



WEDNESDAY SLIDE CONFERENCE 2014-2015

Conference 10

29 October 2014

CASE I: V14-14710 (JPC 4049286).

Signalment: Adult male Maine Coon cat, *Felis catus*.

History: The cat was found dead in the home by a relative taking care of the cat for a hospitalized man.

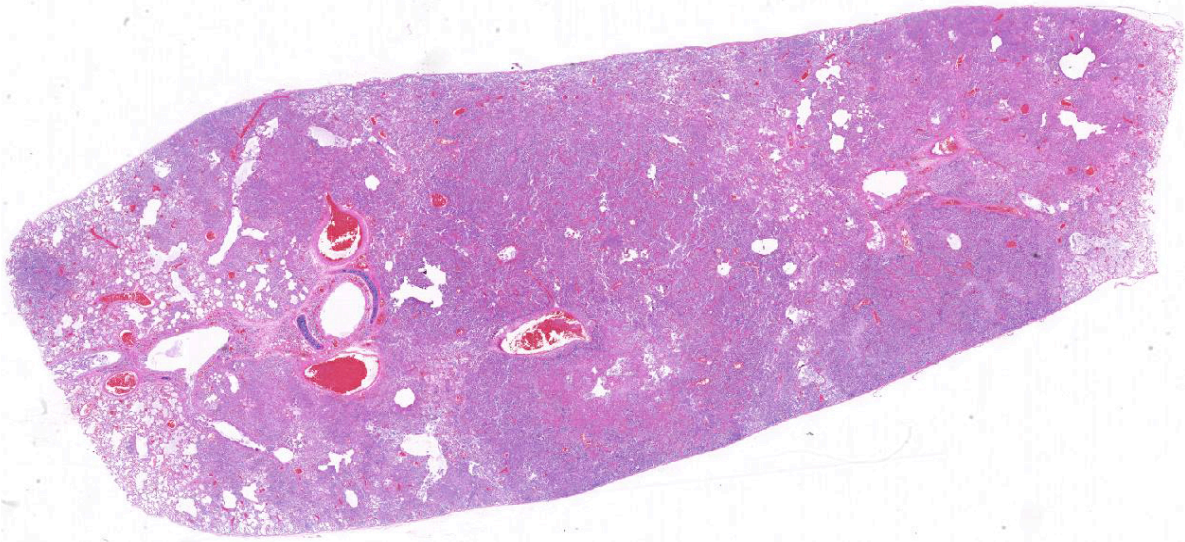
Gross Pathology: The right front foot and the right antebrachium were swollen approximately 2 times their original size. There were open wounds on the cranial aspect of the right carpus with dried exudate on the hair adjacent to the wounds. The subcutis of the right front foot and right antebrachium were edematous and bright red up to the right elbow. The right prescapular lymph node was enlarged 5-6 times its normal size and the right axillary lymph node was enlarged 2-3



1-1. Lung, cat: At necropsy, the right antebrachium and paw were swollen to twice normal size with multiple open cutaneous wounds. (Photo courtesy of: New Mexico Department of Agriculture Veterinary Diagnostic Services, <http://www.nmda.nmsu.edu/vds/>).



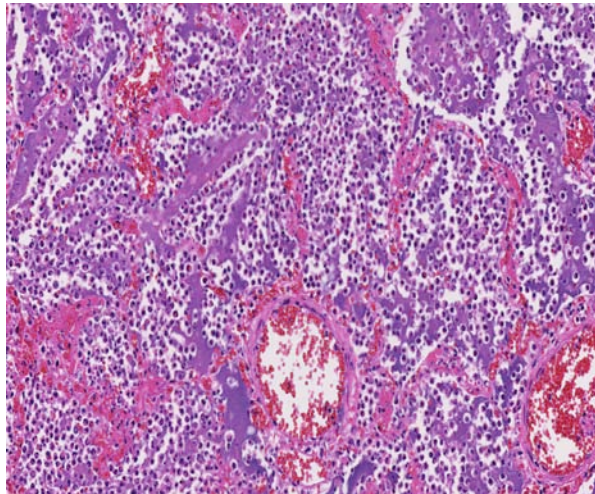
1-2. Lung, cat: The lungs contained multiple randomly distributed firm targetoid foci. (Photo courtesy of: New Mexico Department of Agriculture Veterinary Diagnostic Services, <http://www.nmda.nmsu.edu/vds/>).



1-3. Lung, cat: At subgross examination, 75% of the alveolar spaces are filled with a cellular exudate. (HE 6.3X)

times its normal size. Both of the lymph nodes were mottled tan and bright red with foci of necrosis within the lymph node on cross section. The lungs contained multiple random firm targetoid foci that had a tan center surrounded by a red ring, which was further surrounded by a tan ring. These foci were randomly distributed in all of the lung lobes. There was one pinpoint tan focus on the capsule of the spleen.

Laboratory Results: *Yersinia pestis* was isolated from a swab of the wound on the right front leg, the right axillary lymph node, the lung, the liver, and the spleen.

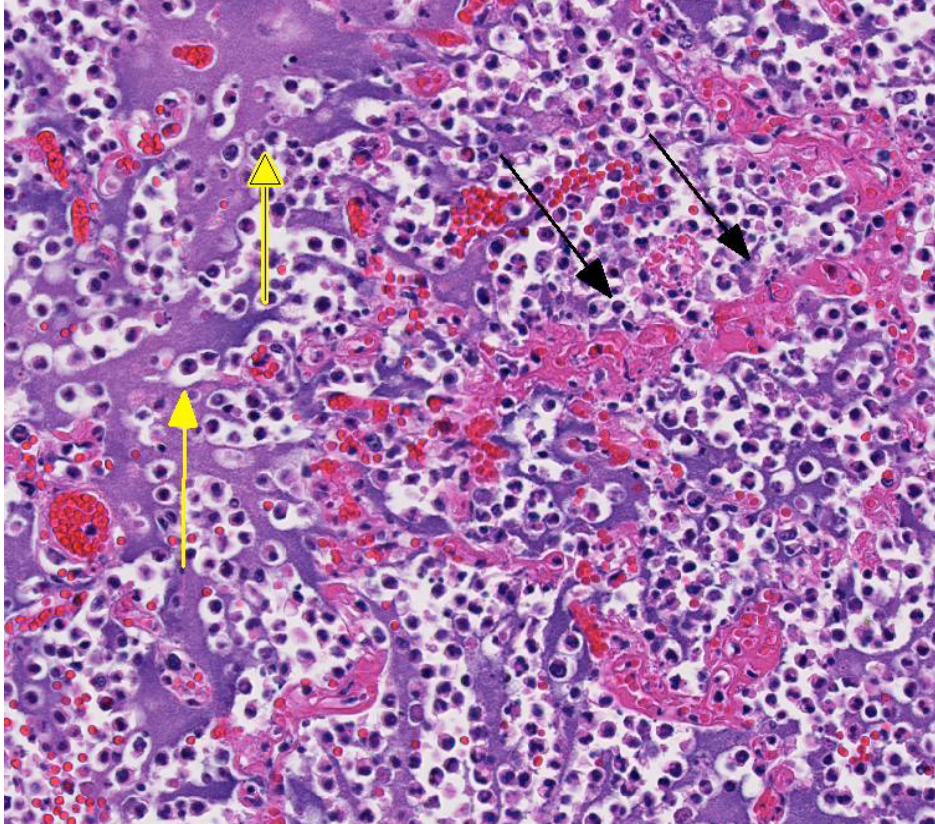


1-4. Lung, cat: Alveoli contain numerous viable and degenerate neutrophils and large basophilic colonies of bacilli, a characteristic finding associated with *Yersinia pestis*. (HE 168X)

Histopathologic Description: The lung contains multiple large foci of necrosis filled with necrotic debris, myriad coccobacilli, and degenerate neutrophils. The necrotic areas often contain an arteriole with a necrotic tunica media that is infiltrated by neutrophils. The affected arterioles are surrounded by myriad coccobacilli, and occasionally contain fibrin thrombi. The foci of necrosis are surrounded by a concentric variably thick layer of numerous neutrophils, fibrin, hemorrhage, and myriad bacteria. The alveoli of the lung between the foci of necrosis contain small variable numbers of coccobacilli and intact and degenerate neutrophils that occasionally become dense enough to coalesce into foci of necrosis. There are rare small arterioles and alveolar capillaries that contain emboli of coccobacilli.

Contributor's Morphologic Diagnosis: Multifocal to coalescing necrotizing suppurative pneumonia with myriad intralesional coccobacilli, necrotizing vasculitis, fibrin thrombi, and bacterial emboli; etiology, *Yersinia pestis*.

Contributor's Comment: *Yersinia pestis* is a gram-negative coccobacillus that is the causative agent of plague.^{5,8-10,13} Plague occurs worldwide, but it tends to occur in endemic regions on different continents.^{5,13} These endemic regions have similar geographic characteristics in that they are cool, semiarid climates near deserts with rodents that have short life spans and high reproductive material.⁵ These endemic regions



1-5. Lung, cat: Infiltrated areas exhibit multifocal septal necrosis, with either interruption and loss of septa (yellow arrows) or marked expansion and replacement by fibrin and cellular debris (black arrows.) (HE 168X)

often have year-round flea activity. In the states of Arizona, Colorado, New Mexico, and Utah (the Four Corners area of the United States), the endemic areas of plague tend to be those locations with elevations up to 2300 meters (7546 feet) and have a piñon pine-juniper habitat or a ponderosa pine habitat. The incidence of plague cases in humans and animals is influenced by annual precipitation, as increased soil moisture favors flea survival and vegetation growth on which rodents feed. In addition, there is evidence that *Yersinia pestis* can survive and remain virulent in soil up to 40 weeks.²

Yersinia pestis is propagated in a flea-mammal (usually rodents) life cycle.^{5,13} A flea capable of transmitting *Y. pestis* first must take a blood meal from a mammal that is septicemic with *Y. pestis*. The bacterium proliferates within the flea's proventriculus, eventually obstructing the flea's gastrointestinal tract. The gastrointestinal obstruction causes the flea to regurgitate *Y. pestis* into a mammalian host when the flea is taking subsequent blood meals. Although this is the accepted paradigm for flea transmission of

plague, other methods of propagation have also been proposed.⁶ Of the domestic species, cats are most susceptible to infection and disease, but dogs may also become infected and occasionally develop disease.^{5,11} Cats are also more likely to transmit plague to people than dogs.^{7,12} However, the cat flea, *Ctenocephalides felis*, is not an effective transmitter of *Y. pestis*.

Once *Y. pestis* is injected into a mammalian host by the flea, it expresses several virulence factors that help it to evade the mammalian host immune system.^{5,9,10} Two virulence factors that help *Y.*

pestis survive in the mammalian host are Yersinia outer coat proteins (YOPS) and a capsule consisting of fraction 1 protein (fraction 1 antigen). YOPS are injected into the host's phagocytic cells via a type III secretory system to inhibit the inflammatory response by reorganizing the host cell cytoskeleton and inhibiting NF- κ B suppressing cytokine production. YOPS can also be injected into endothelial cells, decreasing the expression of adhesion proteins on the cell surface. The capsule of *Y. pestis* is antiphagocytic and helps the bacterium to survive intracellularly when it is phagocytosed by a mammalian phagocyte, particularly monocytes and macrophages. The survival of *Y. pestis* within phagocytes helps it to be distributed from the initial site of infection to the regional lymph nodes and into the circulation.

The pathology of plague is similar in both cats and people.^{5,10,13} The site of injection of *Y. pestis* at the flea bite can develop dermatitis and cellulitis, such as in this case, or more commonly has minimal inflammation. The most common presenting lesion is a swollen lymph node

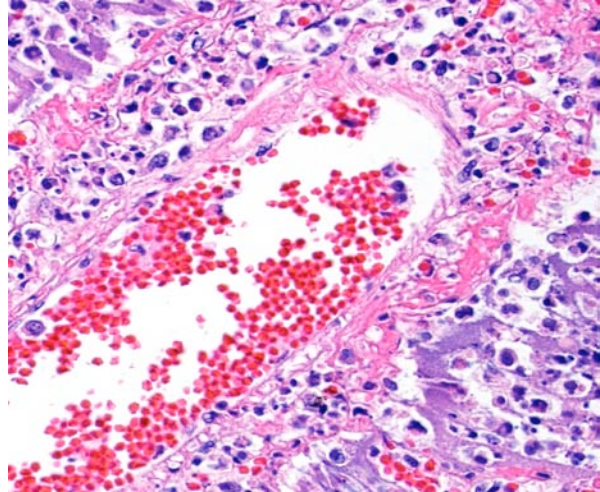
(bubonic plague) that may become necrotic and abscess. *Y. pestis* can then spread lymphogenously to other lymph nodes or hematogenously to other organs, particularly the organs that contain large numbers of resident macrophages (septicemic plague). In addition to the flea-mammal transmission, *Y. pestis* can be transmitted through the inhalation of aerolized *Y. pestis* (pneumonic plague) or through the ingestion of a *Y. pestis* infected rodent. Inhalation and ingestion of *Y. pestis* often results in a shorter incubation period of 1-3 days versus the 2-6 days incubation period after a flea bite due to the fact that the inhaled and ingested *Y. pestis* usually has already developed a capsule allowing the bacterium to spread more quickly in the host.⁵

JPC Diagnosis: Lung: Pneumonia, embolic, fibrinosuppurative and necrotizing, with vasculitis and numerous large colonies of coccobacilli.

Conference Comment: This is a great case illustrating the characteristic appearance of the gram-negative coccobacilli *Yersinia pestis* in tissue section, which is readily distinguishable from other large colony-forming bacteria such as *Actinomyces*, *Actinobacillus*, *Corynebacterium*, *Staphylococcus* and *Streptococcus* spp. Other species of *Yersinia* (*Y. pseudotuberculosis* and *Y. enterocolitica*) more typically affect the gastrointestinal tract of domestic animals, but also have the same histologic appearance as is present in this case, which are often referred to as “microcolonies”.³

Plague is an endemic disease within the southwestern U.S., with prairie dogs being considered highly susceptible and important for disease transmission. A colony of Gunnison’s prairie dogs has been identified as resistant to infection.⁴ Only a minority of these animals mount an antibody response in the face of an outbreak, alluding to the role of the innate immune system as being responsible for conferring resistance to disease. Several proteins of the innate immune response, including VCAM-1, CXCL-1, and vWF, are upregulated in these animals following *Yersinia* exposure.⁴

Conference participants reviewed a vital component of the innate immune system: the pattern recognition receptors known as toll-like receptors (TLR). TLRs recognize pathogen-associated molecular patterns, or PAMPs, which



1-6. Lung, cat: Multifocally, the walls of pulmonary veins are expanded with neutrophils, cellular debris and edema (vasculitis). (HE 360X)

are exogenous microbial products and include LPS, lipoteichoic acid, and peptidoglycans. This recognition of a microbe ultimately results in NF- κ B activation which upregulates transcription of proteins important to the immune response. All TLRs except for two mediate NF- κ B activation via MyD88 signaling, and thus are MyD88-dependent. TLR 4 has the ability to engage MyD88 or bypass it with TRAM and TRIF, resulting in type 1 IFN formation and release. TLR 3 operates exclusively through TRIF, and thus is MyD88-independent. TLRs can be characterized by which specific PAMPs they detect in addition to whether they’re located in the cell membrane or within the membrane of the endosome.¹ Understanding the specifics of TLR-signaling is often an important factor in elucidating disease pathogenesis and the corresponding immune response to a particular pathogen.

The contributor highlighted two important virulence factors of *Yersinia* spp., YOPS and fraction 1 antigen. YOPS are bacterial toxins which are injected into the cell. Three specific proteins (YopE, YopH, YopT) block phagocytosis by inactivating molecules that regulate actin polymerization. YopJ blocks inflammatory cytokine production by inhibiting LPS signaling pathways.¹⁰

Contributing Institution: New Mexico Department of Agriculture Veterinary Diagnostic Services
<http://www.nmda.nmsu.edu/vds/>

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CASE II: S1342/13 (JPC 4050932).

Signalment: 26-year-old thoroughbred gelding horse, *Equus caballus*.

History: The horse was presented to the veterinary clinic with a 14-day history of fever, hematuria and intermittent colic. The referring veterinarian initially treated the animal unsuccessfully with antibiotics due to a suspected cystitis. Urine analysis at the clinic confirmed the initial diagnosis of hematuria. A neoplastic process in the left kidney was suspected after rectal palpation.

Ultrasonographically there was an irregular cavitated mass located cranially of the kidneys of about 30 cm in diameter. Renal parenchyma was only partially recognizable by ultrasound. The urinary bladder was unremarkable. Blood analysis revealed marked azotemia, elevated creatinine, hyperproteinemia with hyperglobulinemia and hyperfibrinogenemia.

Due to the clinical symptoms, the age of the gelding and additional orthopedic problems (founder) as well as a poor prognosis due to the suspected renal neoplasia, the animal was euthanized and submitted for necropsy.

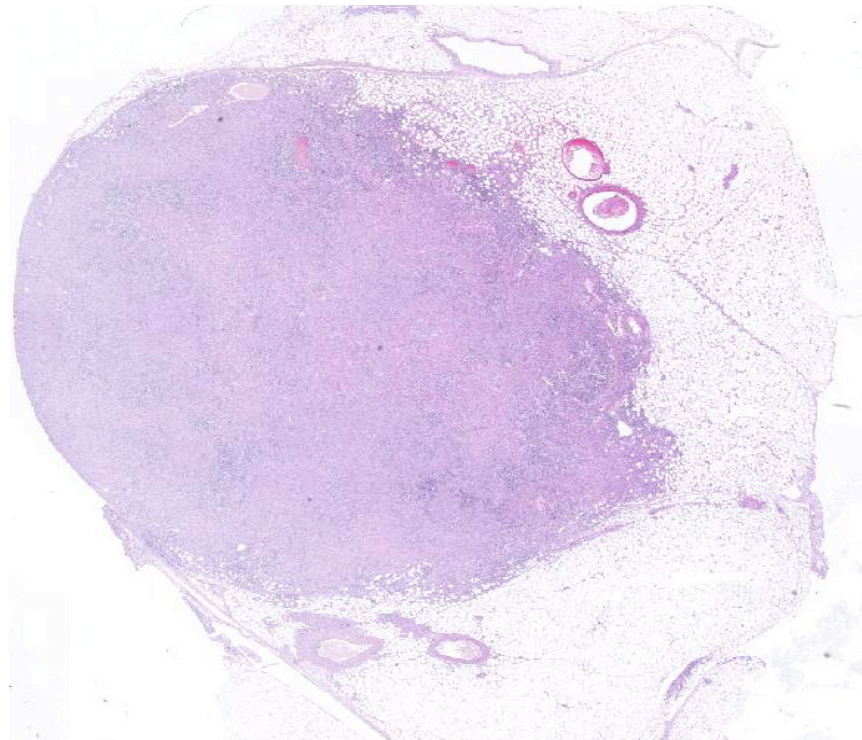
Gross Pathology: At necropsy both kidneys were severely enlarged and firm. The parenchyma contained multiple yellowish-white firm nodules of about 5-15 cm in diameter. The renal pelvis of both kidneys was filled with few milliliters of serosanguineous fluid. The urinary bladder contained pure blood.

Laboratory Results:

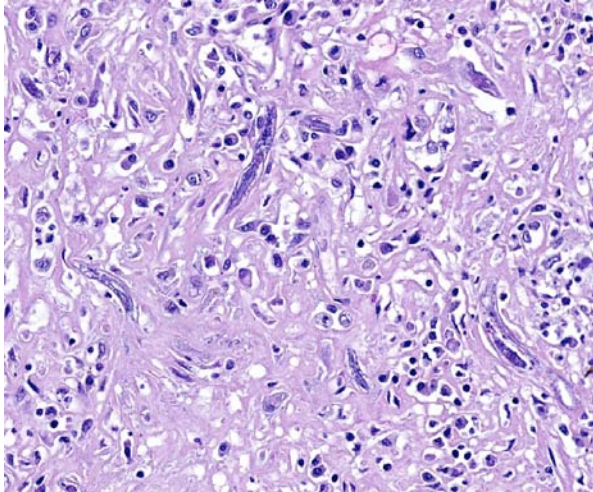
Creatinine μmol/l)	260 μmol/l (ref. 69-155 μmol/l)
Urea mmol/l)	11.41 mmol/l (3.18-7.31 mmol/l)
Serum protein	90.7 g/l (58-74 g/l)
Albumine	26.1 g/l (29.93-37.88 g/l)
Globuline	64.6 g/l (23.07-42.09 g/l)
Fibrinogen	5.14 g/l (1.25-3.29 g/l)

Histopathologic Description: Lymph node and adipose tissue: Affecting approximately 60 % of the section there is a 15 x 10 mm granulomatous and fibrous nodular lesion. The inflammatory infiltrate is interspersed between large amounts of fibrous tissue, and consists of epithelioid cells, occasional multinucleated giant cells of foreign body (haphazardly arranged nuclei) and Langhans (peripherally arranged nuclei) type as well as many plasma cells, fewer lymphocytes and occasional eosinophils. Free within fibrous tissue, surrounded or engulfed by macrophages are multiple cross and tangential sections of nematode parasites. The parasites are 250-300 μm in length and 15-20 μm in diameter and show a thin, smooth cuticle.

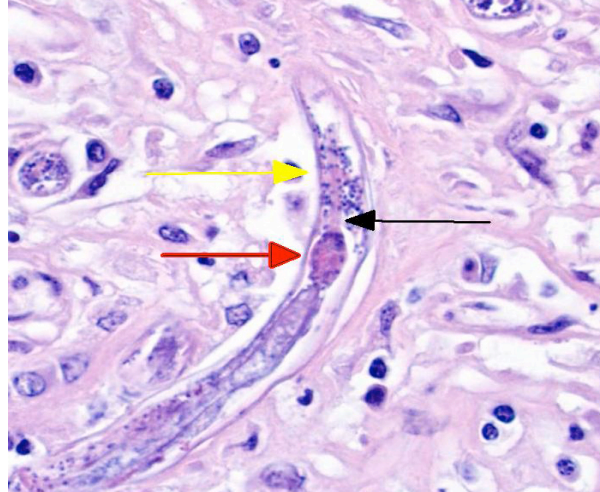
Sometimes a dorsoflexed uterus, occasionally with uninucleated eggs, and a rhabditiform esophagus with



2-1. Lymph node, horse: Nodal architecture is diffusely effaced. (HE 6.3X)



2-2. Lymph node, horse: The lymph node is replaced by fibrous connective tissue, granulomatous inflammation and numerous cross- and tangential sections of nematode parasites measuring 15-20 μm in diameter. (HE 252X)



2-3. Lymph node, horse: Nematode parasites, upon serendipitous section, possess a characteristic rhabditiform esophagus with a corpus (yellow arrow), isthmus (black arrow), and bulb (red arrow) characteristic of *Halicephalobus gingivalis*. (HE 400X)

corpus, isthmus and bulb can be seen. Eggs, measuring about 15 x 20 μm are occasionally observed free within the inflamed tissue. Multifocally, smaller forms of the parasites with rhabditiform esophagus and internal granular structures can be found (larvae). Parasites are multifocally surrounded by areas of lytic necrosis characterized by replacement of tissue with nuclear and cellular debris. Intralesional vessels are dilated (hyperemia) and in one location parasites, surrounded by inflammatory cells, are found within a medium sized artery. At the margins of the granuloma are moderate numbers of macrophages containing a yellow-brown globular pigment (hemosiderin).

Contributor's Morphologic Diagnosis:

Lymphadenitis and steatitis, granulomatous and eosinophilic, focal, moderate with intralesional adult and larval rhabditoid nematodes, etiology consistent with *Halicephalobus gingivalis*.

Contributor's Comment: *Halicephalobus gingivalis* (syn. *Micronema deletrix*, *Halicephalobus deletrix*) is a free-living soil saprophyte worm belonging to the nematode order *Rhabditida*, family *Panagrolaimidae*, and has the ability to produce extensive tissue damage because of its migratory behaviour.^{1,2,6} Equine cases of this parasitosis were reported in Europe, North and South America, Japan, Egypt and South Korea.⁸ One case of a halicephalobosis in a zebra can be found in the literature.⁷ Rare fatalities in man have also been described.¹²

It has been shown that only female worms and larvae induce lesions. In the kidneys, the parasite causes multifocal to coalescing granulomas containing numerous larval and adult rhabditiform nematodes and occasional embryonated eggs. Macroscopically, these granulomas often resemble neoplasms.⁹

The nematodes are 15-20 μm in diameter, 250-430 μm in length and have a thin, smooth cuticle. They possess a platymyarian-meromyarian musculature, a pseudocoelom and a rhabditiform esophagus composed of a corpus, isthmus and bulb. The intestinal tract is lined by uninucleate, low cuboidal cells and a single genital tube/uterus containing one egg/ova.⁵

Other important lesions in horses are severe encephalitis and myelitis,^{1,6,10} orchitis,⁴ osteomyelitis¹³ and posthitis.¹¹ Sometimes disseminated disease can develop.⁷

There are different hypotheses regarding the life cycle and the way of transmission of the nematode. Oral ingestion, inhalation or wound infections with nematode stages are suggested.² In one case vertical transmission on the colostral way from the dam to the foal was described.^{10,15}

Successful surgical therapies of cases with localized lesions are recorded, but it is possible that the parasites may survive within the granulomas; however, in the CNS the parasites can survive because anthelmintics do not easily cross the blood-brain barrier.³

In cases of renal halicephalobosis, also the case in the presented horse, azotemia and renal failure as well as hematuria can be observed. Parasitic lesions in tissues other than kidney and lymph node were not detectable in our case.

JPC Diagnosis:

Lymph nodes:
Lymphadenitis,
granulomatous,
chronic, diffuse,
severe, with
nematode adults,
larva and eggs.

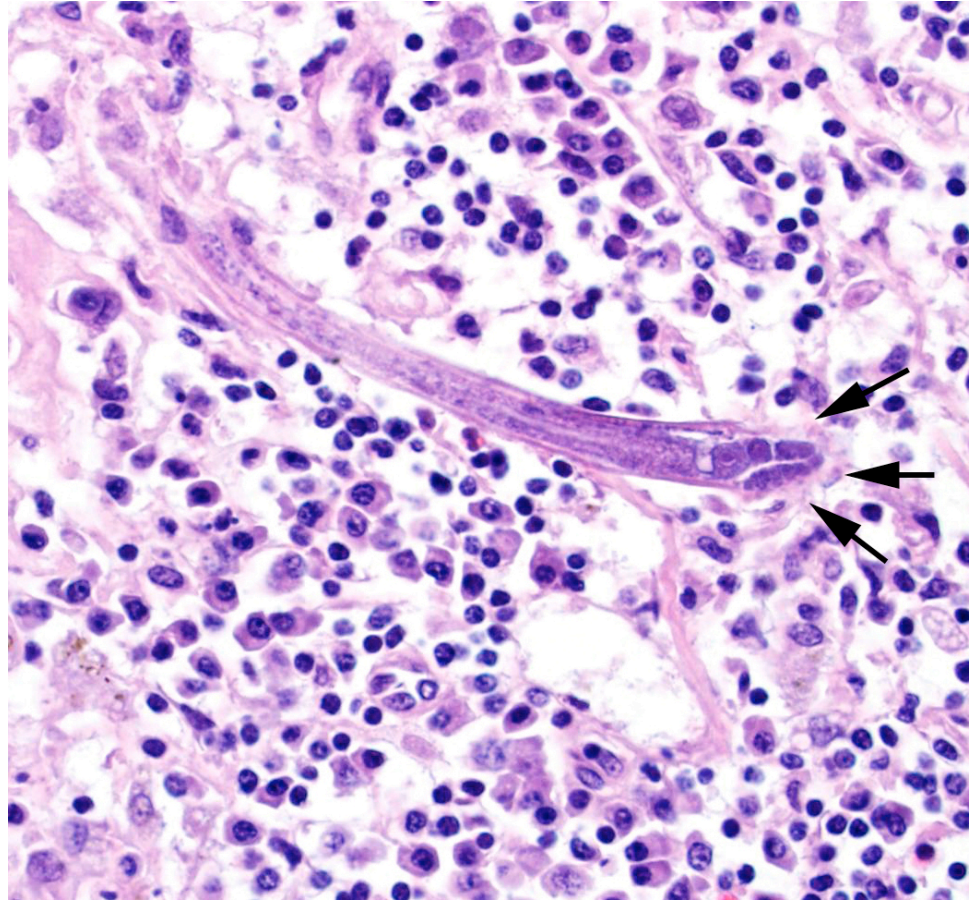
**C o n f e r e n c e
C o m m e n t :**

*Halicephalobus
gingivalis* has a very
characteristic
appearance on
histologic sections
though it is often

difficult to the histologic attributes described adroitly by the contributor. This case, however, presents a unique opportunity to observe all of its morphologic features with all three life stages found in abundance and in good preservation.

There are a number of migrating nematodes capable of inducing disease in the equine. While *H. gingivalis* is readily distinguishable, infections of *Strongylus vulgaris*, *Strongylus equinus*, *Angiostrongylus cantonensis*, *Setaria* spp., and *Draschia megastoma* can all manifest into a variety of clinical presentations to include neurologic signs and thus may be worthy of consideration.⁸ *H. gingivalis* has more affinity for the kidneys, lymph nodes and central nervous system; therefore infected animals most often present with renal signs as in this case or neurologic symptoms such as ataxia, circling, loss of balance, and head tremors.²

There are nine species of *Halicephalobus*, though only *H. gingivalis* is known to cause disease in



2-4. Lymph node, horse: Nematode parasites also possess a dorsoflexed uterus arrows. (HE 400X)

animals.² Its pathogenesis is largely unproven, including routes of infection. Hematogenous spread is widely accepted and supported by the presence of larva within arteries in this case. It is interesting, however, why it has predilection for certain tissues and often spares organs such as the liver and spleen. Only adult females, larval stages, and eggs have been identified in tissue sections, indicating the likelihood of parthenogenetic reproduction.^{2,7} Many details of the pathogenesis of this rarely reported parasitic infection remain undetermined.

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CASE III: N10-103 (JPC 3166502).

Signalment: 16-month-old intact mixed breed male cat, *Felis catus*.

History: The animal was a rescue shelter cat current on all vaccinations. The animal presented with dyspnea and strider upon exercise. Radiographs of the lungs revealed a diffuse interstitial pattern.

Gross Pathologic Findings: The carcass demonstrated an adequate nutritional plane. There was a red watery discharge from both nostrils. Upon reflecting the skin, the subcutaneous tissues were noted to stick to the prosector's gloves. The lungs did not collapse upon opening the thoracic cavity. They were moist and diffusely mottled gray to pink. Approximately 3mls of a pink watery fluid was in the chest cavity. The heart was enlarged and occupied three and a half intercostal spaces. A small amount of fluid oozed from a cut surface of the lungs.

Laboratory Results:

Clinical Pathology:

WBC:10.8 K/ul

NEU:3.47 32.2%N

LYM:5.69 52.9%L

MONO: 0.026 0.239%M

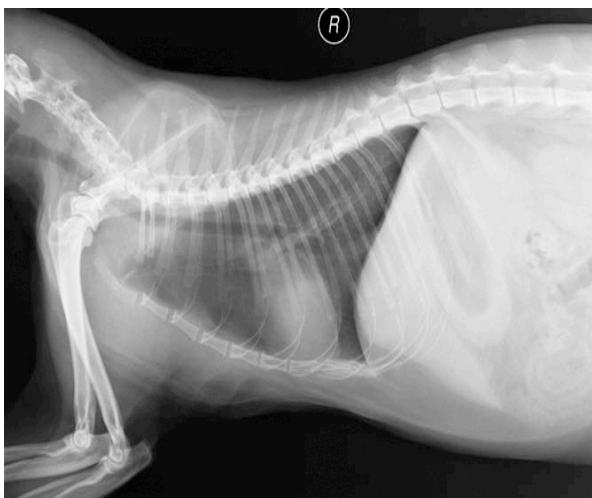
EOS 1.57 14.6%E

BASO 0.002 0.020 %B

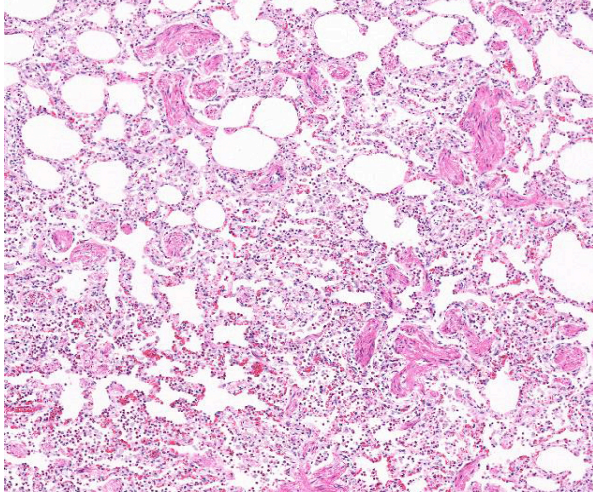
Histopathologic Description: There is moderate to marked hyperplasia and hypertrophy of the tunica muscularis of pulmonary arteries. The smooth muscle of bronchioles and alveolar ducts is also prominent. The epithelial linings of many bronchi are sloughed and there are increased numbers of bronchial glands. Small to moderate numbers of lymphocytes, plasma cells and macrophages infiltrate bronchial and bronchiolar walls, peribronchial connective tissue, and adjacent periarterial tissue. Peribronchial stroma is expanded by small clear spaces (edema).

Contributor's Morphologic Diagnosis: Bronchitis and bronchiolitis, chronic, multifocal, moderate, with alveolar ductal and arterial smooth muscle hyperplasia, and peribronchial glandular hyperplasia, lung.

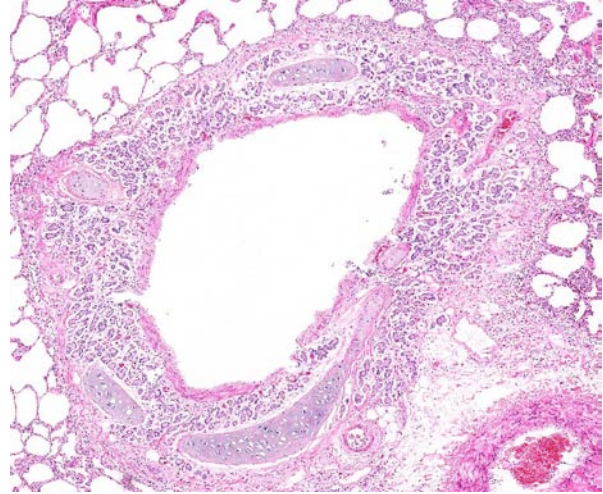
Contributor's Comment: Based on the microscopic lesions, a diagnosis of feline asthma syndrome (FAS) was made. This syndrome is characterized by episodes of coughing, wheezing and or dyspnea which are due to the bronchoconstriction secondary to hyperactivity of airway smooth muscle.¹ It has been referred to as allergic bronchitis or allergic pneumonia. Though the exact cause is unknown, it is associated with a type I immediate hypersensitivity reaction to inhaled antigens. Inhaled cat litter dust, aerosol sprays and cigarette smoke as well as infectious causes have been associated with this syndrome.³ This disease is rarely the primary cause of death



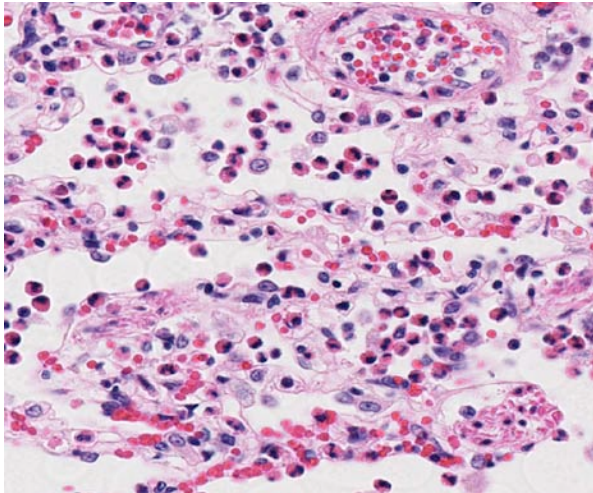
3-1. Lung, cat: Lateral and dorsoventral views demonstrate a marked diffuse interstitial pattern in all lung lobes. (Photo courtesy of: Tuskegee University, School of Veterinary Medicine, Department of Pathobiology, Clinical Anatomy Building, Tuskegee, AL 36088)



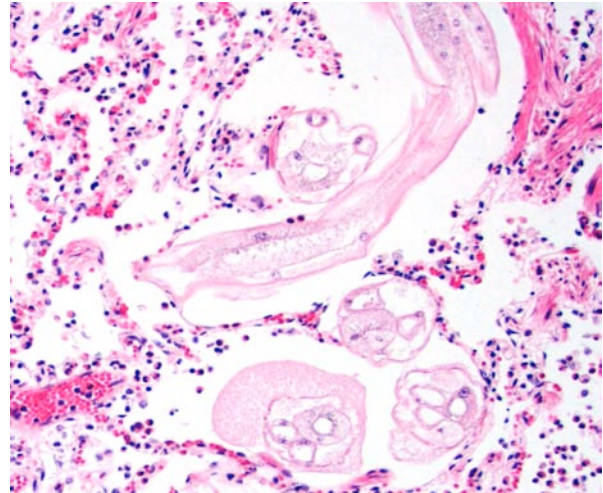
3-2. Lung, cat: There is diffuse hyperplasia of smooth muscle surrounding terminal airways, and alveolar septa are expanded, and alveoli filled by a cellular infiltrate. (HE 96X)



3-3. Lung, cat: There is diffuse hyperplasia of submucosal glands around airways. (HE 36X)



3-4. Lung, cat: Higher magnification of expanded alveolar septa and alveoli containing numerous eosinophils. (HE 356X)



3-5. Lung, cat: Within the section, there are cross- and tangential sections of a strongyle nematode with a smooth cuticle, pseudocoelom, coelomyarian-polymyarian musculature, and an intestine lined by multinucleated cells. Definitive speciation cannot be completed on this single section. (HE 280X)

except when a secondary bacterial pneumonia occurs.

In the early stages of this disease there is a mild eosinophilic inflammatory infiltrate with mucosal edema.³ As seen in this case, eosinophils are not always the prominent cell type. In the more advanced stages the characteristic lesions include bronchial gland hyperplasia along with smooth muscle hypertrophy of arteries and airways.

JPC Diagnosis: Lung: Pneumonia, eosinophilic, chronic, multifocal, moderate with bronchiolar

and smooth muscle hyperplasia, and intrabronchiolar adult nematodes.

Conference Comment: This is an interesting case, not in its classic or dramatic presentation of a lesion as often observed in WSC cases, but rather in its subtlety, effectively delivering a real-world diagnostic challenge to all conference participants. The contributor's diagnosis of feline asthma is based on the presence of smooth muscle and peribronchial gland hyperplasia as corresponding with the animal's clinical signs, as well as a diffuse mild eosinophilic infiltrate, primarily within alveoli. However, a number of

slides contain tangential sections of degenerate adult nematodes which were not described by the contributor, and which we believe are a primary component of this clinical presentation. The level of degeneration precludes definitive diagnosis; however, a large, multinucleated intestine is present in some nematode sections and when coupled with the vague coelomyarian musculature, strongly suggests a metastrongyle. *Aelurostrongylus abstrusus* is considered a ubiquitous nematode of domestic cats and thus the most likely species of metastrongyle in this case.³ Another possibility is the feline parasite *Ollulanus tricuspis*, a trichostrongyle which could have been regurgitated and aspirated into the lung parenchyma.

The changes seen in this case correlate best with a late-stage chronic infection with *A. abstrusus* in cats. In one study, 24 weeks following infection, eggs and larvae were completely absent and adult nematodes present in only 3 of nearly 100 examined histologic sections.² Smooth muscle and peribronchial gland hyperplasia are typical findings in these cases, though it is worth mentioning this is often considered a normal finding in healthy cats with no evidence of parasitism.¹

A. abstrusus is common in cats, with an array of corresponding clinical signs from asymptomatic to chronic coughing and tachypnea. In characteristic lesions, there are nodules formed by masses of eggs and larvae in alveoli and terminal bronchioles with few adult worms. Eosinophils and neutrophils predominate early, with more mononuclear cells and giant cells occurring later. Typically, chronic cases devoid of larvae and eggs have remaining epithelialized alveoli and septa thickened by fibrous tissue and smooth muscle.¹ The infection is usually self-limiting³ and given the mild extent of pathology in most slides, it is possible there were unidentified contributing factors to the clinical presentation described in this case.

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CASE IV: 14-8745 (JPC 4052875).

Signalment: 9-day-old piglet, *Sus scrofa domestica*.

History: This piglet is from a unit with ongoing diarrhea problems.

Gross Pathological Findings: The carcasses were thin and rough-haired. One of two pigs had milk in the stomach. The small intestines were thin-walled and fluid-filled. Spiral colons contained watery feces.

Histopathologic Description: Jejunum and ileum have severe atrophic enteritis. There is villus fusion and epithelial attenuation.

Contributor's Morphologic Diagnoses: Severe atrophic enteritis with villus fusion and epithelial attenuation.

Laboratory Results: Porcine epidemic diarrhea virus, confirmed with PCR. Immunohistochemistry stains are positive also.

Contributor's Comment: Porcine epidemic diarrhea virus (PEDV) was first identified in England in 1971 and was then confirmed in the United States in the spring of 2013.² As of the summer of 2014, the virus has spread to 30 states and has resulted in the loss of millions of pigs. The disease causes severe diarrhea and vomiting in all ages of pigs with mortality in suckling pigs of 90-95%. The original US isolates were nearly

identical to Chinese isolates from 2012. It is not known how PEDV arrived in the US. PEDV is a member of the genus *Alphacoronavirus* together with transmissible gastroenteritis virus (TGEV).

The pathology of PEDV has been described in gnotobiotic pigs.³ The lesions were similar to those observed in conventional pigs infected with PEDV.

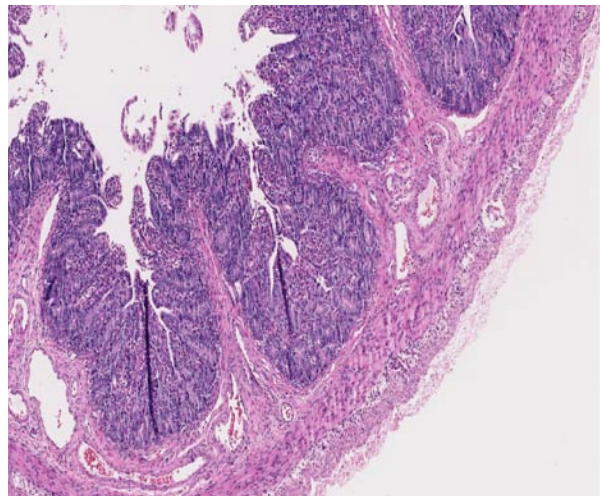
JPC Diagnosis: Small intestine: Enteritis, necrotizing, with villous blunting and fusion, and crypt hyperplasia.

Conference Comment: For an industry that excels in implementing biosecurity practices, the rapid spread of porcine epidemic diarrhea virus proves a major source of concern for our ability to control infectious diseases. In April 2013, hog confinement facilities with closed-herd strategies and shower-in, shower-out facilities broke out with explosive diarrhea and vomiting in suckling pigs. This led to a mortality rate approaching a staggering 95% within 3 days of the onset of clinical signs. Multiple facilities separated by hundreds of miles began to experience the same symptoms and a diarrhea epidemic ensued. Within months, the majority of states in the continental U.S. were reporting cases of PEDV.²

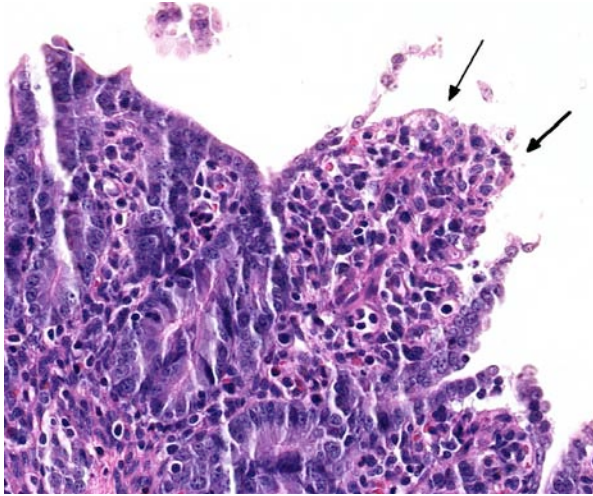
PEDV is an *Alphacoronavirus* that contains an enveloped, single-stranded positive-sense RNA genome.² It was first discovered in the UK in 1971 and continued to cause sporadic outbreaks in Europe and Asia for decades.² Though it is similar in structure and pathogenesis as TGE, its genome



4-1. Jejunum, 9-day-old piglet: Villi are diffusely and severely shortened. (HE 6.3X)



4-2. Jejunum, 9-day-old piglet: Villar epithelium lining shortened villi is multifocally attenuated and lost. (HE 6.3X)

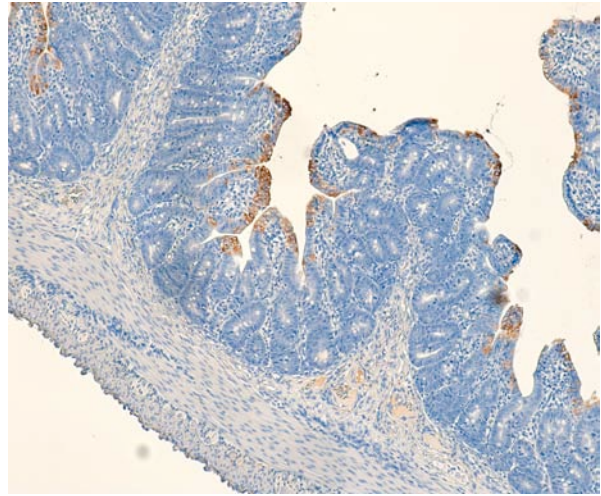


4-3. Jejunum, 9-day-old piglet: Immunohistochemical labeling for porcine epidemic diarrhea coronavirus antigen is diffuse and restricted to villar epithelium. (HE 6.3X)

is more closely related to bat *Alphacoronaviruses*.⁸ The virus targets intestinal epithelial cells of nursing pigs; however, infection of alveolar macrophages has also been demonstrated.⁷ Typical microscopic findings include severe atrophic enteritis throughout the small intestine and viral shedding can precede and continue beyond the observation of clinical signs.⁵ In this case, slides from multiple blocks were submitted and among them, the lesions varied from mild blunting and fusion of villi with moderate crypt hyperplasia to severe necrosis. There are also sections with mild loss of lymphocytes in Peyer's patches. Syncytial cell formation was evident throughout the more severely affected lesions.

There has been much attention on the possible mechanisms of virus transmission. Transportation equipment and contaminated feedstuffs are the most often cited culprits, as this may explain the sporadic, simultaneous outbreaks in facilities separated by hundreds of miles.³ Transmission between animals is largely fecal-oral, but airborne transmission is also suspected.¹

PEDV contains a transmembrane envelope glycoprotein virulence factor called spike, which is responsible for binding and fusion to host epithelial cells and macrophages. Spike contains two domains, S1 and S2, and the S1 domain is the primary target of vaccines due to its specific high-affinity binding to cell receptors.⁶ The first licensed vaccine for PEDV was released in the U.S. in 2014, and now there are several on the market. Incidence rate has been dropping recently



4-4. Treatment of affected sections of intestine with anti-PED antibodies demonstrates positive staining within villar tip enterocytes. (anti-PED coronavirus, 200X)

and, while the disease has killed over seven million pigs in just the last year, it appears the peak of this devastating epidemic has already passed.

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