Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2011-2012

Conference 7

26 October 2011

CASE I: AFIP-3 (JPC 4004305).

Signalment: A 400 pound cross-bred calf (*Bos taurus*), age and gender unknown.

History: Lung and liver tissues of the calf have been submitted to the necropsy section of the ADRDL-SDSU with a history of respiratory signs ("Well vaccinated, small feedlot calves. Having trouble with *Mycoplasma* sp.?").

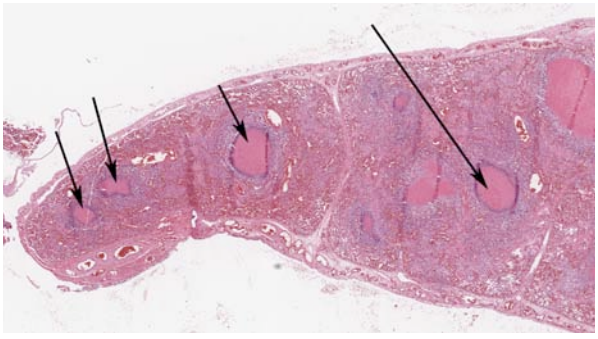
Gross Pathology: Gross necropsy results not reported.

Laboratory Results: *Mycoplasma* sp. and *H. somni* have been isolated from the lung.

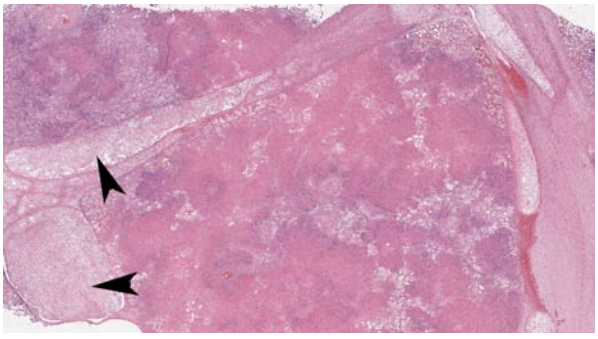
The bovine virus isolation and the FA for BVD, IBR and BRSV results were negative.

Histopathologic Description: Lung: There is diffuse infiltration of neutrophils and accumulation of fibrin and edema fluid in the airways. There are multifocal pulmonary necrotic areas surrounded by a zone of the inflammatory cells, primarily neutrophils and fewer macrophages. In addition to that there is also diffuse infiltration of neutrophils and accumulation of fibrin in the pleura. The pulmonary blood vessels are congested.

Contributor's Morphologic Diagnosis: Bronchopneumonia, fibrino-suppurative, subacute, diffuse, severe, with multifocal areas of abscessation; diffuse fibrinosuppurative pleuritis.



1-1. Lung, calf. Suppurative bronchiolitis and bronchiectasis at lobe margins in one section. (HE 40X)



1-2. Lung, calf. Well-defined coalescing areas of coagulative necrosis are present throughout both sections; massive dilation of interstitial lymphatics by fibrin thrombi (arrowheads). (HE 40X)

Contributor's Comment: Calf pneumonia is one of the major problems in beef and dairy sectors. It is the most common post-mortem diagnosis in calves at 1-5 months of age. Although it is associated with low mortality, it is highly infectious in nature, affecting more than 50% of young calves. Affected calves suffer from low growth rate. It is a multifactorial disease including a number of bacterial, viral and fungal pathogens.

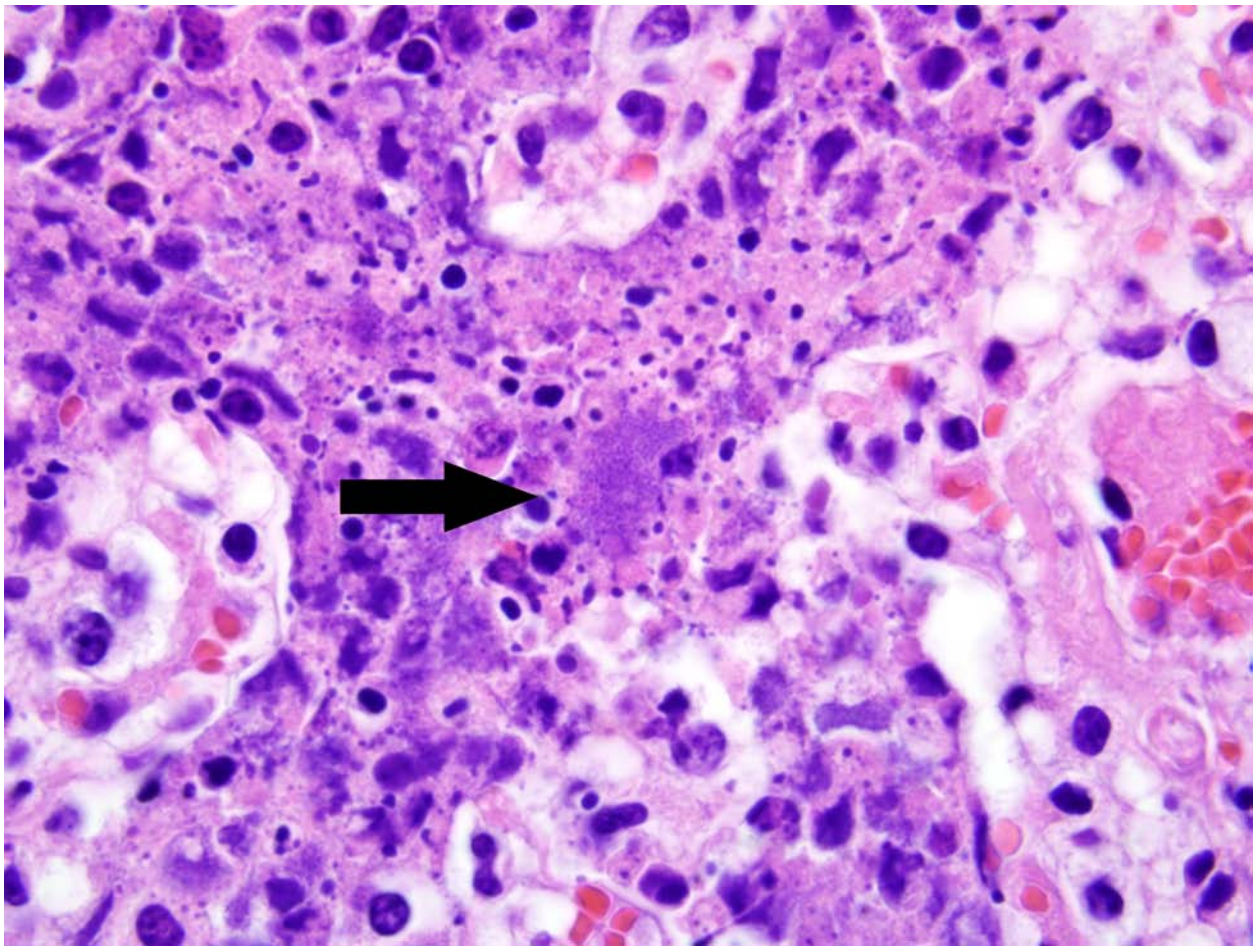
Calf pneumonia occurs due to a complex interaction between host, environment and pathogen. Young calves with low immunity are highly susceptible to this disease. Among various bacterial agents that cause pulmonary infections, *Mycoplasma* and Histophilus are most common.

Mycoplasma bovis was first reported in the United States in the 1970s. The high number of new cases was reported in the summer of 2000. After that, *M. bovis* has been found almost in every herd. A study conducted in 2006 revealed a 46% prevalence of *Mycoplasma bovis* in lungs of normal cattle.[3] Calves suffering from *Mycoplasma* pneumonia show low grade fever, tachycardia and mild depression.

H. somni is another important cause of bovine pneumonia.[1,4] *H. somni* is also associated with a wide variety of other cattle diseases including abortion, infertility and arthritis.[4] *H. somni* pneumonia is characterized grossly by grey to red consolidation of the cranio-ventral lung, involving from 5 to 80% of total lung volume.[1] Tracheobronchial and mediastinal lymph nodes are typically edematous, with fibrinous pleuritis seen irregularly.[1,3] Histologically, the suppurative necrotizing bronchopneumonia is the most common histopathologic identification of bacterial pulmonary infections.

Note: Multiple blocks were used for the slides submission; therefore not all the participants will get the same copy of the slides.

JPC Diagnosis: 1. Lung: Pleuropneumonia, fibrinosuppurative and necrotizing, diffuse, severe, with marked intralobular edema and lymphatic fibrin thrombi.



1-3. Lung, calf. Rare colonies of bacilli consistent with Histophilus somni are present within areas of necrosis (arrow). HE 1000X)

2. Lung: Bronchopneumonia, fibrinosuppurative and necrotizing, with marked suppurative bronchilitis and bronchiectasis.

Conference Comment: There was marked slide variation, and some slides did not contain both sections of lung. The two sections of lung demonstrated the distinctly different histomorphologies of each entity.

One section contains multiple ectatic bronchioles filled with caseonecrotic material within areas of profound atelectasis characteristic of mycoplasmal pneumonia. Bronchiolar-associated lymphoid tissue (BALT) is depleted, which is characteristic of enzootic bovine pneumonia. Affected cattle often present with otitis media, as *Mycoplasma* preferentially colonize areas of the body lined by ciliated epithelium (such as airways).

The other section of lung exhibits necrosuppurative bronchopneumonia, which is more typical of gram-negative bacteria, such as *Mannheimia haemolytica or Histophilus somni.* In affected lungs, alveoli are filled with fibrin and leukocytes and larger areas of coagulative necrosis may become sequestra. Grossly, affected areas of lung will be sharply demarcated from adjacent lung, and the presence of large amounts of fibrin and cellular exudate will give it a firm feel.[2]

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CASE II: NIAH-2 (JPC 3133973).

Signalment: 5-year 3-month-old female Japanese native breed goat, (*Capra aegagrus*).

History: A Japanese native breed goat showed respiratory symptoms including tachypnea and cough. Three months later, the goat developed mild carpal swelling. At the time, the serum was negative for caprine arthritis-encephalitis (CAE) virus. Two months later, many nodules resembling abscesses, up to 10 cm in diameter, developed in the mammary gland and lip. The goat was submitted for necropsy.

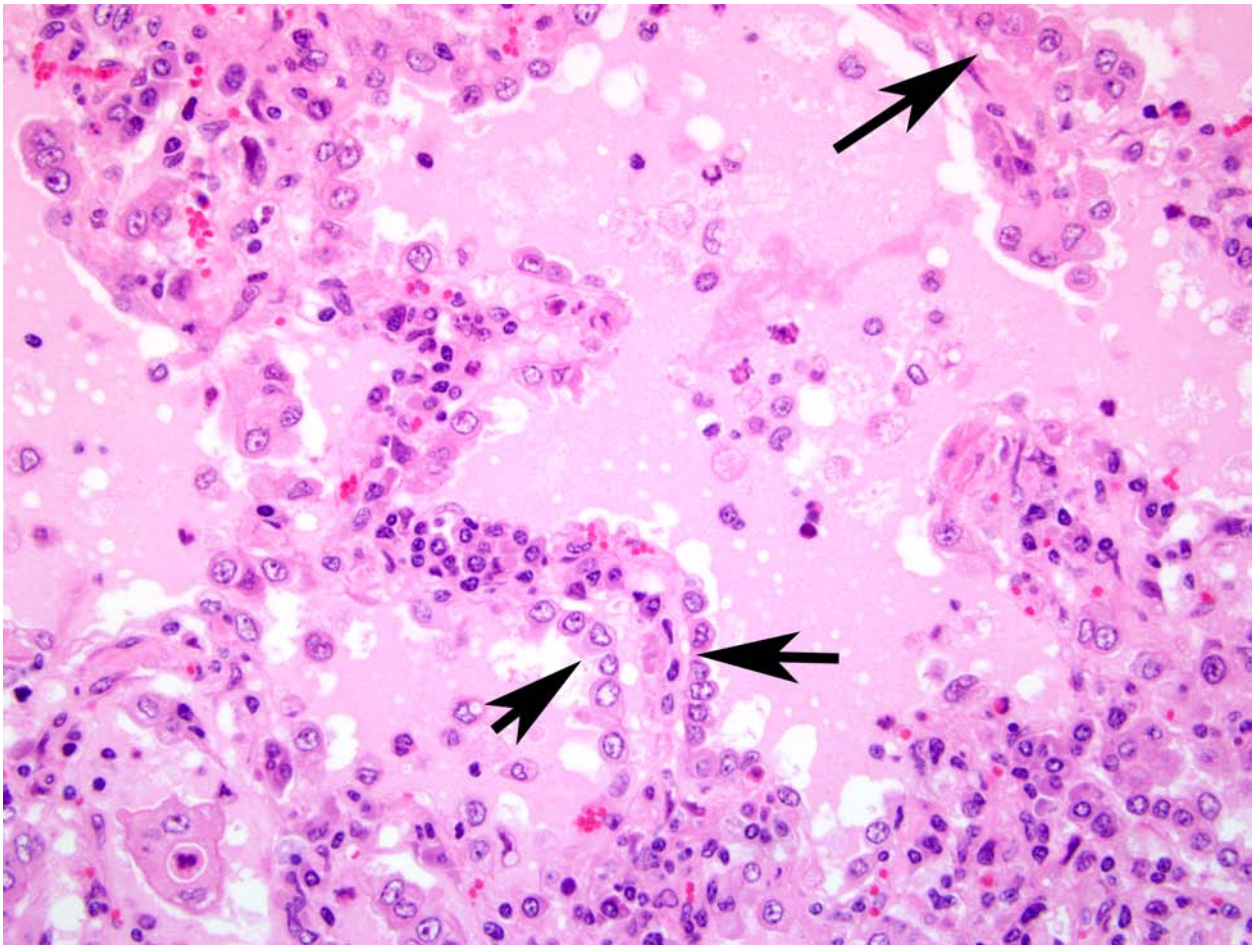
Gross Pathology: The goat was in poor body condition. The lung had distinctive pale firm lesions with ecchymosis throughout the lung. Both carpal joints had mild swelling. Many abscesses were seen in the mammary gland.

Histopathologic Description: Lung: The foci in the lung were demarcated from relatively unaffected areas. Distinctive cuffs consisting of lymphocytes and plasma cells were formed around blood vessels and airways. Alveolar septa were thickened with infiltrates of lymphocytes and the hyperplasia of type II pneumocytes. Alveoli were filled with eosinophilic fluid, small amounts of fibrin, neutrophils and macrophages. Occasionally, macrophages phagocytizing eosinophilic fluid were seen.

Both carpal joints had arthritis and periarthritis characterized by the villous proliferation of the synovial membrane, lymphoplasmacytic infiltration and necrosis of the tendon sheath.

In mammary glands, periductal infiltration of lymphocytes and many abscesses were observed. No lesion was found in the central nervous system.

Immunohistochemically, the eosinophilic materials in alveoli were positive for anti-surfactant protein A antibody (Chemicon). Furthermore, immnohistochemical examination with anti-CD3 (DAKO), anti-CD79a (DAKO), anti-CD68 (DAKO) antibodies showed that most of the lymphocytes



2-1. Lung, goat. Diffuse expansion of alveolar septa and type II pneumocyte hyperplasia (arrows); alveolar lumina are filled with abundant eosinophilic proteinaceous fluid (not just edema). (HE 400X)

around blood vessels and airways were T-lymphocytes that can relate to the cell-mediated immunity. *Pasteurella multocida* antigens were detected in the area of bronchopneumonia. Immunohistochemical detection of CAE virus antigens was not successful.

Contributor's Morphologic Diagnosis: Lung: Pneumonia, interstitial, lymphocytic, with perivascular and peribronchial lymphoplasmacytic infiltration, type II pneumocyte hyperplasia and intra-alveolar eosinophilic proteinaceous materials.
Etiology: CAE.

Contributor's Comment: CAE is a progressive disease of domestic goats caused by the CAE virus and belongs to Lentivirinae of the family Retroviridae. The first case was identified in USA in 1974. In Japan, the first case was identified in 2002.[2] Most infected goats develop subclinical disease. However, affected adult goats may develop the chronic arthritis and mastitis, occasionally leading to the pneumonia and encephalitis. World Organization for Animal Health recommends serological diagnosis like AGID test and ELISA.[7] In addition to these tests, histopathological diagnosis is definitive for CAE.

The lesions of the lung in the present case consisted of those of typical CAE which are characterized by the lymphoplasmacytic infiltration in septa with the type II pneumocyte hyperplasia, infiltration of lymphocytes around blood vessels, bronchi, and bronchioles, and eosinophilic exudates in alveoli.[1,4] Distinctive eosinophilic fluid is an important finding for differential diagnosis between CAE and maedi.[4]

The present case had lymphoplasmacytic arthritis and periarthritis with villous proliferation of the synovium, which are suggestive of CAE.[6] In the mammary gland, many abscesses and periductal cuffs consisting of lymphocytes were seen. Unlike abscesses caused by *Arcanobacterium pyogenes* infection, the infiltration of lymphocytes around ducts was a characteristic finding of the nonsuppurative mastitis caused by CAE virus.[5]

Although the serum was weakly positive for CAE virus antibody by AGID test, pathological findings in this case were identical to those of CAE virus infection. *Pasteurella multocida* infection of the lung might be a secondary infection to CAE.

JPC Diagnosis: Lung: Pneumonia, interstitial, lymphohistiocytic, diffuse, moderate, with marked pulmonary edema, peribronchial and perivascular lymphohistiocytic infiltrates, and type II pneumocyte hyperplasia.

Conference Comment: CAE is primarily transmitted through infected colostrum and milk, and manifests as either nonsuppurative leukoencephalomyelitis in kids or nonsuppurative arthritis and synovitis in adult goats. Pneumonia and mastitis are less frequently seen. There is B cell hyperplasia of BALT and marked tracheobronchial lymphadenomegaly.[4]

Conference participants discussed the primary differential diagnosis for nonsuppurative interstitial pneumonia in sheep and goats, and a primary consideration for many was ovine progressive pneumonia (OPP) - also known as "maedi", to which goats are also susceptible, and which is more common than the pneumonia form of CAE in the United States. One difference between OPP and CAE is that type II hyperplasia and eosinophilic alveolar fluid is not a prominent feature of OPP. Additionally, type II pneumocyte hyperplasia is not prominent in OPP because the type I pneumocytes remain uninjured.[4] Both have a typical gross appearance of heavy, rubbery, pale gray lungs that fail to collapse. Another consideration for the florid type II pneumocyte hyperplasia seen in this case is ovine pulmonary adenomatosis caused by ovine retrovirus (also known as "jaagsiekte sheep retrovirus - JSRV), which rarely affects goats.[1] An associated clinical sign of jaagsiekte is the drainage of fluid from the nose following elevation of the hind limbs. A final cause of lymphocytic interstitial pneumonia in sheep and goats is parasitic pneumonia caused by *Meullerius capillaris*.

The section of lung in this case demonstrates a typical histologic appearance of CAE and other lentiviruses affecting sheep and goats, with a sharp demarcation between affected and unaffected lung. The copious proteinaceous fluid filling the alveoli in this section is visually distinct from edema fluid, and is also very characteristic of this disease. The moderator pointed out that there was no corroborative evidence to attribute the prominent eosinophilic fluid to hydrostatic edema, such as dilated lymphatics and rarefaction around blood vessels. This fluid has been shown to contain pulmonary surfactant, which is consistent with the abundant type II pneumocyte hyperplasia. As the virus destroys type I pneumocytes, and type II pneumocytes proliferate, the local environment becomes hypoxic due to the thickening of the interstitium, which also fills with lymphocytes, plasma cells, and macrophages. As the diffusion capacity of the lung decreases, cells release hypoxia-induced factor-1α, which activates the transcription of vascular endothelial growth factor, increasing vascular permeability and the leakage of high protein plasma fluid.[3] The interstitial pneumonia seen with CAE results from infected macrophages expressing IL-8, which recruits additional inflammatory cells, perpetuating the inflammatory cycle.[8]

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CASE III: 08VD29987B (JPC 3134635).

Signalment: Porcine (*Sus domestica*), 50-60 lbs pigs (approximately 9 weeks of age), crossbreed (unknown), gender unknown (tissues were received for diagnostic evaluation).

History: Sudden death.

Gross Pathology: N/A (tissues were received for diagnostic evaluation).

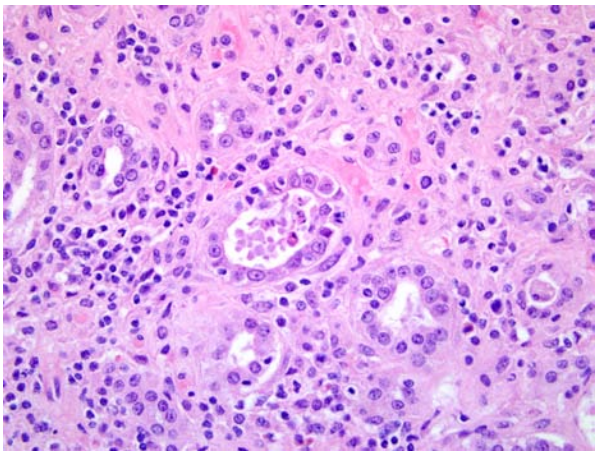
Laboratory Results:
Bacteriology: *Streptococcus suis* and *Arcanobacterium pyogenes* were isolated from lung. Kidney was not cultured (only fixed renal tissue was received)
Mycoplasma hyopneumoniae PCR was negative (lung)

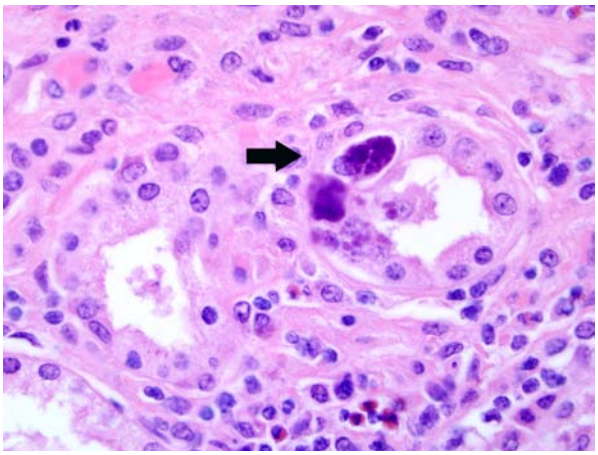
Virology: PRRSV PCR was negative (lung)
SIV PCR was negative (lung)
PCV2 IHC was **positive** (abundant staining, in kidney, spleen, and lymph node)

Histopathologic Description: Kidney: Renal interstitium is multifocally infiltrated by marked inflammatory cells and modest amounts of fibrous connective tissue that frequently coalesce and form linear streaks that extend from the capsule to the medulla. Lymphocytes, plasma cells, macrophages, lesser eosinophils, edema, and scant fibrin separate frequently dilated tubules, surround multifocal glomerular tufts, or cuff arterioles within the cortex and at the corticomedullary junction. Dilated tubules are lined by lost, flattened, swollen (degeneration), or necrotic epithelium that occasionally contain intracytoplasmic basophilic botryoid inclusion bodies ranging in size from 1-5 µm. Proteinic fluid, karyorrhectic cellular debris, and sloughed renal tubular epithelium containing cytoplasmic inclusion bodies are present within multifocal tubular lumens. Multifocally, there is complete loss of tubules (atrophy) or tubules are lined by crowded or stacked epithelium (regeneration). Corticomedullary arterioles are frequently accentuated by proliferation of the tunic intima and smooth muscle hypertrophy and hyperplasia of the tunic media. Blood vessels within the cortex are frequently congested and infrequently contain myriad 1µm coccoid bacteria, and there is mild multifocal hemorrhage. Glomerular tufts are multifocally congested, and mildly hypersegmented and hypercellular.

Contributor's Morphologic Diagnosis: 1. Kidney. Tubulointerstitial nephritis, lymphoplasmacytic and macrophagic, multifocal, severe, chronic with fibrosis and tubular loss, degeneration, necrosis, and regeneration, and botryoid intraepithelial cytoplasmic inclusions (etiology consistent with porcine circovirus type II infection).
2. Kidney. Arteritis, proliferative and perivascular, lymphocytic, multifocal, severe, chronic with intimal and tunic medial proliferation.
3. Kidney. Intravascular coccoid bacteria, multifocal, acute.

Contributor's Comment: In recent years, there has been a marked increase in the number of porcine circovirus associated disease (PCVAD) cases at the Iowa State Veterinary Diagnostic Laboratory. Affected pigs often have classical lesions of lymphoid depletion, interstitial pneumonia, and interstitial nephritis. The severity of these microscopic lesions depends greatly on the timing of viral infection. Interstitial nephritis typically begins with a perivascular accumulation of macrophages, lymphocytes, and fewer plasma cells adjacent to large vessels at the corticomedullary junction. In time, the mononuclear infiltrate extends to



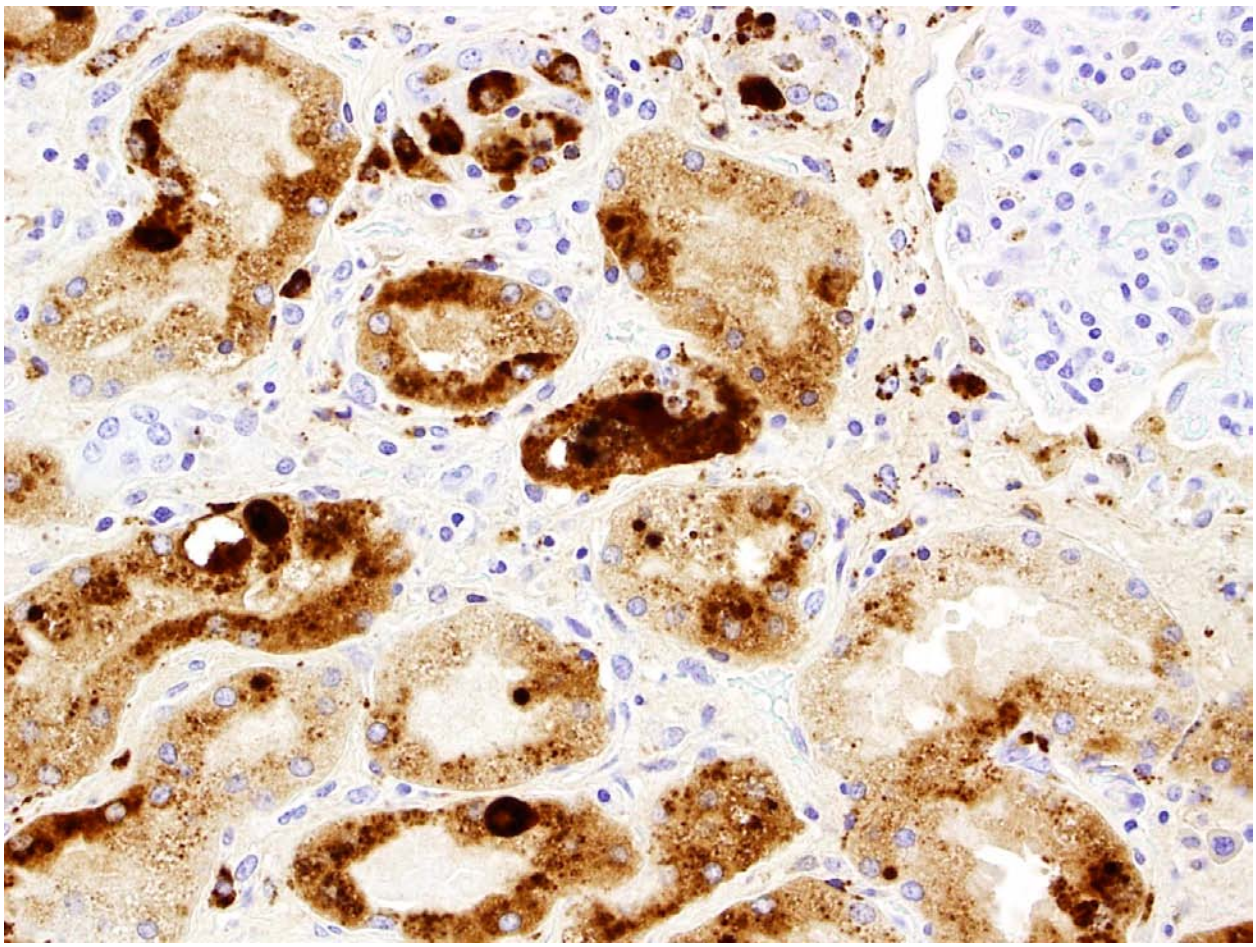


3-1, 3-2. Kidney, pig. Tubules are widely separated by interstitial fibrosis containing moderate numbers of lymphocytes and histiocytes. Multifocally, tubules are filled with necrotic tubular epithelium, or lined by more basophilic, closely spaced epithelial cells. Tubular epithelial cells occasionally contain basophilic, botryoid cytoplasmic inclusions (arrows). (HE 400X)

the cortical interstitium and to a lesser degree to the medulla. Inflammatory cells separate adjacent tubules and occasionally surround glomerular tufts. Renal tubular epithelium is frequently degenerative, sloughed, or regenerative and lumina can contain protein or cellular casts. Another feature that is occasionally seen (often depending on timing of viral infection) are basophilic intracytoplasmic botryoid inclusion bodies.[5] In this particular case, sudden death of the pig was likely due to bacterial septicemia which was predisposed by PCV2 infection. One can only speculate that PCV2 infection may have occurred 2-4 weeks prior to sudden death. Porcine circoviruses (PCV) are non-enveloped, single-stranded, circular DNA viruses of approximately 1.7kb classified in the *Ciroviridae* family, genus *Circovirus*. There are two known PCV species, porcine circovirus type 1 (PCV1) and porcine circovirus type 2 (PCV2). PCV1 was first described in 1974 as a non-cytopathic contaminate of a porcine kidney cell line, PK-15. Experimental studies later determined that PCV1 was non-pathogenic in swine. In contrast, PCV2 is pathogenic in swine and associated with multiple disease entities.

PCV2 is globally distributed and most herds are seropositive for anti-PCV2 antibodies.[7] PCV2 infection occurs as maternally derived antibodies wane in post-weaned pigs (7-15 weeks of age) and results in either subclinical infection or clinical disease. Clinical disease associated with PCV2 infection can have multiple manifestations which include the following: post-weaning multisystemic wasting syndrome (PMWS), respiratory disease, enteritis, porcine dermatitis and nephropathy syndrome (PDNS), myocarditis/vasculitis, and exudative dermatitis.[1,2] Porcine circovirus associated disease (PCVAD) is more common terminology used in North America to summarize the different clinical manifestations associated with PCV2 infection.[7]

Subclinical disease: PCV2 can be detected in normal, healthy pigs without signs of disease. Subclinical PCV2 infection can reduce growth performance, can cause increased susceptibility to other swine-associated pathogens, or result in decreased efficacy of commonly administered swine vaccines.[7] Quantification of PCV2 DNA in serum and tissue has been proposed as a



3-3. Kidney, pig. Renal tubular epithelium demonstrates positive cytoplasmic immunoreactivity for porcine circovirus 2 antigen. Photograph courtesy of Iowa State University College of Veterinary Medicine, Department of Veterinary Pathology, http://www.vetmed.iastate.edu/departments/vetpath/. (200X)

means of differentiating subclinical from clinically affected animals. Subclinically infected PCV2 pigs typically have lower amounts of DNA in serum and tissue ($\geq 10^7$ genomic copies per ml/serum or tissue).

Post-weaning multisystemic wasting syndrome (PMWS): PMWS is a multifactorial systemic disease and clinically manifests at 25-150 days of age with most cases occurring between 7 and 15 weeks. Six fundamental clinical signs are emphasized and include wasting, dyspnea, lymphadenopathy, diarrhea, pallor and jaundice. Coughing, pyrexia, gastric ulceration, and meningitis have also been reported, but are sporadic. Not all clinical signs have to be present in an individual pig, but all six fundamental signs can generally be observed among the population of pigs in affected herds over time.[4] Herd morbidity in PMWS herds is variable with 4-30% of the pigs affected. Mortality rates are often high (20%) with occasional reports of greater than 50% death loss within a group. The most consistent necropsy finding in PMWS pigs is generalized lymph node enlargement. Other macroscopic lesions can include mottled tan non-collapsing lungs and thymic atrophy. PMWS pigs are frequently coinfected with other common bacterial and viral pathogens, and coinfection often complicates gross findings.

Microscopic lesions in PMWS-affected pigs are consistently found in lymphoid tissues and characterized by loss (depletion) of lymphocytes and replacement by histiocytic/granulomatous inflammation. Lymphoid depletion can be associated with paracortical or follicular regions with the latter being more prevalent. Multinucleated giant cells (Langhans-type), epithelioid macrophages and macrophage-associated intracytoplasmic, botryoid-like, basophilic inclusions are also commonly seen in lymphoid tissues (lymph node, tonsil, and spleen). Focal parenchymal coagulative and apoptotic necrosis in lymphoid tissues has also been described. Microscopic lesions in non-lymphoid tissues are composed of lymphomacrophagic inflammation and include interstitial pneumonia, hepatitis, interstitial nephritis and enteritis/colitis.

Clinical signs along with macroscopic and microscopic lesions associated with PCV2 infection are suggestive, but not definitive for a PMWS diagnosis in an individual or group of pigs. A definitive diagnosis of PMWS is based on the following definition: (1) clinical signs of wasting, weight loss or failure to thrive that may or may not include respiratory distress and icterus, (2) microscopic lesions of lymphoid depletion and granulomatous inflammation, and (3) the presence of PCV2 antigen or nucleic acid associated with microscopic lesions.[8] Not all PMWS-affected pigs will have equal distribution of microscopic lymphoid lesions.

PCV2-associated respiratory disease: PCV2-associated respiratory disease can often overlap with PMWS or be a contributing factor in porcine respiratory disease complex (PRDC). In the first cases of PMWS, lymphomacrophagic interstitial pneumonia was a common microscopic lesion. Other hallmark microscopic lung lesions of PCV2 include type II pneumocyte hypertrophy and hyperplasia, peribronchiolar fibrosis, and associated lymphoid hyperplasia.[2]

PCV2-associated enteritis: The suspected major route of PCV2 transmission is fecal-oral, suggesting that the alimentary mucosa, intestinal M-cells, and gut-associated lymphoid tissue (GALT; Peyer's patches) are exposed to varying amounts of infectious virus. Peyer's patches can exhibit hallmark microscopic lesions of lymphoid depletion and granulomatous inflammation in both PCV2-associated enteritis and PMWS-affected pigs. The diagnosis of PCV2-associated enteritis is appropriate when (1) there is clinical diarrhea, (2) the hallmark microscopic lesions are present in Peyer's patches but not in other lymphoid tissues, and (3) PCV2 DNA or antigen can be demonstrated within the lesions.[2]

PCV2-associated enteritis may occur anytime in the grow-finish phase, and can be associated with the small or large intestine. Affected intestinal segments are sometimes thickened and necrotic resembling gross lesions of *Lawsonia intracellularis* infection and can be misdiagnosed as such. Microscopically, PCV2-associated enteritis has been described as having variable amounts of macrophages infiltrating the mucosa with PCV2 antigen present in crypt epithelium, the lamina propria, and submucosa. Villous atrophy and fusion along with multinucleated giant cells within the lamina propria have also been described.

Porcine dermatitis and nephropathy syndrome (PDNS): PDNS is a distinctive, acute clinical entity of growing swine that was first recognized in 1993 and is now globally distributed.[2] Affected pigs have circular to coalescing, red to purple macules or raised papules and plaques, occasionally with black centers, that originate on the skin of the hind legs and perineal region. Lesions may become exudative, crust-over, and eventually regress leaving dermal scars. Bilateral swollen kidneys with widely disseminated cortical petechial hemorrhages are common features of the syndrome. Increased mortality is seen in affected pigs older than three months of age, the syndrome is sporadic, and herd-outbreak mortality can range from 0.25 to > 20%.

The hallmark microscopic lesion in PDNS-affected pigs is necrotizing vasculitis and glomerulonephritis. Small to medium sized dermal and subcutaneous arterioles are cuffed by neutrophils, macrophages, lymphocytes, and plasma cells that are sometimes present within vascular walls. Arterioles are lined by plump endothelial cells, occasionally occluded by fibrin thrombi and walls can display multifocal hyalinization. The corresponding dermis is necrotic and hemorrhagic. Kidney sections are characterized by distension of urinary spaces by fibrin intermixed with necrotic cellular debris and hemorrhage, periglomerular and interstitial mononuclear cell infiltration, and distension of renal tubules that contain cellular and proteinaceous casts. Perirenal lymph nodes are sometimes depleted and hemorrhagic.

Skin and glomerular lesions are characteristic of a type III hypersensitivity reaction with deposition of antigen-antibody complexes (immune complexes). Immune complexes have been demonstrated in glomerular tufts. Multiple viral and bacterial pathogens have been implicated in PDNS, but PCV2 is considered a contributing factor. To date, PDNS has not been reproduced with PCV2 infection.

JPC Diagnosis: 1. Kidney: Nephritis, interstitial, lymphohistiocytic, diffuse, moderate, with tubular degeneration, necrosis, and regeneration, granular and cellular casts, intraepithelial intracytoplasmic botryoid inclusions, and proliferative, eosinophilic and histiocytic arteritis.
2. Kidney, glomeruli and vasa recta: Intravascular bacterial emboli.

Conference Comment: The contributor has provided an excellent and comprehensive overview of circovirus-associated disease in swine.

A central nervous system manifestation of PCV2 infection is cerebellar hemorrhage and edema from necrotizing and lymphohistiocytic vasculitis and thrombosis. Gross findings include multiple cerebellar petechiae and fibrinopurulent meningitis. PCV2 antigen has been demonstrated in macrophages and cerebellar endothelial cells in affected areas.[3]

A differential diagnosis discussed by conference participants is leptospirosis, which results in clinical illness in only a small portion of infected swine. The primary effect on swine is abortion and the birth of weak piglets, but leptospirosis may also result in interstitial nephritis and renal papillitis with infiltration by mononuclear cells and numerous bacteria in the medulla.[6]

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CASE IV: IPTA Berne Case 1 (JPC 3164992).

Signalment: 4-month-old male calf (*Bos primigenius taurus*).

History: The animal is from a dairy farm and presented for necropsy in October 2009. Clinical signs included fever and bloody diarrhea. Antibiotic treatment was attempted but the animal died after two days from the onset of the clinical signs. Vaccination history was unknown and the animal tested negative for Bovine Viral Diarrhea virus as required by the eradication program (October 2009).

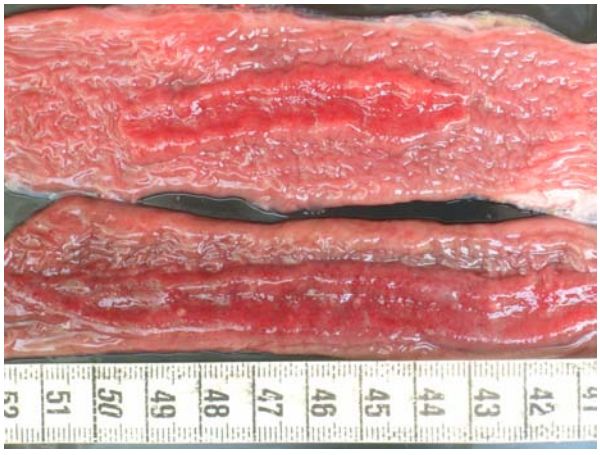
Gross Pathology: A general poor body condition was noted at necropsy. The small and large intestines contained a large amount of fibrino-hemorrhagic exudates. The mucosa was edematous and hyperemic with multifocal, pinpoint areas of necrosis more evident at the level of the Peyer's patches with occasional wider foci of ulceration.

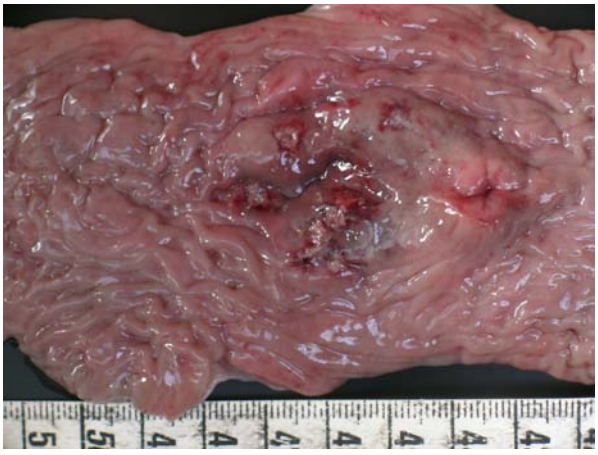
Laboratory Results: Bacteriology for *Salmonella* spp. was negative. Virology for BVDV (Ag ELISA method) was negative.

Histopathologic Description: Small and large intestine sections: The lymphoid follicles at the level of the Peyer's patches contain large areas of necrosis characterized by hypereosinophilic cellular debris mixed with fibrinous exudate. Lymphocytolysis is evident in the more preserved lymphoid follicles. Numerous intranuclear, basophilic to amphophilic, completely or partially filling the nuclei, round to oval inclusion bodies are present in the endothelial cells of mucosal and submucosal small blood vessels. Multifocally, the mucosa shows loss of tissue architecture and cellular detail; replaced by hypereosinophilic cellular debris (coagulative necrosis) mixed with fibrin and extravasated erythrocytes (hemorrhage). Moderate edema is present in the submucosa adjacent to the lymphoid tissue. Multifocally, few crypts are markedly dilated and filled with necrotic epithelial cells, viable and degenerate neutrophils and, occasionally mucinous material (crypt abscesses). In some places this is associated with the herniation of the overlying mucosal glands into the necrotic lymphoid centers. Few foci of granulation tissue are present around some lacunar spaces filled with neutrophilic exudates in the submucosa (cecum). In the new-formed blood vessels of the granulation tissue are visible intranuclear inclusion bodies. Distended lymphatic vessels (edema) are scattered throughout the muscular layer. Bacterial colonies (not present in all sections) are associated with the necrotic mucosa and present within the inflamed herniated cystic glands.

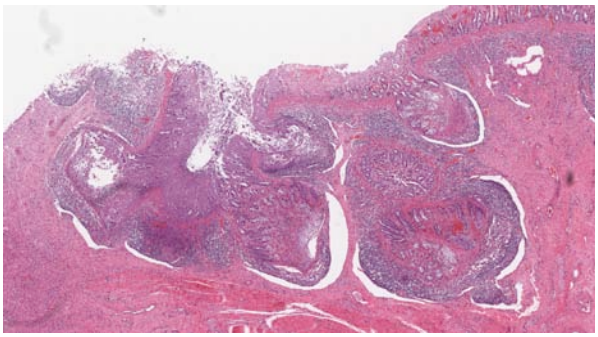
Contributor's Morphologic Diagnosis: 1. Enterocolitis, multifocal, necrotizing and fibrino-hemorrhagic, severe, acute with severe Peyer's patch necrosis and intranuclear inclusion bodies (adenoviral type). 2. Colitis, multifocal, submucosal, neutrophilic, chronic moderate with granulation tissue formation and intralesional bacterial colonies.

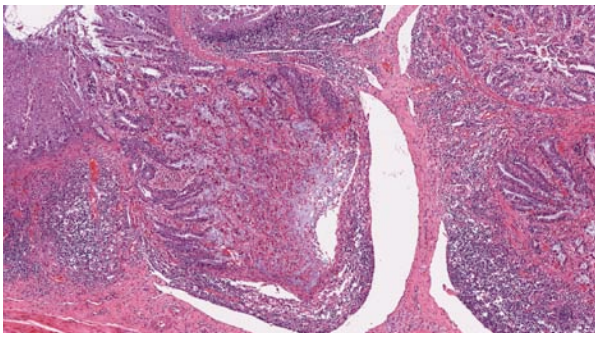
Contributor's Comment: After human and fowl adenoviruses, bovine adenoviruses (BAdVs) present the third largest group of adenoviruses originating from one host species.[7] They have been classified into two separate genera: Atadenovirus (namely types 4-8) and Mastadenovirus (types 1-3 and 9). The most recently described, BAdV 10, is the cause of a well-defined disease in cattle, particularly in calves, characterized by acute severe fibrinous, necrotizing and hemorrhagic enterocolitis of worldwide occurrence.[1,6,7] Another uncommon characteristic of this virus is the variation in the genome size of various isolates, which justifies its classification as a separate BAdV species.[1,4] Electron microscopical examination showed the



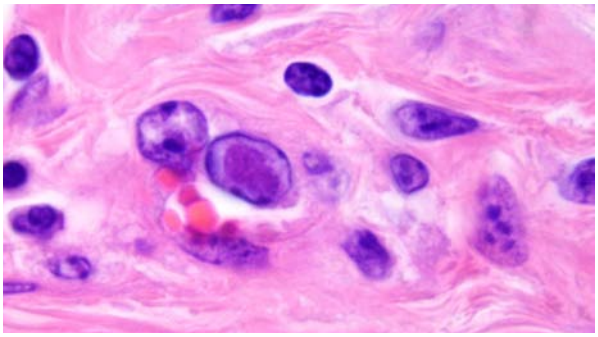


4-1, 4-2. Small and large intestine, Peyer's patches, cow. The mucosa is edematous and hyperemic and there is multifocal necrosis of lymphoid tissue. Photographs courtesy of University of Berne, Berne, Switzerland, http://www.itpa.vetsuisse.unibe.ch/html.





4-3, 4-4. Ileum, cow. Crypt herniation and necrosis happens over Peyer's patches. (HE 100X and 280X)



4-5. Arteriole, ileum,cow. Oblong basophilic intranuclear viral inclusions expand the nucleus and marginate chromati of endothelial cells throughout the section. (HE 1000X)

densely stained virus particles measured 70 to 75 nm in diameter.[1,6]

Microscopic lesions were found in the respiratory (bronchiolitis and bronchopneumonia) and intestinal tract (necrosis, fibrinous exudates, hemorrhage, mild infiltration with mononuclear cells and granulocytes) whereas the basophilic or amphophilic vascular inclusion bodies were identified in the lung, kidney, liver, abomasum, small intestine and colon.[2,4] Necrosis preferentially affected Peyer's patches with extension to the overlying mucosa. In the described cases the pathologic findings were related to the primary vascular damage produced by the virus, supported by the absence of other enteric pathogens.[3,4,5] Bacteria, when present, are considered secondary opportunists, but potential contributors to the ultimate pathologic process.[3] The vessels sometimes contained thrombi with many leukocytes and neutrophils present in the walls.[3] However, further experimental studies are needed to determine the virulence of BAdV and to establish if its presence in the vascular endothelium is a cause or a consequence of a co-existing enteric disease.[5]

In other domestic species like horses and pigs, enteric adenovirus infection targets the epithelial cells, yielding to villus atrophy, epithelial sloughing and mild diarrhea. This differs from what is seen in calves in which the intestinal pathology is associated with primary infection of blood vessels resulting in necrosis of the mucosa and lymphoid tissue.

The disease must be differentiated from common causes of fibrinous and hemorrhagic enterocolitis, including coccidiosis, bovine viral diarrhea, salmonellosis and bovine malignant catarrhal fever. There is very limited information available on the prevalence of BAdVs, particularly BAdV 10 infection within cattle populations.[5] At present, adenoviral infection of cattle with enteric disease is probably underdiagnosed especially because there is no test suitable for diagnosis of the disease in live animals and, second, because diagnostics require histopathologic or immunocytochemical examination of the intestine.[4,5] It has been speculated that the sporadic cases of fatal BAdV 10 infection can be the result of some type of immunological incompetence.[2] Further confirmation through electron microscopy, in situ hybridization, or virus isolation in tissue cell cultures was not possible at that time.

JPC Diagnosis: Small intestine: Enteritis, necrotizing, multifocal to coalescing, severe, with villar blunting, crypt herniation, lymphoid depletion, and endothelial intranuclear viral inclusions.

Conference Comment: The contributor does an excellent job of summarizing and describing the lesions associated with BAdV 10. Although difficult to reflect in the morphologic diagnosis, the lesions in this case are most severe within and directly overlaying the necrotic Peyer's patches. There are two different gross lesion presentations associated with BAdV 10 infection. The first includes hemorrhagic bands along the serosa, while the second is a more generalized hemorrhagic enteritis overlain by a fibrinous exudate and with associated Peyer's patch necrosis.[1,4] Other gross lesions occasionally associated with BAdV 10 infection include pulmonary edema and abomasal ulceration.[4]

The use of the term "crypt abscess" to describe the material filling the crypts is considered by some to be a misnomer as the material is often composed of necrotic

epithelial and inflammatory cells within a crypt lumen, rather than suppurative inflammation of the crypt epithelium. The moderator prefers "cryptitis" as a more descriptively accurate term for the lesions in this case. Crypt abscess would more appropriately describe the lesions associated with ulcerative colitis where a suppurative inflammatory process of the epithelium predominates; however, the term "crypt abscess" is widely used by veterinary pathologists and is generally understood.

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