The Armed Forces Institute of Pathology
Department of Veterinary Pathology

Conference Coordinator
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WEDNESDAY SLIDE CONFERENCE 2010-2011

Conference 10

27 October 2010

Conference Moderators:
Edward Stevens, DVM, Diplomate ACVP

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CASE I: 3090525001 (AFIP 3144268).

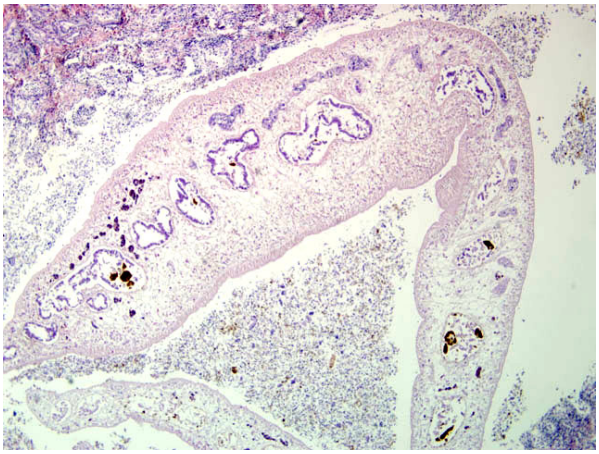
Signalment: 10-month-old, intact male, pony, horse (*Equus ferus caballus*).

History: A ten month old male pony was submitted for necropsy with a history of poor growth and poor body condition. The submitting veterinarian suspected a congenital defect.

Gross Pathology: The animal was in poor body condition, with pale muscles and mucous membranes as well as marked subcutaneous edema. The liver was firm, tan to grey in color, and numerous cords of fibrous tissue coursed through the parenchyma. The entire left lobe and portions of the quadrate lobe were markedly atrophied (~50% of normal size). The right lobe was diffusely enlarged. Multifocally, fibrous villous proliferations were present on the serosal surface (perihepatitis villosa). Many adult trematodes, between 2-2.5 cm long, were evident within dilated and thickened bile ducts. The femoral metaphyseal bone marrow was reddened.

Laboratory Results: Clinical biochemistry: anemia, hypoalbuminemia.

Histopathologic Description: Liver: Liver sections reveal marked multifocal, mainly portal bridging fibrosis admixed with multifocal infiltrates of moderate numbers of eosinophils and large numbers of lymphocytes and plasma cells. There is marked bile duct hyperplasia.



1-1. Liver, horse. Within a dilated bile duct there is an adult trematode characterized by an outer tegument, spongy parenchyma, ceca containing blood pigment, and vitellaria. (HE 40X)

Large bile ducts contain an adult trematode characterized by a cuticle without spikes, a digestive tract, and vitellaria within a spongy parenchyma. Sections through adult trematodes show testicles with mature sperm, uteri with eggs, and also occasional miracidia larvae (morphologically consistent with *Fasciola hepatica*).

Contributor's Morphologic Diagnosis: Marked diffuse chronic lymphoplasmacytic and eosinophilic hepatitis and (peri-)cholangitis with marked portal bridging fibrosis and intralesional adult trematode (morphologically consistent with *Fasciola hepatica*).

Contributor's Comment: In our experience (4 reports over a 21 year period), trematode infection is rare in equids in The Netherlands, and there are only a few reports of its prevalence in the literature. The reported prevalence of infection of horses in Europe ranges from approximately 1% in central Europe to 77% of horses from Ireland and the United Kingdom.[4] A German study found that between 38 and 71% of horses and 11% of donkeys were positive for the presence of eggs in their feces, while a similar Turkish study reported that the feces of 4.7% of equids were positive for eggs.[2,5]

Fascioliasis is common in cattle and sheep. The life cycle of *Fasciola hepatica* includes a Lymnead snail as an intermediate host. The snail is found in damp environments, such as marshy ground, ponds, and along the banks of slow moving streams. The miracidia of *Fasciola hepatica*, which are ingested along with the feces of the final host, infect the snail by burrowing through its body wall. Once within the snail, the larvae pass through a number of developmental stages including a sporocyst, three generations of rediae, and finally a cercarial stage which leaves the snail and encysts on vegetation to become a metacercaria. The infective metacercariae are ingested by the final host and excyst within the duodenum and migrate to the liver. Adult flukes reside in the bile ducts.[3]

In comparison to cattle and sheep, equids appear to mount an, as yet poorly understood, early immunological challenge to infection, which leads to the destruction, immobilization or developmental retardation of the larval flukes, the result being that only a few trematodes reach maturity in the bile ducts of equids.[2]

AFIP Diagnosis: Liver: Cholangiohepatitis, proliferative and fibrosing, chronic and eosinophilic, diffuse, marked with hepatocellular loss, dark brown anisotropic pigment, and few trematode eggs and adults.

Conference Comment: Based on the histologic findings, a reasonable differential diagnosis list would include *Fasciola hepatica*, *Fasciola gigantica*, and *Dicrocoelium dendriticum*. All three of these trematodes reside in the bile ducts of affected animals; *Fascioloides magna* inhabits the liver parenchyma and therefore would be an unlikely etiologic agent. Speciation of trematodes in histologic samples is nearly impossible. With the exception of *F. magna*, the histologic lesions are similar, and thus identification of flukes at gross necropsy is more reliable, as the morphology can be more adequately characterized. To that end, *F. hepatica* is approximately 2.5 cm long and leaf shaped; *F. gigantic* is double or triple the size of *F. hepatica*; *D. dendriticum* is 0.5-1cm long and lancet-shaped; and *F. magna* is 8 cm in length.[3]

Given the limited clinical information and history provided to participants, i.e. species of animal affected, most favored *D. dendriticum* as the causative agent. In addition to infecting horses, this trematode also infects ruminants, pigs, dogs and cats. *Fasciola hepatica* and *F. gigantica* primarily affect sheep and cattle. Wild cervids are the natural host for *F. magna*, though it can infect cattle and sheep. Other trematodes infecting domestic animals include: *Eurytrema pancreaticum* and *E. coelomaticum* in ruminants; *Opisthorchis viverrini* in cats and dogs; and *Pseudamphistomum truncatum*, *Metorchis* spp., *Parametorchis complexus*, *Concinnum procyonis*, and *Platynosum fastosum* in cats and dogs.[1]

Two possible sequelae to hepatic trematodiasis are black disease in sheep and bacillary hemoglobinuria in sheep and cattle. Black disease occurs when anaerobic, necrotic foci in the liver resulting from *F. hepatica* migration allow ingested *Clostridium novyi* spores in the liver to germinate. Once active, *C. novyi* elaborates a necrotizing beta toxin and hemolytic phospholipase C, and together, these toxins produce large areas of coagulative necrosis in the liver resulting in severe edema, congestion, hemorrhage and death, often with no premonitory signs. The pathogenesis of bacillary hemoglobinuria, caused by *Clostridium haemolyticum*, is similar to black disease with respect to the fluke involved, germination of spores, and toxin production. The toxins of *C. haemolyticum* produce intravascular hemolysis with associated anemia and hemoglobinuria.[1]

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CASE II: D-10-0751 (AFIP 3164918).

Signalment: 2-week-old, male, pig (*Sus scrofa*).

History: The young pig was submitted for necropsy with a history of sudden death.

Gross Pathology: The coronary bands of all four feet were pale and blanched, but there were no vesicles. A pale, sloughed, necrotic area measuring 1.5 cm in length and 1 cm in width was present on the dorsum of the tongue. There was severe hydropericardium, with 5-6 ml of yellowish fluid with fibrin clots present in the pericardial sac. The heart was diffusely involved, with pale streaks separated by darker areas noted on the epicardium and cut surfaces of the heart. Fibrin strands were found in the abdominal cavity.

Laboratory Results (clinical pathology, microbiology, PCR, ELISA, etc.)**:** Heart, nail, tongue and pericardial fluid samples were positive for Foot and Mouth Disease Virus type O by antigen capture ELISA.[1,2] Results were from the World Foot and Mouth Disease Reference Laboratory at Pirbright.

Heart, nail, tongue and pericardial fluid samples were positive for FMDV type O, Southeast Asia (SEA) topotype, Mya-98 lineage, by nucleotide sequencing.[10] Results were from the World Foot and Mouth Disease Reference Laboratory at Pirbright.

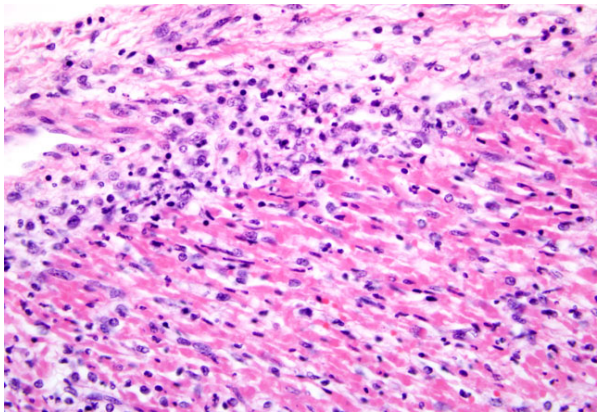
Histopathologic Description: Heart: Severe diffuse myocardial necrosis. Necrotic cardiomyocytes were intensely eosinophilic, fragmented, had lost their cross striations and had pyknotic nuclei. Moderate numbers of macrophages and smaller numbers of lymphocytes and neutrophils were present in the necrotic areas. Similar inflammatory cells were present on the epicardial surface.

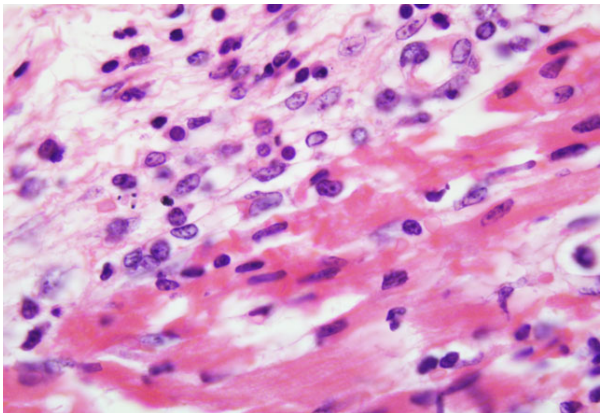
Contributor's Morphologic Diagnosis: Heart: Myocardial necrosis, acute, severe with histiolymphocytic infiltrates, pig (*Sus scrofa*). The lesion is consistent with Foot and Mouth Disease.

Aetiologic diagnosis: Aphthovirus myocarditis

Contributor's Comment: Foot and mouth disease (FMD) affects cloven hoofed animals, with the most dramatic clinical infections of domestic swine and cattle.[7] It is caused by seven serologically distinct types (A, O, C, Asia 1, Southern African Territories [SAT] 1, 2, and 3) of Foot and Mouth Disease Virus (FMDV) in the genus Aphthovirus, family Picornaviridae.[1] Type O and Asia 1 viruses are the most widespread viruses and are endemic in Asia.[9] The SAT type viruses have never been reported in Asia.

FMDV is a single stranded RNA virus with a protein capsid consisting of four viral proteins enumerated as VP1, VP2, VP3 and VP4.[1] Subtype-specific neutralization epitopes have been identified among the





2-1, 2-2. Pig, heart. Within the myocardium and epicardium are moderate numbers of macrophages, with fewer lymphocytes and neutrophils. There is degeneration and necrosis of subjacent ventricular cardiomyocytes. (HE 400X, 1000X)

four capsid proteins, primarily within VP1.[6,8] The serotype prevalent in Hong Kong SAR has been and continues to be serotype O.[4] However, the topotype has recently changed from Cathay to the South East Asia topotype with a subsequent increase in clinical signs and mortalities. The Southeast Asia (SEA) topotype, Mya-98 lineage, has been confirmed by the World Foot and Mouth Disease Reference Laboratory at Pirbright. Similar topotypes have been identified in the Republic of Korea and Japan recently. This recent spread of FMD in the Far East indicates the possibility of disease spread both within and outside the region, as happened during the FMD O PanAsia pandemic of 1999-2001.[4,10]

In swine, vesicles often form on the rostrum of the snout and around the nares. Foot lesions, when present, frequently extend along the coronary bands and dewclaws, and in severe cases can cause sloughing of the claw. Tongue lesions tend to coalesce and ooze a serous fluid when ruptured, leaving behind a visible raw and denuded stratum germinativum.[6]

Mortality is not commonly seen in FMD cases unless young pigs are affected. Young pigs up to 14 weeks of age, but particularly those less than 8 weeks of age, may die without developing any clinical signs of FMD due to heart failure, which is characterized by acute myocarditis that at times may be seen macroscopically as whisps of blanched areas on the epicardium that extend into the endocardium, a consequence of the damage caused by viral replication to the developing myocardium.[3,9,11]

AFIP Diagnosis: Heart: Myocarditis and epicarditis, necrotizing, subacute, diffuse, severe, with lymphohistiocytic and neutrophilic interstitial inflammation and perivasculitis.

Conference Comment: Conference discussion focused on the differential diagnosis for myocarditis in the pig. Encephalomyocarditis virus (EMCV), a *Cardiovirus* of the Picornaviridae family, was the favored etiology by most participants. Histologic findings are similar to those found in this case with diffuse myocardial necrosis, and the inflammatory infiltrate with EMCV is typically mononuclear. Other viruses associated with myocarditis in the pig include porcine parvovirus and porcine circovirus 2 associated with postweaning multisystemic wasting syndrome.[7] Vitamin E/selenium deficiency causes myocardial necrosis; however, inflammation is minimal. Additionally, several parasitic etiologies can cause myocarditis, including *Toxoplasma gondii*, *Sarcocystis* spp., *Taenia* spp., *Trypanosoma* spp. and *Trichinella spiralis*.[12]

The exact cause of death in myocarditis is unknown. Death could be due to the effects of the offending agent (e.g. viral damage to myocytes), the ensuing inflammatory response, or both. Infiltrating cytotoxic T lymphocytes can produce direct myocyte necrosis. Activated histiocytes and lymphocytes produce a cytokine milieu resulting in myocyte metabolic disturbances, reduced contractility, and dysrhythmia. Death during the acute phase of myocarditis is often attributed to dysrhythmias.[7] Animals surviving the acute phase begin resolution in which macrophages arrive to remove the necrotic debris. Due to the continuous contraction of cardiac myocytes, their regenerative capabilities are limited; therefore, healing most often occurs through fibrosis.[5]

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CASE III: HN2585 (AFIP 3167483).

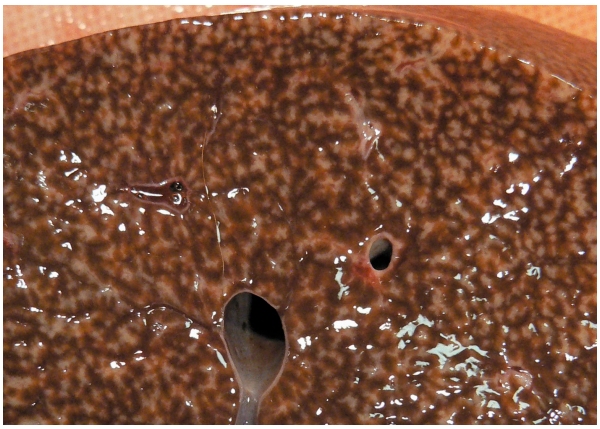
Signalment: 3-year-old, male, Tokara (Japanese native) goat (*Capra hircus domesticus*).

History: Four goats and nine sheep were kept in a zoological garden. The present case was born at the garden in 2006, and the zoo staff noticed that the goat showed decreased appetite and weight loss from January 2009. He had intermittently excreted soft feces since May 2009 and overt diarrhea was noted in October of the year. He died in November 2009.

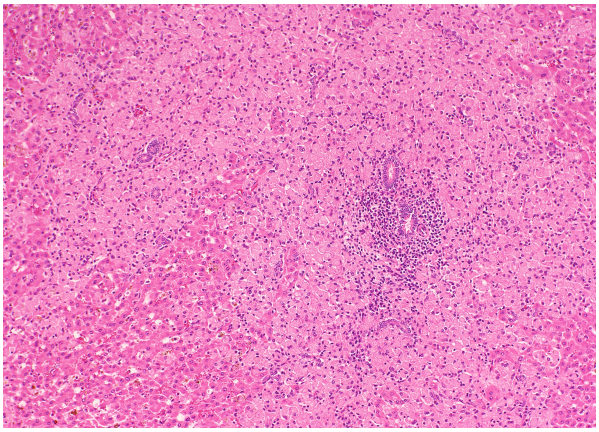
Gross Pathology: The carcass was in poor nutritional condition and post mortem autolysis was mild. The oral mucosa and conjunctiva were pale white. The liver diffusely showed centrilobular congestion and periportal white discoloration, such as in nutmeg liver. There was a foreign body (tight handkerchief) in the content of rumen. Numerous white small foci due to mucosal thickening, approximately 2 mm in diameter, were visible from the serosa of the small intestine. About 50% of lung lobes, mainly in both cranial lobes, were dark red, wet and consolidated.

Laboratory Results: Tissues from this goat were not examined microbiologically. After the necropsy, a monitoring study in the herd was performed for *Mycobacterium avium subsp. paratuberculosis* (MAP) with johnin reaction, complement fixation (CF) test, and the isolation from feces five times in all for 5 months. MAP was not isolated from any animals, but 6 sheep were positive in both johnin reaction and CF test.

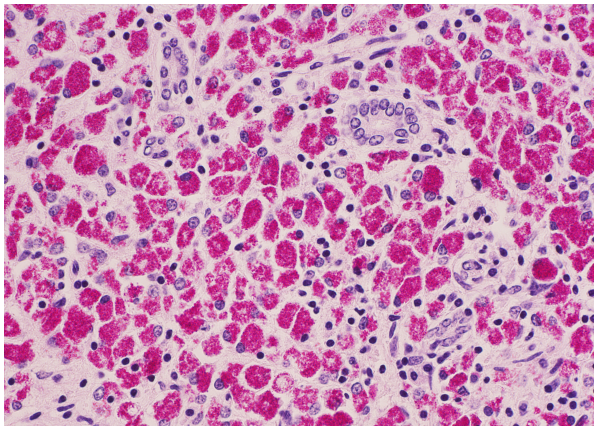
Histopathologic Description: Liver: The liver showed severe interlobular, periportal, and intralobular infiltration of macrophages, epithelioid cells and a small number of lymphocytes. There was atrophy, degeneration and loss of the hepatocytes adjacent to the foci due to the extensive invasion of the macrophages. Mild proliferation of bile ducts and arterioles was noted in expanded portal areas. Hemosiderin-laden macrophages (Kupffer cells) were scattered in sinusoids throughout the parenchyma. The Ziehl-Neelsen stain showed a massive presence of acid-fast rod-shaped bacteria in the epithelioid cells.



3-1. Liver, goat. Diffusely throughout the hepatic parenchyma are numerous periportal white foci. Photograph courtesy of Laboratory of Comparative Pathology, Graduate School of Veterinary Medicine, Hokkaido University, Sapporo, Japan, umemura@vetmed.hokudai.ac.jp



3-2. Liver, goat. Diffusely expanding periportal areas are many macrophages with abundant foamy cytoplasm and indistinct cell borders. Photograph courtesy of Laboratory of Comparative Pathology, Graduate School of Veterinary Medicine, Hokkaido University, Sapporo, Japan, umemura@vetmed.hokudai.ac.jp



3-3. Liver, goat. The staining by the Ziehl-Neelsen method reveals numerous acid-fast bacilli within the cytoplasm of macrophages. Photograph courtesy of Laboratory of Comparative Pathology, Graduate School of Veterinary Medicine, Hokkaido University, Sapporo, Japan, umemura@vetmed.hokudai.ac.jp

Additionally, epithelioid cells diffusely infiltrated and proliferated in lamina propria mucosae of the ileum and colon. Epithelioid cell aggregates were occasionally observed around the vessels and lymphatics under the serosa. Similar foci were also noted in the mesenteric adipose tissue. These epithelioid cells also contained numerous acid-fast rod shaped bacilli in the cytoplasm. Obvious necrosis and mineralization could not be found in any granulomatous foci.

Contributor's Morphologic Diagnosis: Liver: Hepatitis, granulomatous, multifocal to coalescing, marked, with numerous intrahistiocytic acid-fast bacilli.

Contributor's Comment: Paratuberculosis, or Johne's disease, caused by MAP infection mainly occurs in domestic ruminants and is responsible for considerable economic losses all over the world.[2,5] The disease has been spontaneously recognized in pigs, free-ranging and captive wild ruminants, camelids, and rarely in equids and captive primates. Speculation exists that Johne's disease is zoonotic and associated with Crohn's disease in human beings, although MAP has still not been accepted as the cause of the human disease.

MAP is very resistant to environmental stressors, particularly in regions with acid soils. The bacterium enters the M cells that cover the intestinal Peyer's patches, and ingested bacteria are subsequently phagocytized by macrophages.[2] In cattle, susceptibility to infection is greatest in the first 30 days of life, although clinical disease does not usually develop until 2-5 years of age. The progression from asymptomatic to clinical Johne's disease is associated with a decrease in peripheral cell-mediated immunity and increasing production of non-protective IgG1 antibodies.[7,8] The disease is clinically characterized by untreatable diarrhea accompanied by progressive weight loss and hypoproteinemia. The characteristic gross lesion in the symptomatic cattle is chronic segmental thickening of the ileum, mesenteric lymphadenopathy, and lymphangitis. Histologically, cattle usually have non-caseating granuloma in the affected bowel and lymphoid tissues.[2]

Although the pathogenesis of Johne's disease in small ruminants is assumed to be similar to that in cattle, there are several differences in clinical signs and pathology. Sheep and goats reveal emaciation and hypoproteinemia, but overt diarrhea is unusual.[2,5] In sheep, goats, and deer, enteric gross lesions are often mild, with little obvious thickening, and no transverse ridges.[2,4]

Two main pathological forms of the intestinal lesion have been described in symptomatic sheep.[3,9] The first form is multibacillary or lepromatous, in which macrophages filled with numerous mycobacteria are the main inflammatory cells. The second form is paucibacillary or tuberculoid, in which the inflammatory infiltrate is composed of lymphocytes and few macrophages and caseous necrosis and calcification may be observed. It is difficult to find acid-fast mycobacteria in macrophages in the latter form. It is uncertain whether the two distinct forms represent sequential or divergent stages. Asymptomatic sheep may have small granulomas in the interfollicular and basal areas of ileal Peyer's patches, usually with no visible intracellular organisms.[9]

Corpa et al.[4] characterized the intestinal lesions of caprine tuberculosis in four categories: focal, diffuse multibacillary, diffuse lymphocytic, and diffuse mixed. Histological classification for sheep was valid for goats, and the lower frequency of focal lesions in goats compared to sheep appears to indicate that the former species has only limited ability to control the infection. In this species, granulomatous lesions are likely to be more severe in the jejunum than in the ileum, although the distribution could not be determined in this case. Currently, the similar histological classification is applicable also in bovine paratuberculosis.[6]

The ileum of the present case showed diffuse multibacillary lesions. The monitoring study in remaining sheep and goats supported the histological diagnosis. Previously, focal granulomas have been seen in lymph nodes elsewhere in the body, liver, lung, spleen, and other organs in symptomatic sheep and goats.[2-4] However, the number of histiocytic infiltrates in the liver was unusual.

AFIP Diagnosis: Liver: Hepatitis, portal and random, histiocytic, diffuse, marked with numerous intrahistiocytic acid-fast bacilli.

Conference Comment: The pathogenesis of *Mycobacterium avium* ssp. *paratuberculosis* (MAP, Johne's) is assumed to be similar in cattle and sheep. The greatest susceptibility to infection is within the first 30 days of life. Infection occurs when MAP is ingested, taken up by M cells overlying intestinal Peyer's patches, and transported to resident macrophages. The bacteria localize in the mucosa and draining lymph nodes; rarely in small ruminants, MAP-associated lesions can be found in the walls of blood vessels, meninges, liver and spleen.[2] These disseminated lesions are thought to result from irregular lymphogranulomatous foci; affected animals typically have a negative response to intradermal johnin testing.[2]

Mycobacteria species utilize a complex interplay of virulence factors and the host immune system to evade

Organism Factor	Cell Pathway	Mechanism	Result
Man-LAM	TLR2-MAPK-p38	IL-10 overexpression	Decreased: IL-12, IL-8, and TNF-α, MHC class II, apoptosis, phagosome acidification, and organism killing
Man-LAM	IL-10-mediated	Decreased: IL-12, IL-8, and TNF α expression	Attenuation of: 1. Inflammatory response 2. Th 1-type immune response
Man-LAM	IL-10-mediated	Decreased MHC class-II expression	Decreased antigen presentation
Unknown	IL-10-mediated; decreased TNF-α	Decreased apoptosis	Increased cell survival
Man-LAM	IL-10-mediated; TLR2-MAPK-p38 signaling	Decreased phagolysosome fusion and acidification	Increased organism survival

being killed. The chart above, adapted from Weiss and Souza,[10] summarizes the mechanisms by which MAP suppresses monocyte-macrophage microbicidal response.

Interleukin 10, as noted in the chart above, plays a pivotal role in the MAP-directed immune modulation; a brief review of IL-10 follows. IL-10 is produced by a variety of cells, including T regulatory lymphocytes, Th 2 lymphocytes, and dendritic cells. The primary function of IL-10 is to direct the immune system to a Th 2-type immune response by enhancing Th 2 activity and suppressing Th 1 activity; Th 1 suppression is accomplished by inhibiting macrophage IL-12 production. Antigen presentation by dendritic cells is decreased through IL-10 mediated down-regulation of MHC class-II.[1]

As commented by the contributor, the distribution and extent of the histiocytic infiltrate in the liver is striking. While most participants interpreted the lesion as consistent with *Mycobacterium avium subsp. paratuberculosis* infection, they were nevertheless impressed by the number of infiltrating macrophages filled with acid- fast bacilli. A similar histopathologic presentation is reported in dogs infected with *M. avium-intracellulare* complex (MAC), as exemplified by Wednesday Slide Conference 2009 Conference 5 Case 1, and in the absence of special stains may result in the histologic interpretation of histiocytic neoplasia or a sarcomatous lesion, rather than an infectious process.

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CASE IV: 518-10-1 (AFIP 3167496).

Signalment: Juvenile (18.5 kg), female, pig (*Sus scrofa*).

History: In a finishing herd there were some pigs with a decreased rate of body weight gain and a couple of pigs had died during the previous week.

Gross Pathology: This pig was one of four growing pigs submitted for necropsy at the same time. The pig was in poor nutritional condition. The main gross lesions were observed in the lungs. There were pneumonic lesions in the cranial lung lobes and the caudal part of the left diaphragmatic lobe was covered with thick fibrinous exudate and attached to the wall of the pleural cavity. The cranial part of the left diaphragmatic lobe also contained abscesses.

Laboratory Results (clinical pathology, microbiology, PCR, ELISA, etc.)**:** Bacteriology: *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* were cultured from the lungs. Salmonella bacteria were not cultured.

Virology: Swine influenza was not detected (RT-PCR).

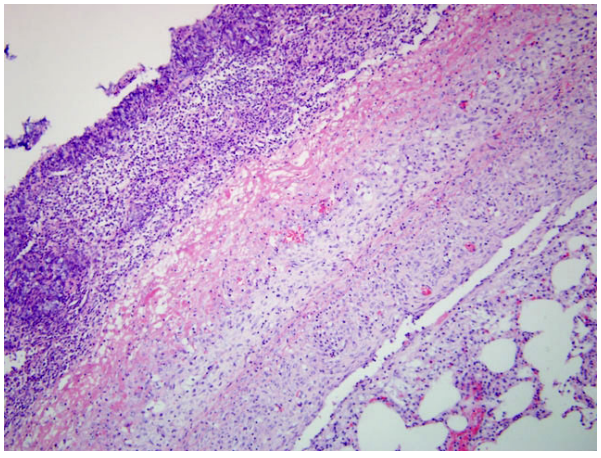
Immunohistochemistry: Porcine circovirus-2 antigen was demonstrated in lymph nodes.

Histopathologic Description: Lung: The lung parenchyma contains multifocal demarcated pale or basophilic areas bordered by a thick band of degenerate neutrophils and macrophages, often with elongated, "streaming" or "oat cell" nuclei, eosinophilic fibrillar material and nuclear dust, and occasionally also fibroblasts. The alveolar walls inside are pale and necrotic, congested or thickened with inflammatory cells. The alveolar space is often filled with variable numbers of degenerate macrophages and neutrophils. The lobular septae are severely dilated and contain pale edema fluid, eosinophilic fibrillar material, macrophages and few neutrophils. The pleura is severely thickened by fibroblasts and covered by a thick eosinophilic fibrillar membrane with large numbers of degenerate macrophages and neutrophils with streaming nuclei and occasional bacterial colonies. The bronchi are multifocally filled with degenenerate neutrophils, macrophages and sloughing bronchial epithelial cells. Multifocally some arteriolar walls are disrupted and infiltrated with degenerate neutrophils (vasculitis).

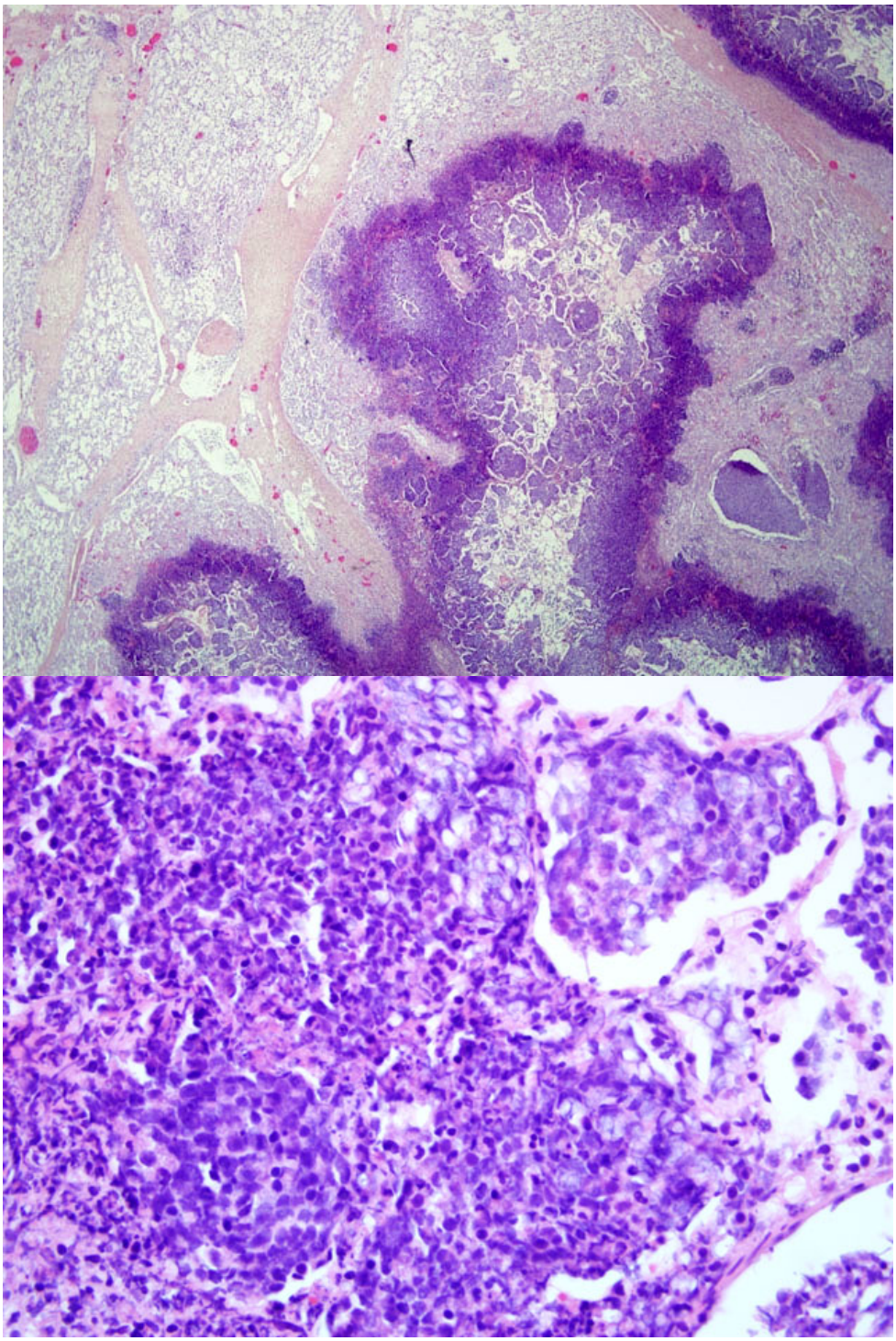
Contributor's Morphologic Diagnosis: Severe, subacute, multifocal and locally extensive necrotizing and fibrinosuppurative bronchopneumonia and pleuritis.

Contributor's Comment: Pleuropneumonia caused by *Actinobacillus pleuropneumoniae* is one of the most important respiratory infections of swine. The disease is common worldwide and causes severe morbidity and mortality, especially in growing pigs, but pigs of all ages can be affected. The disease can be peracute, acute, subacute or chronic.

In peracute cases, pigs can be found dead before clinical signs are observed. In acute cases, pigs have high fever, apathy and anorexia, occasionally dyspnea and diarrhea or vomiting, cyanosis of skin and blood-tinged discharge from the nostrils is often seen. Gross lesions can be observed anywhere in the lungs, but often one or both of the caudal lung lobes is affected. Blood-stained froth fills the trachea. Fibrinous pleuritis and pleural adhesions are characteristic. Histologically there is a lobar fibrinosuppurative hemorrhagic and necrotizing pneumonia and fibrinous pleuritis. Vasculitis with thrombosis is often seen. Differential diagnoses in acute cases include



4-1. Lung, pig. The visceral pleura is covered by abundant fibrin, necrotic cellular debris, and many degenerate neutrophils and expanded by increased amounts of fibrous connective tissue and edema. (HE 20X)



4-2, 4-3. Lung, pig. Filling and replacing bronchioles and alveoli and expanding interlobular septae are many degenerate neutrophils and macrophages admixed with abundant fibrin and necrotic cellular debris. Alveoli contain oat cells. (HE 400X, 20X)

Salmonella choleraesuis and *Actinobacillus suis* infections.

The disease is caused by a gram negative, encapsulated coccobacillus, *Actinobacillus pleuropneumoniae.* The bacterial agent is divided into two biovars according to the requirement of NAD (nicotinamide adenine dinucleotide). Biovar 1 strains are NAD- dependent and biovar 2 strains are NAD- independent. There are 15 serotypes based on capsular polysaccharides.

Clinical signs and pathological findings are associated with several bacterial virulence factors combined with the host reaction. In addition to capsular components and cellular lipopolysaccharides, *A. pleuropneumoniae* produces several cytotoxins and proteolytic enzymes

and can resist macrophage and complement killing. Acute disease is often followed by chronic encapsulated necrotic lung lesions and local pleuritis with adhesions. Chronic pleuritis seen at slaughter is common in herds with endemic infection. Asymptomatic carrier pigs spread the disease by direct contact or by aerosols.

A. pleuropneumoniae is capable of causing severe disease without predisposing factors, but the severity of the disease is affected by the immune status of the pigs and environmental factors, such as crowding, ambient temperature or moving and mixing of animals. There are also differences in the virulence within and between the strains. Disease problems can be enhanced by other concurrent pathogens, for example *Mycoplasma hyopneumoniae*, swine influenza virus, PRRS (porcine respiratory and reproduction syndrome virus) or PMWS (porcine circovirus-2).

Other uncommon lesions associated with *A. pleuropneumoniae* include endocarditis, pericarditis, arthritis, osteomyelitis, meningitis, otitis media, granulomatous hepatitis and granulomatous pneumonia.[3]

A. pleuropneumoniae was cultured from lung lesions of all four examined pigs. In this case, *Pasteurella multocida* was also isolated from the lungs. *Pasteurella multocida* can cause suppurative pneumonia in pigs, but it is often a secondary invader. The lymph nodes exhibited depletion of lymphocytes and loss of the follicular architecture. Porcine circovirus-2 antigen was also detected by immunohistochemistry in lymph nodes of this pig. These lesions were indicative of PMWS (postweaning multisystemic wasting syndrome). However, in this pig the lesions associated with PCV2 were considered to be an additional finding.

AFIP Diagnosis: Lung: Pleuropneumonia, fibrinosuppurative and necrotizing, subacute multifocal to coalescing, severe, with oat cells, fibrinonecrotizing vasculitis, and colonies of coccobacilli.

Conference Comment: The moderator focused the discussion on recognizing patterns of pneumonia and lung injury. Participants classified patterns of pneumonia as bronchopneumonia, interstitial, bronchointerstitial, embolic and granulomatous. The authors of McGavin and Zachary's *Pathologic Basis of Veterinary Disease* provide an excellent overview of pneumonia. The table below summarizes key points of each pattern.[1,2]

The moderator discussed additional patterns of lung injury. Bronchitis and bronchiolitis result from direct damage to and subsequent necrosis of airway epithelium leading to airway inflammation. Potential etiologic agents or disease syndromes resulting in this

Pneumonia	Route of exposure	Anatomic Distribution	Lung Texture	Anatomic Location of Injury	Example	Common Pulmonary Sequelae
Broncho-pneumonia	Aerogenous	Cranioventral	Firm, hard	Bronchiolar-alveolar junction	Enzootic pneumonia; Pneumonic mannheimiosis	Abscesses, pleural adhesions
Interstitial	Aerogenous or hematogenous	Diffuse	Elastic, rubbery	Alveolar or interlobular septae	PRRS, PCV2	Edema, type II pneumocyte hypertrophy, alveolar fibrosis
Broncho-interstitial	Aerogenous	Multifocal	Firm to rubbery	Bronchioloar and alveolar epithelium	BRSV, swine influenza	Mix of broncho- and interstitial-pneumonias
Granuloma-tous	Aerogenous or hematogenous	Multifocal	Nodular	Non-specific	Tuberculosis, blastomycosis	Dissemination of infection
Embolic	Hematogenous	Multifocal	Nodular	Pulmonary vasculature	Vegetative endocarditis	Random abscesses

Adapted from Table 9-4, McGavin and Zachary's *Pathologic Basis of Veterinary Disease*[2]

pattern include feline asthma, viral infection, inhalation of toxic gases, toxins metabolized by P450 cytochrome oxidase of Clara cells, and inhaled irritants.[1]

As noted by the contributor, *Actinobacillus pleuropneumoniae* has several virulence factors which play a unique role in the pathogenesis of porcine pleuropneumonia. The organism produces three RTX toxins (Apx I, II, and III) which are cytolytic for neutrophils, erythrocytes, alveolar macrophages, and epithelial cellsonce—lysed, the contents of neutrophils and macrophages damage host tissue. Macrophages activated by lipopolysaccharide secrete neutrophil chemoattractants, activate complement, and promote coagulation. In addition to resisting macrophage phagocytosis, the bacterial capsule prevents complement activation. In order to survive in the milieu of cytotoxins and reactive oxygen species from lysed leukocytes, *Actinobacillus pleuropneumoniae* produces a variety of antioxidant enzymes, including superoxide dismutase, catalase and hydrogen peroxide reductase.[1]

Contributor: Finnish Food Safety Authority Evira, Oulu, Finland
http://www.evira.fi

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