Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2025-2026

Conference #5 — 24 September 2025

CASE I:

Signalment:
10-week-old, female intact, mixed breed, *Canis lupus familiaris,* canine.

History:
The submitted dog was from a litter of puppies that was found living underneath a shed in Texas. A rescue organization acquired the puppies, and the dog was later adopted by a family in Colorado. The dog was apparently healthy up until 10 weeks of age when she suddenly developed a bloated appearance and began vomiting. The animal's condition worsened overnight, becoming lethargic and not acting herself. The next morning, the dog went outside and tried to vomit but subsequently collapsed and died.

Gross Pathology:
A 7.55 kg, intact female, mixed breed puppy was submitted for necropsy, one day post-mortem, and in good condition. The lungs and heart were grossly unremarkable. The peritoneal cavity contained approximately 400 ml of serosanguinous fluid. All liver lobes had numerous, multifocal to coalescing, pinpoint, flat, tan foci that extended into the hepatic parenchyma on cut section. The stomach contained a black plastic clothing hook and yellow to green mucoid material. The small intestines contained yellow to tan liquid material and the large intestines had no intraluminal contents.

Laboratory Results:
N/A

Microscopic Description:
Expanding and infiltrating all layers of the heart, with the greatest severity in the myocardium, are large numbers of plasma cells, lymphocytes, and macrophages. Cardiomyocytes in areas of inflammation are multifocally hypereosinophilic, shrunken, and have striation loss with fragmented to absent nuclei (necrosis). There is mild, multifocal, interstitial fibrosis often associated with cardiomyocyte degeneration and inflammation. Throughout the myocardium, there are occasional cardiomyocytes that contain intrasarcoplasmic, variably sized (up to 100 µm in length) pseudocysts with numerous, 2-3 µm, round protozoal amastigotes.

Figure 1-1: Heart, dog. A section of heart is submitted for examination. Numerous hypercellular foci within the myocardium are visible at subgross magnification. (HE, 10X)

Contributor's Morphologic Diagnoses:
Heart: Severe, multifocal, chronic-active, lymphoplasmacytic and histiocytic pancarditis with intrasarcoplasmic pseudocysts containing amastigotes

Contributor's Comment:
The histologic findings within the heart are most consistent with the protozoal organism, *Trypanosoma cruzi*, also known as Chagas disease or American trypanosomiasis. *Trypanosoma cruzi* is a flagellate protozoan organism that primarily harbors in an insect vector of the *Triatominae* family, most commonly the kissing bug or triatomine bug.[5,8-10] It affects a variety of mammalian species across South, Central, and North America, including humans, domestic animals, and non-human primates.[5,8-10] It is estimated that approximately 8 million people worldwide have this disease, and around 280,000 reside within the United States.[5] Between 60 to 70% of people infected with *T. cruzi* will never develop clinical signs or symptoms, the remaining 30-40% will develop chronic symptomatic forms within 10 to 30 years.[8]

The life cycle of *T. cruzi* is complex and begins when the triatomine bug feeds on a host's blood infected with trypomastigotes. Once in the insect's midgut, the trypomastigotes differentiate into the epimastigote form where they later become the infective metacyclic trypomastigotes at the rectal ampulla.[5] The infective trypomastigotes are then excreted into the feces. As the now-infected bug moves on to its next victim, it will take a blood meal from the host and subsequently defecate near the bite wound. In humans, triatomine bugs will frequently bite along the face and near the mouth, hence their name "kissing bug", due to their attraction to the carbon dioxide and warmth produced by the face. The parasites can then enter through the mucous membranes, the bite wound, or a cut/abrasion to the skin, as infected hosts will often scratch at the time of

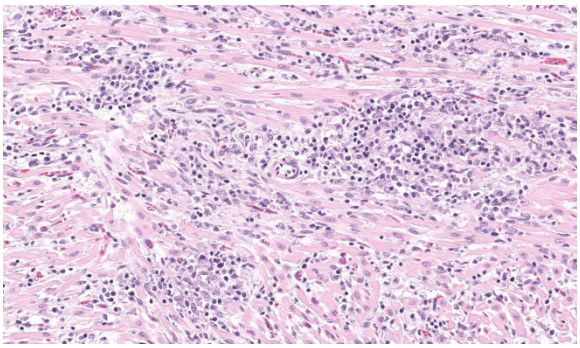

Figure 1-2: Heart, dog. Hypercellular foci consist of numerous lymphocytes and plasma cells within the myocardial interstitium which multifocally efface cardiomyocytes. (HE, 315X)

the bite. Once in the bloodstream, the metacyclic trypomastigotes will invade the host cells and begin the intracellular transition to amastigotes. Amastigotes will replicate by binary fission differentiating back to metacyclic trypomastigotes and rupturing the cell making their way back into the bloodstream.

T. cruzi can infect myocytes, endothelial cells, fibroblasts, and adipocytes, but has a tropism for cardiac muscle tissue.[11] Grossly, there are no pathognomonic lesions for Chagas disease. Histologically, the cardiomyocytes will be expanded by a pseudocyst containing amastigotes. While best observed ultramicroscopically, the amastigotes will have a large nucleus and an adjacent rod-shaped kinetoplast, like *Leishmania* spp. Unlike the defined perpendicular orientation of the kinetoplast in *Leishmania*, the location of the kinetoplast relative to the nucleus changes during the life cycle and cannot be a diagnostic feature in Chagas disease.[10] Unfortunately, additional diagnostics including PCR, culture, and serology were not performed so leishmaniasis cannot be completely ruled out, but the geographic and anatomic location of the organism along with the histologic appearance is most likely consistent with *T. cruzi*. Infection results in marked inflammation of the heart, often not associated with the intracellular pseudocysts. Myocarditis can lead to heart failure with cardiac arrest and potentially fatal arrhythmias. In this case, there was multi-organ evidence of

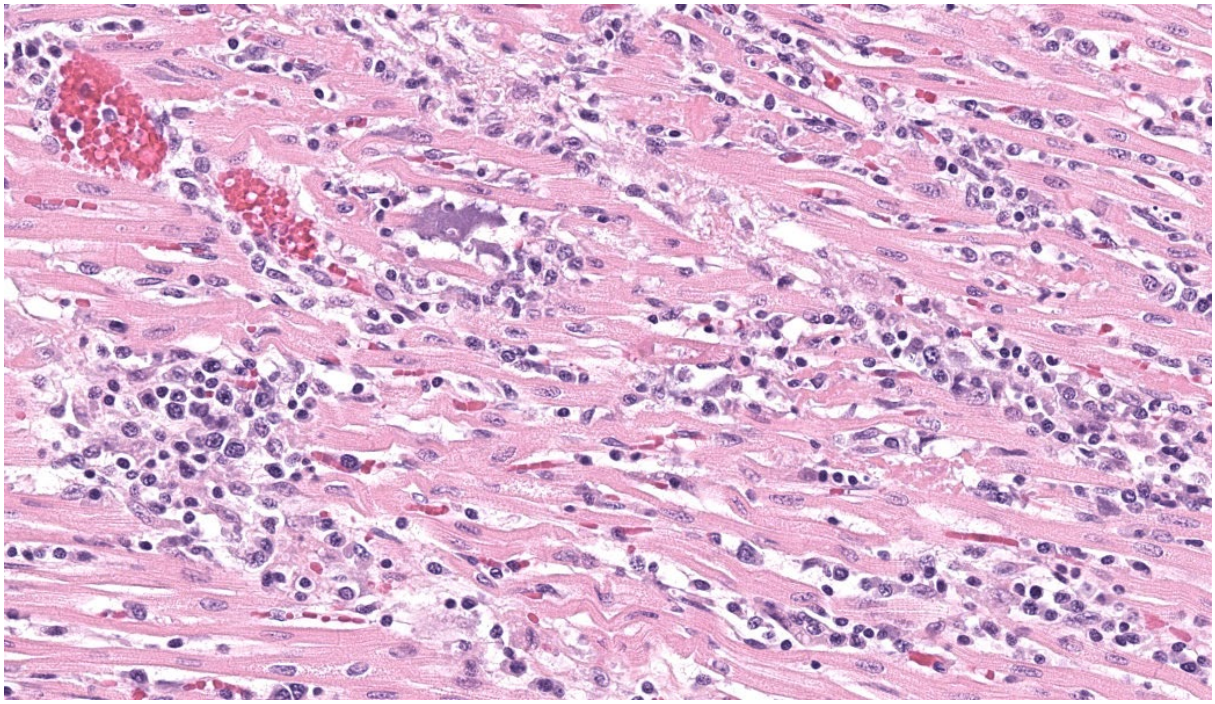

Figure 1-3: Heart, dog. In areas of dense inflammatory infiltration of the myocardium, cardiomyocytes multifocal are lost, fragmented, atrophic and hypereosinophilic, and rarely mineralized. (HE, 600X)

heart failure including ascites (abdominal effusion) and centrilobular hepatocyte necrosis due to hypoxia.

Dogs play a crucial role in the domestic life cycle and are excellent reservoir hosts to continue parasite transmission. Cases have been reported in domestic and working dogs in South America and the southern United States, especially Texas and Gulf Coast states. Interestingly, the vectorial transmission that occurs in humans is less likely in dogs. Transmission is suspected to occur orally through ingestion of the infected vectors, ingestion of meat from infected mammals, or through ingestion of milk from infected lactating bitches.[5,11] The human-companion animal relationship has become increasingly more important, and it is proposed that dogs could act as a sentinel for human exposure, environmental risks, and continued surveillance.[5] Shelter and stray dogs with greater exposure to the outdoors are more likely to encounter *T. cruzi* and with increased human encroachment the interactions with wildlife reservoirs will also likely increase.[3] There are no commercially available vaccines for dogs but potential vaccines are being tested including live-attenuated vaccines, recombinant protein and vector vaccines, and DNA and mRNA vaccines.[3] Current prevention strategies include vector control methods and prophylactic treatment options.[3]

Contributing Institution:
Colorado State University Veterinary Diagnostic Laboratory
https://vetmedbiosci.colostate.edu/vdl/

JPC Diagnoses:
Heart: Pancarditis, lymphoplasmacytic and histiocytic, subacute, multifocal to coalescing, marked, with numerous sarcoplasmic amastigotes.

JPC Comment:
Moderated by MAJ William Baskerville, the 5th WSC of the year started off with a great

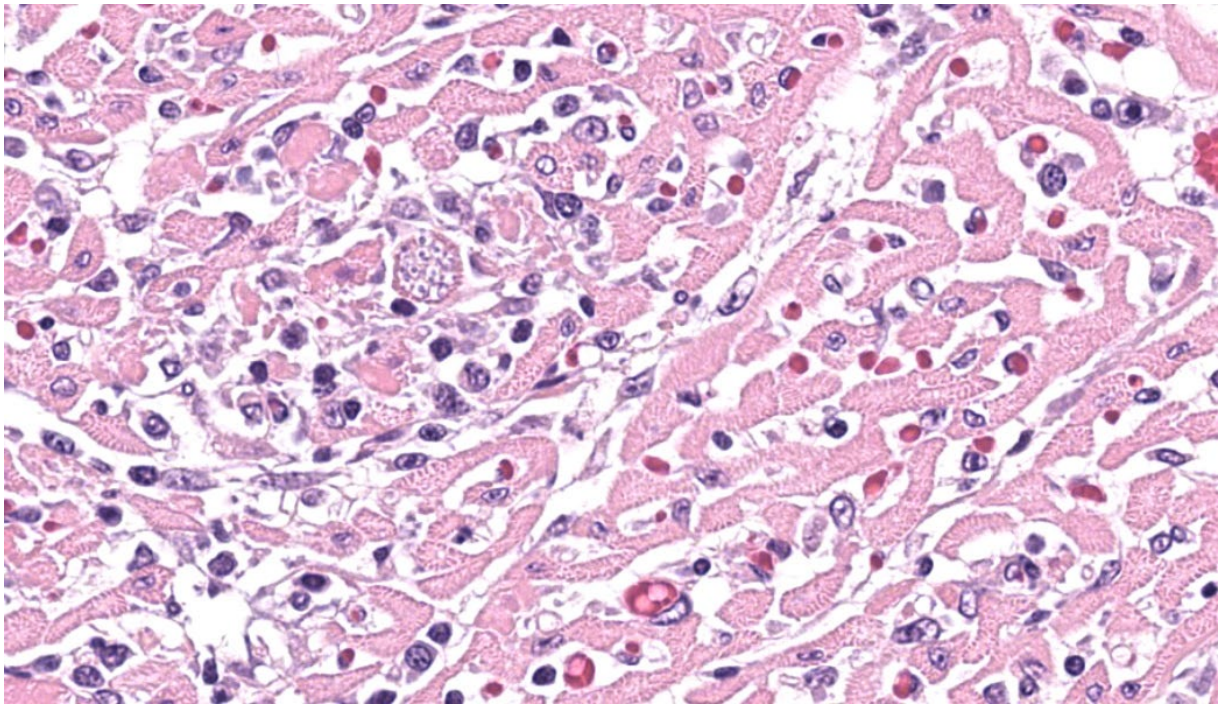

Figure 1-4: Heart, dog. Cardiomyocytes occasionally contain sarcoplasmic pseudocysts contain numerous round 2-4um amastigotes compatible with *Trypanosoma cruzi*. (HE, 1400X)

case of a relevant infectious disease that is gathering more attention as it spreads within the United States: American trypanosomiasis (Chagas disease). Chagas disease was recently designated as endemic in the southern United States.[5] Current data also indicate that, as temperatures continue to trend warmer, the triatome vectors of Chagas are increasing and expanding their range further north in the United States. Conference discussion largely centered on this being a growing health concern within the US for both humans and veterinary species, especially domestic dogs that are housed outdoors in kennel situations and have higher rates of exposure to insect vectors. This has been exceptionally relevant for military working dogs (MWDs) housed in Texas kennels, where there has been a disproportionally high number of MWDs contracting Chagas Disease compared to other locations within the US. Due to the likelihood of contact with vectors in these housing situations, dogs are currently being looked at as a sentinel species for this condition.

The causative protozoa's tropism for specific tissues can result in fatal chronic disease in the heart, esophagus, and/or colon.[6] While most infections are asymptomatic, in humans, approximately 30% of chronically infected people will develop cardiomyopathy, megacolon, or megaesophagus with chronic Chagas disease.[5] In fact, this condition is the current leading cause of infectious myocarditis in humans and most robust blood-banking operations are now testing for *Trypanosoma cruzi* before administering blood to patients. Trypomastigotes of *T. cruzi* detect and subsequently alter their movement in the presence of mammalian cells and, in the presence of specific cell types, will respond more strongly to and invade these cells over alternative cell lineages.[2]

Across multiple studies, it has been demonstrated that *T. cruzi* shows particular tropism for cardiomyocytes.[1,2,6,13] Studies in rats have demonstrated that cardiomyocytes infected with *T. cruzi* lose their gap junctional commu-

nication, which results in decreased automaticity of the cardiac muscle with subsequent electrical alterations.[7] Gap junction proteins (connexins) enable transmission of ions and signaling molecules between cells, making them critical to proper cardiac function.[6] Similarly, mouse cardiac myocytes infected with *T. cruzi* trypomastigotes had significant alterations in connexin43 (Cx43) distribution with an initial increase in their expression in peracute infection followed by a marked decrease in acute and chronic infections. These gap junction disruptions are thought to contribute to the heart's electrical dysregulation observed in some *T. cruzi* infections.[1]

It has also been suggested that *T. cruzi* exploits a HIF-1α-dependent, stress-related activation of glycolysis that is intrinsic to cardiomyocytes, further promoting intracellular infection and replication.[15] These chronic stress responses by cardiomyocytes lead to dysfunction, cell death, and, ultimately, development of cardiac disease. More recently, in vitro studies have demonstrated possible cell-to-cell transfer of the parasite between cardiomyocytes, although the mechanism by which this occurs is not yet known.[5]

Along with exploiting cellular pathways, *T. cruzi* also utilizes a handful of virulence factors to invade host cells, including a trans-sialidase to allow the parasite to bind to host cells, a penetrin to mediate invasion into a host cell, neuraminidase and hemolysins to destabilize and disrupt lysosomes, and galectin-3 (gal-3).[10] Gal-3 in particular is being studied as a potential target for therapeutics, as it is involved in the stimulation of cardiac fibroblasts to synthesize Type I collagen and resultant cardiac fibrosis. One study found, in vivo, that mice infected with *T. cruzi* that were subsequently treated with a gal-3 blocker had significantly reduced cardiac fibrosis and inflammation.[10] With this disease on the rise in the Southern U.S. and South American nations, the growing body of research on Chagas disease will become ever more important as scientists and medical professionals attempt to further the development of treatments and preventatives for this condition.

References:

1. Adesse D, Garzoni LR, Huang H, Tanowitz HB, de Nazareth Meirelles M, Spray DC. Trypanosoma cruzi induces changes in cardiac connexin43 expression. *Microbes Infect.* 2008;10(1):21-8.
2. Arias-Del-Angel JA, Santana-Solano J, Santillán M, Manning-Cela RG. Motility patterns of Trypanosoma cruzi trypomastigotes correlate with the efficiency of parasite invasion in vitro. Sci Rep. 2020;10(1):15894.
3. Barr SC. Canine Chagas' Disease (American Trypanosomiasis) in North America. Veterinary Clinics: Small Animal Practice. 2009;39(6):1055-1064.
4. Busselman RE, Meyers AC, Zecca IB, et al. High incidence of Trypanosoma cruzi infections in dogs directly detected through longitudinal tracking at 10 multi-dog kennels, Texas, USA. PLoS Negl Trop Dis. 2021;15(11):e0009935.
5. CDC. About Chagas Disease. Chagas Disease. September 4, 2024. Accessed June 16, 2025. https://www.cdc.gov/chagas/about/index.html.
6. Contreras-Ortiz JME, Hernández-Mendoza D, Márquez-Dueñas C, Manning-Cela R, Santillán M. In vitro characterization of Trypanosoma cruzi infection dynamics in skeletal and cardiac myotubes models suggests a potential cell-to-cell transmission in mediating cardiac

pathology. PLoS Negl Trop Dis. 2024;18(6):e0012288.
7. de Carvalho AC, Tanowitz HB, Wittner M, Dermietzel R, Roy C, Hertzberg EL, Spray DC. Gap junction distribution is altered between cardiac myocytes infected with Trypanosoma cruzi. Circ Res. 1992;70(4):733-42.
8. Durães-Oliveira J, Palma-Marques J, Moreno C, et al. Chagas Disease: A Silent Threat for Dogs and Humans. International Journal of Molecular Sciences. 2024;25(7):3840.
9. Sousa AS de, Vermeij D, Ramos AN, Luquetti AO. Chagas disease. The Lancet. 2024;403(10422):203-218.
10. Souza BSF, Silva DN, Carvalho RH, Sampaio GLA, Paredes BD, Aragão França L, Azevedo CM, Vasconcelos JF, Meira CS, Neto PC, Macambira SG, da Silva KN, Allahdadi KJ, Tavora F, de Souza Neto JD, Dos Santos RR, Soares MBP. Association of Cardiac Galectin-3 Expression, Myocarditis, and Fibrosis in Chronic Chagas Disease Cardiomyopathy. Am J Pathol. 2017;187(5):1134-1146.
11. Rassi A, Marin-Neto JA. Chagas disease. The Lancet. 2010;375(9723):1388-1402.
12. Hodo CL, Wilkerson GK, Birkner EC, Gray SB, Hamer SA. Trypanosoma cruzi Transmission Among Captive Nonhuman Primates, Wildlife, and Vectors. Ecohealth. 2018;15(2):426-436.
13. Montalvo-Ocotoxtle IG, Rojas-Velasco G, Rodríguez-Morales O, et al. Chagas Heart Disease: Beyond a Single Complication, from Asymptomatic Disease to Heart Failure. Journal of Clinical Medicine. 2022;11(24):7262.
14. Teixeira ARL, Hecht MM, Guimaro MC, Sousa AO, Nitz N. Pathogenesis of Chagas' Disease: Parasite Persistence and Autoimmunity. Clin Microbiol Rev. 2011;24(3):592-630.
15. Venturini G, Alvim JM, Padilha K, Toepfer CN, Gorham JM, Wasson LK, Biagi D, Schenkman S, Carvalho VM, Salgueiro JS, Cardozo KHM, Krieger JE, Pereira AC, Seidman JG, Seidman CE. Cardiomyocyte infection by Trypanosoma cruzi promotes innate immune response and glycolysis activation. Front Cell Infect Microbiol. 2023;13:1098457.

CASE II:

Signalment:
5 years old, male intact, cynomolgus macaque (*Macaca fascicularis*)

History:
A 5-year-old training animal from the stock colony, not actively enrolled in a study presented with decreased activity and reactivity and was emaciated, pale, dehydrated, and hypothermic. Cardiothoracic examination revealed increased respiratory effort, muffled

Figure 2-1: Right ventricle and atrioventricular valve, cynomolgus macaque. There is a large septic thrombus attached to the right AV valve. (HE, 10X)

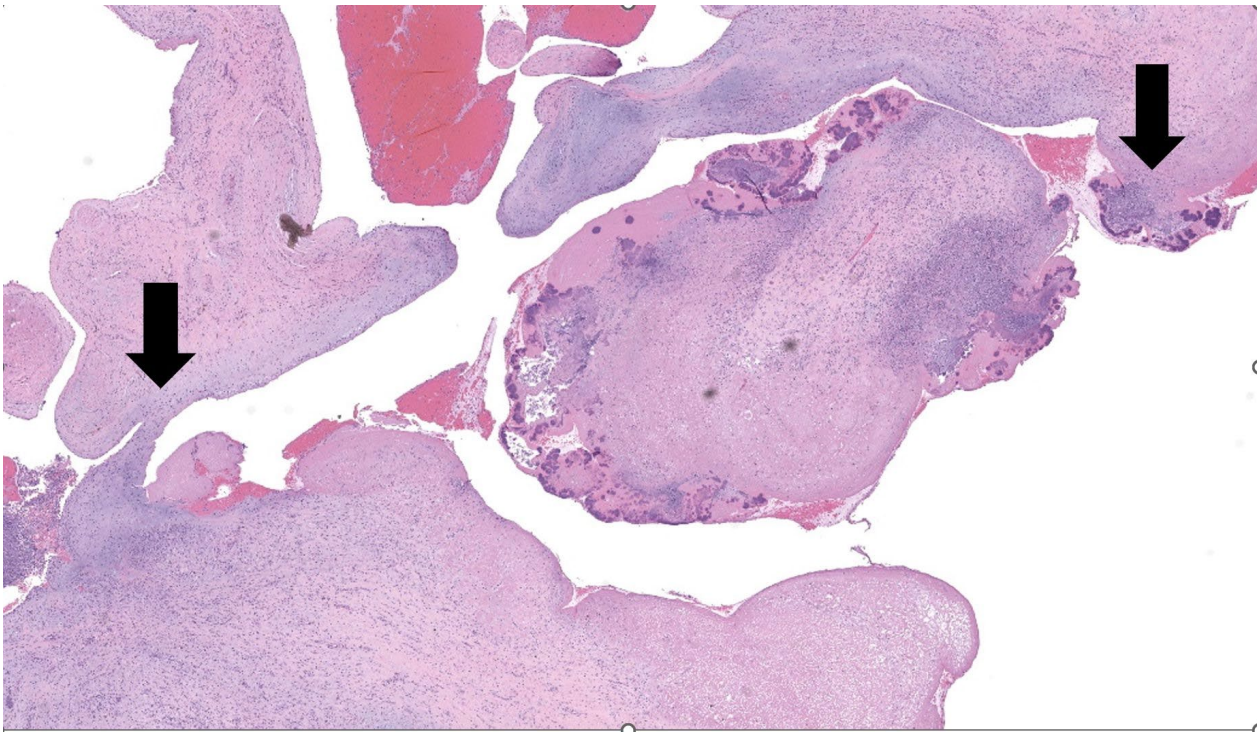

Figure 2-2. Right atrioventricular valve, cynomolgus macaque: The septic thrombus is multifocally attached to the AV valve (arrows). (HE, 35X)

cardiac sounds with a suspected systolic murmur, and thoracic edema. The animal was euthanized *in extremis*.

Gross Pathology:
Lung: Discoloration, dark, brown, diffuse
Heart: Irregular surface, right AV valve, 100% affected

Laboratory Results:
Aerobic bacterial culture, heart: Moderate *Escherichia coli*, Few *Staphylococcus warneri*, Few *Streptococcus mitis*

Microscopic Description:
Representative sections of heart and lungs are examined.

In the heart, the right atrioventricular valve is extensively overlain by large mats of fibrin, admixed with numerous degenerate and viable neutrophils and multiple coccobacilli bacterial colonies. The valvular stroma is diffusely expanded by moderate myxedema and there are moderate numbers of neutrophils and lesser numbers of hemosiderin-laden macrophages, plasma cells and lymphocytes scattered throughout the valvular stroma and expanding the endocardium of the adjacent papillary muscles. The epicardium and surrounding adipose tissue are mildly infiltrated by small numbers of neutrophils, lymphocytes, and plasma cells.

Regionally, sharply demarcated areas of the pulmonary parenchyma are markedly necrotic and replaced by abundant hemorrhage, fibrin, inflammatory infiltrates composed mainly of neutrophils and macrophages, and necrotic cellular debris. In these areas, multiple blood vessels contain thrombi consisting of large numbers of degenerate neutrophils, organizing fibrin, occasional colonies of bacterial coccobacilli, and necrotic cellular debris that variably obscure the lumen and vessel walls. Affected vessels often have smudgy, hypereo-

sinophilic walls that are transmurally infiltrated by neutrophils, lymphocytes, and macrophages. In less affected regions, the alveolar spaces contain a small amount of fibrin, numerous foamy alveolar macrophages (some of which contain brown granular hemosiderin pigment), and fewer neutrophils and erythrocytes. There are moderate numbers of hemosiderin-laden macrophages mostly concentrated around pulmonary arteries, multifocally. Regionally, along the pleural surface there is a large amount of fibrin admixed with numerous degenerate neutrophils and necrotic cellular debris. The pleura itself is mildly thickened by fibrous connective tissue and edema and is multifocally lined by markedly

reactive mesothelium, characterized by plump, rounded mesothelial cells.

Contributor's Morphologic Diagnoses:
Heart, right atrioventricular valve: Marked, chronic, fibrinosuppurative valvular endocarditis with intralesional bacterial colonies; Mild, multifocal, suppurative epicarditis

Lungs: Marked, regional, suppurative, necrotizing embolic pneumonia with vascular thrombosis and intrathrombotic bacteria; Marked, regional, fibrinosuppurative pleuritis

Contributor's Comment:
Endocarditis refers to the inflammation of the endocardium, primarily of the heart valves, and can affect most animal species.[7] Mechanistically, endothelial lesions tend to start at areas of highest trauma, particularly the lines of apposition of the valvular surface exposed towards the direction of blood flow.[2,5] Bloodborne microorganisms may become adhered to these regions, resulting in a localized infection, which can cause valvular injury and subsequent insufficiency.[2,5] Infectious causes are

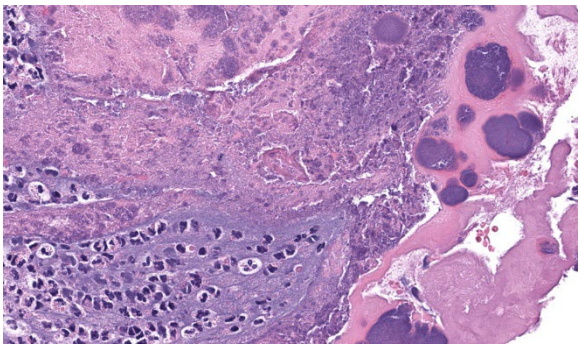

Figure 2-3: Right atrioventricular valve, cynomolgus macaque. The septic thrombus contains numerous dispersed bacilli and colonies of cocci. (HE, 748X)

usually of bacterial origin, usually from systemic infection, but can also be of mycotic or parasitic origin.[5] The bacteria most commonly involved in valvular endocarditis varies among species, but *Streptococcus* sp., *Staphylococcus* sp., and *Enterococcus* sp. have been implicated in endocarditis in humans and most animal species.[5] In cattle, *Trueperella pyogenes* is the most common agent involved in bacterial endocarditis, whereas in pigs, *Erysipelothrix rhusiopathiae* is most common. Bacterial endocarditis is less common in horses, dogs, and cats.[5]

Valvular endocarditis usually involves the left atrioventricular valve, followed by the aortic valve, right atrioventricular valve, and pulmonic valve.[5] In non-human primates, valvular endocarditis is an uncommon spontaneous finding, with an incidence of 0.6% of all spontaneous cardiovascular lesions observed.[1] Endocarditis can be associated with systemic bacterial infections or, particularly in the laboratory environment, contaminated venous indwelling catheters, the latter more commonly affecting the right atrioventricular valve.[6] Interestingly, in cattle, the right atrioventricular valve is mostly affected, most

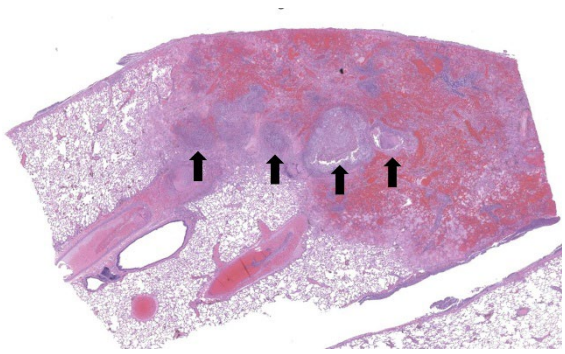

Figure 2-4: Lung, cynomolgus macaque. Multiple branches of the pulmonary artery contain septic thrombi (arrows) (HE, 14X)

likely due to the increased incidence of liver abscesses and subsequent bacterial venous spread to the caudal vena cava and right side of the heart.[4]

As the adherence of bacteria and blood components to the valve leaflets progresses, irregular, raised vegetations replace the smooth valvular surface.[5] Portions of such vegetations may become detached and travel throughout the body as septic emboli.[5] Emboli arising from the right side mainly affects the lungs, while emboli from the left side may dislocate and travel to distant organs, such as kidney and spleen.[5]

In the current case, right-sided valvular endocarditis was observed, most likely a consequence of a contaminated venous injection. Septic emboli translocated to the lungs, causing pulmonary thrombosis and infarction. Bacterial cultures of the heart and lungs revealed large numbers of *E. coli* and fewer *Staphylococcus* sp.

Contributing Institution:
Charles River Laboratories Mattawan
(criver.com/products-services/safety-assessment/preclinical-facilites/Mattawan-michigan)

JPC Diagnoses:
1. Heart, right AV valve: Valvulitis, fibrinosuppurative, chronic, focally extensive, severe, with valvular remodeling and numerous colonies of coccobacilli.

2. Lung: Pneumonia, embolic, necrotizing and suppurative, chronic, multifocal to coalescing, severe, with septic arterial thrombi and suppurative pleuritis.

JPC Comment:
This second case provides a beautiful example of an infective endocarditis with subsequent embolic bacterial pneumonia, stimulating value-added educational discussion of a classic pathogenesis that the contributor sums up nicely in their comment. Other major points of discussion included clinical signs associated with either right or left-sided emboli and associated gross lesions with endocarditis, including those seen in acute cases where only irregular ulcerations on swollen valve leaflets may be seen instead of the more classic irregular "vegetations" on affected valves.

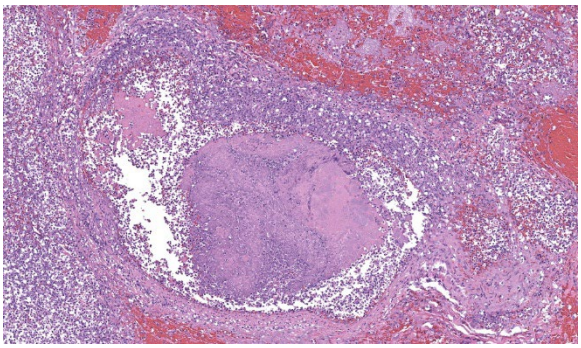

Figure 2-5: Lung, cynomolgus macaque. Higher magnification of septic thrombus within the pulmonary artery, with numerous neutrophils effacing the arterial wall. (HE, 150X)

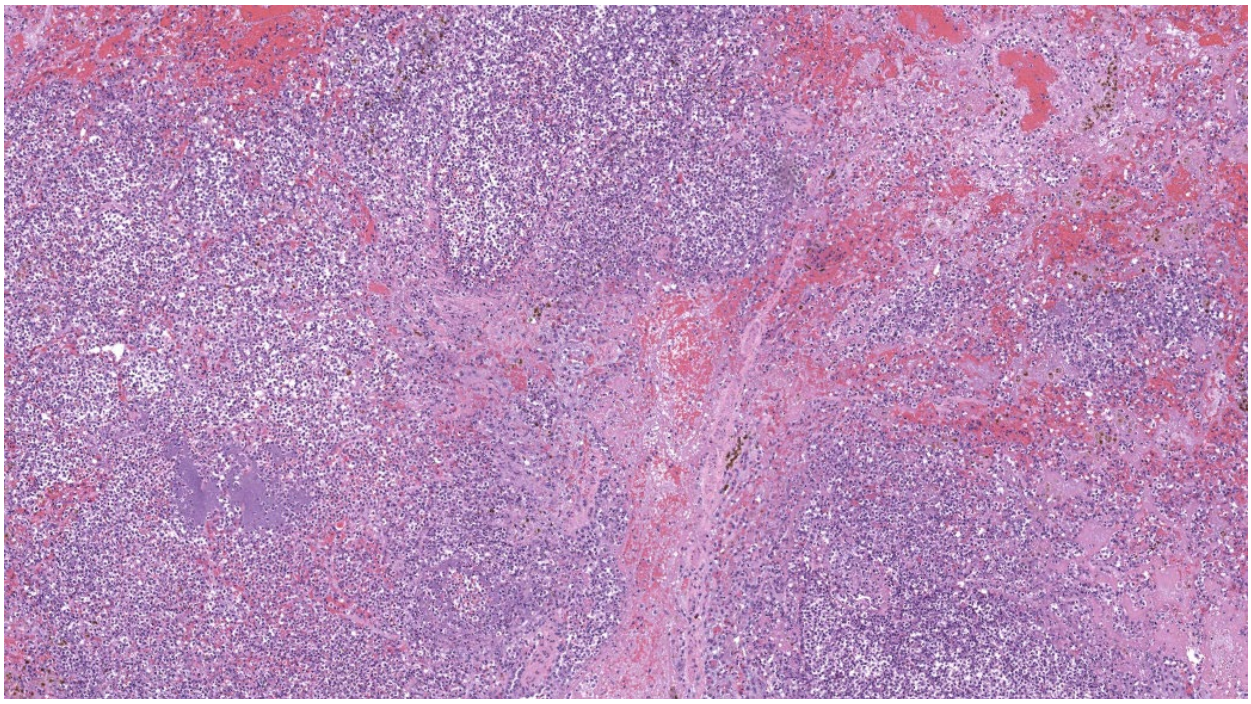

Figure 2-6: Lung, cynomolgus macaque. Suppurative inflammation and colonies of bacteria extend into the pulmonary parenchyma adjacent to effaced pulmonary arterial branches. (HE, 150X)

Conference participants were again asked to recall the "YAACSS-NT" acronym of large colony-forming bacteria, which was previously spelled out in this year's Conference 3, if a refresher is needed. (Repetition is key!) To drive home the dramatic degree of valvular expansion seen in the heart in this case, a review of valvular anatomy followed and included discussion of the normal composition of valves, which are made up of collagen, ground substance (proteoglycans and elastin fibers), and endothelium lining both sides of the valve leaflets.

Endocarditis was first documented almost 350 years ago.[3] The term "vegetative" in the term "vegetative valvular endocarditis" refers to the clumps of bacteria, fibrin, platelets, and other cellular material that adhere to a damaged heart valve. This conglomeration has traditionally been referred to as a "vegetation".

This term was first used by French physician Jean-Nicolas Corvisart in 1806 to describe "wart-like growths" he observed on the heart valves of patients with endocarditis at autopsy, stating that they appeared to resemble natural plant life.[3] Considering this information, one must wonder of Dr. Corvisart had, in fact, ever seen a plant in his own natural life to have named it thus. Despite its historical use, the medical community as a whole is has moved away from that term in favor of either "infective endocarditis" when microorganisms are present, or "nonbacterial thrombotic endocarditis" when the lesion is sterile.

References:

1. Chamanza R, Parry NM, Rogerson P, Nicol JR, Bradley AE. Spontaneous lesions of the cardiovascular system in purpose-bred laboratory nonhuman primates. *Toxicol Pathol*. 2006;34:357-363.

2. Chorianopoulos E, Bea F, Katus HA, Frey N. The role of endothelial cell biology in endocarditis. *Cell Tissue Res*. 2009;335**:**153-163.
3. Geller SA. Infective endocarditis: a history of the development of its understanding. *Autops Case Rep*. 2013;3(4):5-12.
4. Gudmundson J, Radostits OM, Doige CE. Pulmonary thromboembolism in cattle due to thrombosis of the posterior vena cava associated with hepatic abscessation. *Can Vet J*. 1978;19**:**304-309.
5. Robinson WF, Robinson NA. Chapter 1 - Cardiovascular System. In: Maxie MG, ed. *Jubb, Kennedy & Palmer's Pathology of Domestic Animals: Volume 3 (Sixth Edition)*. W.B. Saunders; 2016:1-101.e101.
6. Saravanan C, Flandre T, Hodo CL, et al. Research Relevant Conditions and Pathology in Nonhuman Primates. *ILAR Journal*. 2020;61**:**139-166.
7. Vilcant V, Hai O. *Bacterial Endocarditis*-StatPearls Publishing, Treasure Island (FL);2023.

CASE III:

Signalment:
11-years-old, male, mixed breed canine, *Canis familiaris*.

History:
"Enucleated right eye**".** No other history was provided.

Gross Pathology:
An entire formalin-fixed eye was submitted for histopathology.

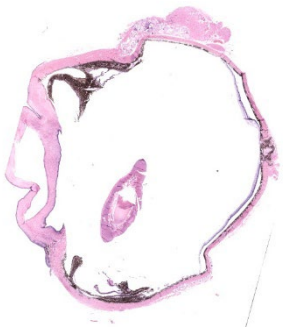

Figure 3-1: Eye, dog. A cross -section of the globe is submitted for examination. There are cross-sections of larval nematodes embedded in the sclera on both sides of the globe. (HE 5X).

Laboratory Results:
N/A

Microscopic Description:
Enucleated right eye: Expanding and infiltrating the sclera, and occasionally extending to and dissecting the periocular skeletal muscle, are multiple cross and oblique sections of nematode parasites. Nematodes are characterized by a thick cuticle with annular ridges seen as raised areas in oblique sections, coelomyarian/polymyarian musculature that is atrophied and multifocally replaced by hypodermal tissue, a very small intestinal cross section, and reproductive organs. Mild hemorrhage, fibrin, and edema are present in affected sclera, and occasional nematode cross sections are surrounded by epithelioid macrophages. The cornea is hypercellular with low numbers of neutrophils and areas of neovascularization.

Contributor's Morphologic Diagnoses:
Granulomatous scleritis and myositis with intralesional *Onchocerca lupi*

Contributor's Comment:
Onchocerca lupi is a parasitic, filarid nematode that is the causative agent of ocular onchocerciasis in domestic dogs.[1] Cases have also been described in cats, one case was reported in a wolf, and coyotes in the southwestern United States have been reported to be

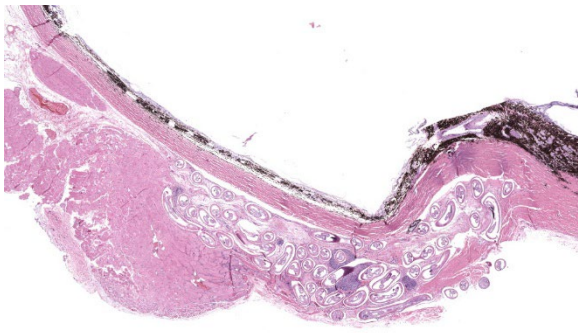

Figure 3-2: Eye, dog. On one side of the globe, cross-sections of one or more larval nematodes are embedded in an inflammatory nodule in the sclera and adjacent orbital skeletal muscle. (HE 28X).

probable reservoirs.[1,2,3] Canine infections with *Onchocerca lupi* have been reported in Europe, North America, and in Asia.[1,3,4,5] *Onchocerca lupi* is also zoonotic, and human cases of *Onchocerca lupi* have been reported in the United States, Europe, North Africa, and in the Middle.[4,6,7] Outside of the United States, reported human cases are mostly in adults, manifesting as localized ocular disease, however, human cases in the southwestern United States have been predominately seen in children, including at least 4 neuroinvasive cases.[7,8]

The life cycle of *Onchocerca lupi* has not been completely described, but it is thought to be similar to that of other filarid nematodes. Canids are described as definitive hosts.[4] Adult male and female nematodes develop within canine periocular tissues, and, after mating, females release microfilariae, which travel to the subcutaneous tissues, especially of the head, and the inter-scapular and lumbar areas.[4] Rare cases of intraocular onchocerciasis, and of extensive aberrant migration of onchocerciasis have been reported in domestic dogs.[9,10] *Wolbachia* spp. have been described in adult *Onchocerca lupi*, and this bacteria is necessary for the reproduction and survival of other *Onchocerca* species, as well as of *Dirofilaria immitis* , another filarid nematode.[8] Presumably, the intermediate host becomes infected with microfilaria while feeding on the definitive host. The exact intermediate host is unknown, but is thought to be a species of black fly (*Simulium* spp), as is the case in other *Onchocerca* species, and *Onchocerca lupi* DNA has been isolated from *Simulium tribulatum* in California, USA.[11] *Onchocerca lupi* DNA has also been found within *Ceratopogonidae* sp. (biting midges) in Northern Arizona and New Mexico, USA.[12] Presumably, the larvae develop into infective L3s within the intermediate host, which then infects the definitive host during feeding.[4]

Clinically, canine cases of *Onchocerca lupi* may present with single or multiple, variably sized nodules on the bulbar conjunctiva, conjunctival hyperemia, episcleral injection, chemosis, periocular swelling, retinal detachment, and corneal edema.[13,14] Typical gross lesions include nodules affecting the conjunctiva, episcleral tissue, and periorbital soft tissues.[13] Some cases do not have reported clinical signs directly attributable to Onchocerciasis, and are diagnosed as an incidental lesion on biopsy secondary to other presenting causes like neoplasia.[13] Bilateral involvement is described.[14]

Onchocerca lupi is typically diagnosed via histopathology, and to our knowledge no commercially available polymerase chain reaction (PCR) tests is available, although PCR assays have been described in the peer reviewed literature.[7,14] Typical histologic lesions include nematodes with very small intestinal cross sections, atrophied coelomyarian/polymyarian musculature, and annular cuticular ridges that can be seen in longitudinal or oblique sections. Microfilaria may be seen within female worms. Variable amounts of inflammation

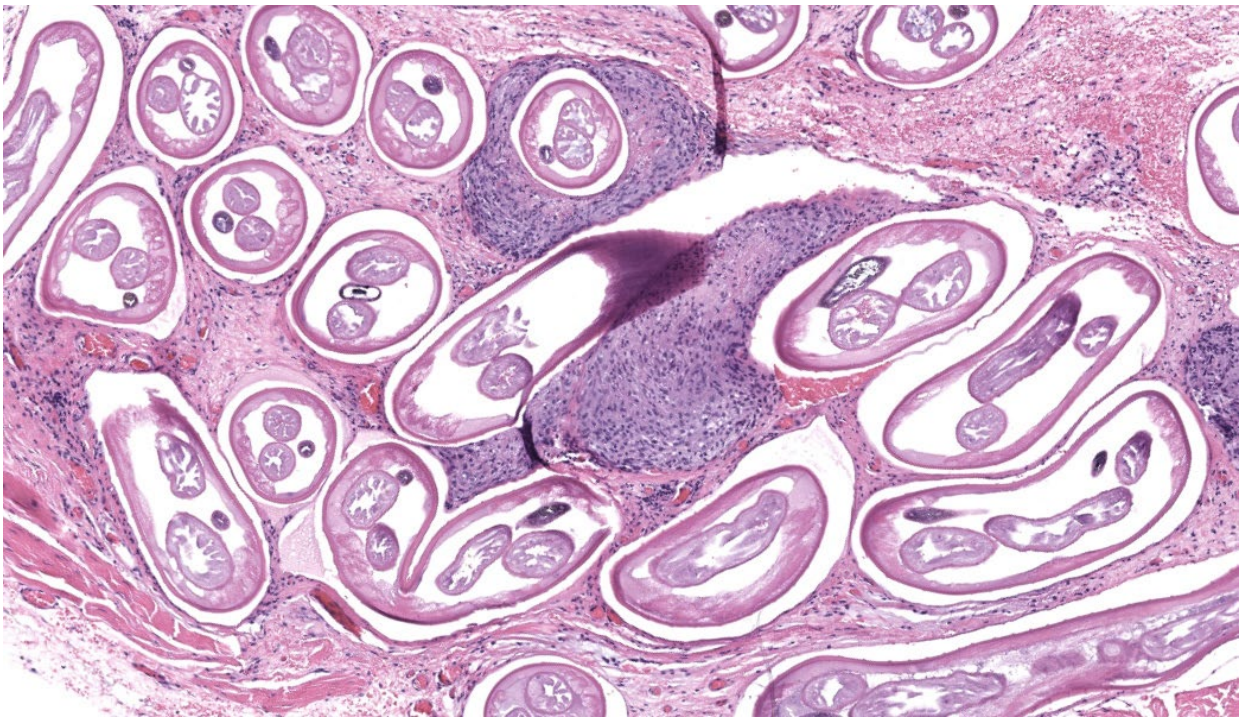

Figure 3-3: Eye, dog. Higher magnification of the mass of nematode larvae within the sclera. Some of the larvae are surrounded by granulomatous inflammation. At the periphery of the nodule, larvae extend into the adjacent atrophic orbital skeletal muscle. (HE 131X)

ranging from mild to severe, and including macrophages, lymphocytes, and eosinophils may be seen, as can fibroplasia. We have seen pyogranulomatous inflammation as well in our laboratory. Currently, a commercially available serology test is not available, although serologic tests are in development.[15]

Contributing Institution:
NMDA Veterinary Diagnostic Services, 1101 Camino de Salud NE, Alberquerquw, NM 87102,
https://nmdeptag.nmsu.edu/labs/veterinary-diagnostic-services.html

JPC Diagnoses:
1. Globe and periocular tissue: Scleritis and orbital rhabdomyositis, granulomatous, chronic, multifocal, moderate, with adult filarids.
2. Retina, ganglion cell layer: Degeneration and atrophy, chronic, diffuse, severe.
3. Globe, lens: Cataract.
4. Globe, cornea: Keratitis, neutrophilic and histiocytic, chronic, multifocal, moderate.

JPC Comment:
This third case stimulated excellent discourse on ocular pathology and the associated changes seen in this eye. While the nematodes in the periocular tissues were striking, the other ocular lesions were a point of discussion focus for conference participants to ensure residents in attendance understood the importance of not latching on to one lesion ("search satisfaction") before examining the tissues in their entirety. This eye had multiple other lesions, some of which were subtle, and these caught the attention of the more experienced participants in the room. The keratitis in this eye served as a springboard to discuss the other changes, and conference participants suspect the keratitis was secondary to melanosis and inflammation causing occlusion of the drainage angle in this case, resulting in secondary glaucoma (as evidenced

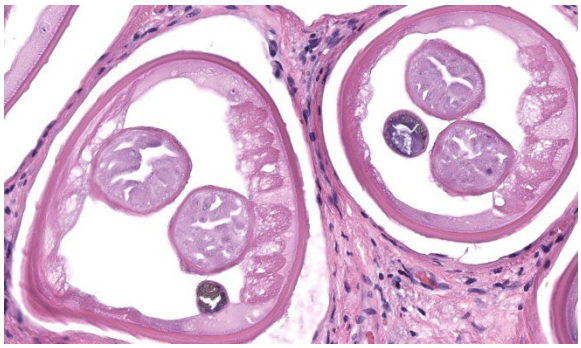

Figure 3-4: Eye, dog. Higher magnification of a larva in cross section. Larvae have no developed reproductive tracts. The nematodes have a tegument with thin spikes, coelomyarian-polymyarian musculature which is interrupted by a hypodermis, a small triradiate esophagus, and sections of a small multinucleated intestine.

by degeneration of inner retinal cells and retinal ganglion cell loss) and subsequent buphthalmia. One of the more common sequelae to buphthalmia is an exposure keratitis due to inability of the eyelids to completely close over the enlarged eye. Coupled with possible irritation from the nematodes, participants felt that the keratitis and precluding factors were important features to discuss in this case.

Conference participants unanimously agreed that the nematodes in section were consistent with *Onchocerca lupi*. For the sake of educational discussion, differentials for ocular nematodes in a dog were: *Toxacara canis* (ascarid), *Onchocerca lupi* (spirurid), *Angiostrongylus vasorum* (metastrongylid), *Dirofilaria immitis* (spirurid), *Ancylostoma caninum* (strongylid), *Trichinella spiralis* (aphasmid), and *Thelazia spp.* (spirurids). Of these, *Thelazia spp.* are the true ocular parasite and tend to reside in the conjunctival sacs and lacrimal ducts of infected animals. *Onchocerca spp*. in other species were briefly discussed, and honorable mentions included *O. cervicalis*, which sets up shop in the nuchal ligament of horses, *O. gutturosa* and *O. lienalis*, both of which invade the nuchal and gastrosplenic ligaments of cattle, and O. volvulus, the causative agent of "river blindness" in humans.

References:

1. Labelle AL, Maddox CW, Daniels JB et al. Canine ocular onchocercosis in the United States is associated with *Onchocerca lupi*. *Vet Parasitol*. 2013;193(1-3):297-301.
2. Tudor P, Ionașcu I, Mateescu CI, Bezerra-Santos MA et al. Feline ocular onchocercosis by *Onchocerca lupi*: Phylogenetic insights and implication for veterinary health. *Acta Trop*. 2023; 237:106723.
3. Roe CC, Yaglom H, Howard A, et al. Coyotes as Reservoirs for *Onchocerca lupi*, United States, 2015-2018. *Emerg Infect Dis*. 2020 Dec;26(12):2989-2993.
4. Rojas A, Morales-Calvo F, Salant H, Otranto D, Baneth G. Zoonotic Ocular Onchocercosis by *Onchocerca lupi. Yale J Biol Med*. 2021;94(2):331-34
5. McGarry JW, Carrozza R, Bradley C, Latrofa MS, Makepeace BL, Otranto D. *Onchocerca lupi* in imported dogs in the UK: implications for animal and public health. *BMC Vet Res*. 2022 Feb;18(1):66.
6. Otranto D, Sakru N, Testini G, Gürlü VP, Yakar K, Lia RP, Dantas-Torres F, Bain O. Case report: First evidence of human zoonotic infection by Onchocerca lupi (Spirurida, Onchocercidae). *Am J Trop Med Hyg*. 2011;84(1):55-8.
7. Bowers Wu D, Ko B, Lopez Hernandez G, et al. Neuroinvasive *Onchocerca lupi* Infection in a Ten-Year-Old Girl. *Case Rep Infect Dis*. 2022; 2022:9773058
8. Cantey PT, Weeks J, Edwards M, et al. The Emergence of Zoonotic Onchocerca lupi Infection in the United States--A Case-Series. *Clin Infect Dis.* 2016 15;62(6):778-83
9. Komnenou AT, Thomas AL, Papadopoulos E, Koutinas AF. Intraocular

localization of *Onchocerca lupi* adult worm in a dog with anterior uveitis: A case report. *Vet Ophthalmol.* 2016 ;19(3):245-249.
10. Wallitsch K, Jaffey JA, Ferguson S, et al. Extensive Aberrant Migration of *Onchocerca lupi* in a Dog. *Top Companion Anim Med.* 2022;49:
11. Hassan HK, Bolcen S, Kubofcik J, et al. Isolation of *Onchocerca lupi* in Dogs and Black Flies, California, USA. *Emerg Infect Dis*. 2015;21(5):789-96.
12. Roe CC, Holiday O, Upshaw-Bia K, et al. Biting midges (Diptera: Ceratopogonidae) as putative vectors of zoonotic *Onchocerca lupi* (Nematoda: Onchocercidae) in northern Arizona and New Mexico, southwestern United States. *Front Vet Sci*. 2023 15;10:1167070.
13. Dubielzig RR, Ketring KL, McLellan GJ, Albert DM. Veterinary Ocular Pathology: A comparative review. Saunders Elsevier; 2010.
14. McLean NJ, Newkirk K, Adema CM. Canine ocular onchocerciasis: a retrospective review of the diagnosis, treatment, and outcome of 16 cases in New Mexico (2011-2015). *Vet Ophthalmol.* 2017;20(4):349-356.
15. Latrofa MS, Louzada-Flores VN, Maia C, et al. Development of an indirect ELISA for the serodiagnosis of canine infection by *Onchocerca lupi*. *Sci Rep*. 2024;14(1):3348

CASE IV:

Signalment:
2.5-year-old spayed female domestic shorthair cat (*Felis catus*)

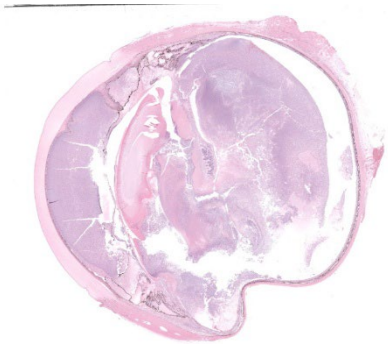

Figure 4-1: Eye, cat. There are profound inflammatory changes in all segments of the eye. (HE, 10X)

History:
Dental procedure performed 6 weeks prior with multiple extractions, including right maxillary arcade. Right eye discomfort was noted by the owner one day post-surgery. Medical management (full details not available) was attempted by the primary veterinarian, but the patient was refractory to treatment. The cat was referred to an ophthalmologist who documented severe anterior uveitis, iris bombe, and lens capsule rupture via ultrasound. Enucleation was performed due to suspicion of septic endophthalmitis secondary to dentistry-related ocular trauma.

Gross Pathology:
Submitted fixed in 10% neutral buffered formalin for evaluation is an enucleated eye (diameter: 31mm; cornea diameter: 18mm; axial length: 22mm) with a less than 1mm segment of optic nerve. On section of the eye, the ocular chambers contain abundant amounts of thick off-white purulent material.

Laboratory Results:
N/A

Microscopic Description:
Filling all ocular chambers and coating the surfaces of intraocular structures are vast accumulations of exudate consisting of myriad

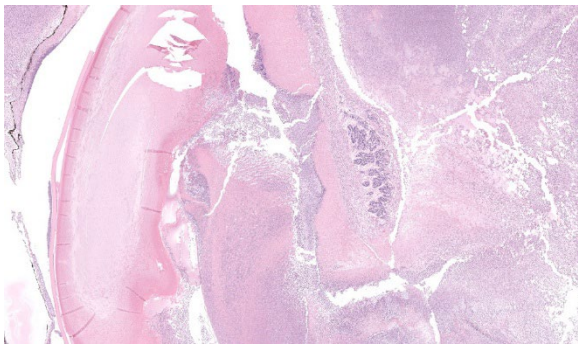

Figure 4-2: Eye, cat. The lens is ruptured. HE, 25X)

degenerate and intact neutrophils, many macrophages, abundant amounts of fibrinous to proteinic material, abundant necrotic cellular debris, occasional pools of extravasated erythrocytes, and multifocal colonies of mixed bacteria (rods and coccobacilli). Centrally incorporated into the inflammatory exudates is a ruptured lens which lacks a capsule in many areas and has highly undulating free capsule margins regionally. The lenticular stroma is variably vacuolated with the following features: streaks of pallor, Morgagnian globules, many infiltrating leukocytes (mostly neutrophils), and occasional pockets of similar bacteria. The retina is diffusely detached and largely inapparent apart from remnant segments of atrophied and degenerate retina enmeshed within the exudate. Suppurative to pyogranulomatous inflammatory infiltrates multifocally extend into the iris, ciliary body, choroid, optic nerve which is significantly gliotic with rarefied neuropil, and optic nerve meninges. The iris is displaced anteriorly and multifocally abuts the posterior aspect of the cornea. The anterior chamber is severely narrow, and the drainage angle is collapsed and inapparent. The corneal stroma is moderately to markedly oedematous and contains small to moderate numbers of scattered neutrophils. The anterior corneal epithelium appears attenuated in areas. The sclera is variably thinned with multifocal often perivascular infiltrates of lymphocytes and plasma cells with variable numbers of admixed neutrophils and occasional macrophages. There are increased numbers of perilimbal pigmented cells. A thin to moderately thick layer of oedematous and inflamed granulation tissue regionally lines the mid and posterior scleral margins outside the globe and extends into a bundle of periocular skeletal muscle. In addition to infiltrates of the aforementioned inflammatory cells, the granulation tissue also contains many golden-brown pigmented macrophages (siderophages) which are concentrated at the level of the ciliary body. There is abundant haemorrhage in the retrobulbar loose connective tissue.

Contributor's Morphologic Diagnoses:
Endophthalmitis, diffuse, suppurative to pyogranulomatous, severe, with lens rupture, retinal detachment and degeneration/atrophy with intraocular exudation and intralesional mixed bacteria, drainage angle collapse, keratitis, corneal oedema, scleritis and regional periscleral fibrosis

Contributor's Comment:
Ophthalmic complications associated with scleral penetrating injuries are infrequently reported in dogs and cats with a recent history of dental procedures. Iatrogenic globe trauma as

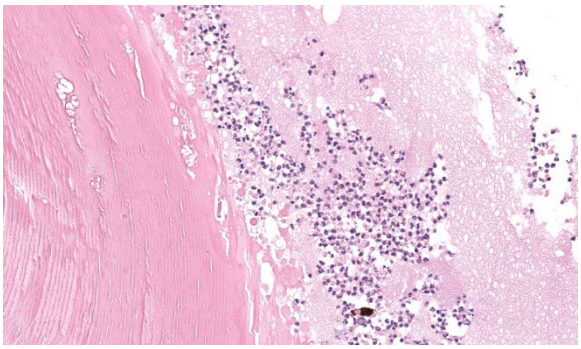

Figure 4-3: Eye, cat. The ruptured lens is infiltrated by numerous neutrophils which are attracted to lens protein. The posterior lens capsule is at right. (HE, 457X)

a complication of routine dentistry may occur secondary to slippage of dental instruments during maxillary tooth extraction or inadvertent needle perforation of the globe when placing infra-orbital and maxillary nerve blocks. Endophthalmitis is a common sequela of dental-associated globe penetration due to implantation of bacteria and/or lens rupture. Medical management is often poor and most cases of post-dentistry endophthalmitis lead to palliative and diagnostic enucleation.

Compared with other species, cats may be at increased risk of traumatic globe injury during exodontic procedures due to a large globe size that nearly fills the orbit, lack of bony orbital floor, and close proximity of maxillary tooth roots (especially PM4 and M1) to the ventral orbit. Bone resorption associated with periodontal and endodontic disease may further compromise the narrow rim of alveolar bone surrounding the roots of the maxillary premolars and molars, increasing vulnerability to iatrogenic ocular trauma. Older cats may be at increased risk of penetrating ocular trauma during dental procedures compared with younger cats due to age-associated atrophy of orbital fat pads and closer globe position to the oral cavity.

Clinical findings in animals following orbital penetration during a dental procedure include vision loss, epiphora, mucopurulent ocular discharge, blepharospasm, exophthalmos, buphthalmos, glaucoma, hyphema, hypopyon, miosis, iris bombe, cataract, and orbital cellulitis. Gross examination of the globe commonly demonstrates opacification of the aqueous and vitreous humor and may reveal a site of scleral penetration. Histopathologic lesions include severe suppurative endophthalmitis or panophthalmitis, varying degrees of orbital cellulitis and episcleral fibrosis of the ventral

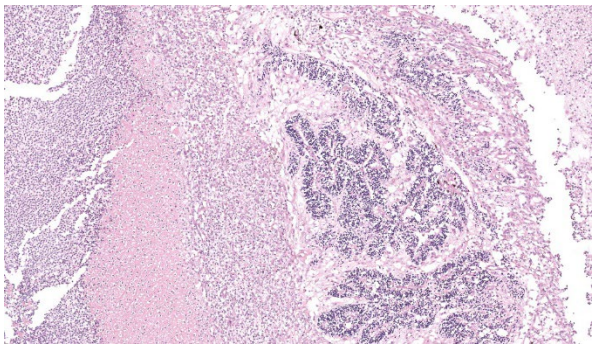

Figure 4-4: Eye, cat. The markedly atrophic and coiled retina is floating free within a mass of fibrinosuppurative inflammation within the vitreous behind the ruptured lens. (HE, 121X)

aspect of the globe, and in some instances rupture of the posterior or equatorial lens capsule and/or presence of intraocular bacteria. Ventral scleral perforation may be appreciated in some cases, but a site of penetrating injury is not always detected. In this case, a scleral penetration site was not appreciated grossly or histologically despite review of multiple step sections.

Contributing Institution:
University of Sydney
https://sydney.edu.au/science/schools/sydney-school-of-veterinary-science/veterinary-science-services.html

JPC Diagnoses:
Globe: Endophthalmitis, fibrinosuppurative, subacute, diffuse, severe, with lens rupture, synechiae, fibrovascular membranes, retinal detachment and atrophy, and bacterial colonies.

JPC Comment:
Talk about a descriptive case that made, for obvious reasons, an excellent sales pitch on why pathology is the best profession! This case provides an excellent opportunity for participants to push themselves on their ocular descriptive abilities. Many thanks to this contributor for a fantastic case! Much like the previous eye case in this conference,

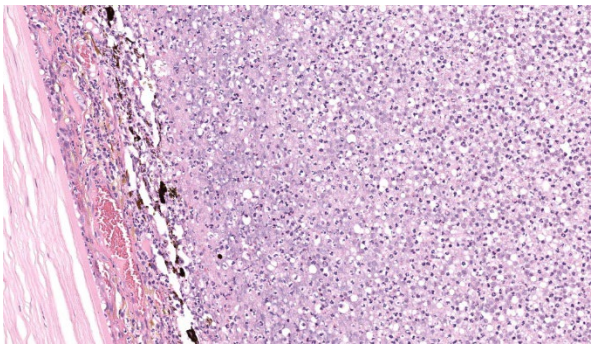

Figure 4-5: Eye, cat. The iris is adhered to the posterior of the cornea (anterior synechia) and expanded by pre- and post-iridal fibrovascular membranes. The anterior segment is filled with neutrophils. (HE, 379X)

there was substantial discussion on ocular pathology. The most informative nuggets from that conversation included utilizing the lens capsule, which is an easily identifiable structure in the eye, to assist with orientation in a busy ocular slide such as this one. The pigmented irideal stroma, as well as the "golden" fibers of the iris, can also be used to help identify structures that might otherwise be difficult to ascertain due to the degree of damage and/or inflammation.

This case had beautiful examples of iris bombe (iris pushed forward into the anterior chamber and adhered to the back of the cornea), numerous types of fibrovascular membranes (retrocorneal, preiridial, cyclitic, etc.), and a fantastic phakoclastic panuveitis from lens rupture. The six types of uveitis and their definitions were discussed and included: 1) anterior uveitis (inflammation of the iris and ciliary body), 2) posterior uveitis (inflammation of the ciliary body and choroid), 3) panuveitis (iris, ciliary body, and choroid affected), 4) chorioretinitis (inflammation of the choroid and retina), 5) endophthalmitis (inflammation of uvea, retina, and ocular cavities), and 6) panophthalmitis (all ocular structures are affected, including sclera). Being able to recognize and accurately use these terms as pathologists can provide crucial information to ophthalmologists when it comes to treating these patients.

As anyone who has owned a cat will tell you, cats are no strangers to ocular trauma. Common causes include fights (especially with claws), foreign bodies, blunt trauma, chemical burns, and, less commonly, iatrogenic (such as dental work or local nerve blocks). Of the frequently encountered domestic species in veterinary medicine, cats are more likely to end up with traumatic globe injury following dental procedures due to their complete lack of a bony orbital floor, their objectively massive eyes that stare straight into the void, and the close proximity of their maxillary roots (PM4 and M1) to their ventral orbit. Additionally, they get a fair amount of periodontal disease, which can lead to bone resorption and thinning of the alveolar bone around the tooth roots. Older cats, as if they needed any additional help getting their eyeballs stabbed, also have age-associated atrophy of their orbital fat pad, putting their globes in even closer proximity to the oral cavity.

An unfortunate possible sequela to chronic ocular trauma in cats is the development of feline post-traumatic ocular sarcoma (FPTOS), which is an aggressive malignant neoplasm of the eye in cats and the third most common primary intraocular tumor in feline patients.[6] It can take up to seven years for these sarcomas to develop following ocular trauma or disease, and they are thought to arise from malignant transformation of lens

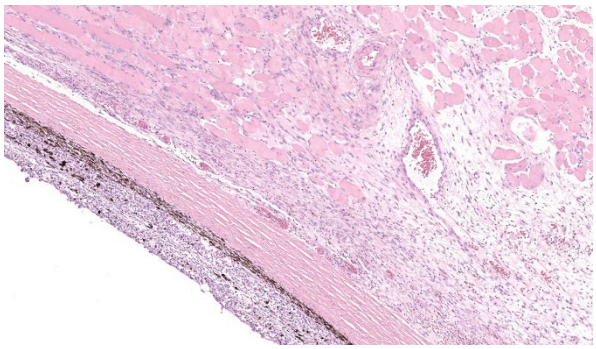

Figure 4-6: Eye, cat. The retina is detached and the choroid is expanded by moderate numbers of infiltrating neutrophils. The sclera is thinned. The periorbital fat and atrophic orbital skeletal muscle are infiltrated by edematous fibrous connective tissue.

epithelium, as there is a history of lens rupture is almost all cases of FPTOS.[6] Most of these tumors look very similar to fibrosarcomas, but there can be variation in their morphology; some may look like osteosarcomas, others like giant cell neoplasms.[6] Recently, there has been a link established between the development of FPTOS and the use of intravitreal gentamicin injections used to ablate the ciliary body in cases of unresolving glaucoma.[6] Medicine is ever-evolving, and one of the great burdens of clinicians is making treatment decisions that carry risk knowing that, for some patients, the benefit of such treatment outweighs that risk. For cats afflicted with these aforementioned conditions, though, it seems that all roads lead to enucleation.

References:

1. Dubielzig RR, Ketring KL, McLellan GJ, Albert DM. *Veterinary Ocular Pathology, a Comparative Review*. Philadelphia, PA: Elsevier; 2010:330-336.
2. Duke FD, Snyder CJ, Bentley E, Dubielzig RR. Ocular trauma originating from within the oral cavity: clinical relevance and histologic findings in 10 cases (2003-2013). *J Vet Dent.* 2014;31(4):245-248.
3. Perry R, Moor D, Scurrell E. Globe penetration in a cat following maxillary nerve block for dental surgery. *J Feline Med Surg*. 2015;17(1):66-72.
4. Smith MM, Smith EM, La Croix N, Mould J. Orbital Penetration Associated with Tooth Extraction. *J Vet Dent.* 2003;20(1):8-17.
5. Volk HA, Bayley KD, Fiani N, Bilson FM. Ophthalmic complications following ocular penetration during routine dentistry in 13 cats. *N Z Vet J.* 2019;67(1):46-51.
6. Wood C, Scott EM. Feline ocular post-traumatic sarcomas: Current understanding, treatment and monitoring. *J Feline Med Surg.* 2019;21(9):835-842.