which can be transplacentally transmitted to her fetus during pregnancy. Some of these infected pregnancies may abort, but many will produce a congenitally infected calf and a congenitally infected heifer calf is capable of transmitting the infection onto the next generation when she becomes pregnant, thus maintaining the infection in the herd. Cows that abort a neospora-infected fetus may have additional abortions or infected fetuses in subsequent pregnancies. Cows and heifers that are seropositive are at an increased risk of abortion.[44-45]

There are no signs of clinical illness in cows that abort and while abortions have been diagnosed in both heifers and cows from three months gestation to term, but the majority of abortions occur in the second trimester of pregnancy, four to six months gestation, which is a distinctive feature of this disease. Fetal mummification has been associated with neospora outbreaks. A rare outcome of fetal neospora infection is the birth of a full-term calf with central nervous system signs. However, the majority of calves that acquire a neospora infection during gestation are born clinically normal. These calves have a high precolostral antibody titer to *Neospora caninum* which is useful in diagnosing *in utero* infection.

The aborted fetuses are autolyzed with serosanguinous fluid in body cavities. Subtle gross lesions, consisting of pale white foci or streaks in the skeletal muscles or the heart may be rarely observed. There are widespread histologic lesions in many organs, the most diagnostically significant in the brain consisting of scattered foci of cellular infiltrates and/or foci of necrosis. Other routinely identified lesions include nonsuppurative epicarditis and/or myocarditis and myositis. Liver lesions consist of portal hepatitis with foci of paracentral hepatic necrosis. Lung and kidney often have scattered nonsuppurative interstitial infiltrates. Placentitis varies in severity but may be the primary cause of fetal death and abortion.

Immunohistochemistry using antibodies raised against *Neospora caninum* antigens is an effective method to identify the tachyzoite and tissue cyst stages of the parasite in fetal tissues. Neospora immunohistochemistry is most successful in sections of brain, lung, kidney, skeletal muscle and placenta. The evidence of neospora infection in an aborted fetus as the cause of the abortion can be questioned because a fetus can be infected and not abort due to the infection. A diagnosis of neospora infection as the cause of abortion should take in consideration the gestational age, autolyzed condition, compatible disseminated inflammatory lesions, detectable parasites and no other identified causes. A fetus with mild lesions, often limited to focal encephalitis in late term fetuses, may likely have an incidental neospora infection so other causes for the abortion should be investigated. Neospora PCR techniques have been used to identify fetal *Neospora caninum* infection and are reported to be more sensitive than immunohistochemistry in identification of fetal infection.[46] However, establishing neospora infection as the cause for the abortion on the basis of a positive neospora PCR should employ the same criteria for diagnostic significance as for a positive neospora immunohistochemistry test.

A variety of serologic tests are available to assist in the diagnosis of neosporosis. These include the indirect fluorescent antibody test, the modified agglutination test, and a number of enzyme-linked immunosorbent assays.[47-48] The assays utilize *Neospora caninum* tachyzoites or specific derived antigens. The specificity and sensitivity of the various serologic tests are comparable depending on the minimum antibody titer that has been established as the cut-off for a positive result. Laboratories utilizing any of the serologic tests for neospora should establish appropriate cut-off titers using sera from known infected and noninfected cattle. In some tests, the positive cut-off titer has been selected based on the antibody titer in a cow that has aborted an infected fetus so this cut-off may not be the most appropriate for the serologic diagnosis of a chronic infection in cattle which vary in age and pregnancy status. A single serum sample from an individual cow may not accurately reflect her infection status since titers in known positive cattle fluctuate and may fall below the cut-off value for some period of time. In rare instances, cows that abort a neospora-infected fetus may not have a significantly elevated titer. Also, previously elevated titers at abortion may decline over several months following abortion. In newborn calves, neospora serology on precolostral serum is an effective method to determine fetal exposure. In aborted fetuses, neospora serology is less useful in diagnosis. An infected fetus may have a negative titer because of the gestational age, duration of infection prior to death, or autolysis. A negative fetal titer does not rule-out infection nor does a positive titer prove that this infection caused the abortion. In the individual aborting cow, a positive serology result does not prove that the abortion was due to neosporosis but it can assist the diagnosis. Serology can be used on a herd basis to investigate the association between seropositivity and abortion by comparing results among aborting and non-aborting cattle to estimate the extent that the abortions can be attributed to neospora infection.[44]

Toxoplasma gondii. *Toxoplasma gondii*, a protozoan parasite similar to *Neospora caninum*, is an important cause of reproductive disease in sheep and goats. The parasite has a two-host life cycle with cats as the definitive host which shed infective oocysts following intestinal infection that are capable of infecting a wide variety of mammals and birds which serve as intermediate hosts. Infection and/or exposure is not uncommon in small ruminants with little evidence of clinical disease other than during pregnancy. Reproductive disease is most commonly seen in younger, previously unexposed animals. In the susceptible pregnant animal, transplacental infection can result in resorption, fetal death, mummification, abortion or stillbirth. The infection can also be congenitally transmitted to the fetus with the birth of healthy lambs that are capable of infecting their offspring although the significance of vertical transmission is still unclear. The various outcomes appear to be dependent on the stage of gestation at which infection occurs. Aborted fetuses can vary from autolyzed to fresh, even among the same pregnancy. Gross fetal lesions are usually not apparent. Placenta lesions, if visible, are diagnostically useful. The cotyledons contain numerous small white foci with a grossly normal intercotyledonary placenta. On histologic examination there are foci of necrosis of the cotyledonary villi often with mineralization and mononuclear inflammation. Rarely individual tachyzoites or tissue cysts can be identified in or adjacent these lesions with conventional histology. Fetal lesions are variable and may be absent in some cases but the most distinctive lesion is found in the brain consisting of multifocal necrosis and gliosis. Scattered mononuclear inflammation may be present in other organs including the lung, heart and liver. Diagnosis most commonly is based on the presence of the placental and fetal lesions coupled with demonstration of the organism by specific antibody using an immunohistochemistry stain. Toxoplasma DNA PCR procedures have been used by some laboratories to detect infection with good results even on autolyzed specimens. Serology on the aborting dam may be useful to help rule out toxoplasma infection if negative but a positive result is not diagnostic as exposure is common. Fetal serology is occasionally useful in cases when the aborted fetus has sufficient maturity and duration of infection to mount an antibody response.[49]

Sarcocystis. Infection with *Sarcocystis* species is very common in the muscular tissues of domestic ruminants but clinical disease or abortion is rare. The protozoal parasite has a two-host life

cycle with a sexual intestinal stage in the carnivore definitive host and an asexual tissue stage in the ruminant intermediate host. There are a number of *Sarcocystis* species identified in ruminants but the most important are *S. cruzi* in cattle, *S. tenella* in sheep and *S. capracanis* in goats which all have canid definitive hosts. Abortions are rare and sporadic. The fetus is usually autolyzed with no gross lesions. Histologic examination reveals disseminated inflammation with some similarities to fetal neosporosis in cattle including encephalitis with necrosis and gliosis, myocarditis, myositis and hepatitis. The protozoal schizonts are associated with the endothelium of most organs. On occasion, a distinctive rosette formation of mature schizonts within endothelial cells can be identified which is useful in distinguishing this parasite from *Neospora* and *Toxoplasma* species.[50]

Summary

The laboratory results obtained from the abortion submissions should be interpreted by the veterinarian to determine whether they provide a sufficient answer to the herd abortion problem. On occasion, aborted fetuses may present with incidental infections, have multiple infections, or the fetus submitted may not be representative of the herd problem. When laboratory testing is completed, the clinical situation and laboratory diagnosis can be compared to assess whether the abortion submission is a representative sample and if the identified cause is a significant factor in the herd abortion problem. Identification of an infectious cause in abortion submissions is usually successful in less than half of submissions. The failure to find an infectious cause may be a correct interpretation in cases in which there are abnormal genetic, hormonal, metabolic, developmental or other factors responsible which are often difficult or impossible to confirm in diagnostic laboratory submissions. The lack of significant findings in multiple fetuses submitted from a herd can be used as evidence by the veterinarian to investigate other possible noninfectious factors. Among the bovine fetuses submitted to veterinary diagnostic laboratories for which no etiologic diagnosis was obtained a significant minority have inflammatory lesions compatible with an infectious etiology, suggesting that there is room for improvement. It is reasonable to presume that with improved detection methods and further investigations the diagnosis rate on abortion submissions can be improved and new causes identified.

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