The Armed Forces Institute of Pathology
Department of Veterinary Pathology

WEDNESDAY SLIDE CONFERENCE 2007-2008

Conference 12

2 January 2008

Moderator:

Bridget Lewis, DVM, DACVP

CASE I – A7-005112 (AFIP 3069593).

Signalment: Ten-week-old, female, Border collie dog, *Canis familiaris*.

History: The 10-week-old puppy was euthanized and submitted for necropsy with a history of ascending progressive muscle weakness, neutrophilic leukocytosis, non-regenerative anemia, and elevated alkaline phosphatase levels.

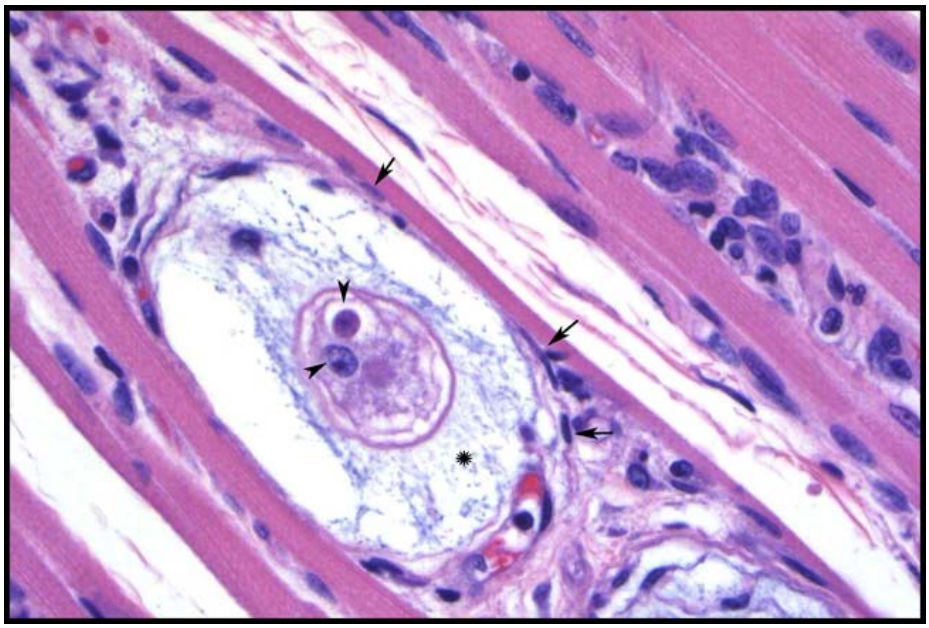
Gross Pathology: The carcass was in good physical condition and post mortem autolysis was mild. Mucopurulent ocular discharge and crusts were present bilaterally. Mucus membranes, subcutaneous tissues and viscera were uniformly pale. Small numbers of petechia were present in the peritoneum overlying the ventral abdominal muscles. A diffuse copper tint was present throughout the liver parenchyma. Intestinal contents were bright yellow and watery. No additional significant gross abnormalities were identified.

Laboratory Results: FA negative for canine distemper and infectious canine hepatitis viruses.

Histopathologic Description: Skeletal muscle: Endomysial areas are infiltrated by scattered small mixed populations of neutrophils and macrophages. Combinations of macrophages and neutrophils also commonly form multifocal, large, vascularized nodular aggregates containing myofiber fragments. Within these pyogranulomas, macrophages often possess an eccentric nucleus due to the presence of single, small, round, amphophilic, intracytoplasmic **parasite (fig. 1-1)**. Scattered throughout are numerous, round to oval, 50-100 µm structures containing a central, finely granular, pale eosinophilic core, with 1-2 ill-defined nuclei. Surrounding the core are multiple layers of lacy, pale basophilic material and a thin outer wall of flattened cells with elongated nuclei ("onion cysts"). These structures elicit little or no direct inflammatory response. Present in some sections are similarly sized structures (meronts) with a large pale eosinophilic core lined peripherally by either marginated nuclear material or elongated bodies (merozoites) with deep basophilic nuclei. Blood vessels contain increased numbers of neutrophils and macrophages.

Contributor's Morphologic Diagnosis: Skeletal muscle: Myositis, pyogranulomatous, widespread, chronic, severe, with multifocal intralesional *Hepatozoon americanum* zoites and meronts

Contributor's Comment: The history and histopathologic findings are consistent with American canine hepatozoonosis, a debilitating, tick-borne disease of dogs in the south-central and southeastern United States. The



1-1. Skeletal muscle, Boxer. Expanding and separating myocytes are 50 to 100 micrometer intracellular meronts, characterized by a central finely granular eosinophilic core with 1-2 nuclei (arrowheads). These are surrounded by layers of a myxomatous to lacy, pale basophilic material (star) and further bounded by a rim of compressed cells with flattened nuclei (arrows). Photomicrograph courtesy of the Department of Pathology, College of Veterinary Medicine, The University of Georgia, 501 D.W. Brooks Drive, Athens, GA 30602

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diagnosis was confirmed by PCR and sequence analysis. Discovered in 1978, *H. americanum* was advanced as a distinct species from its Old World counterpart, *H. canis*, in 1997.[1,8] At least 46 Hepatozoon species infect mammals and more than 120 infect snakes. Transmission of the apicomplexans to their vertebrate intermediate hosts occurs through hematophagous invertebrates. Like their *Plasmodium* and *Babesia* spp. relatives, many hepatozoons occur in erythrocytes. However, most of the mammalian parasites infect leukocytes and use acarines as definitive hosts or vectors. Interestingly, *H. americanum* is spread by the ingestion of infected ticks rather than through their feeding activities.[3]

It is believed that *H. americanum* crossed into canids from unknown vertebrates only recently, whereas *H. canis* has a long history with dogs. The vector for *H. americanum* is *Amblyomma maculatum*, gamonts are found in monocytes, and merogony occurs in host cells lodged between striated muscle fibers. In contrast, *Rhipicephalus sanguineus* is a primary vector for *H. canis*, the neutrophil is the favored host cell, and merogony takes place in a wide variety of tissues. Meronts of *H. americanum* develop most consistently in striated muscle within "onion skin" cysts created by layers of host secreted mucopolysaccharide. No similar lesion is associated with *H. canis*, which rarely occurs in muscle. Disease from *H. americanum* is more severe than that seen with *H. canis*. Developing organisms are shielded from the dog's immune system, but elicit intense local pyogranulomatous inflammation, systemic reaction, and overt illness when merozoites are released. Local lesions evolve into vascular granulomas. Diseased dogs are often febrile and lethargic, with stiff gaits, mucopurulent ocular discharge, and atrophy of the head muscles. Clinicopathological findings include mature neutrophilia, increased alkaline phosphatase, and hypoalbuminemia. Periosteal bone proliferation may be seen radiographically and at necropsy.[2,3,5]

AFIP Diagnosis: Skeletal muscle: Myositis, pyogranulomatous, multifocal, moderate, with fibrosis, and intracellular protozoal cysts and zoites etiology consistent with *Hepatozoon americanum*, Border collie (*Canis familiaris*), canine.

Conference Comment: The disease course of *Hepatozoon canis*, the causative agent of Old World hepatozoonosis, is generally mild with low levels of parasitemia, but severe illness occurs occasionally with nearly 100% of neutrophils containing parasites.[1,2] In the case of *Hepatozoon americanum* infection, the causative agent of American canine hepatozoonosis, parasitemia remains very low, and often less than 0.1% of leukocytes are infected, even in cases of severe illness.[1,2]

When *H. americanum* was first identified, *Rhipicephalus sanguineus* was thought to be the vector for transmission, as it is a known vector for *H. canis*. Even current literature has implied the role of *R. sanguineus* in transmission of *H. americanum*.[6] In fact, the primary vector for *H. americanum* appears to be *Amblyomma maculatum*, as *R. sanguineus*, *Dermacentor variabilis*, and *Amblyomma americanum* appear refractory to infection.[3,8]

In addition to the lesions within skeletal and cardiac mus-

cle, *H. americanum* is known to cause severe periosteal bone proliferation of proximal limbs.[3] Flat bones can be markedly, but less commonly, affected, and distal limbs are often spared.[3] The periosteal reaction shares common features with hypertrophic osteopathy in dogs.[3] The pathogenesis of the reaction is unknown, as there are no parasites identified with the bone lesions, and the inciting factors have not been identified.

Severe muscle wasting, especially of the temporal muscles, is also a feature of *H. americanum*.[3]

We thank Dr. C. H. Gardiner, PhD, veterinary parasitology consultant to the AFIP, for his review of this case.

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http://www.vet.uga.edu/VPP/index.php

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CASE II – Pfizer-05/Case2 (AFIP 3024116).

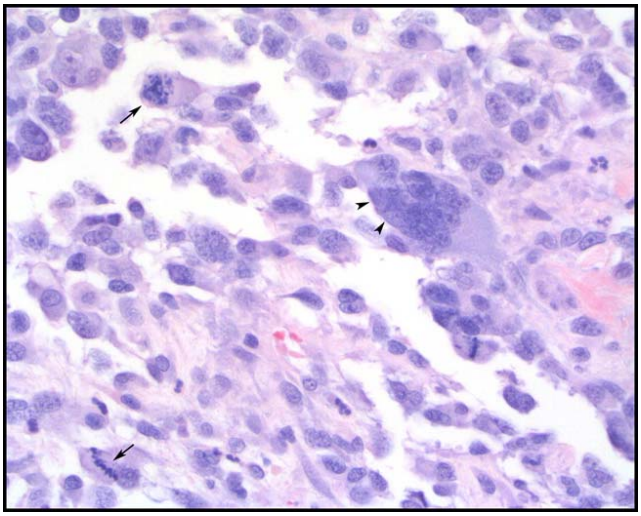
Signalment: Five-year-old, intact, beagle dog (*Canis familiaris*)

History: Dog had diarrhea for 2-3 days with unproductive vomiting starting on the third day. At the onset of vomiting a physical exam revealed a palpable abdominal mass and the dog was euthanized.

Gross Pathology: There were numerous multifocal 1-3 mm, white masses throughout the mesentery with 3-5, 3-10 mm white masses on right renal capsule.

Laboratory Results: Pan Cytokeratin (+), Vimentin (+), S-100 (-), SMA (-), Desmin (-)

Histopathologic Description: Overlying the serosa and throughout the mesentery are hypercellular papillary projections and disorganized mats of cells (forming layers and clumps) that overlay cores of fibrovascular stroma. The plump, pleomorphic, neoplastic mesothelial cells have indistinct cell margins, variable amounts of lightly eosinophilic cytoplasm, round nuclei with stippled chromatin and 1 nucleolus. There are 4-7 mitotic figures per high power field. Throughout the neoplastic tissues there



2-1. Mesentery, beagle. Neoplastic cells display marked anisocytosis and anisokaryosis with occasional multinucleate giant cells (arrowheads) and frequent bizarre mitoses (arrows). Photomicrograph courtesy of Pfizer Groton (PRGD), Groton, CT —>

is anisokaryosis, bizarre mitoses, **multinucleate giant cells (fig. 2-1)**, apoptotic cells and large cells with fragmented nuclei. Neoplastic cells are pancytokeratin and vimentin positive while negative for smooth muscle actin (SMA), desmin, and S-100.

Contributor's Morphologic Diagnosis: Biphasic mesothelioma

Contributor's Comment: Mesotheliomas are rare primary tumors of the squamous epithelium lining the pericardial, peritoneal, and pleural cavities. They rarely metastasize and are locally invasive.[8] Though they are most commonly reported in calves and dogs[8] they are also found in rodents[10,18], fish[6], horses, cattle, sheep, cats and pigs.[2] Peritoneal mesotheliomas are most frequent in a majority of species with the exception of pleural mesotheliomas in pigs.[2] Clinical signs vary with location. Pericardial signs include cardiac tamponade and congestive heart failure.[8] Pulmonary tumors may cause pleural effusion and dyspnea[1] while peritoneal tumors may cause ascites.[5]

Mesotheliomas in calves and other neonates are suspected to be due to spontaneous developmental disturbances.[9] Dog and human mesotheliomas linked to mineral fibers such as asbestos and erionite exposure may be due to physical irritation of mesothelium, disruption of the mitotic process leading to chromosome damage, increased reactive oxygen intermediate generation and/or persistent kinase-mediated signaling.[9,14] Mesotheliomas are also reported to be linked to exogenous hormones, metals and hydrocarbons as well as viruses (including SV40 virus).[6]

Mesotheliomas have three histological presentations with epitheloid, sarcomatous and biphasic forms. Epitheloid forms often have papillary structures lined by cuboidal basophilic mesothelial cells while sarcomatous forms have spindle cells and large anisocytotic cells with abundant eosinophlic cytoplasm and distinct cell margins.[5] Biphasic forms have characteristics of both.

Differential diagnosis include serous carcinomas and normal activated / reactive mesothelium. Differentiation of the set three entities can be challenging. Reactive mesothelium usually is not invasive and has less cytologic atypia while carcinomas form acinar structures.[8] Immunohistochemistry is useful in differentiating mesotheliomas from carcinomas. Mesotheliomas often stain positive for vimentin, cytokeratin[2], LP 34 and also stain for tumor glycoprotein BER EP4, S-100 and HMB 45.[1] They stain negatively for carcinoembryonic antigen, CD15 (LEU M1).[1] Electron microscopy of mesotheliomas often reveals long, slender, branching and undulate microvilli on apical surfaces while serous carcinomas have fewer, variably lengthed straight microvilli.[11]

AFIP Diagnosis: Fibroadipose tissue, mesentery (per contributor): Mesothelioma, Beagle (*Canis familiaris*), canine.

Conference Comment: Mesotheliomas are tumors of low grade malignancy that usually metastasize by exfoliation and implantation of neoplastic cells.[1] In humans mesotheliomas have been linked to exposure to asbestos fibers, and there is suggestive evidence in animals that a similar link occurs as well. Ferruginous bodies, asbestos fibers coated by ferritin and an amorphous protein[4], have been found in the lungs of dogs with mesotheliomas.[3,4] In addition to asbestos fiber exposure, mesotheliomas are reported to arise in response to non-fibrous and fibrous non-asbestiform agents.[8]

Cytologic diagnosis of mesotheliomas is difficult as neoplastic mesothelial cells are similar in appearance to reactive mesothelial cells in non-neoplastic effusions.[8] Immunohistochemistry can be useful in distinguishing mesotheliomas from other epithelial or non-epithelial neoplasms, although in some instances electron microscopy (EM) is necessary. Characteristic EM features of mesothelial cells include long slender, branching and undulating microvilli on all cell surfaces and prominent desmosomes.[1,11] The cytoplasm contains numerous bundles of tonofilaments that are arranged circumferentially around the nucleus.[8]

F344 rats are predisposed to mesotheliomas in the tunica vaginalis of the testes with occasional subsequent implantation on the serosal surfaces of the peritoneum.[1,10,12]

Other neoplasms that have positive immunoreactivity for both cytokeratin and vimentin include meningioma[8], chordoma[8], clear cell adnexal carcinoma[16], ciliary body adenoma/adenocarcinoma[7], anaplastic carcinoma[8], synovial cell sarcoma (biphasic)[8], and carcinosarcoma.[15]

Contributor: Pfizer Groton (PRGD), Groton, CT

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CASE III – 06-0115 (AFIP 3054023).

Signalment: 30-year-old, male, American flamingo (*Pheonicopterus ruber*)

History: Self-isolation from flock. On presentation, flamingo was weak and thin. Supportive care was given, but bird was found dead two days later.

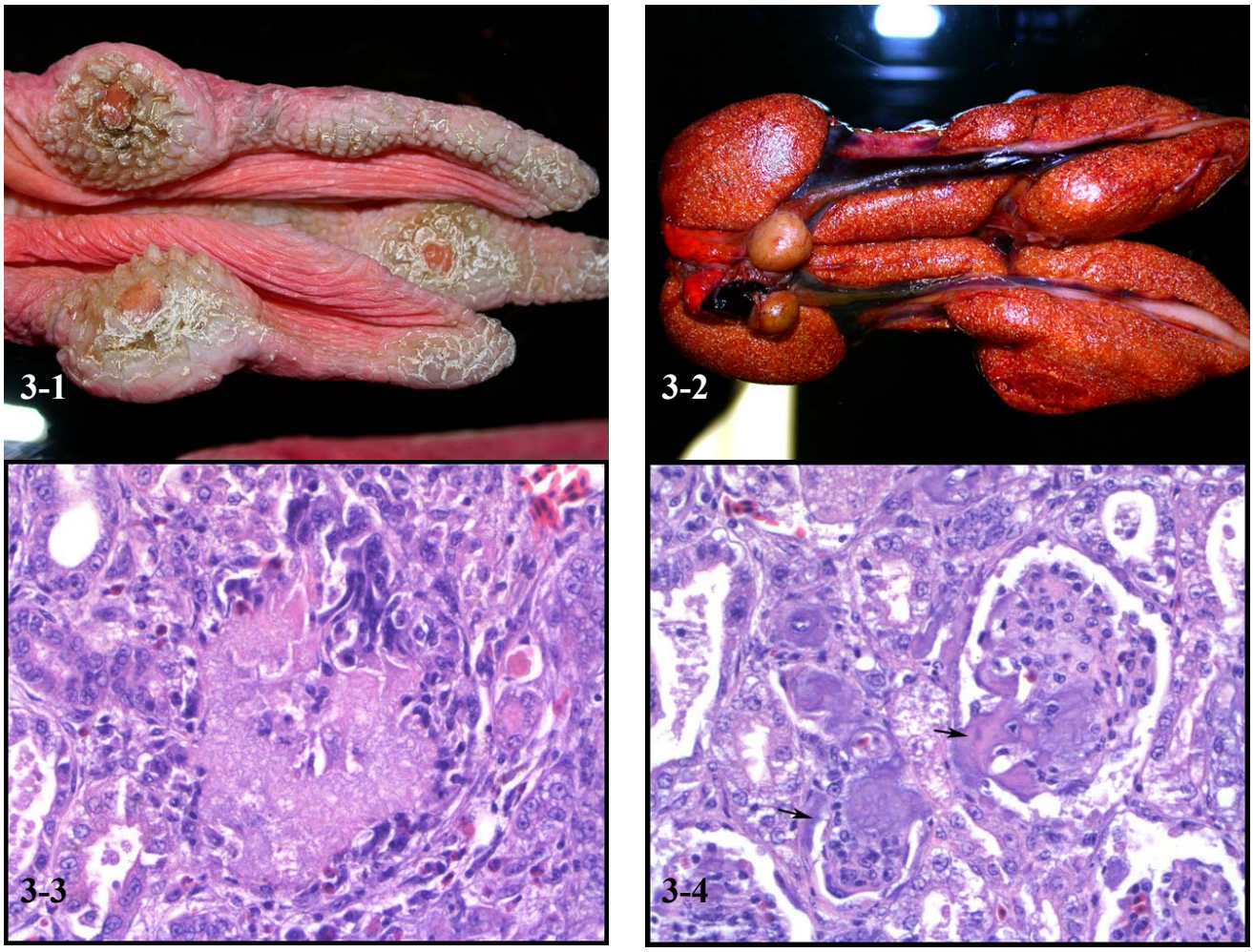
Gross Pathology: The plantar aspects of both **feet (fig. 3-1)** have thickened/calloused 1-1.5 cm diameter lesions with a small central crater over the proximal joints of digits one, two, and three. Associated joints contain cloudy, viscous fluid. The abdominal air sacs, primarily on the right side, have pinpoint gritty, white foci. The liver is firm and subtly mottled yellow brown to red brown, primarily on the edges and right lobe. On section, there are multifocal pinpoint, cream-to-yellow nodules in the hepatic parenchyma. The **kidneys (fig. 3-2)** are discolored yellow to light brown with pinpoint, gritty, palely yellow foci. The ureters are prominent.

Laboratory Results:
Joint fluid cytology at necropsy: Articular gout.
CBC revealed a leukocytosis (20.6 k/uL) with a heterophilia, lymphopenia and monocytosis. Hyperfibrinogenemia (700mg/dl), hypoglycemia (98mg/dl), hyperphosphatemia (11.2mg/dl), and hyponatremia (120mEq/L) were evident on CP. CP also showed elevations of uric acid (99.6mg/dl), CPK (3770 IU/L), and LDH (511 IU/L).

Histopathologic Description: Kidney: Multifocally, the renal architecture is disrupted by tubulocentric gouty **tophi (3-3)** that are composed of an inner, radiating array of eosinophilic, acellular spicules surrounded by macrophages and multinucleated giant cells with few heterophils. Rarely the centers of these tophi are mineralized. Within glomerular loops and occasionally expanding tubular basement membranes, there are lakes of homogenous, eosinophilic material **(amyloid-like) (fig. 3-4)**. There is a moderate increase in interstitial fibrosis and tubules are mildly ectatic and tortuous. Multifocally, lymphocytes and fewer macrophages are present in the interstitium.

Contributor's Morphologic Diagnoses: 1. Kidney: Gout, visceral, multifocal, marked, with tubular degeneration and necrosis, and chronic, interstitial nephritis, American flamingo (*Phoenicopterus ruber*)
2. Kidney: Amyloidosis, glomerular and interstitial, American flamingo (*Phoenicopterus ruber*)

Contributor's Comment: Of the many avian species,



3-1. Plantar surface of foot, American flamingo. Multifocally, the joints are markedly swollen with central craterform ulcers.
3-2. Kidneys, American flamingo. Multifocally, the kidneys have a military pattern of white to yellow pinpoint foci of mineralization.
3-3. Kidney, American flamingo. Multifocally, expanding renal interstitium, separating, surrounding and replacing uriniferous tubules and glomeruli are radiating acicular gouty tophi surrounded by granulomatous inflammation.
3-4. Kidney, American flamingo. Multifocally markedly expanding and replacing glomerular tufts, tubular and glomerular basement membranes and bowman's capsule is an amorphous, eosinophilic, acellular homogenous material (amyloid-like material) (arrows)

Gross photgraphs and photomicrograph courtesy of the Department of Pathology, National Zoological Park, 3001 Connecticut Ave NW, Washington DC, 20008

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waterfowl are most often affected by amyloidosis. Though mammals produce over 15 kinds of amyloid protein, birds are known only to deposit amyloid AA.[1] Accumulation of this protein in the extracellular spaces is a result of chronic antigenic stimulation and may be associated with such diseases as bumblefoot, chronic enteritis, or pneumonic aspergillosis. Deposition of amyloid AA occurs most frequently in the liver, spleen, and intestine, but may occur in any organ of the body.

Gout occurs in two forms: articular and visceral.[1] Articular gout is a chronic process with an uncertain etiology that results in deposition of urates and resultant granulomatous inflammation in the joint spaces, most

Extracted from Diseases of Poultry, Crespo, et al.[1]

	Visceral Gout	Articular Gout
Onset	Usually acute	Usually chronic
Frequency	Common	Rare
Kidney Lesions	Almost always involved, grossly abnormal, with white chalky deposits	May become involved with dehydrations
Joints	May or may not be involved	Always involved, especially the feet
Pathogenesis	Failure of urate excretion (renal failure)	Possibly due to metabolic defect in secretion of urates by kidney tubules
Causes	Dehydration Nephrotoxicity Infectious agents Vitamin A deficiency Urolithiasis Neoplasia Immune mediated glomerulonephritis Others	Genetics High protein diet Others

often of the feet. It is proposed that genetics or a high protein diet may contribute to this condition. Visceral gout occurs more acutely than articular gout and is characterized by small gouty tophi within the renal parenchyma and on the surface of the liver, heart and air sacs. In severe cases, gouty tophi may be seen within the liver and spleen parenchyma as well. These tophi incite little to no inflammatory response, as compared to deposits in articular gout, as their accumulation is more rapid. Visceral gout may occur due to dehydration or renal damage.

Renal function, in birds, is evaluated with the measurement of uric acid. This compound is the final result of nitrogen catabolism in avians and is produced in the liver.[1] If renal function is impaired, uric acid may build up in the bloodstream and precipitate as crystals in the tissues.[4] The validity of this test is not absolute as plasma uric acid may rise with normal feeding or ovulation, and may be normal in some cases of renal disease.[3]

We hypothesized that this aged flamingo developed articular gout over a period of time which led to severe amyloidosis in the kidney, liver and spleen. There was no other post mortem evidence of chronic disease, though this may have resolved by the time of death, leaving only amyloidosis as evidence of past pathology. The deposition of large amounts of protein in the interstitial spaces of the kidneys caused tubular degeneration and ischemia, leading to renal failure, decreased uric acid clearance, marked hyperuricemia and visceral gout.

Of the 62 American flamingos necropsied at the National Zoological Park since 1975, 21 (34%) have had amyloid deposition in at least one tissue. Amyloidosis was listed as the cause of death in 14 (23%) flamingos. This finding may indicate that this group of American flamingos, a closed flock since 1996, has a genetic predisposition to amyloid deposition.

AFIP Diagnosis: 1. Kidney, glomeruli, tubules and vessels: Amyloidosis, multifocal, marked, American flamingo (*Pheonicopterus rubber*), avian.
2. Kidney: Nephritis, tubulointerstitial, granulomatous and heterophilic, multifocal, moderate, with protein casts and urate tophi.

Conference Comment: Gout is the deposition of sodium urate crystals or urates in tissue; it occurs in species that lack the enzyme uricase such as humans, birds, and reptiles.[9] Uricase, or urate oxidase, is an enzyme that catalyzes the oxidation of uric acid to 5-hydroxyisourate. In those animals lacking this enzyme, uric acid is the final step in purine catabolism. Uric acid and urates are eliminated as semisolid urates in birds and reptiles.[4]

Visceral and articular gout are two separate syndromes with different etiologies, morphologies, and pathogenesis.

The diagnosis of visceral gout should not be considered a

disease entity itself, but rather a sign of severe renal dysfunction leading to hyperuricemia.[1]

True gout must be distinguished from pseudogout in which crystals other than sodium urate, such as calcium pyrophosphate dehydrate or hydroxyapatite, are deposited in joints. Grossly, pseudogout appears as cream-colored gritty material surrounding the joint capsule. This is in contrast to urates which are found inside the joint capsule and within the synovial fluid. Tophi are not present in pseudogout. Additionally, urates are radiolucent, whereas calcium deposits are radiopaque. True gout affects the kidneys, pericardium, liver, and other internal organs, whereas pseudogout only affects the joints and does not appear to occur in other locations. Pseudogout has been reported in humans, Rhesus macaques, dogs, and turtles.[5,6]

Contributing Institution: Department of Pathology, National Zoological Park, 3001 Connecticut Ave NW, Washington DC, 20008

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CASE IV - W406/07 (AFIP 3074808).

Signalment: 12-month-old, female spayed, Bengal cat, *Felis catus*, feline.

History: Three week history of pyrexia, progressive inappetance, weight loss, unilateral uveitis, upper respiratory stertor with serous nasal discharge. Respiratory rate and effort was slightly increased. Thoracic **radiographs (fig. 4-1)** revealed a severe generalized mixed parenchymal pattern (fluffy increase in opacity throughout all lung lobes, coalescing into small nodules). The cat failed to respond to antimicrobial and supportive therapy and was euthanized.

Gross Pathologic Findings: The carcass of a young adult, spayed female, feline was in poor body condition and of adequate hydration. There was a tan-brown crust over the anterior nares. Transverse sectioning of the nasal cavity revealed almost complete **effacement (fig. 4-2)** of the turbinate architecture by soft pink moist tissue with smaller areas of green-brown discoloration. The trachea contained a small amount of cream-colored stable foam. At the level of the bifurcation there was a moderate amount of pink tinged clear viscid fluid. The pleural surface of the **lungs (fig. 4-3)** was extensively mottled dark red. On cut section the mottling extended throughout the parenchyma.

The liver had a pronounced acinar pattern. Multifocal irregularly shaped maroon discolorations, which were often depressed, were present on the capsular **surface (fig. 4-3)**.

All other organ systems were examined with no further gross lesions detected.

Laboratory Results: Routine hematology and biochemistry were within normal limits, except for elevated globulins (globulins 55 g/L, albumin 24 g/L, total protein 79 g/L).

Bronchoalveolar lavage contained large numbers of degenerate nucleated cells and an abundance of cellular debris. Markedly increased numbers of neutrophils (85%) and an abundance of mucous were also noted.

Serology

Toxoplasmosis IFAT (IgG)	negative
Toxoplasmosis IFAT (IgM)	negative
Feline Calicivirus IFA Titre	>= 1:80
Feline Herpes Virus IFA Titre	= 1:20
Feline Panleukopaenia Virus IFA Titre	= 1:20
Feline Coronavirus IFA Titre	>= 1:2560

PCR

Feline Immunodeficiency Virus PCR	negative

Using a monoclonal antibody against Feline Coronavirus (FCoV), immunohistochemistry was performed on several sections of paraffin embedded formalin fixed tissue. FCoV-infected macrophages were detected in large numbers throughout the nasal submucosa.

Histopathologic Description: Nasal turbinates: The respiratory epithelium was generally intact with cilia present and sufficient numbers of goblet cells, however, there were small to locally extensive areas of epithelial erosion and surrounding attenuation and fibrinous exudation. There was moderate, predominately mononuclear inflammatory exocytosis. Turbinate structure was largely obliterated by a necrotizing inflammatory infiltrate. The submucosa contained a diffuse severe mixed, predominately lymphoplasmacytic inflammatory infiltrate. Numerous **veins (fig. 4-4)** were occluded by intense aggregations of monocytes and macrophages admixed with neutrophils. Many of these leucocytes were disintegrating. Vascular walls were often effaced by the inflammatory infiltrate. Bony trabeculae had irregular margins and were lined by abundant numbers of osteoclasts with surrounding proliferation of osteoprogenitor cells in some areas. The inflammatory reaction extended to cancellous marrow spaces and bone marrow of the maxilla and periodontal ligament and vessels of the dentine. Tooth dentine was necrotic.

Lung: There was a diffuse interstitial pneumonia with widely distributed foci of intense pyogranulomatous inflammation. Multifocal moderately sized areas of parenchyma were necrotic and surrounded by fibrinous effusion.

Liver: There was severe diffuse hydropic change of hepatocytes with mild bridging fibrosis and mild periportal lymphoplasmacytic inflammatory infiltrates. Multifocal moderately sized areas of telangiectasia were present and most noticeable towards the capsular surface. Leukocyte numbers were increased within the sinusoids.

Lymph nodes: Cortices contain numerous follicles with prominent germinal centers. The paracortices were expanded by numerous small mature lymphocytes. Numerous plasma cells were present within the medullary cords. There was a sinus histiocytosis. Multifocal granulomas of varying size were scattered throughout the nodes.

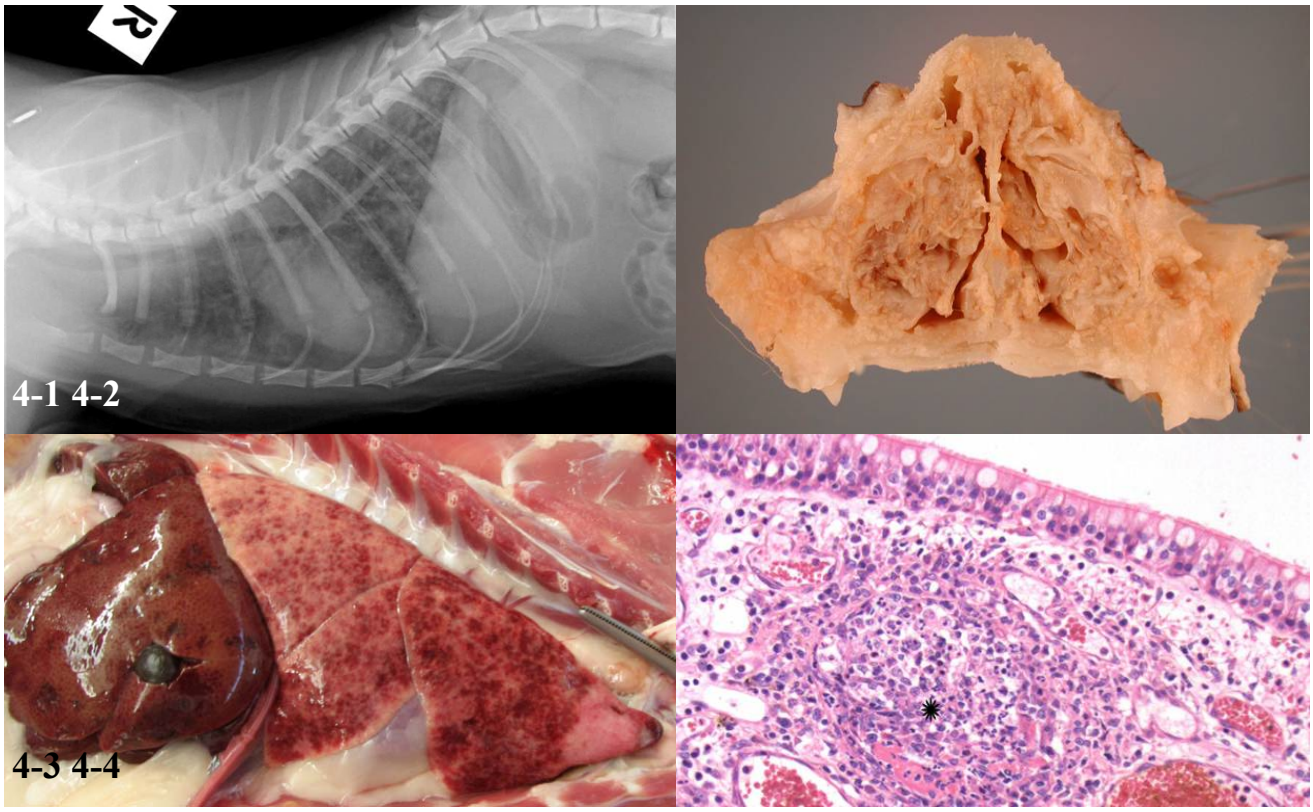
Bone marrow: There was a marked increase in myeloid to erythroid ratio

Contributor's Morphologic Diagnosis: 1. Nasal turbinates: Rhinitis and phlebitis, pyogranulomatous, chronic-active, diffuse, severe.
2. Lung: Bronchopneumonia, necrotising, granulomatous chronic, multifocal to coalescing, severe.
3. Lymph nodes: Lymphadenitis, granulomatous, chronic, multifocal, moderately severe.

Contributor's Comment: Feline infectious peritonitis (FIP) is a worldwide fatal systemic disease of wild and domestic felids which is triggered by infection with FCoV. The disease syndrome was first described in 1963 with the etiological agent identified in 1978.[3] Granulomatous vasculitis and perivasculitis (especially of venules), fibrinous to granulomatous serositis, pyogranulomatous inflammation and granulomas in organs are characteristic histopathological lesions. [1,3,4] These result in the spectrum of "wet" (with large amounts of highly proteinaceous cavitory effusions) to "dry" (multifocal granulomas) clinical presentations.

FCoV is a member of the family Coronaviridae, genus *Coronavirus*. Coronaviruses are enveloped positive stranded RNA viruses averaging 100 nm in diameter and have characteristic petal shaped surface projections (peplomers) which are responsible for the crown like (corona) electron microscopic appearance.[3] Coronaviruses have relatively low species specificity. Canine coronavirus is closely related to FCoV and can infect cats causing diarrhea. Exposed cats develop antibodies which cross-react with FCoV. Infection with FCoV results in a spectrum of outcomes, from asymptomatic enteric infection and healthy lifelong carrier status, through to systemic enteric infection to virulent systemic infection (FIP).

Coronavirus antibodies are present in up to 90% of cats in catteries and in up to 50% of cats in single cat households.[3] However, FIP morbidity is low, with only approximately 5% of FCoV infected cats developing FIP[3,4], and those cats that do develop the disease are usually under 2 years of age.[1] Infection usually takes place oral-nasally from exposure to FCoV-containing feces. Transmission in saliva can occur as the virus replicates in the tonsils in the early stages of infection.[3] Respiratory droplet and urine are also considered possible vehicles for



4-1. Thoracic lateral radiograph, Bengal cat. The radiograph shows a diffuse parenchymal nodular pattern of radiolucency within the lungs.
4-2. Transverse section, nasal turbinates, Bengal cat. Diffusely, the nasal turbinates are effaced by necrosis.
4-3. Thorax and abdomen, Bengal cat. Multifocally, both the lungs and liver have an irregular pattern of necrosis and hemorrhage characterized by a mottled discoloration.
4-4. Nasal turbinates, Bengal cat. Multifocally veins within the subepithelial connective tissue are expanded and occluded by fibrin thrombi characterized by a coagulum of fibrin, necrotic debris, viable and degenerate neutrophils (star).

Radiograph, photographs, and photomicrograph courtesy of the University of Melbourne, School of Veterinary Science, 250 Princess Highway, Werribee, Victoria, Australia 3030

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transmission.[3] Trans placental transm ission has bee n shown to o ccur but is r are.[3] FC oV rep licates in en terocytes eith er asy mptomatically or causi ng transient a nd usually clinically mild diarrhea and/or vomiting.[3] A short episode of mild upper respi ratory tract dis ease may also occur.[3]

FIP only e nsues i n i ndividual affected a nimals whe n FCoV undergoes sp ontaneous m utation during r eplication. Deletions in o pen reading frames 3 an d 7 wh ich code for non s tructural proteins a re res ponsible f or s urface cha nges which allow the vi rus pha gocytozed by macrophages t o bind t o t he ri bosomes of t he m acrophages.[3,4] M utated viruses have a 99.5% genetic homology with the parent virus.[3] The mutation allows the virus to rep licate within m acrophages. FC oV i nfected m onocytes are c onsidered r esponsible f or vi ral dissemination within th e host.[4] FCoV vi remia is detectable in both virulent (m utated FIP infection) and n on m utated FCoV infected cats.[3,4]

The pat hogenesis of F IP i s complex. Th e vi rus i tself does no t cau se major cytopath ic d amage; rath er lesi ons result from th e ho st's own immu ne r esponse.[3] Fibrinogen, C 3 an d viral a ntigen demonstrated within FIP lesions, and evidence of FCoV-specific immune complexes within the blood and vessels, together with high levels of gamma globulin in affected cats support an immune com-

plex-mediated, type III hypersensitivity pathogenesis.[3,4] However, an alternative pathogenesis has been proposed where lesion initiation appears to begin with endothelial adherence and extravasation of FCoV positive, activated monocytes and progresses to venous and perivenous, macrophage dominated, focal to circular infiltrates.[4] The presence of a peripheral rim of B lymphocytes in older FIP lesions, the paucity of neutrophils and T lymphocytes within the lesions and a lack of non-specific perivascular lymphocytic cuffing during one study are cited as significant differences between FIP and classical immune-complex mediated vasculitides.[4]

A definitive antemortem diagnosis of FIP is often challenging, complicated by the often insidious onset and non-specific signs displayed by infected animals. Laboratory tests including FCoV antibody titer (blood and CSF), RT-PCR to detect virus, ELISA to detect antibody-antigen complexes and measurement of acute phase proteins (mainly serum alpha-1 acid glycoprotein) are relatively insensitive and/or poorly specific.[3,4] This is mainly due to the inability to differentiate sero conversion or viremia caused by FCoV from that caused by mutated FCoV (FIP causing) strains. Serum alpha-1 acid glycoprotein has been shown to be elevated in other inflammatory conditions. Histopathology with immunohistochemistry to detect FCoV infected macrophages remains the only conclusive means of diagnosing FIP.[1,4]

This case demonstrates classic characteristic FIP vasocentric granulomatous lesions. It is unusual in that the most severe lesions are within the nasal submucosa, this distribution has not previously been reported.

AFIP Diagnosis: Nasal turbinates, maxillary bone, and hard palate: Vasculitis, pyogranulomatous, multifocal, severe, with rhinitis, erosions, fibrin thrombi, and bone remodeling, Bengal cat (*Felis domesticus*), feline.

Conference Comment: The contributor provides an excellent overview of feline infectious peritonitis virus. Conference participants discussed the definition of vasculitis, the histomorphologic features needed for the diagnosis of vasculitis, and the differential diagnosis for vasculitis in various other species.

The diseases that cause vasculitis in animals are summarized in **table 4-1** below from Pathologic Basis of Veterinary Disease.[5]

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Table 4-1. Causes of Vasculitis in Animals

VIRAL
Equine viral arteritis (arterivirus), malignant catarrhal fever (gammaherpesvirus), hog cholera (porcine pestivirus), feline infectious peritonitis (coronavirus), bluetongue (orbivirus), African swine fever (asfarvirus), equine infectious anemia (lentivirus), bovine virus diarrhea (bovine pestivirus)

BACTERIAL
Salmonellosis, erysipelas (*Erysipelothrix rhusiopathiae*), *Hemophilus* spp. infections (*Hemophilus suis*, *Histophilus somni*, *Hemophilus parasuis*)

MYCOTIC
Phycomycosis, Aspergillosis

PARASITIC
Equine strongylosis (*Strongylus vulgaris*), dirofilariasis (*Dirofilaria immitis*), spirocercosis (*Spirocerca lupi*), onchocerciasis, elaeophoriasis (*Elaeophora schneideri*), filariasis in primates, aelurostrongylosis, angiostrongylosis

IMMUNE-MEDIATED
Canine systemic lupus erythematosus, rheumatoid arthritis, Aleutian mink disease (parvovirus), polyarteritis nodosa, lymphocytic choriomeningitis, drug-induced hypersensitivity

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