



WEDNESDAY SLIDE CONFERENCE 2011-2012

Conference 9

09 November 2011

CASE I: HSRL-425/00724637 (JPC 4002934).

Signalment: 4-year-old intact female German shepherd canine (*Canis lupus familiaris*).

History: The animal was presented after she fell down the steps in the house a few weeks ago. Owner noted that after the fall she has been wobbling and weak. One week before referral, the owner also reported some bloody vaginal discharge. The referring veterinarian described the patient as bright, alert, responsive, and calm. The dog was reported to have been in heat two months ago. The oral mucosa was pink with a normal capillary refill time; temperature was 101.6° F (38.6° C). The animal weighed 37 kg; a loss of 2 kg since last visit.

Ultrasound revealed a distended bladder; the uterus was distended with fluid in both horns. Pyometra was considered but hemogram and serum biochemical analyses were normal, except for a mild serum globulin concentration. Radiographs showed no pulmonary involvement.

Clinical pathology findings at this time:

Low positive Lyme titer. CBC profile: HTC 40.3 (37-55 %); WBC 14.38 (6.5-15.90 th/ul); & neutrophils 80, lm 5%, mono 12 % eos 3 %. Mild moderate platelet clumping.
BUN creatinine within normal limits.
Total protein 8.6 (5.2-8.2)

Albumin 2.9 (2.5-4)
Globulin 5.7 (2.5-4.5)

Two days after the animal's initial visit she was walking sideways, not defecating, and falling down. The animal had a mild head tilt to the left, walked in circles, and bilateral nystagmus. Vestibular disease, Lyme disease and Leptospirosis were included in the differential diagnosis. The dog was treated with tetracycline. The owner wanted an ovariohysterectomy performed on the animal. Cytology performed during surgery revealed numerous degenerated neutrophils and long thin septated fungal hyphae. The animal started fluconazol therapy. The owner was advised of the cytology findings and the owner decided on euthanasia 3 days after surgery. The animal collapsed just before arriving to the clinic and arrived unconscious. The animal was euthanized.

Gross Pathology: The postmortem examination performed by the local veterinarian revealed multifocal, white- gray well demarcated lesions in the liver, heart and kidney. Heart, uterus, and kidney were submitted for histopathology. No brain samples were submitted.

Laboratory Results:

Uterine content were submitted for microbiology: *Bulbithecium spp.* (closely related to *Bulbithecium hyalosporium*) was isolated. The anamorph of this fungus is *Acremonium spp.*

Contributor's Microscopic Description: Uterus:

There is a marked thickening of the endometrial wall with severe proliferation of the endometrial glands and lining epithelial cells, partially or completely occluding the uterine lumen. The abundant hyperplastic endometrium forms variable sized cystic dilations filled with eosinophilic acellular granular proteinaceous material admixed with variable numbers and combinations of neutrophils mixed with numerous fungal hyphae. The hyphae are thin (2-4 μ m), long (100-200 μ m), septate, and occasionally branch out, suggestive of *Acremonium* spp. The inflammatory reaction extends to the myometrium and to the serosal surface.

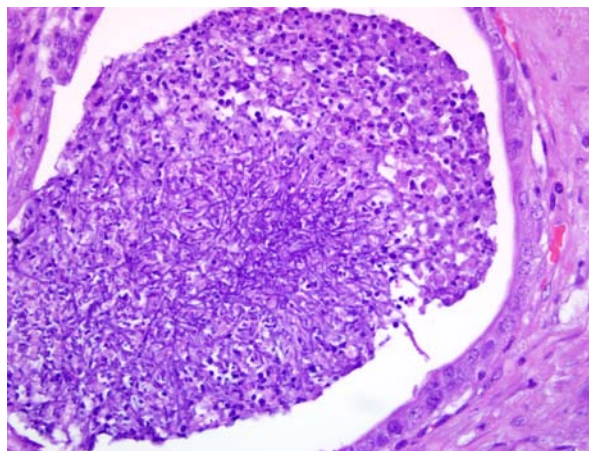
Contributor's Morphologic Diagnosis: Uterus:

Severe, transmural neutrophilic subacute endometritis with intralesional fungal hyphae and marked severe endometrial cystic hyperplasia.

Contributor's Comment: Mycotic uterine infections in dogs are very rare and have been associated with systemic fungal infection rather than exclusive uterine infections. Young German shepherds (GS) have been over represented in cases of systemic aspergillosis or acremoniosis.^{4,10,12} It has been described that GS have an immunologic disorder that makes them predisposed for these type of invasions with saprophytic organisms.⁶ This case described a mycotic systemic infection due to *Bulbithecium* spp., the anamorph phase of *Acremonium*. Unfortunately in this case no nervous tissue was submitted for histopathology to confirm that the systematic involvement explains the entire clinical presentation. The multifocal, well delimited white nodules in the heart and the kidney are the classic findings in these systemic mycotic infections. GMS stain done on the uterus sections were positive and not necessary since the fungal hyphae and typical morphology can be seen in the H&E sections submitted for the conference.

The classification of *Acremonium* spp. has changed; previously it was described as hypomycetes, and currently it is classified as one of the two members under the group *Dyckaria* in the sub group *Ascomycotas*. It is still classified as Imperfect fungi (Deuteromycota), and nondematiaceous (not pigmented), but the term hyphomycetes is obsolete.

Pyometra is inflammation of the uterus that has variable symptomology from genitourinary disease to non-specific systemic disease. In the dog, pyometra is associated with cystic endometrial hyperplasia predisposed for by luteal activity (progesterone). During this phase, progesterone inhibits the intrauterine leukocyte response, decreases muscle contractibility and stimulates development and secretion of endometrial glands.^{2,8} Clinically, pyometra



1-1. Uterus, dog. Ectatic endometrial glands are filled with tangles of fungal hyphae enmeshed with abundant cellular debris. (HE 400X)

can be associated with or without vaginal discharge depending on whether the cervix is closed or open. If the cervix is closed, the prognosis is more serious since the possibility of septic or uterine peritonitis exists.^{2,9}

Fungi are a very variable group of eukaryotic organisms that belong to the fungi kingdom.⁷ The old classification was based on morphologic microscopic features that classified the kingdom in 6 phyla. Classification of fungi is confusing and based on several criteria including formation of hyphae, pseudohyphae, or yeast forms. Another feature important in classification is the presence of a sexual stage of reproduction (teleomorph stage) or the absence of sexual reproduction (anamorphous stage). Biochemical and physical properties can be used to distinguish different species. However, more recently, molecular genetics and DNA analysis have played a role in taxonomy.⁷

Unfortunately, at the present time, there are no agreements on specific rules for an international system to facilitate the fungal nomenclature. There are some efforts to create an organized fungal classification scheme.⁷

The kingdom of Fungi is classified in 7 or 8 phyla or subdivisions.⁵

Infections by hyalohyphomycosis with nondematiaceous or not pigmented fungi have been described in other species such as horse, reptiles, and humans.⁶

JPC Diagnosis: Uterus: Endometritis, necrotizing, diffuse, severe, with marked cystic endometrial hyperplasia and numerous fungal hyphae.

Conference Comment: The contributor mentioned the predisposition of German shepherd dogs to

disseminated infection with saprophytic fungi, and conference participants discussed *Aspergillus terreus* as the most common culprit, with reported lesions including pneumonia, myositis, myocarditis, endometritis, encephalitis, nephritis, splenitis, osteomyelitis, and lymphadenitis due to hematogenous spread of the fungal aleurospores.³ In addition to bacterial and rare fungal and viral causes of endometritis in dogs, a differential diagnosis should include other non-infectious etiologies such as pseudopregnancy, caused by retained corpora lutea which can contribute to cystic endometrial hyperplasia-pyometra complex, and placental sub-involution, which manifests as necrosis and hemorrhage of the endometrium with invasion of trophoblasts into adjacent myometrium and blood vessels, producing a hemorrhagic vaginal discharge.¹¹

In mares, a reported fungal cause of abortion is fescue grass toxicity caused by *Neotyphodium* (formerly *Acremonium*) *coenophialum*. This fungal endophyte infects grass and produces the ergot alkaloid ergovaline, which causes dysmaturation of foals and infrequent abortion. Ergovaline, in addition to its well known alpha-2 adrenergic agonistic effects causing vasoconstriction seen in fescue foot in cattle, is a potent dopamine D₂ receptor agonist which blocks prolactin, which is important in maintaining the corpus luteum and mammary gland growth and milk production. The lack of prolactin with decreased progesterone and increased estradiol in the mare during pregnancy can lead to fetal death. Fetal death also occurs from suffocation due to a thick edematous placenta that does not rupture at the cervical star. The mares are also agalactic with minimal colostrum, and if the foal survives to term, they often die due to failure of passive transfer.

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CASE II: 8-456-11 (JPC 4003080).

Signalment: Adult cow bison, *Bison bison*.

History: Placenta submitted from a bison cow that recently aborted in a capture facility in Yellowstone National Park.

Gross Pathology: The non-cotyledonary regions of the chorioallantois were diffusely opaque, edematous and white/pink. The cotyledons were tan and had scattered hemorrhage.

Laboratory Results: *Brucella abortus* biovar 1 was isolated from the placenta.

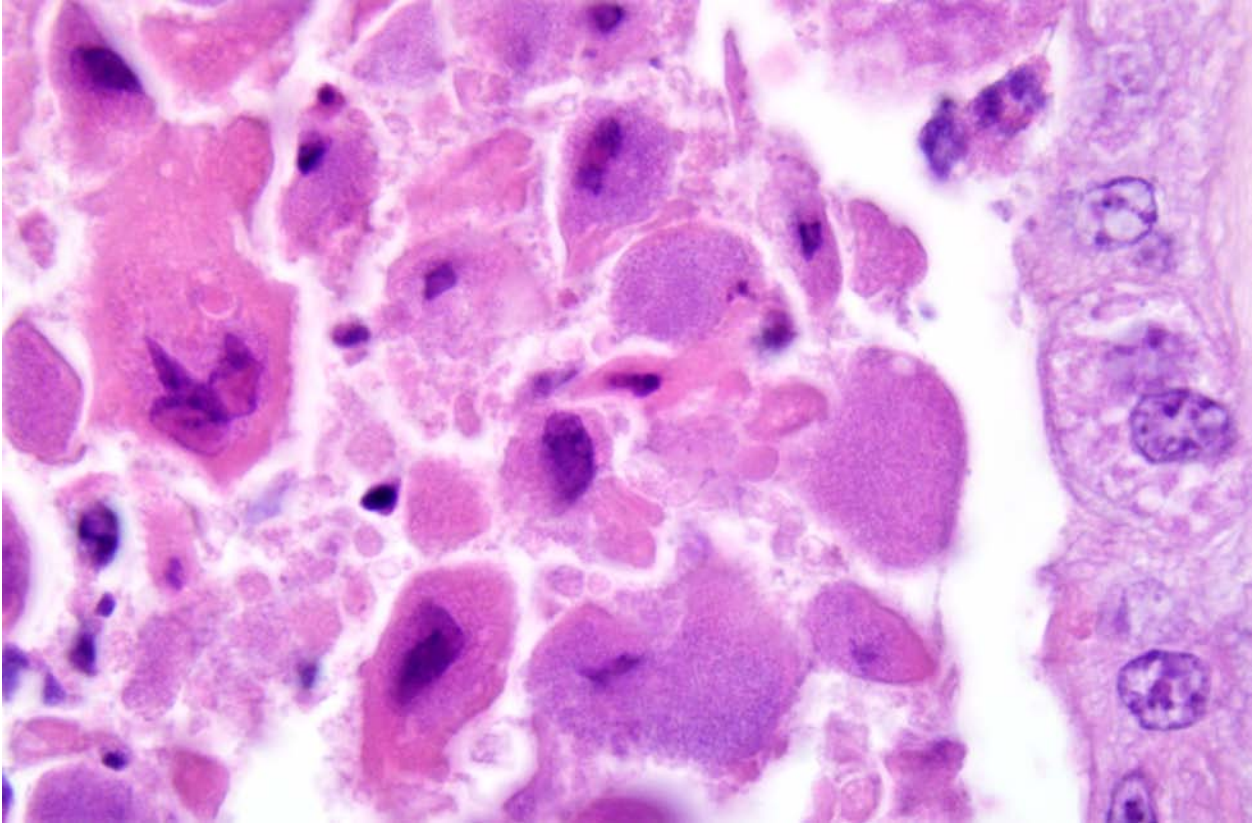
Contributor's Microscopic Description: Placenta: Multifocally, the cotyledons of the chorioallantois are necrotic as characterized by loss of distinct villar architecture with replacement by a granular eosinophilic material containing karyorrhectic debris including necrotic leucocytes. Intracytoplasmic bacteria occur within trophoblasts. The deeper connective tissue is edematous with scattered infiltrates of neutrophils and fewer macrophages.

Contributor's Morphologic Diagnosis: Placentitis, necrotizing, acute, multifocal, severe, with intracytoplasmic bacteria and severe edema, chorioallantois, placenta.



2-1, 2-2. Fetus and placenta, bison. The cotyledons are tan with multifocal hemorrhages and the intercotyledonary portions of the placenta are opaque and edematous. Photographs courtesy of Montana Veterinary Diagnostic Laboratory <http://liv.mt.gov/liv/lab/index.asp>.





2-3. Placenta, bison. Trophoblasts are shrunken and hyper-eosinophilic (necrosis) and often contain many lightly basophilic intracytoplasmic coccobacilli. (HE 1000X)

Contributor's Comment: The primary consequences of brucellosis in domestic animal populations are economic losses due to decreased production. Infections also occur in wild populations and in the United States; bison and elk in the Greater Yellowstone Area (GYA) and wild/feral swine in other areas of the US are natural reservoirs hosts. The recent *Brucella abortus* outbreaks in cattle within the GYA are considered to be the result of transmission from infected elk herds. Disease management practices in bison herds of Yellowstone National Park have been controversial and polarizing for several decades. Permanent solutions for disease control or population management in the bison and elk herds of this region will be difficult to implement because of a multitude of factors including the following: large wild animal populations within a large geographic area; differing jurisdictional boundaries of governmental agencies; differing state and federal agency missions and mandates; naïve understanding and exaggerated fears of the disease by various groups and entities; the urbanization of the populace; and financial interests. Although brucellosis has been eradicated in domestic herds in some advanced countries, the disease is still significant in animals and humans throughout most of the world. The agent's zoonotic potential also lead to the propagation and incorporation of the agent into

national bio-warfare arsenals.

Brucellosis is caused by small gram-negative bacilli of the genus *Brucella*; these bacteria are facultative intracellular organisms. The organism lacks many of the typical virulence factors of pathogenic bacteria and how the organism resists phagocytic degradation and is able to replicate within professional and non-professional phagocytes is poorly understood. There are multiple species within the genus and include: *B. abortus* biovars 1-9 (cattle), *B. suis* biovars 1-5 (swine), *B. ovis* (sheep), *B. melitensis* biovars 1-3 (sheep and goats), *B. canis* (dog), *B. neotomae* (rodents), and species that infect pinnipeds and cetaceans. *B. abortus*, *B. suis* and *B. melitensis* are further subdivided into biovars but contrary to the species name, these organisms can also cause disease in numerous other domestic and wild animal hosts and these are the common species infecting man. *B. canis* and marine *Brucella* species have also rarely been associated with disease in man, whereas *B. ovis* and *B. neotomae* are recognized to only infect sheep and rodents, respectively.

Brucellosis in animals is characterized by third trimester abortion with necrotizing placentitis, retained placentas and metritis, weak calves, mastitis, arthritis/

hygromas/bursitis, and in males, orchitis/epididymitis and seminal vesiculitis. The disease in susceptible domestic animal populations has significant economic consequences due to calf loss, infertility, decreased milk production and disease regulatory consequences. Infected animals can eventually become resistant but could still act as intermittent shedders that serve as a reservoir of infection within the herd. Transmission is usually through ingestion or contamination of mucous membranes after exposure to infected fetuses, fetal membranes or contaminated body fluids. Venereal transmission occurs with *B. suis*, *B. ovis* and *B. canis* but is uncommon with *B. abortus* or *B. melintensis*. Abortions also can occur after vaccination of pregnant females with live vaccine strains.

Brucellosis in man has multiple synonyms such as undulant fever and Malta fever. In countries where the disease is common, infection in man is normally acquired by ingestion of contaminated dairy products or exposure to infected animal reproductive tissues and fluids. Infection can result from exposure to the agent after ingestion, inhalation, through open wounds, accidental injection when vaccinating animals, and congenitally from infected mothers. Effective animal disease control programs and pasteurization of dairy products are major contributors in the low rates of human infections in modern societies. Laboratory personnel, veterinarians and agricultural and slaughterhouse workers are at higher risk for acquiring infections. Laboratory personnel are extremely vulnerable and can readily be exposed if safety precautions are not utilized. Centers for Disease Control and Prevention Biosafety in Microbiological and Biomedical Laboratories (CDC BMBL) recommends strict adherence to BSL-3 safety practices in conjunction with sound laboratory techniques when culturing the organism. The infectious dose for man varies depending on the species. In man, only 1-10 CFU of *B. melintensis* can cause disease. Reported infectious doses for immune-competent people with the following species are: *B. suis* (1000-10,000 CFU), *B. abortus* (100,000 CFU) and *B. canis* (greater than 1,000,000 CFU).

Acute disease in man usually results in incapacitating flu-like illness, cyclic fevers, gastrointestinal upsets, epididymitis/orchitis, and in severe cases, CNS or endocardial disease. Chronic infections can manifest as chronic fatigue-like syndromes, depression, arthritis, endocarditis, hepatitis, cholecystitis, meningitis, uveitis, and osteomyelitis. Mortality rate is less than 5%. Treatment involves long term antibiotic therapy and currently, there is no human vaccine.

JPC Diagnosis: Chorioallantois: Placentitis, necrotizing, multifocal to coalescing, moderate, with marked edema, diffuse vasculitis, and with numerous

intratrophoblastic bacilli.

Conference Comment: Transmission of brucellosis is by contact with infected tissues, secretions or excretions, such as milk, urine, and fetal and placental tissues. The bacteria penetrate the mucosa and migrate to local and regional lymph nodes after being engulfed by local macrophages or dendritic cells, within which the bacteria grow and replicate. The bacteria kill the phagocytes and incite a pyogranulomatous lymphadenitis due to the lipopolysaccharide composition of the bacterial cell wall. The bacteria are systemically disseminated via leukocyte trafficking, enabling them to infect the mammary glands, reproductive organs, placenta and fetus. Chorionic epithelial cells naturally produce erythritol around the fifth month of gestation, which is a carbohydrate growth promoter for *Brucella abortus*, and the bacteria multiply in the rough endoplasmic reticulum of chorionic trophoblasts. Other intratrophoblastic bacterial agents causing abortion include *Leptospira interrogans*, *Coxiella burnetti*, *Listeria monocytogenes*, *Campylobacter fetus* and *C. jejuni*, and *Chlamydophila abortus* and *C. pecorum*; intratrophoblastic protozoa include *Toxoplasma gondii*, *Neospora caninum*, and *Sarcocystis* spp., although protozoal cysts are more commonly found in other tissues, especially in the central nervous system.¹¹

Fetal death and abortion are attributed to placental disruption and endotoxemia; fibrinous bronchopneumonia, pleuritis and pericarditis are seen in the fetus. In addition to *Arcanobacterium pyogenes*, *B. abortus* is the most common cause of bacterial fetal pneumonia. The bacterial infection induces hypoxia through placental inflammation, and this disruption of the placenta induces a breathing response in the fetus, and death is due to aspiration of the amniotic fluid.^{3,5,14} Typical gross placental lesions include extensive cotyledonary necrosis; intercotyledonary edema with a tough, yellow to gray, leathery surface; necrosis and inflammation of the placental arcades; and inflammation of the maternal septa, leading to placental interlocking and retained placenta.⁵ *Brucella abortus* is also commonly associated with bursitis in horses, known colloquially as poll evil and fistulous withers.¹³

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CASE III: NF-08-747
(JPC 3134538).

Signalment: Term fetus female Alpine dairy goat, (*Capra hircus*).

History: Twin female American Alpine dairy goat fetuses were submitted for determination of the cause of abortion. These were from a newly assembled dairy goat herd which had experienced multiple abortions over the last week.

Gross Pathology: On physical exam, the fetuses were moderately autolytic, and contained serosanguinous fluid within their pleural cavities. No other gross lesions were detected in the fetuses or their accompanying placentas. All samples were taken from the larger of the two fetuses.

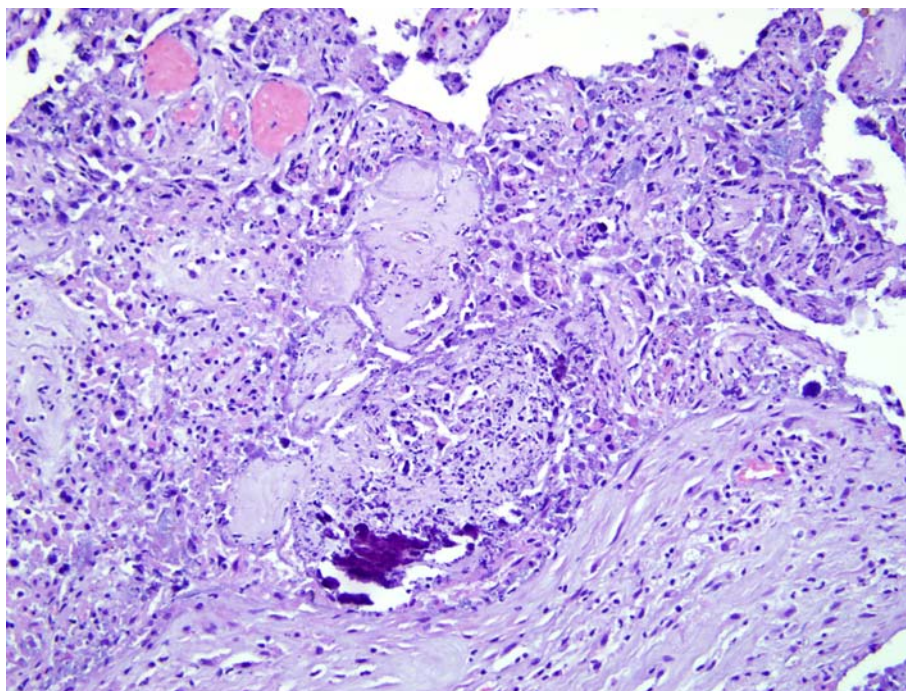
Laboratory Results: PCR for *Coxiella burnetii* was positive on placenta; PCR for *Chlamydophila* sp. was negative. Mixed coliforms and *Streptococcus* sp. were isolated from the placenta. Cultures of lung, liver, and stomach contents were negative.

Contributor's Microscopic Description: Slides contain sections of chorioallantois. Chorionic villi are necrotic, and the surface has adherent necrotic cellular debris and degenerate neutrophils. A mixed infiltrate of neutrophils, lymphocytes, plasma cells, and histiocytes extends throughout the interstitium of the chorioallantois. Numerous trophoblasts are distended by intracellular colonies of palely basophilic bacteria. Gram stains of the chorionallantois demonstrate these colonies consist of gram-negative short bacilli. Depending on the section, there is variable partial mineralization of the epithelium.

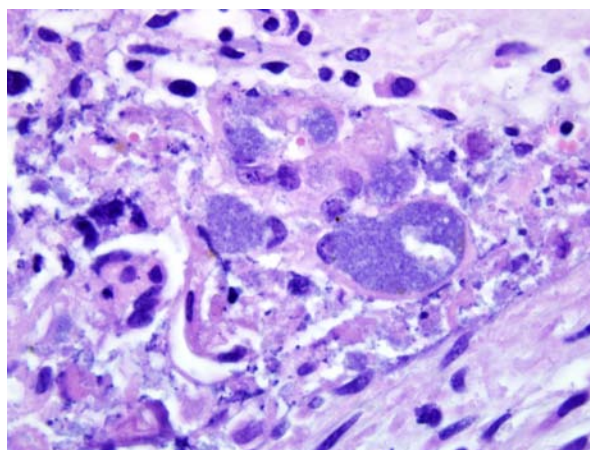
Immunohistochemistry using a generic antibody against *Coxiella burnetii* was strongly immunopositive for the intracytoplasmic bacterial colonies.

Contributor's Morphologic Diagnosis: Chorioallantois: Severe acute necrotizing placentitis with intracellular bacterial colonies.

Contributor's Comment: *Coxiella burnetii* is a member of the Rickettsiaceae family, which are small,



3-1. Placenta, goat. Chorionic villi are collapsed and largely replaced by necrotic cellular debris, degenerate neutrophils and multifocal mineralization. (HE 200X)



3-2. Placenta, goat. Trophoblasts are distended by numerous intracytoplasmic basophilic coccobacilli (HE 1000X)

non-motile gram-negative bacteria that replicate only within host cells. Infection with *Coxiella burnetii* is relatively common in domestic cattle, sheep and goats, which serve as the reservoir hosts. Infection is persistent, and shedding of the organism through urine, feces, milk and placental fluids contaminates the environment. Acute infection in domestic ruminants may manifest itself as late third trimester abortions, stillbirths, delivery of weak neonates, retained placentas, endometritis and infertility. When the placenta is infected, the obligate intracellular bacteria are encountered within the cytoplasm of trophoblasts. Gross lesions in the placenta (not noted in this case)

include thickened and leathery appearance, and off-white exudates which are most prominent in the intercotyledonary regions of the chorioallantois. However, histologically, the predominantly necrotizing and suppurative placentitis frequently extends into cotyledonary regions as well. The principal differential for *C. burnetii* in the placenta is *Chlamydophila* infection, which produces a similar placentitis with intracytoplasmic colonies.

In humans, *C. burnetii* results in the zoonotic condition known as Q fever. Acute infection may include mild flu-like symptoms, pneumonia, or hepatitis. The organism infects monocytes and macrophages which internalize the organism into phagolysosomes. In the environment, the organism survives as the highly resistant extracellular small cell variant. But once inside monocytes or macrophages, the organism switches to the large cell variant. The more debilitating chronic form of the disease in humans is characterized by endocarditis, hepatitis, and chronic fatigue syndrome. Due to *C. burnetii*'s resistance to environmental conditions of heat and pressure, and its highly infectious nature, it is classified as a "Category B" biological warfare agent.

JPC Diagnosis: Chorioallantois: Placentitis, necrotizing, multifocal to coalescing, marked, with numerous intratrophoblastic bacilli.

Conference Comment: *Coxiella burnetii* is transmitted by most tick species and can be acquired by aerosolization and direct contact. Although infection occasionally causes abortions in cattle, abortion is a more common result in small ruminants and typically presents as isolated abortions rather than as an abortion storm. Unless infection is overwhelming, as in this case, the organisms may not be visible with hematoxylin and eosin (H&E) staining, but silver stains and immunohistochemistry are useful.³ Because of concerns for safety of laboratory personnel, the organism should only be cultured within a biosafety level-3 laboratory.

Brucella abortus, another differential for this case, also causes cotyledonary and intercotyledonary necrosis, but the fetus usually has bronchopneumonia, which helps differentiate infection with this organism from *Coxiella*. Other differential causes for necrotizing placentitis are *Chlamydophila abortus*, which commonly also causes vasculitis, and *Toxoplasma gondii*, which primarily affects the cotyledons and spares the intercotyledonary areas.³ Multifocal epithelial mineralization around blood vessels in small ruminant placentas can be a normal physiologic process and contributes to ossification of the fetal skeleton.

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CASE IV: 648-11 (JPC 4003704).

Signalment: 8-day-old female Aberdeen Angus (*Bos taurus*), bovine.

History: This calf was from a cow-calf herd with 55 suckler cows. The herd had suffered from increased morbidity and mortality of suckling calves aged 1-9 days old. Clinical signs of this calf included diarrhea, petechiae on the conjunctival and buccal membranes, fever and generalized weakness.

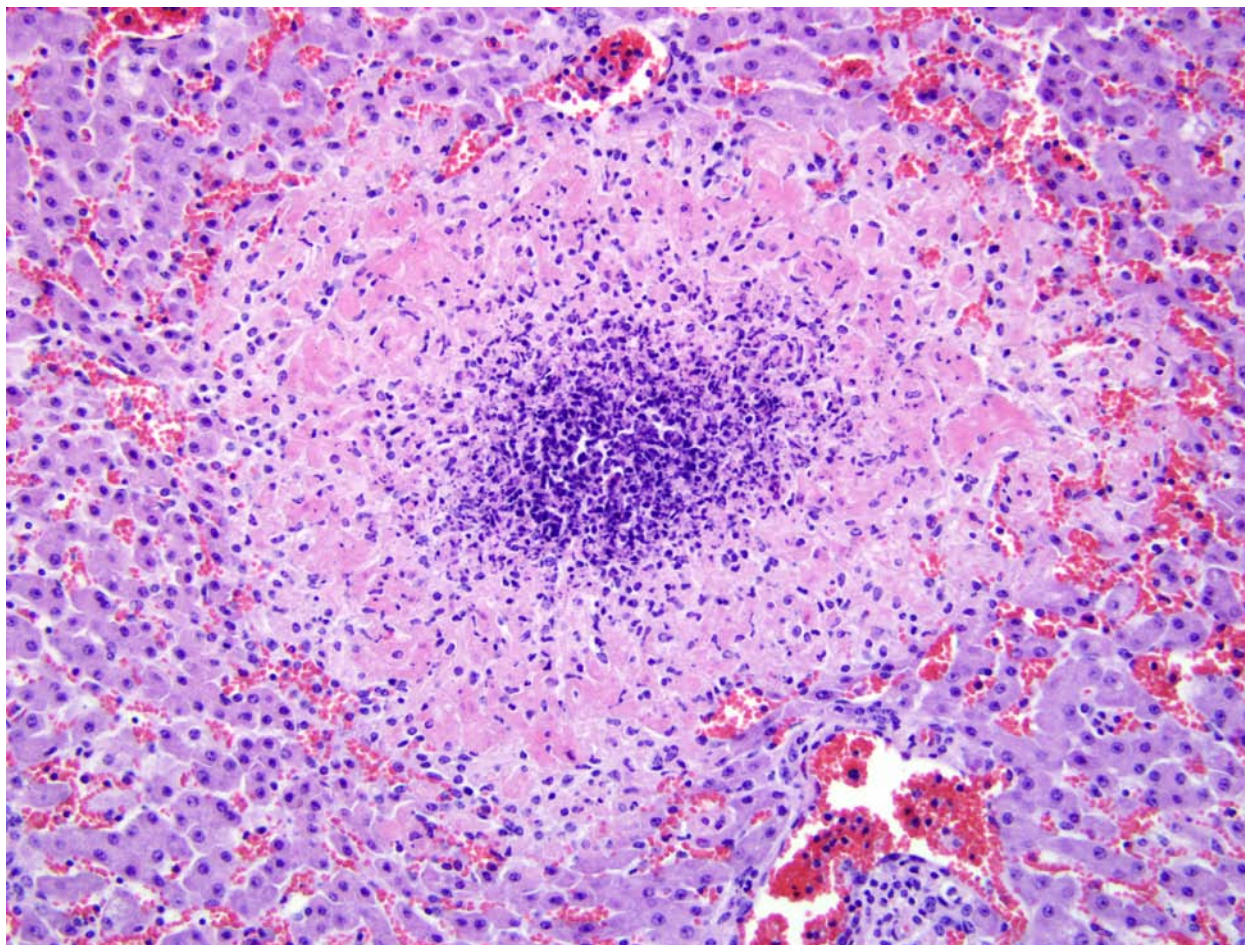
Gross Pathology: Weight 39 kg, moderate post mortem changes, moderate fat stores, and severely dehydrated. All visible lymph nodes were swollen. The umbilical arteries were swollen and deep red. The spleen was moderately enlarged. The liver contained multiple disseminated 2-3 mm pale yellow spots all over the parenchyma. The abomasum contained 1 liter of coagulated milk, mucosa was moderately red and swollen. The distal parts of the jejunal and the ileal serosa and mucosa were red, and ileal lymph nodes were severely swollen and reddish gray. Pale purulent

exudate covered the meninges of the brain stem. Fibrinous pale exudate was detected in the joint cavities of the legs.

Laboratory Results: *Listeria monocytogenes* was isolated in pure growth from the spleen, liver, lung, ileal lymph node and brain. *Salmonella* was not detected.

Contributor's Microscopic Description: Liver: Multifocal, disseminated, random, variable sized foci of deeply eosinophilic (coagulation necrosis) hepatocytes, infiltrated with variable, usually moderate, numbers of degenerating neutrophils and a few macrophages. Brown-Benn staining showed multiple gram-positive short rod shape bacteria in these foci. In other tissues (samples not submitted), a suppurative synovitis and meningitis, and a necrotizing lymphadenitis and enteritis were detected.

Contributor's Morphologic Diagnosis: Liver: Multifocal moderate subacute necrotizing hepatitis.



4-1. Liver, calf. There are numerous randomly distributed foci of lytic necrosis bordered by a rim of hepatocytes undergoing coagulative necrosis. (HE 200X)

Contributor's Comment: The genus *Listeria* includes 6 species, of which two, *L. monocytogenes* and *L. ivanovii*, are known to cause disease in animals. *L. ivanovii* has been detected causing abortions in ruminants. *L. monocytogenes* is ubiquitous in the environment, in the soil, plants and feces of animals. It is a gram-positive short non-spore forming rod capable of growing from 1° C to 45° C and pH 4.5-9.6. *L. monocytogenes* is an opportunistic pathogen and causes disease in several animal species including mammals, birds and fish. Of the domestic species, most commonly ruminants are affected, rarely also foals or pigs.^{2,6} Feeding of poorly fermented silage with pH over 5 has commonly been associated with occurrence of the disease in ruminants. Listeriosis is a zoonosis.

The three main types of disease caused by *Listeria* are meningoencephalitis, abortions and septicemia. Meningoencephalitis is the most common form of the disease and occurs mainly in adult ruminants. Abortions in the last third of the pregnancy or stillbirths are most often detected in sheep, goats and cattle. Septicemia occurs in young ruminants and neonate monogastric animals. Less common forms of the disease are conjunctivitis, keratitis or uveitis in ruminants and horses¹; mastitis, endocarditis, meningitis in young animals; spinal myelitis in sheep; and enteritis in adult sheep. Recently, a fatal mesenteric lymphadenitis was described in adult cattle.⁵ Also, skin infections have been described in veterinarians. *L. monocytogenes* septicemia occurs also in rabbits, chinchillas, hares, and has been described in semi-domesticated reindeer calves associated with silage feeding.³ The disease is often sporadic but small epidemics occur.

Infection occurs via ingestion, from the contaminated feed or udder, via milk or umbilical cord, or in the uterus. The bacteria penetrate the intestinal mucosa and cause a subclinical bacteremia. Encephalitis in ruminants has a different pathogenesis and is probably acquired via cranial nerves from oral mucosal abrasions or an infected tooth cavity. In these cases the bacteria reach the brain stem by using axonal transport. This is supported by the special distribution of the lesions in the brain stem. The incubation period varies from 2 days to several weeks. Only a small proportion of infected animals develop clinical disease. The predisposing factors include stress, pregnancy, parturition, poor nutritional state, large dose and failure of passive transfer. In humans the infection is usually foodborne and pregnant women, elderly and immunocompromised individuals are predisposed.

Listeria is a facultative intracellular parasite and invades cells, macrophages, monocytes, neutrophils and epithelial cells by using a special surface protein,

internalin.² In the cell, bacteria escape from the phagosomes by producing a haemolysin called listeriolysin O and phospholipases. The bacteria are motile and have a special cell to cell movement system. Cell-mediated immunity has a role in causing tissue damage. Gross pathological findings in septicemic forms of the disease consist of multiple random pale necrotic foci or microabscesses, most commonly in the liver and spleen.

Histologically, in the septicemic form, multiple necrotic foci or microabscesses with variable numbers of neutrophils and macrophages are seen in the liver, and are often also in the spleen or other tissues.

The differential diagnoses for necrotic hepatitis include *Salmonella*, *Bacillus piliformis* (Tyzzer's disease), *Yersinia pseudotuberculosis*, and in rodents also *Toxoplasma gondii*.

JPC Diagnosis: Liver: Hepatitis, necrotizing, multifocal and random, moderate.

Conference Comment: Glycogen vacuoles present in the liver suggest this is a young animal. Because infection occurs following ingestion, *Listeria* causes individual abortions rather than an abortion storm. It also causes placentitis with cotyledonary necrosis and vasculitis of the chorioallantois but not the amnion. Necrotizing hepatitis and enteritis may also be prominent features in the aborted bovine fetus. With early third trimester infection and following abortion, the placenta is often retained due to mild metritis; however, the dam usually does not suffer severe illness. Conversely, if infected near term, the dam often suffers from dystocia, severe metritis and septicemia.⁴ Neutrophils are the primary inflammatory cell in listeriosis, due in part to *Listeria* infected endothelial cells expressing P- and E-selectin, intracellular adhesion molecule-1 (ICAM-1), and vascular cell-adhesion molecule-1 (VCAM-1), which activate the neutrophil adhesion cascade and neutrophil binding.⁷

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