



Cardiac inflammatory and non-inflammatory diseases

Gisela Martinez-Romero,
DMV, MSc, PhD, DACVP
emarti18@tufts.edu

Acknowledgments

Thank you for all the photos!

Cummings Veterinary School of Veterinary Medicine-Tufts University

Dr. Emily Brinker- Department of Pathobiology
Dr. Francisco Conrado- Department of Pathobiology
All Anatomic Pathologists

Dr. John Rush- Department of Clinical Sciences
Dr. Emily Karlin- Department of Clinical Sciences
Dr. Lisa Freeman- Department of Clinical Sciences

Great Ape Heart Project

Dr. Sushan Han- Denver Zoo, GAHP Pathology Advisor
Dr. Linda Lowenstein- UC Davis, Emeritus Professor, GAHP Pathology Advisor
Dr. Ritha McManamon- University of Georgia, GAHP Pathology Advisor
Dr. Karen Terio- University of Illinois, GAHP Lead Pathology Advisor
Dr. Marieta Dindo Danforth- GAHP director

Dr. Francisco Carvallo- Virginia-Maryland College of Veterinary Medicine
Dr. Francisco Uzal- UC Davis School of Veterinary Medicine
Dr. Laura Nordio, Division of Pathology, San Marco Veterinary Clinic and Laboratory, Veggiano, Italy

Facultad de Medicina Veterinaria y Zootecnia-UNAM Mexico

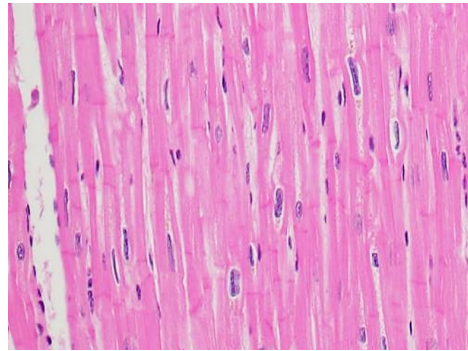
Dr. Feliz Sanchez Godoy- Departamento de Aves
Dr. Elizabeth Morales Salinas- Departamento de Patologia
Dr. Gerardo Salas Garrido- Departamento de Patologia



Myocardial fibrosis

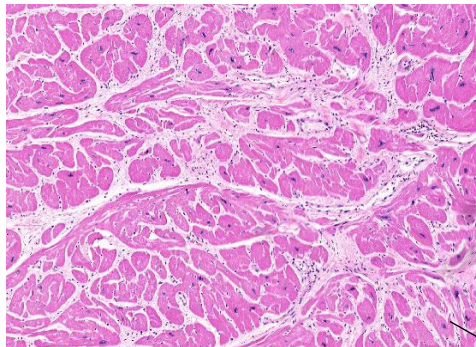
Myocardial fibrosis is defined as an increased amount of collagen in the myocardium relative to cardiac myocytes, associated with changes in collagen fiber type composition (excess of collagen type I versus type III) and physical-chemical properties (increased cross-linking of collagen fibers).

Healthy myocardium



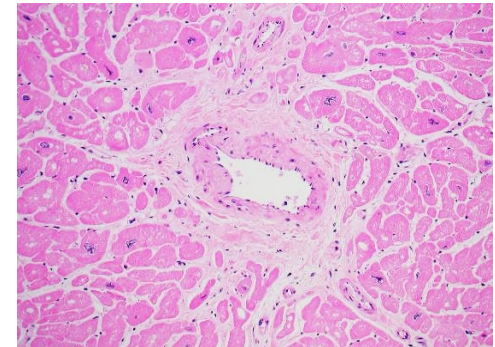
Interstitial fibrosis

-hypertension -diabetes -genetic
-aging -LV pressure-overloaded



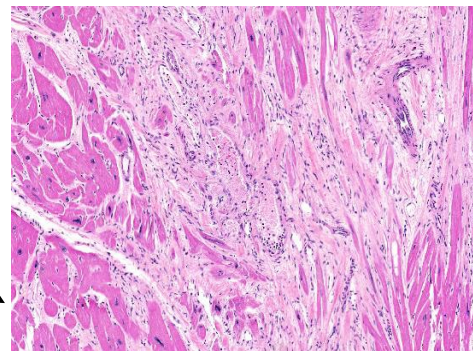
Perivascular fibrosis

-pressure overload -vascular stress



Replacement fibrosis

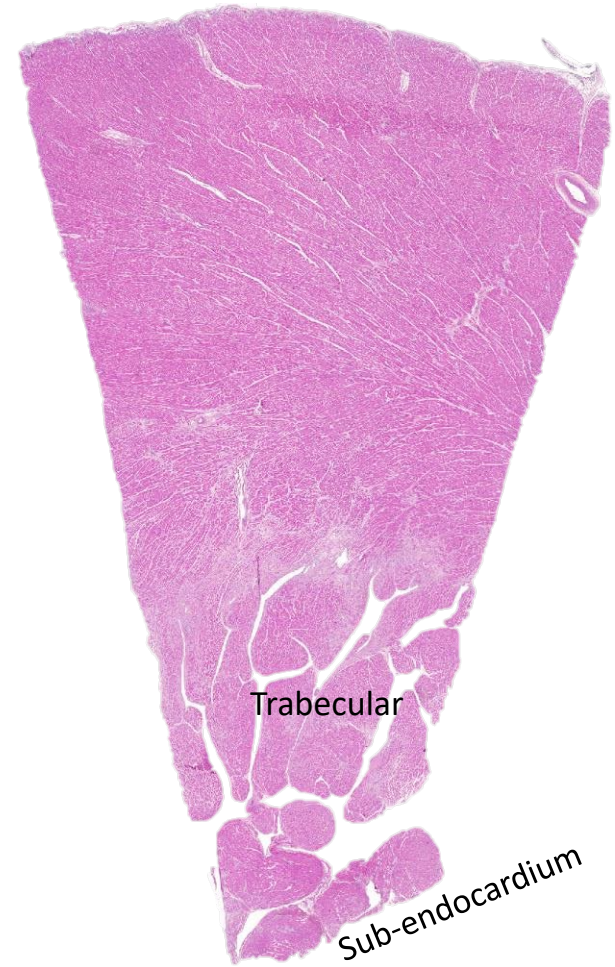
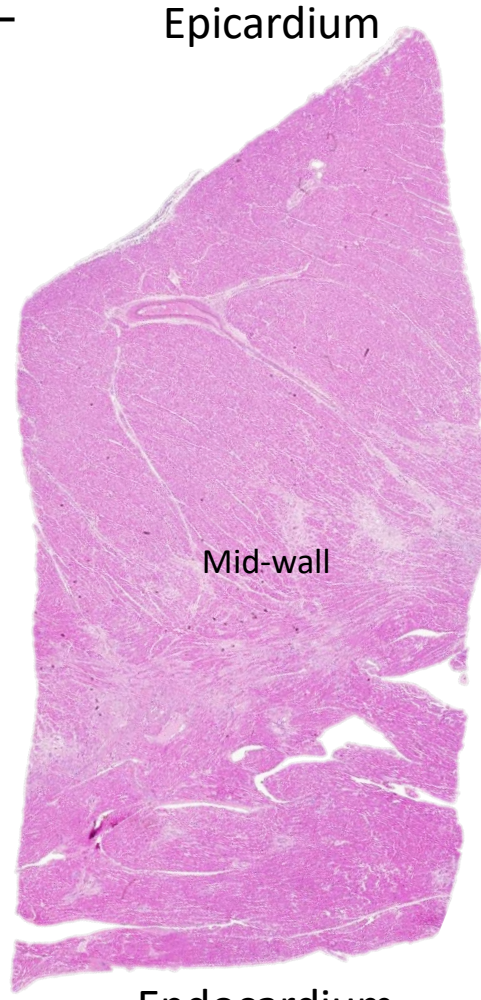
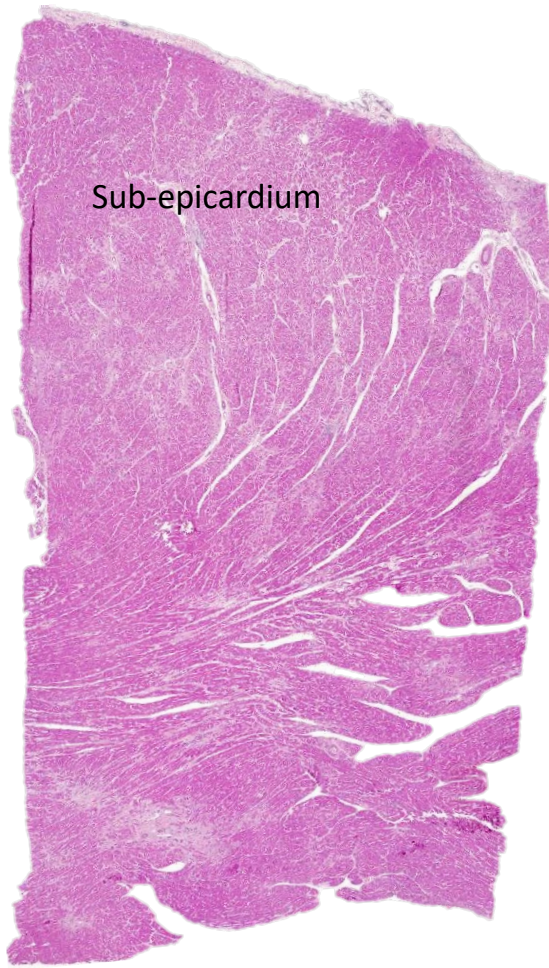
-myocarditis -infarction -chronic renal failure
-genetic -toxic

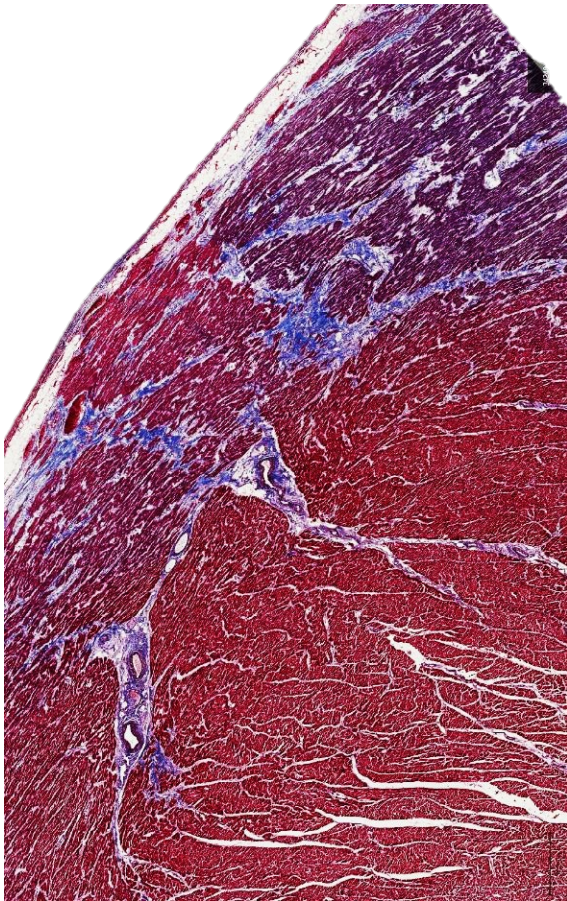


TOPOGRAPHICAL DISTRIBUTION OF MYOCARDIAL FIBROSIS

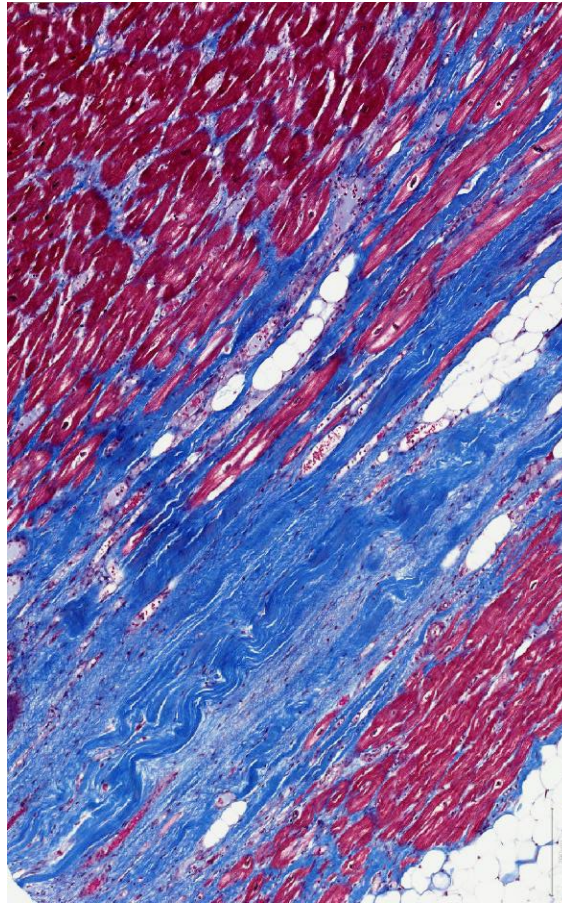


OFFICIAL
**TOPOGRAPHICAL DISTRIBUTION
OF MYOCARDIAL FIBROSIS**

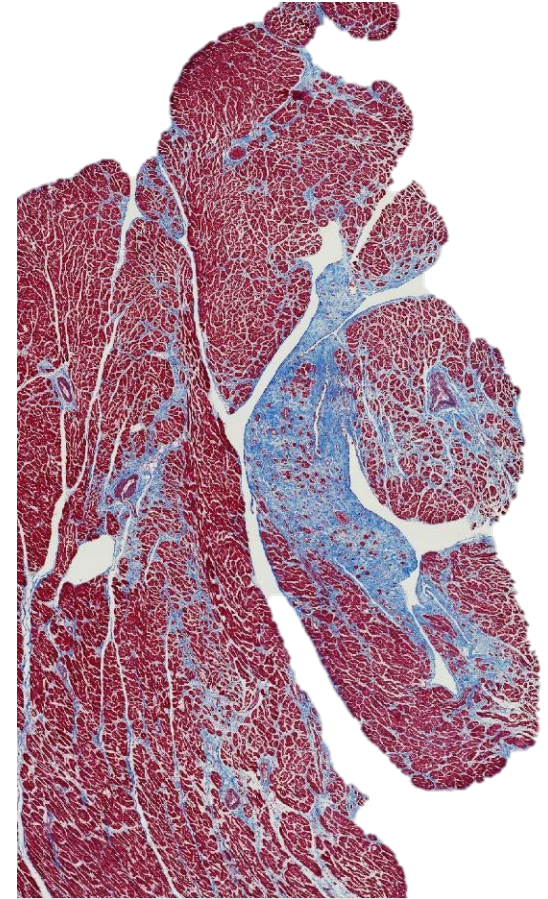




Sub-epicardium



Mid-wall

Trabecular myocardium
Subendocardium

PATTERNS OF MYOCARDIAL FIBROSIS

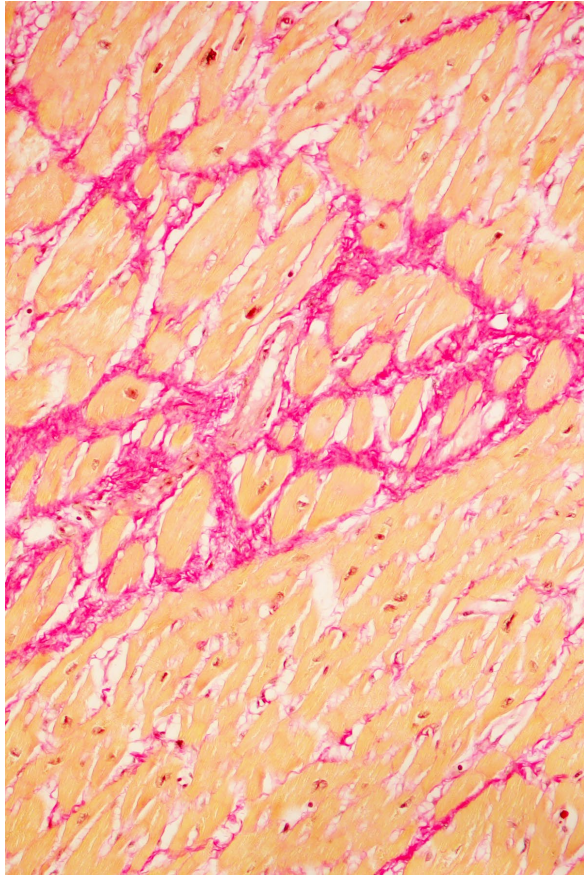
THE GREAT APE
HEART PROJECT



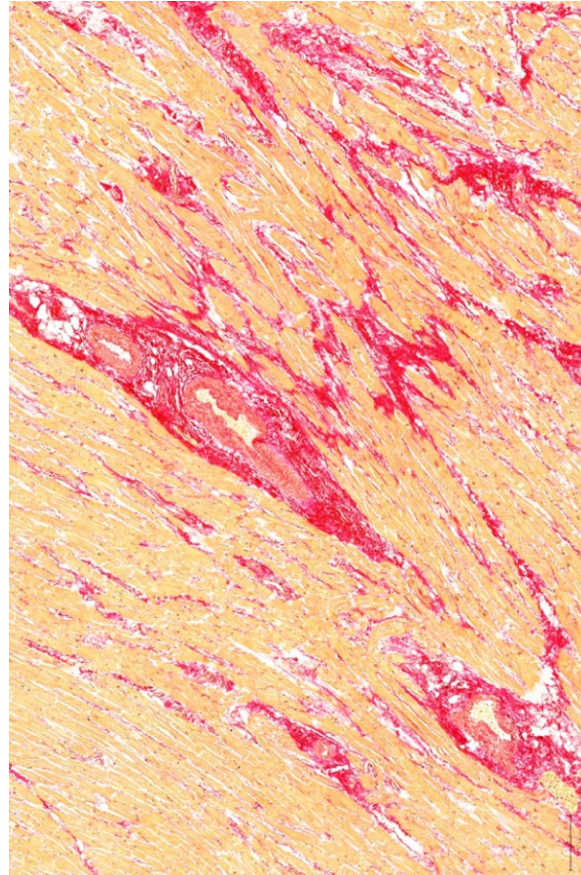
OFFICIAL

PATTERN OF FIBROSIS

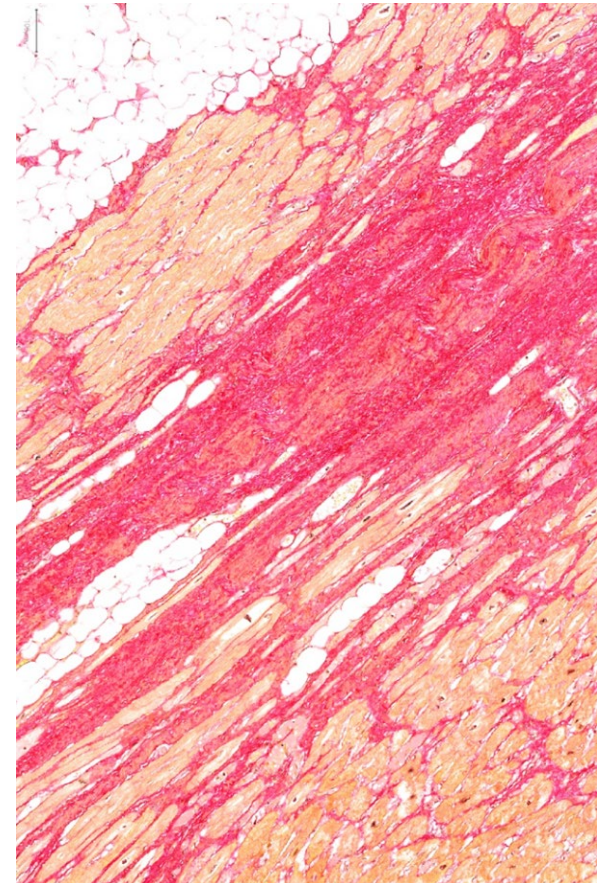
Interstitial



Perivascular



Replacement

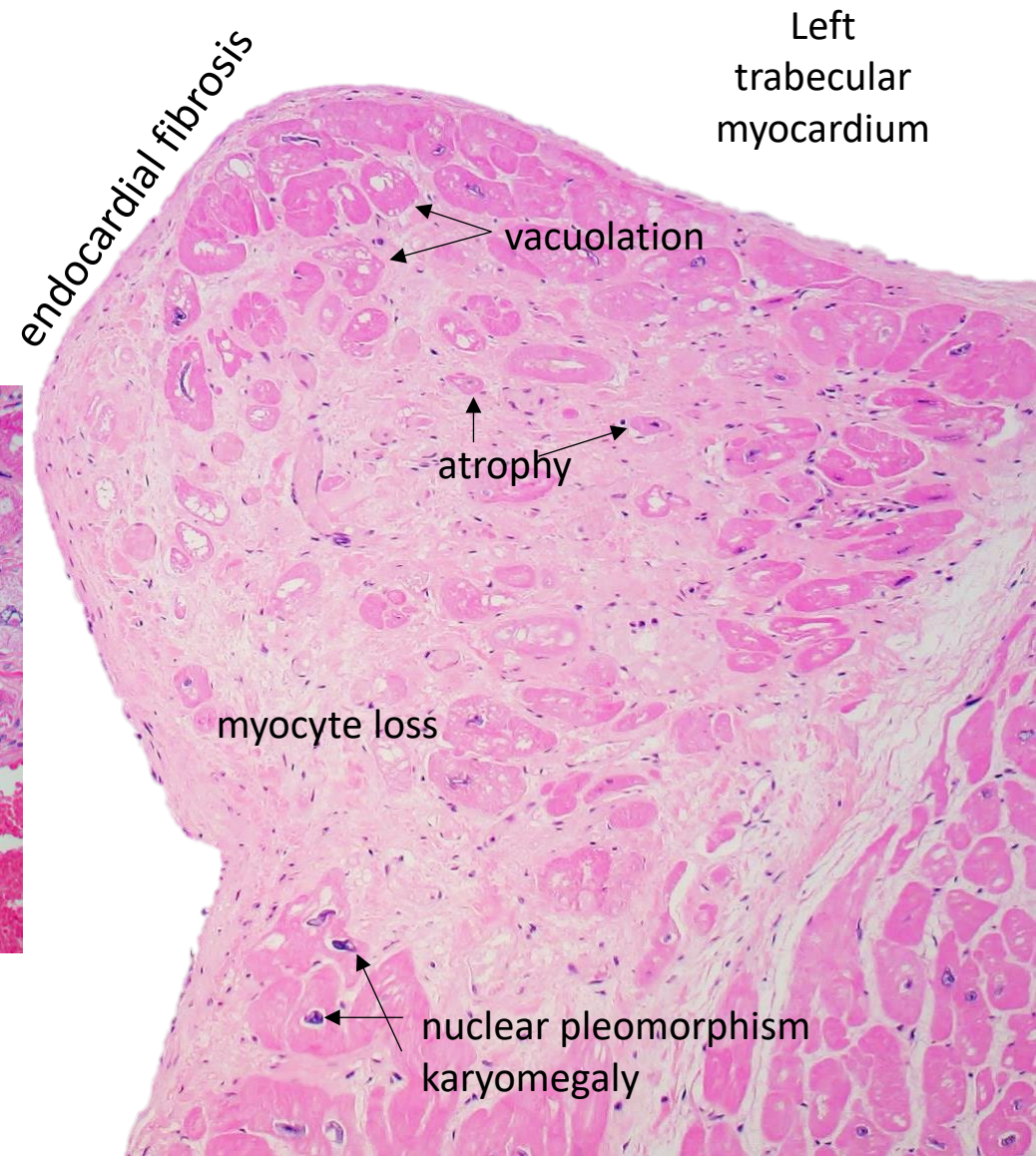
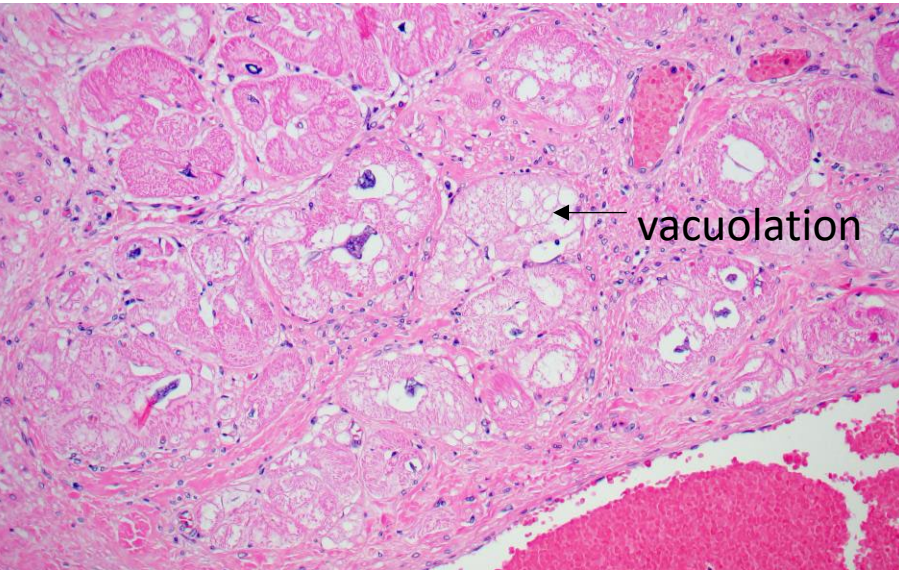


Sirius red stain

OFFICIAL

**THE GREAT APE
HEART PROJECT**

ALTERATIONS IN CARDIOMYOCYTES AND ENDOCARDIUM

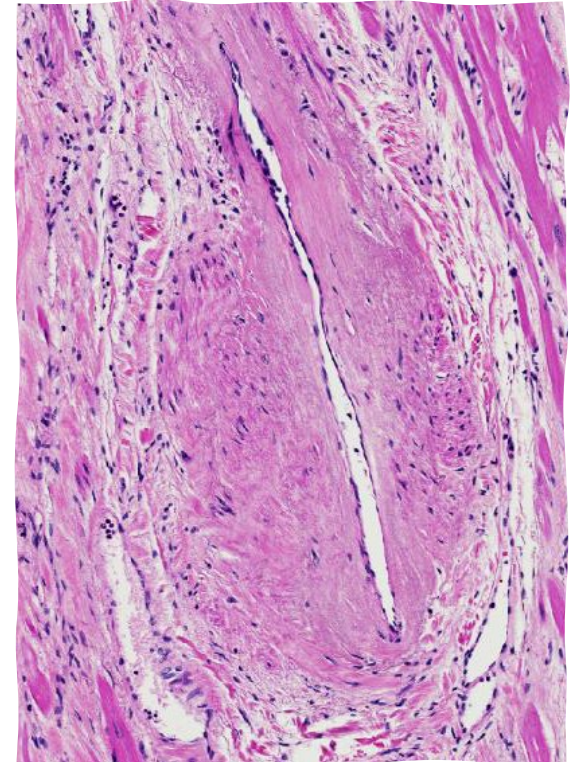
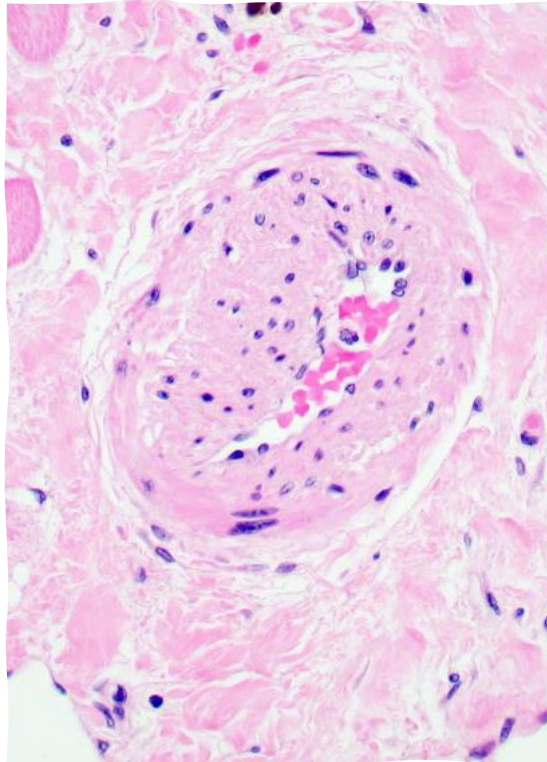
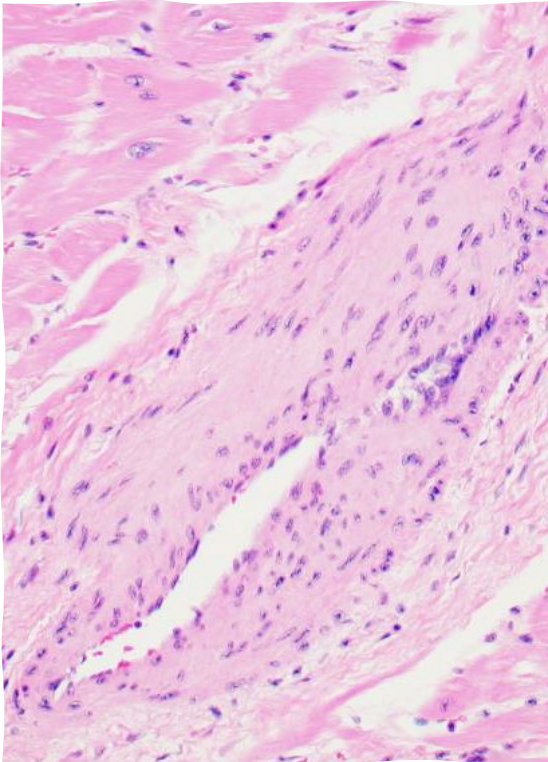


ALTERATIONS IN CORONARY ARTERIES

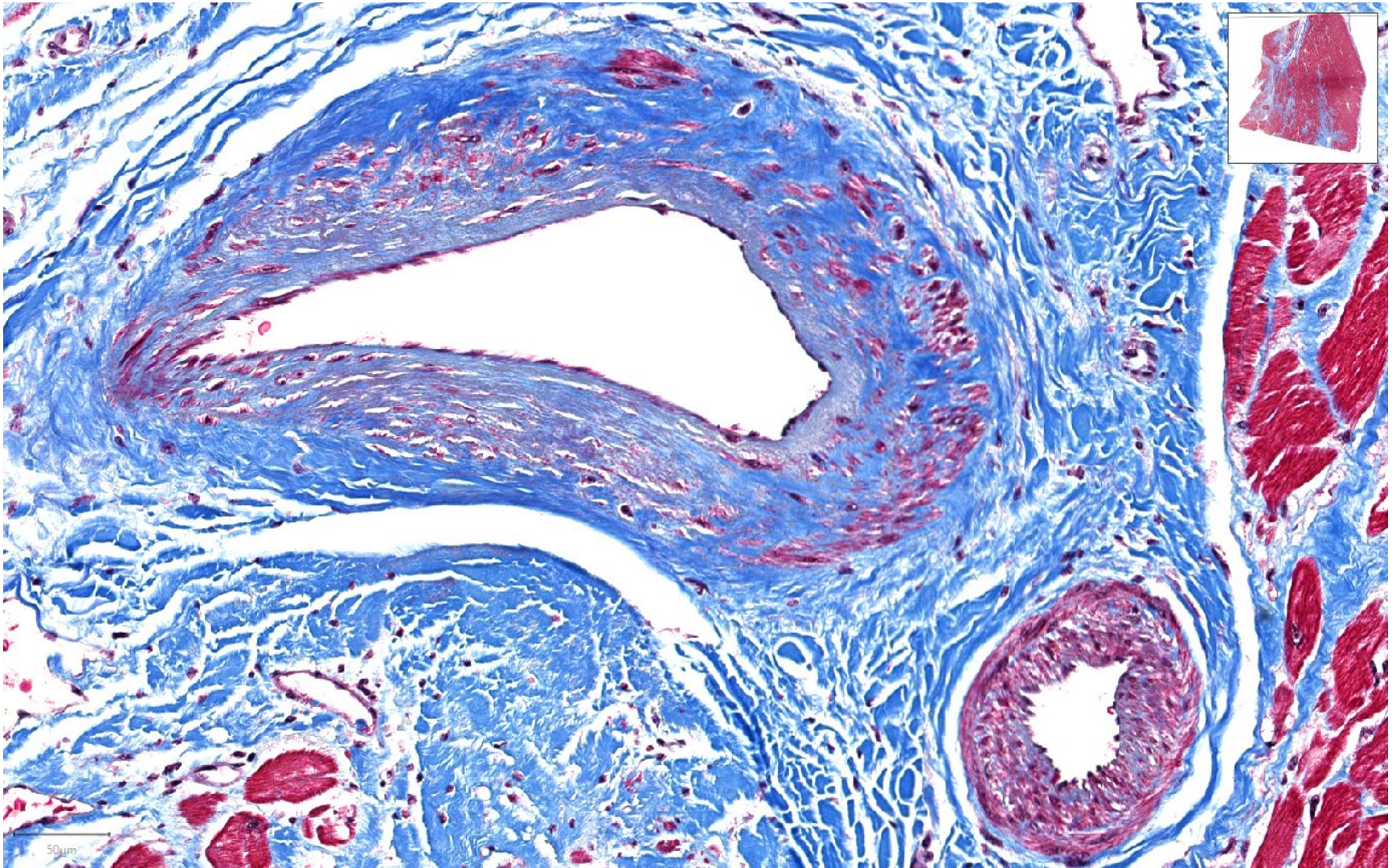
Medial hypertrophy/fibrosis

Hypertension, subaortic stenosis, cardiomyopathies

Intramural arteries



Medial hypertrophy/fibrosis

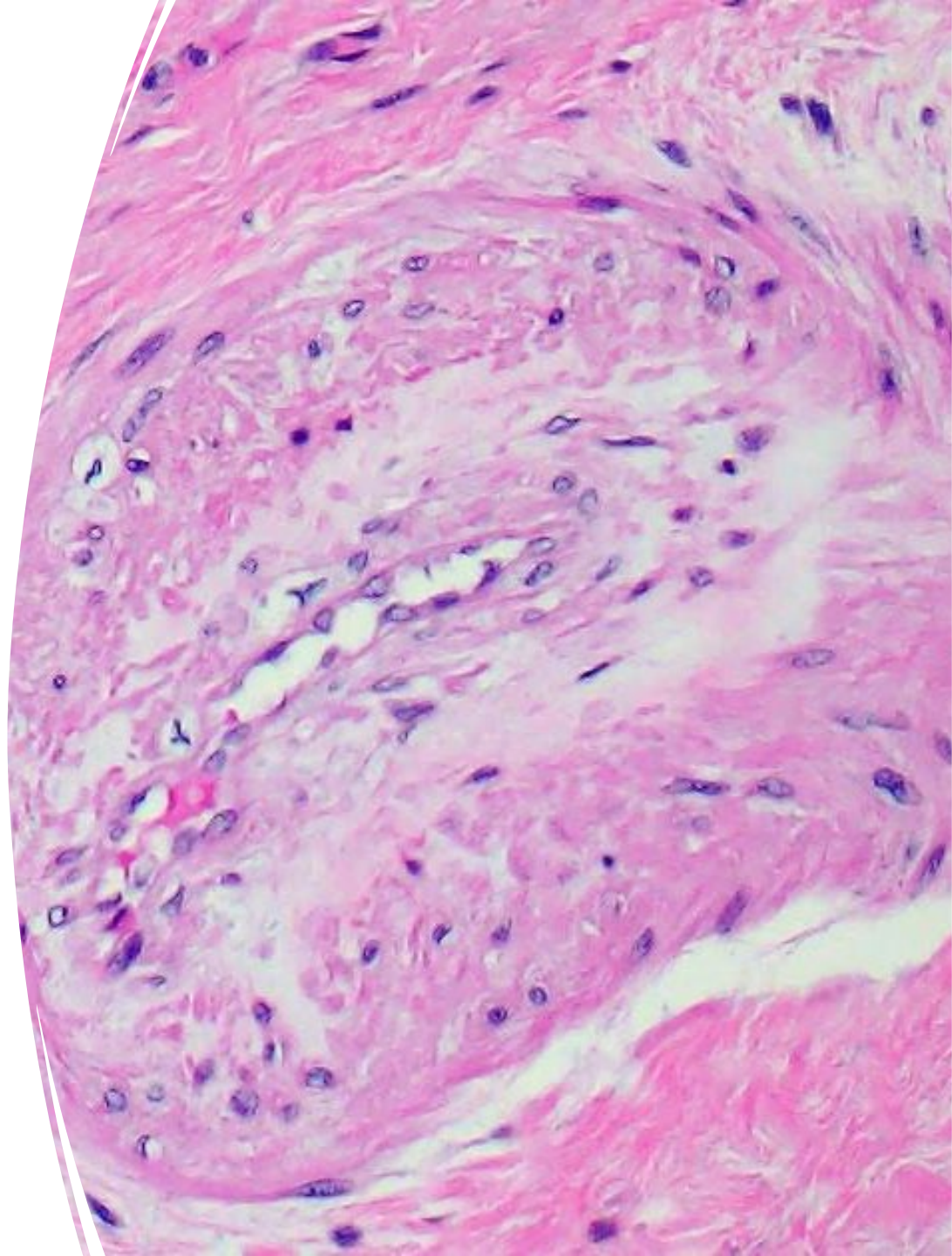


Intimal hyperplasia

Non-specific signals;
aging, hypertension

Intramural artery

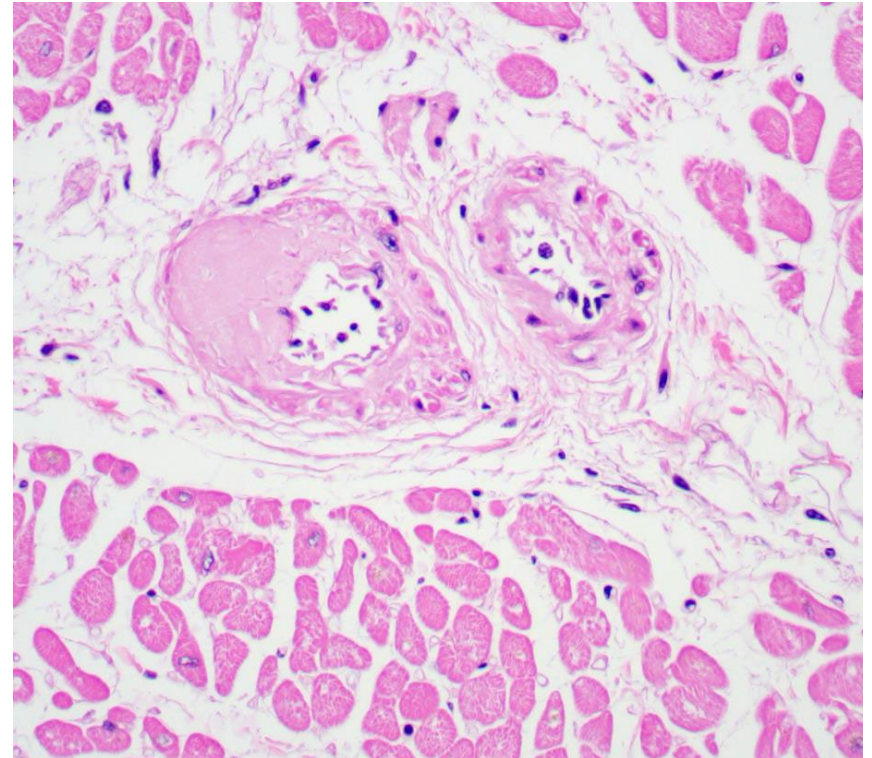
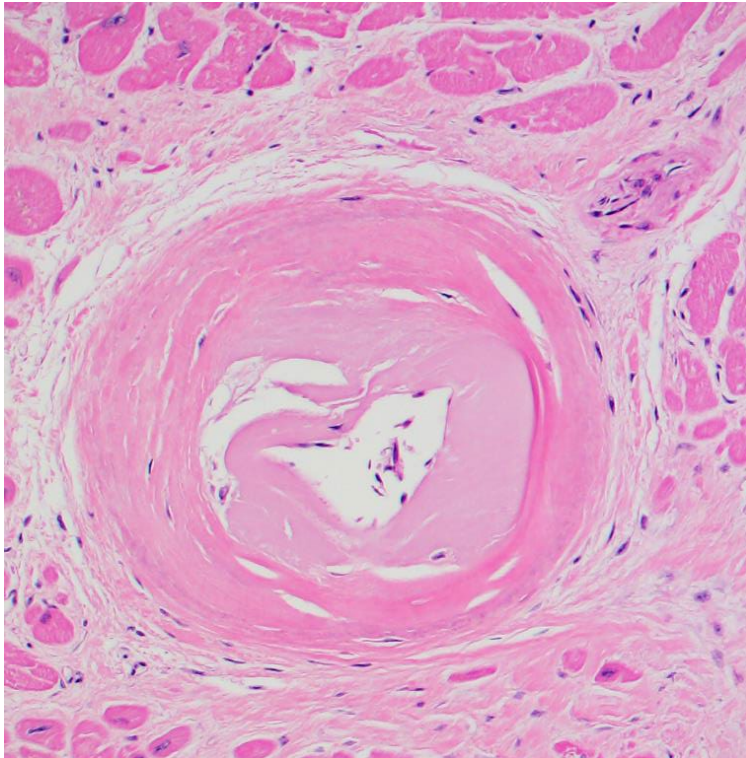
- Medial hypertrophy
- Intimal hyperplasia



Hyaline arteriolosclerosis

Hypertension, diabetes, aging

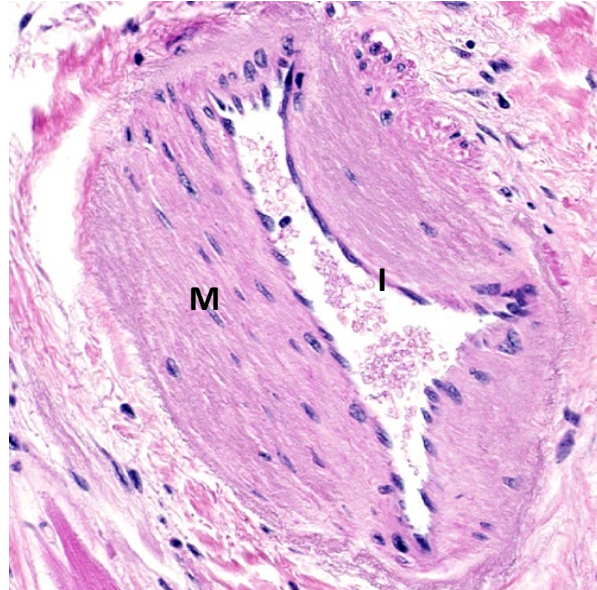
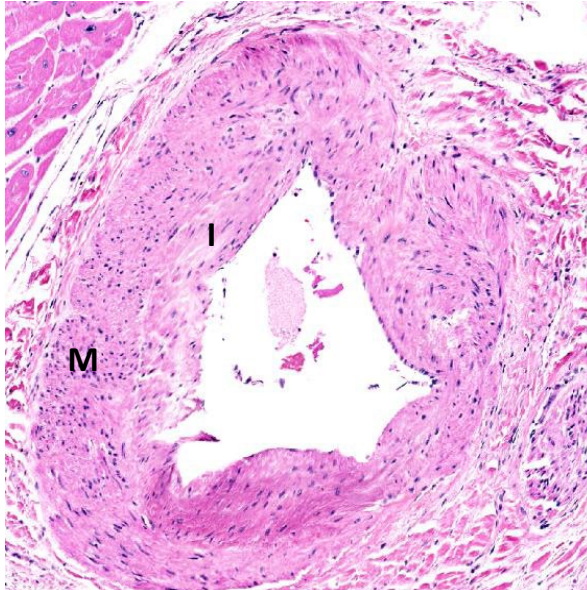
Intramural arteries



SYSTEMIC ARTERIAL HYPERTENSION

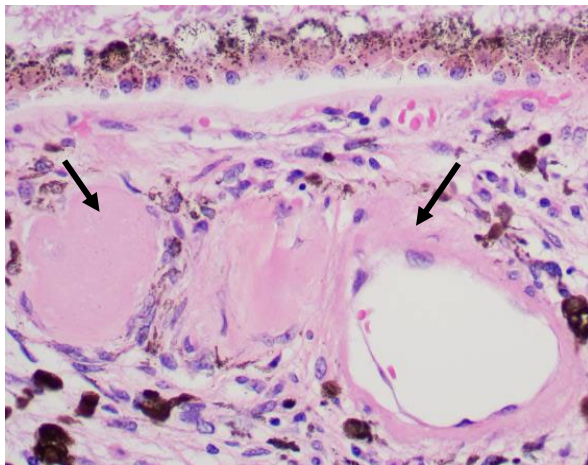
Intramural coronary arteries

Thickened
media/intima

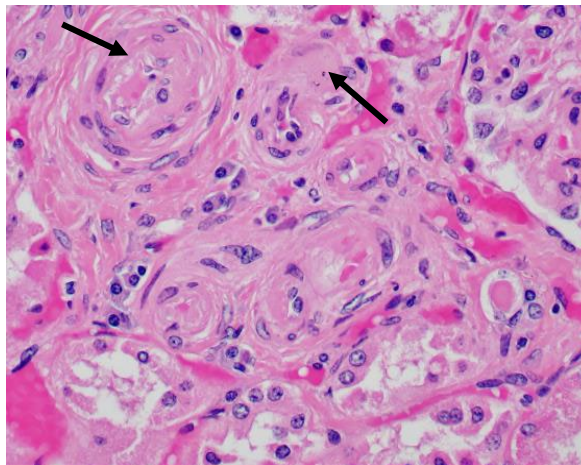


Thickened
media

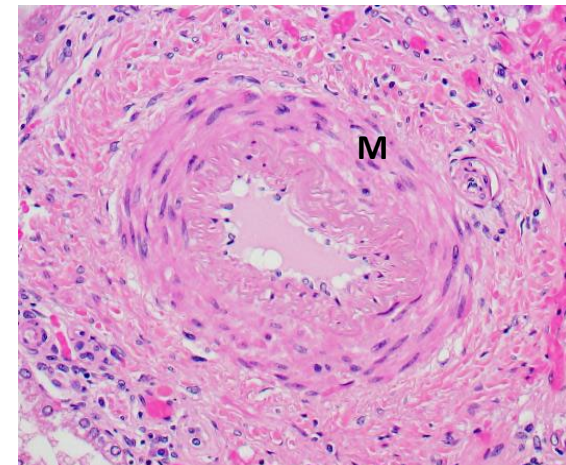
Hyalinization of choroidal arteries



Hyalinization of afferent arterioles



Arcuate artery with thickened media



Infectious myocardial diseases

MYOCARDITIS

Viral

- Canine Parvovirus
- West Nile Virus
- Encephalomyocarditis Virus
- Foot and Mouth Disease Virus
- Pseudorabies Virus
- Canine Distemper Virus
- Cytomegalovirus
- Newcastle Disease Virus
- Eastern and Western Encephalitis Viruses

Fungi

- *Aspergillus*, *Candida*, *Histoplasma*, *Blastomyces*, *Coccidioides*

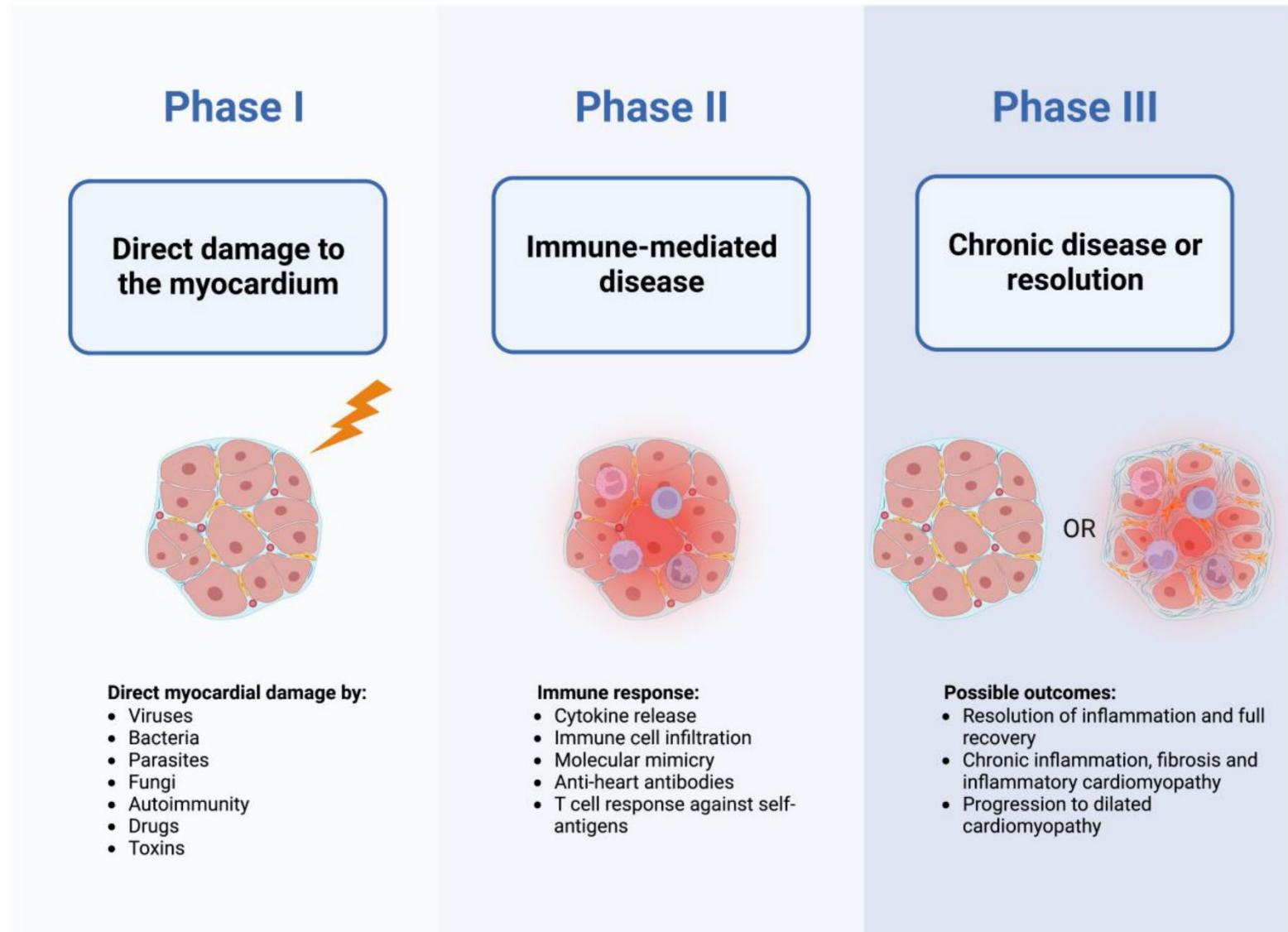
Bacterial

- *Clostridium chauvoei*
- *Listeria monocytogenes*
- *Clostridium piliformis*
- *Fusobacterium necrophorum*
- *Mycobacterium* spp.
- *Corynebacterium pseudotuberculosis*
- *Actinobacillus equuli*
- *Streptococcus equi*
- *Borrelia burgdorferi*
- *Bartonella vinsoni*

Parasites

Trypanosoma, *Toxoplasma*, *Neospora*,
Sarcocystis, *Leishmania* spp.
Trichinella, *Cysticercus cellulosae*

Triphasic model of myocarditis pathogenetic mechanisms based on clinical observations and experimental data



Myocarditis

Classification: type of exudate/lesion

Suppurative

Lymphoplasmacytic

Eosinophilic

Granulomatous

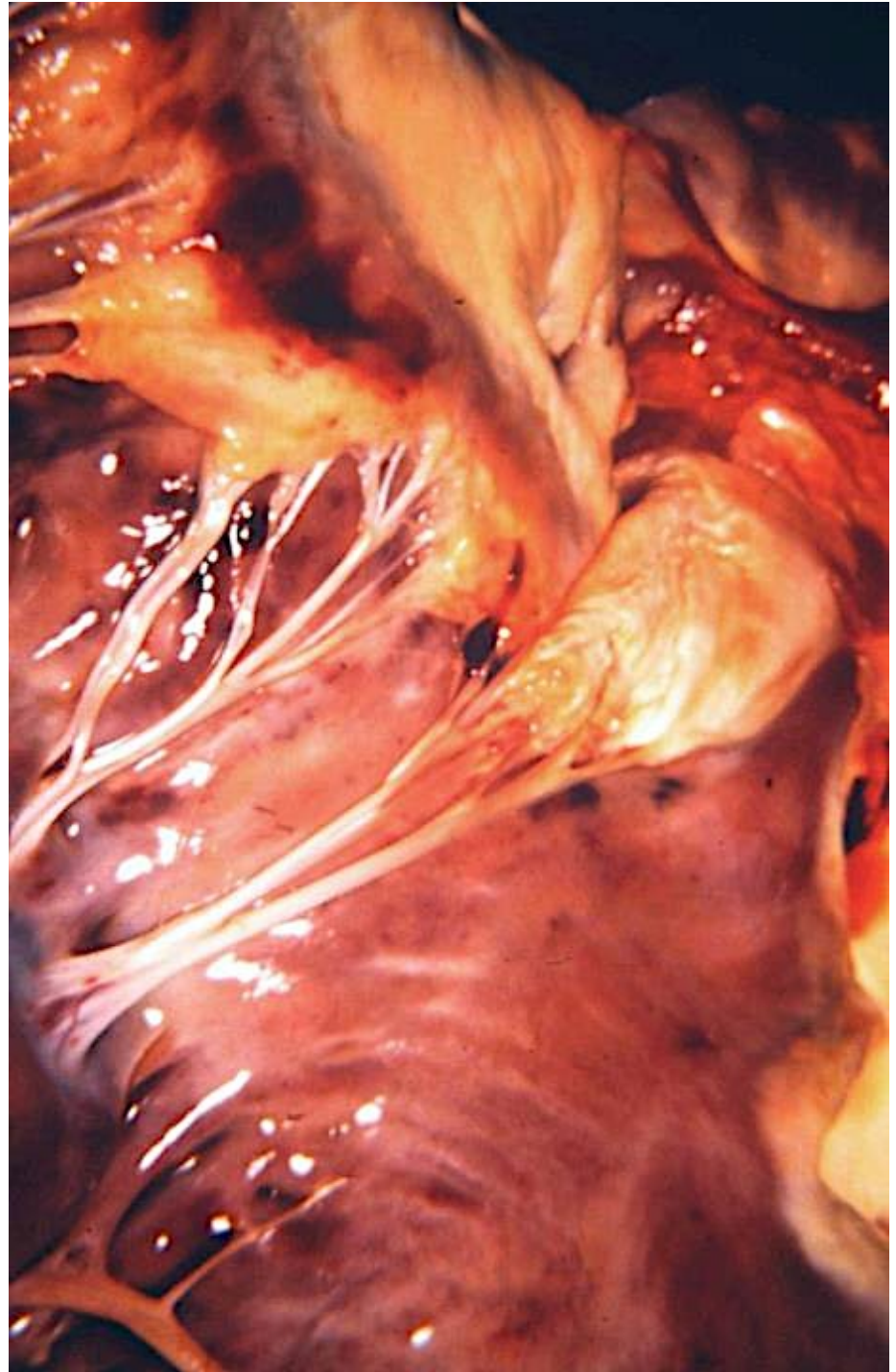
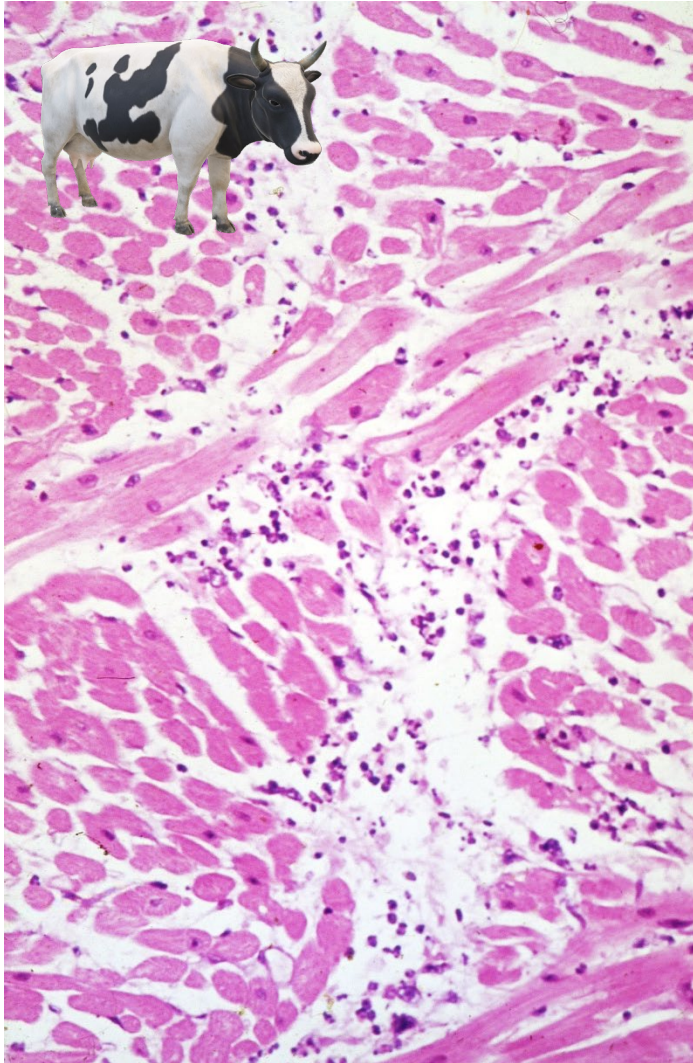
Pyogranulomatous

Hemorrhagic

Necrotizing

Necrotizing myocarditis

Clostridium chauvoei

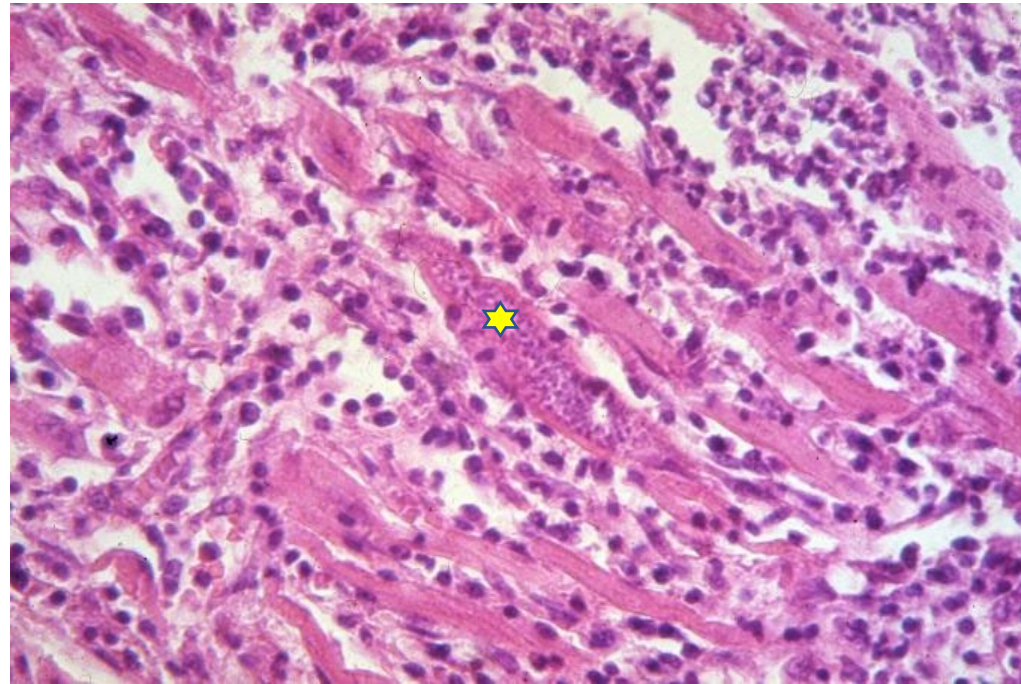


Trypanosoma cruzi

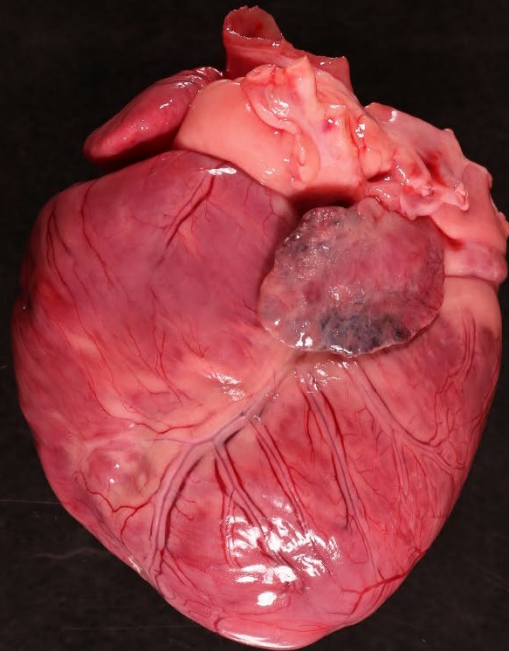
Lymphoplasmacytic/histiocytic/necrotizing
myocarditis



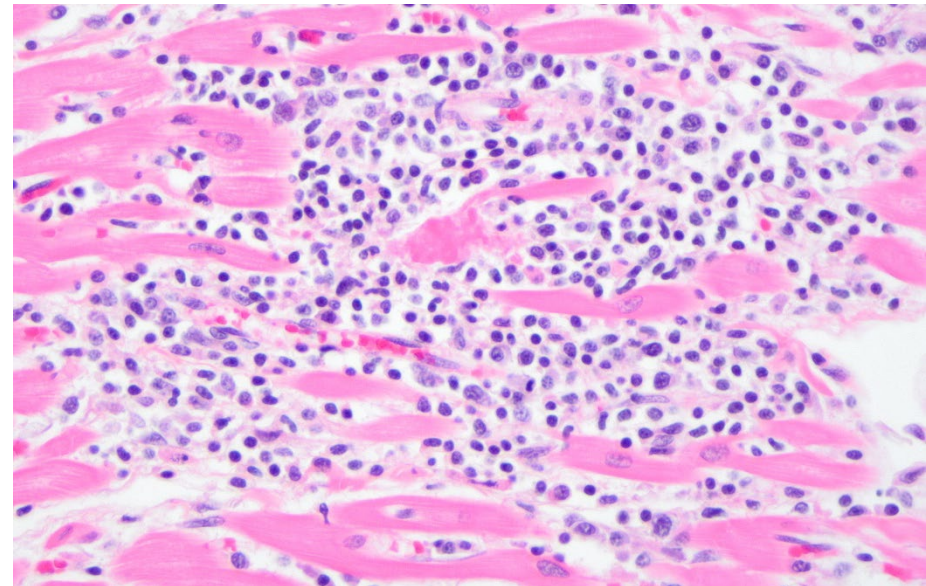
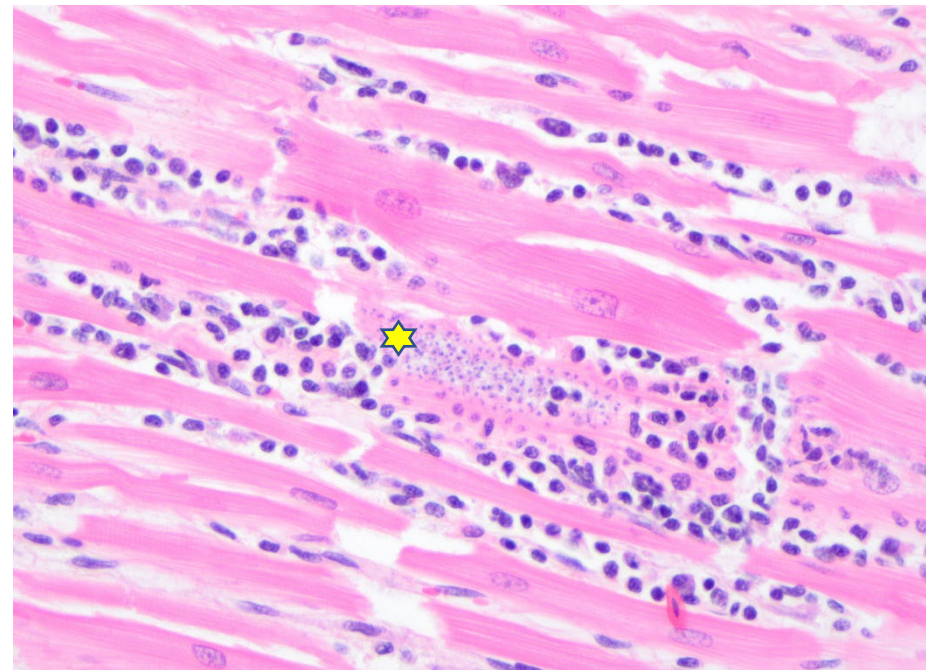
Dilated RV



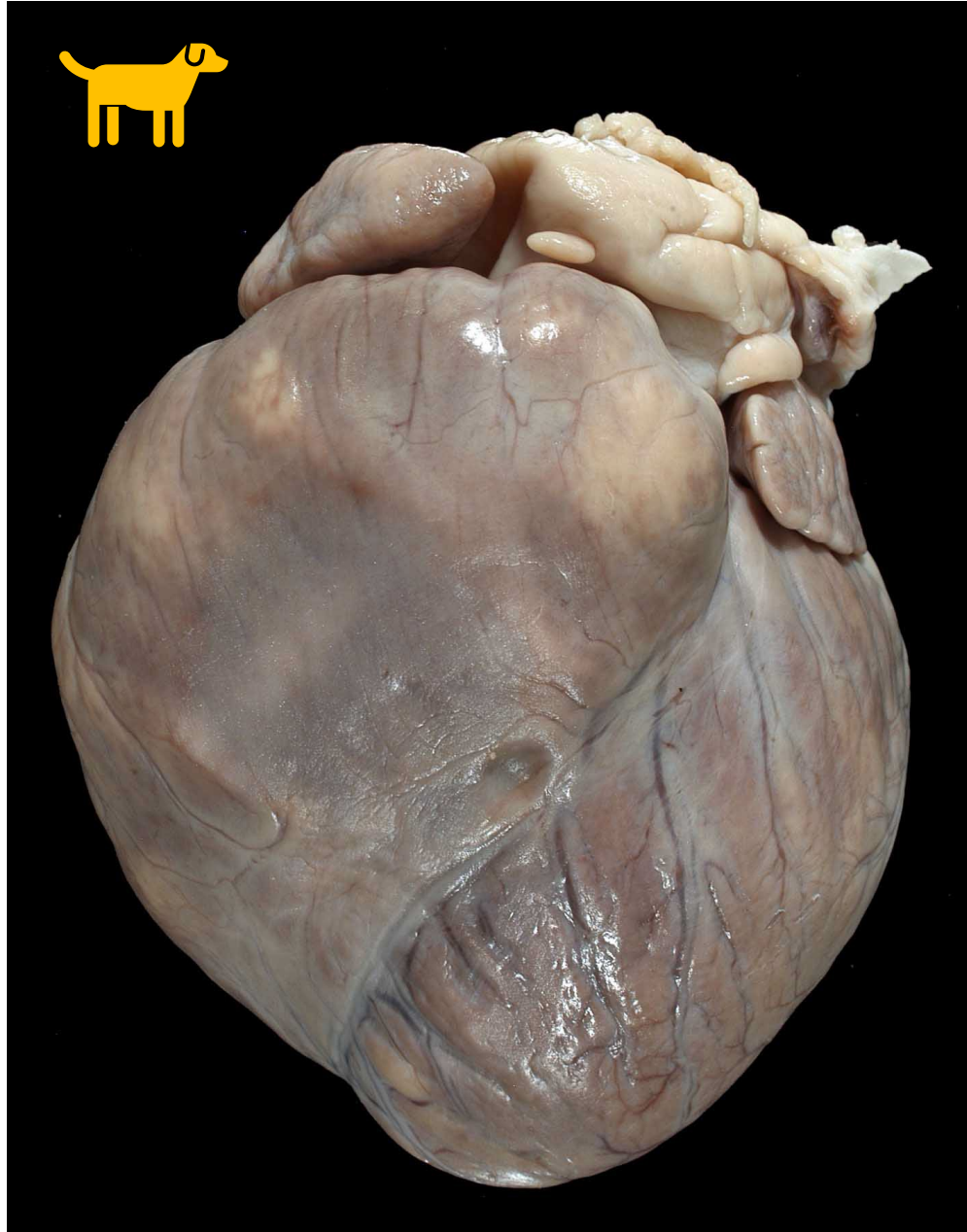
Amastigotes



Trypanosoma cruzi

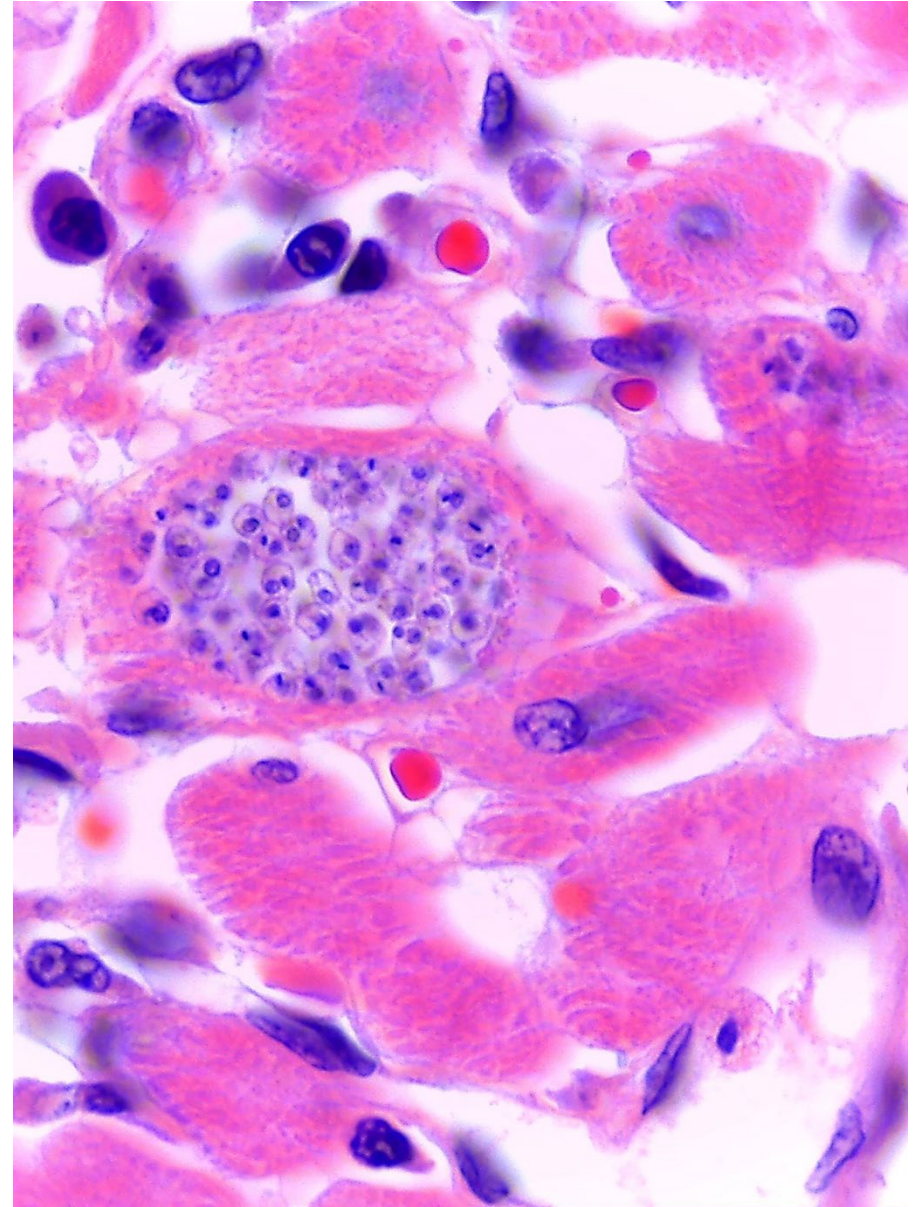
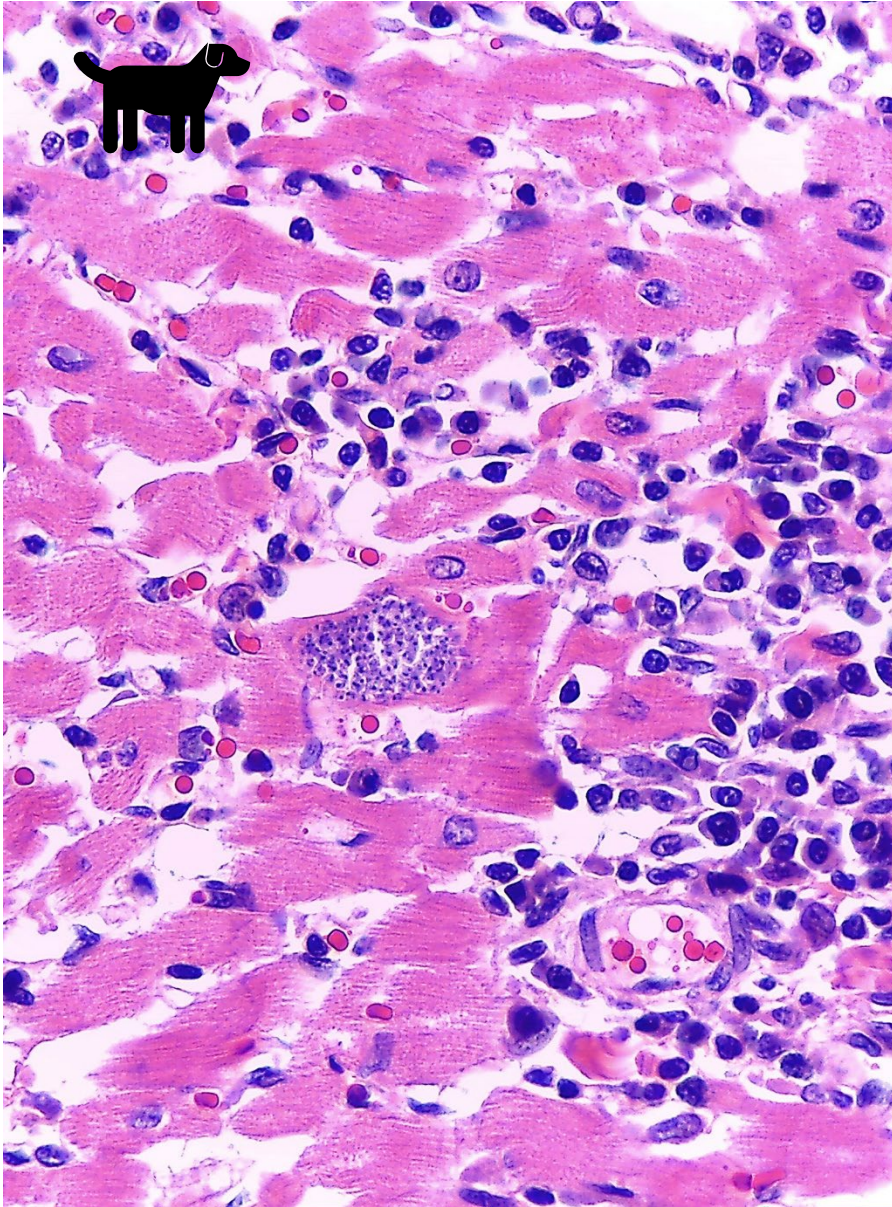


OFFICIAL
Trypanosoma cruzi



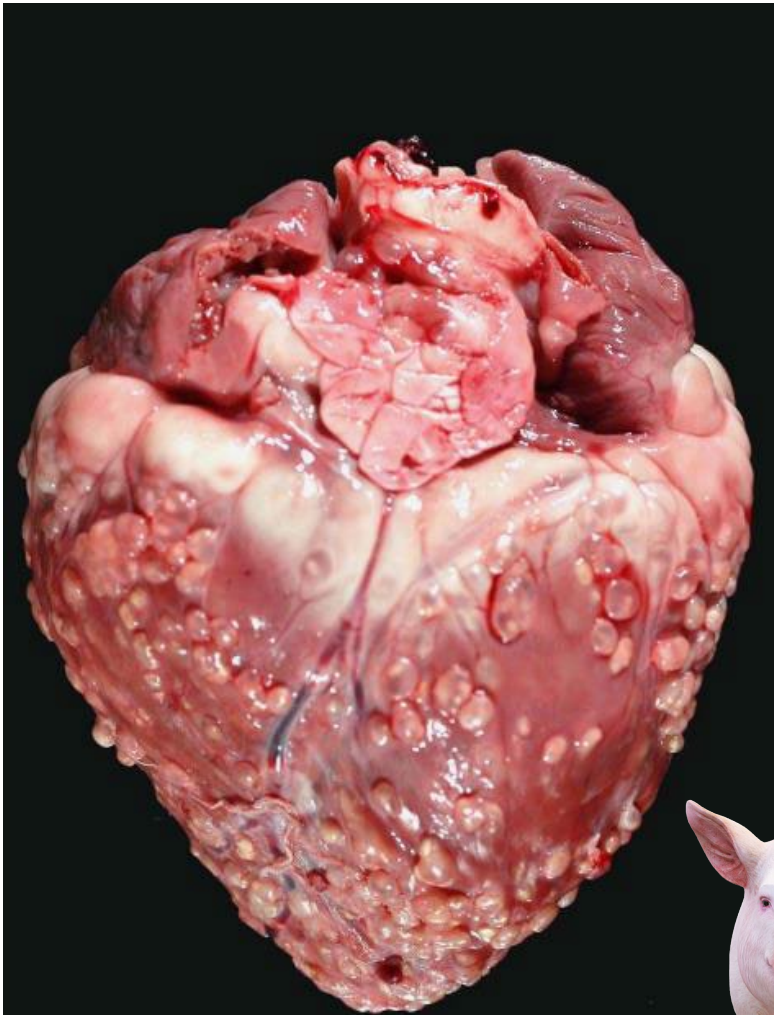
OFFICIAL

Trypanosoma cruzi/amastigotes

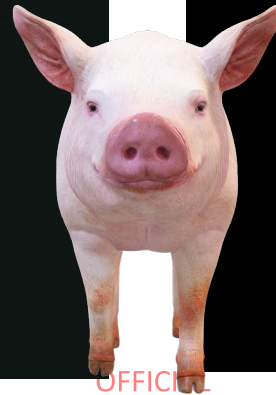


Cysticercus cellulosae

Multiple small, translucent, fluid-filled vesicles (cysticerci)



UNAM-FMVZ
PATOLOGIA



Viable cysticerci have a transparent membrane, a clear vesicular fluid, and an invaginated scolex



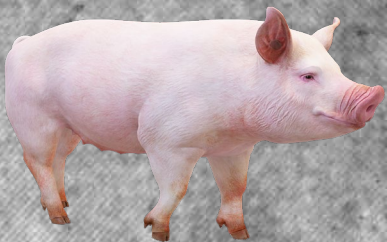
Taenia solium

Scolex

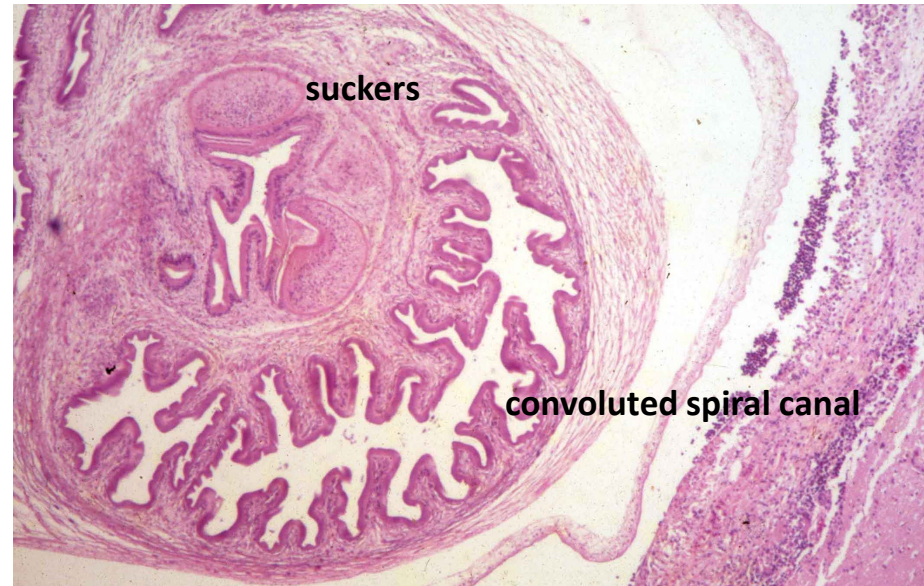
Two rows of hooks

rostellum

suckers



Dead cysticerci are surrounded by lymphocytes and fibrosis



Septicemia due to ^{OFFICIAL} *Pasteurella multocida*

Hemorrhage and fibrinous pericarditis



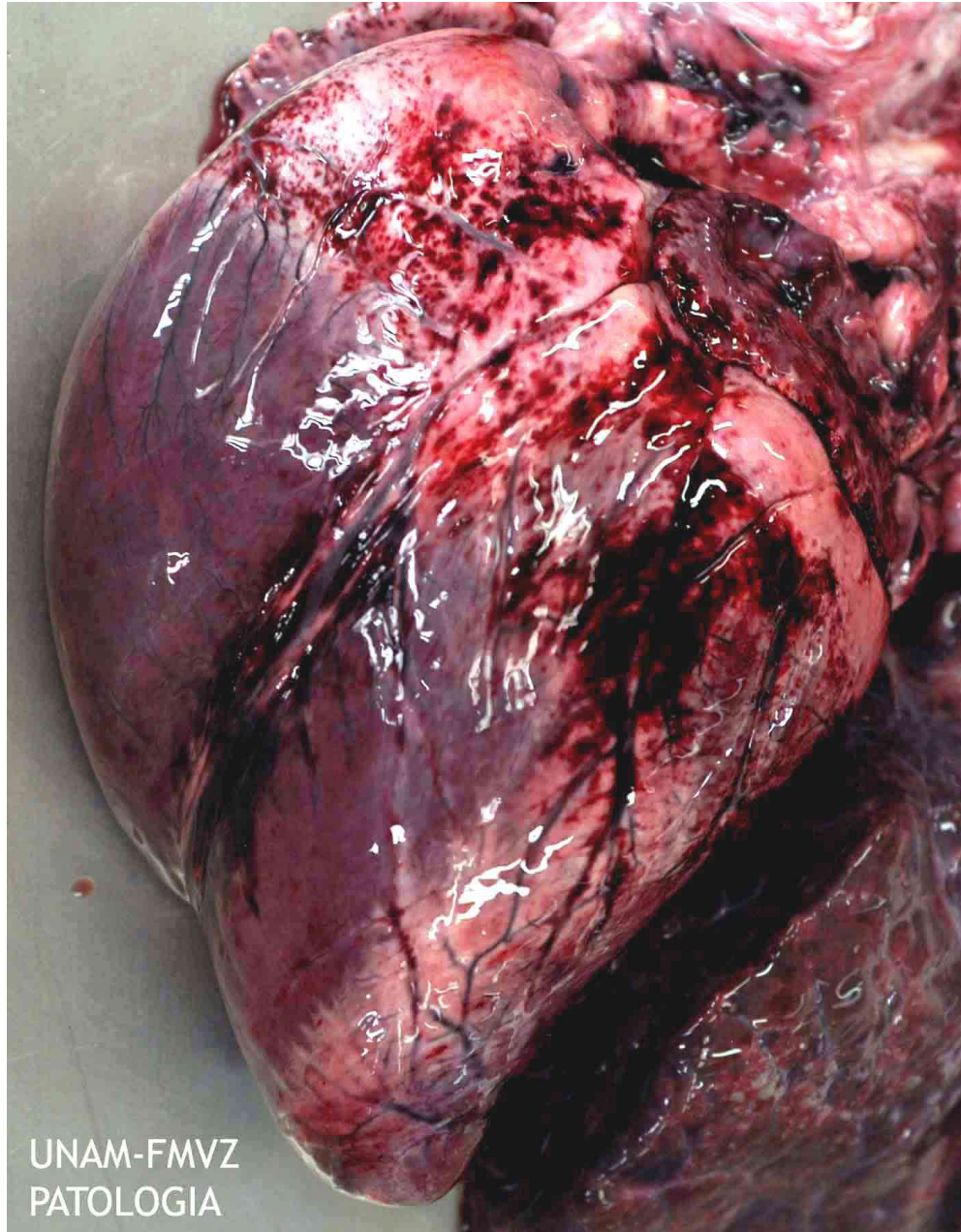
OFFICIAL

Hemorrhage Epicardial or endocardial

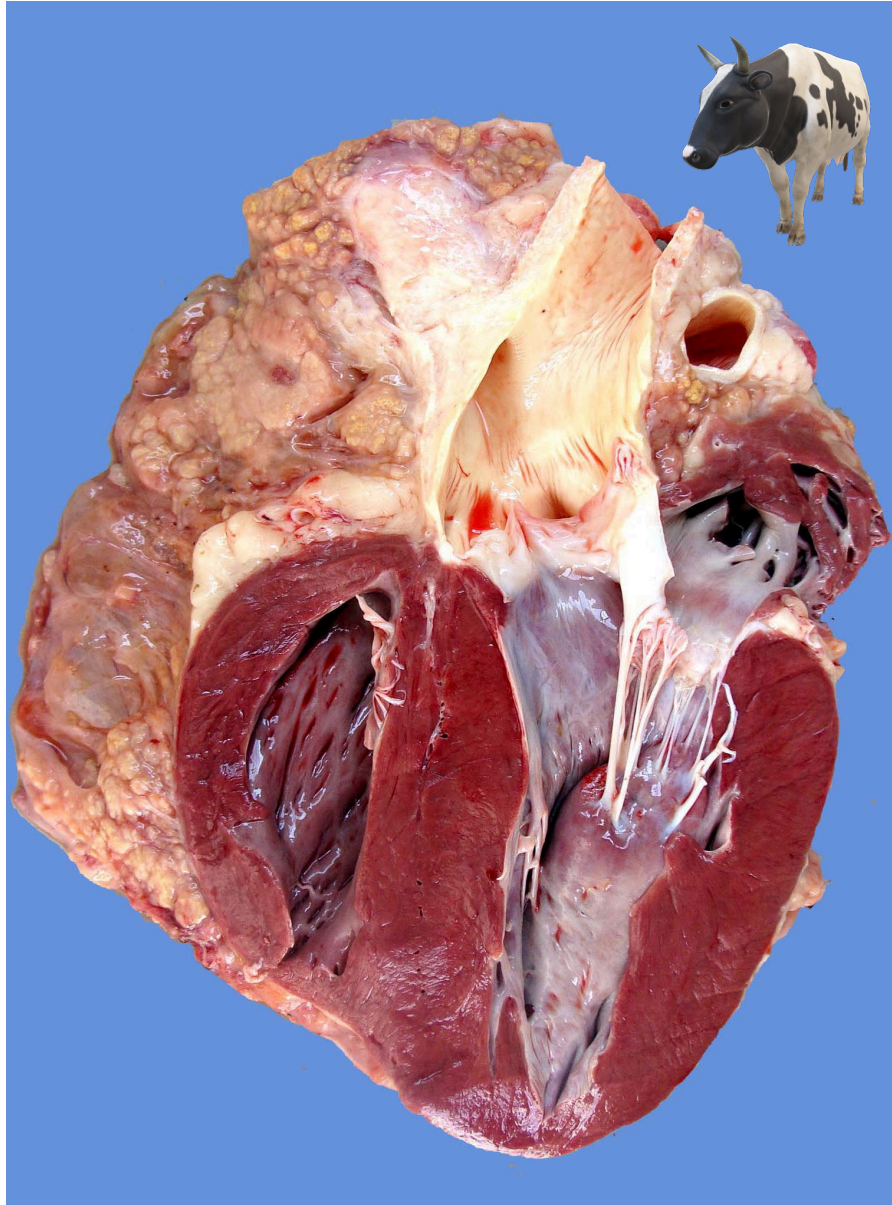
- Septicemia
- Endotoxemia
- Electrocution
- Anoxia
- Agonal



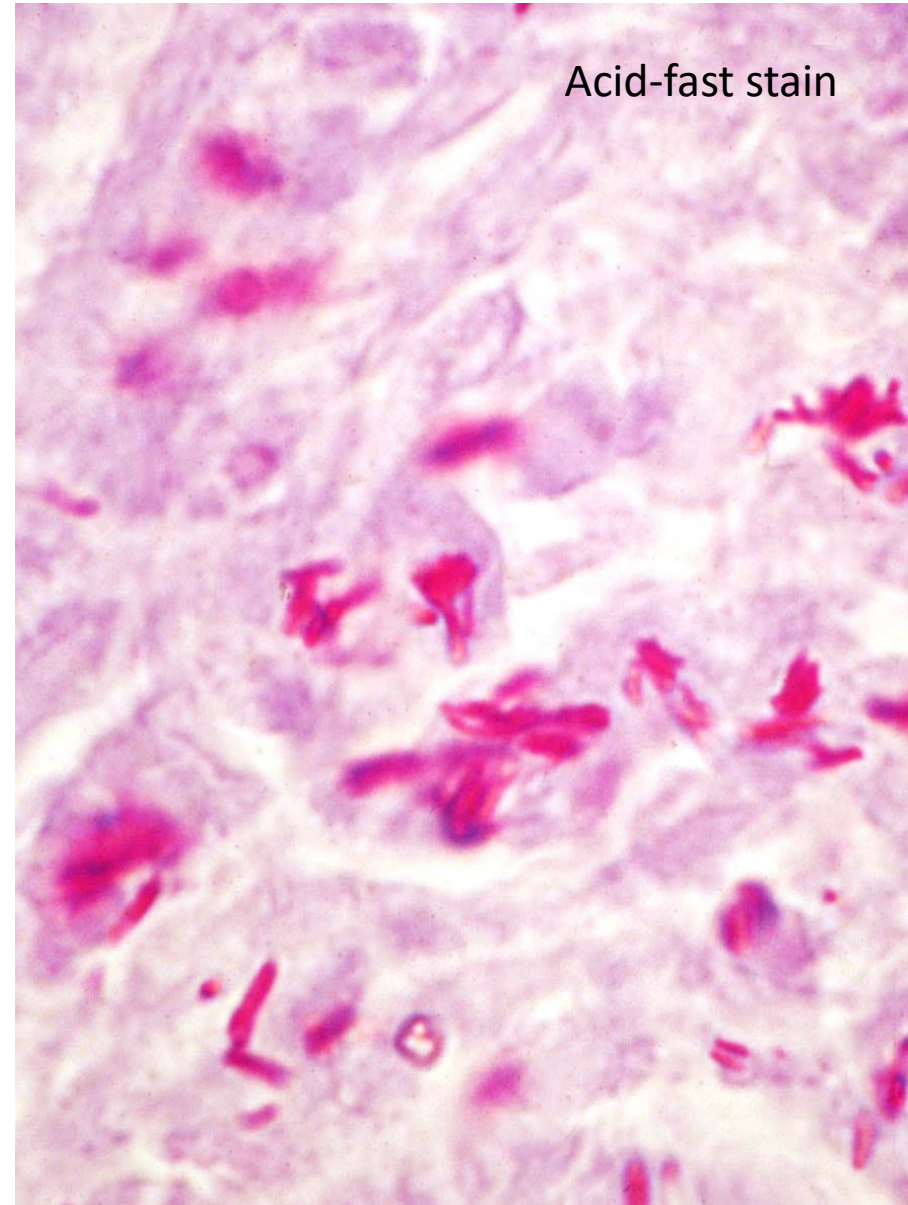
OFFICIAL
Hemorrhages due to septicemic salmonellosis



Tuberculosis



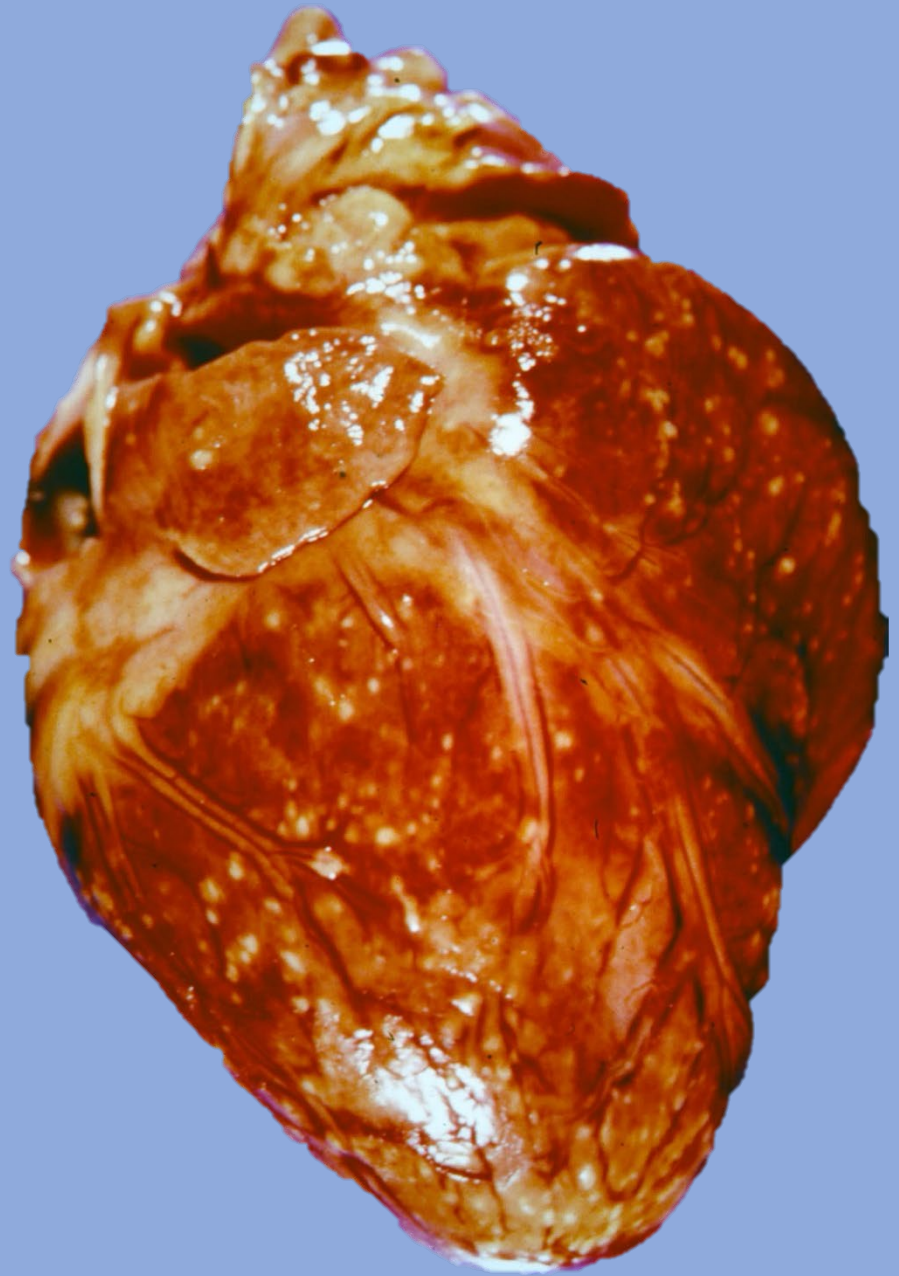
Granulomatous pericarditis



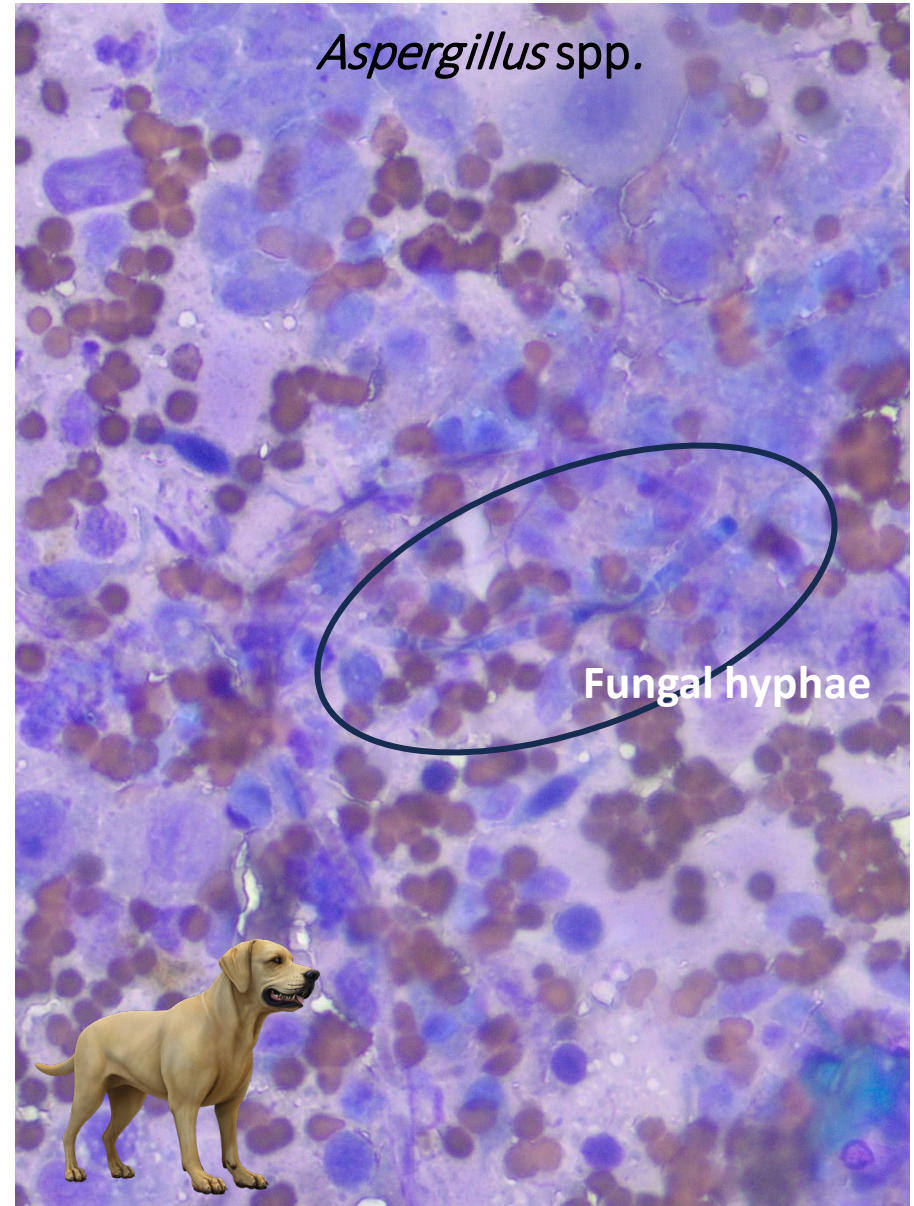
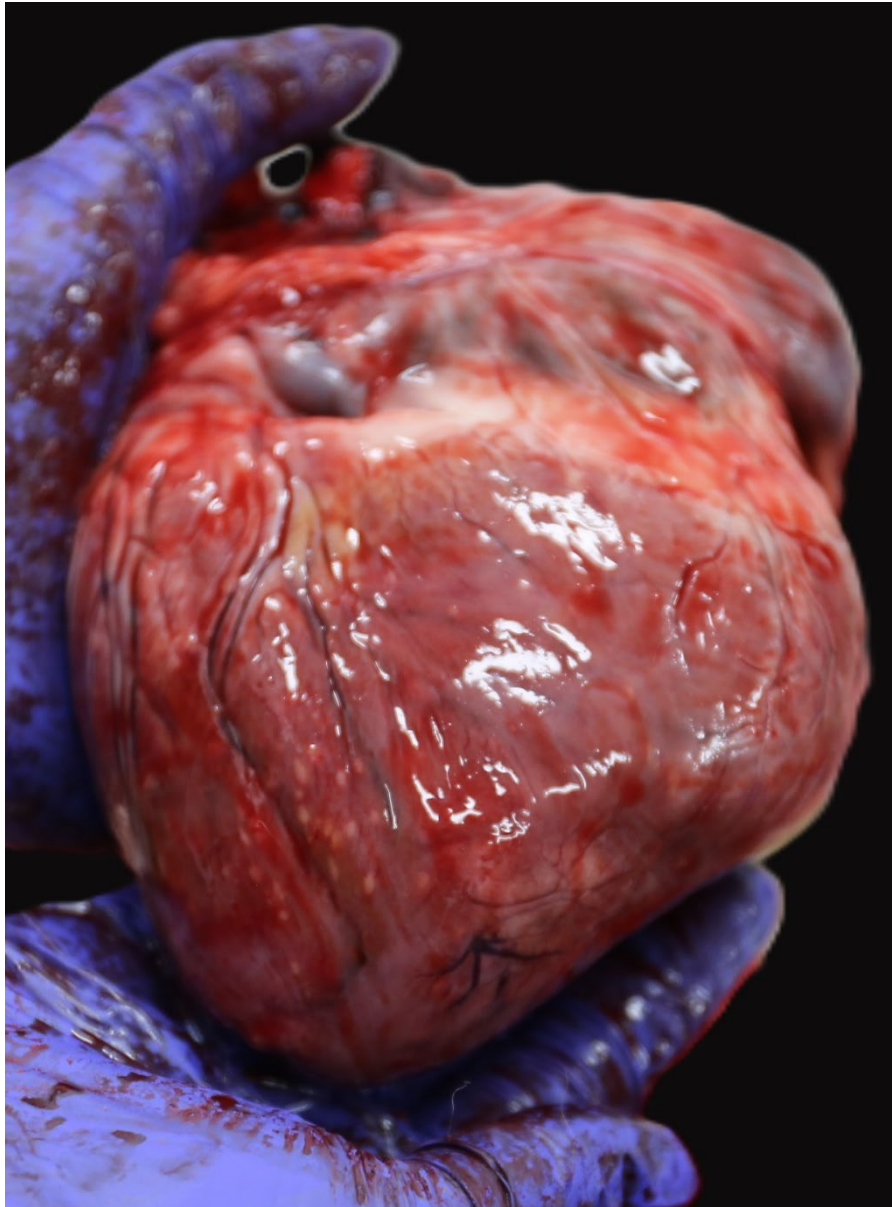
Necrotizing myocarditis

Multifocal to coalescing yellow foci

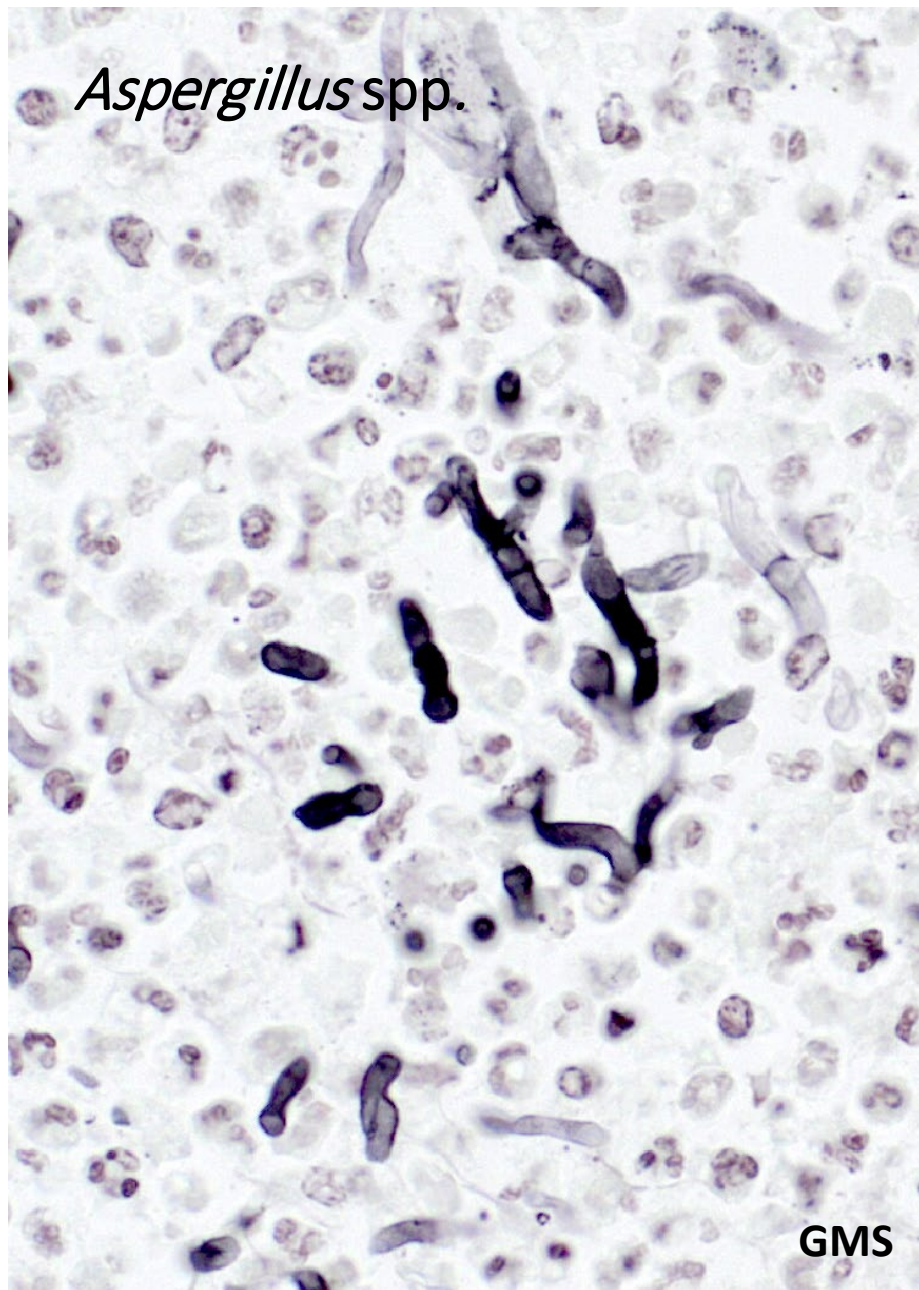
Aspergillus spp.



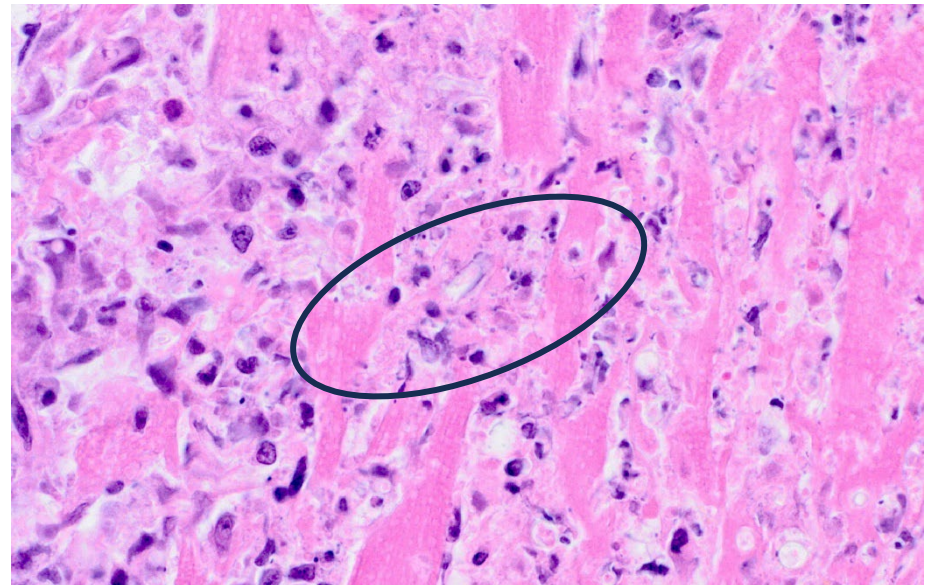
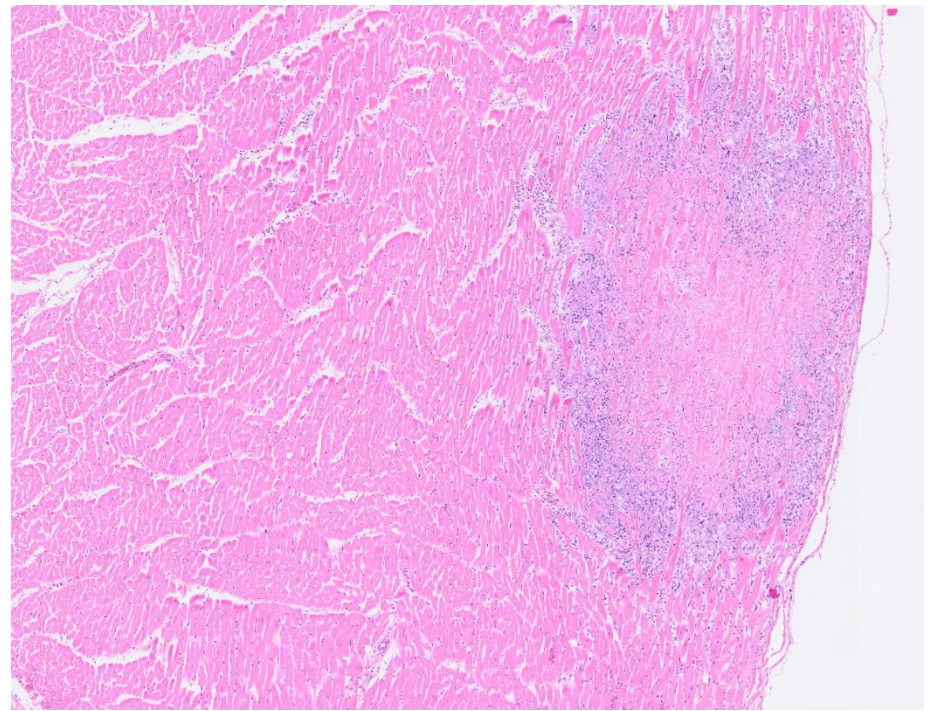
Myocardium with multifocal to coalescing yellow foci/areas of necrosis



Aspergillus spp.



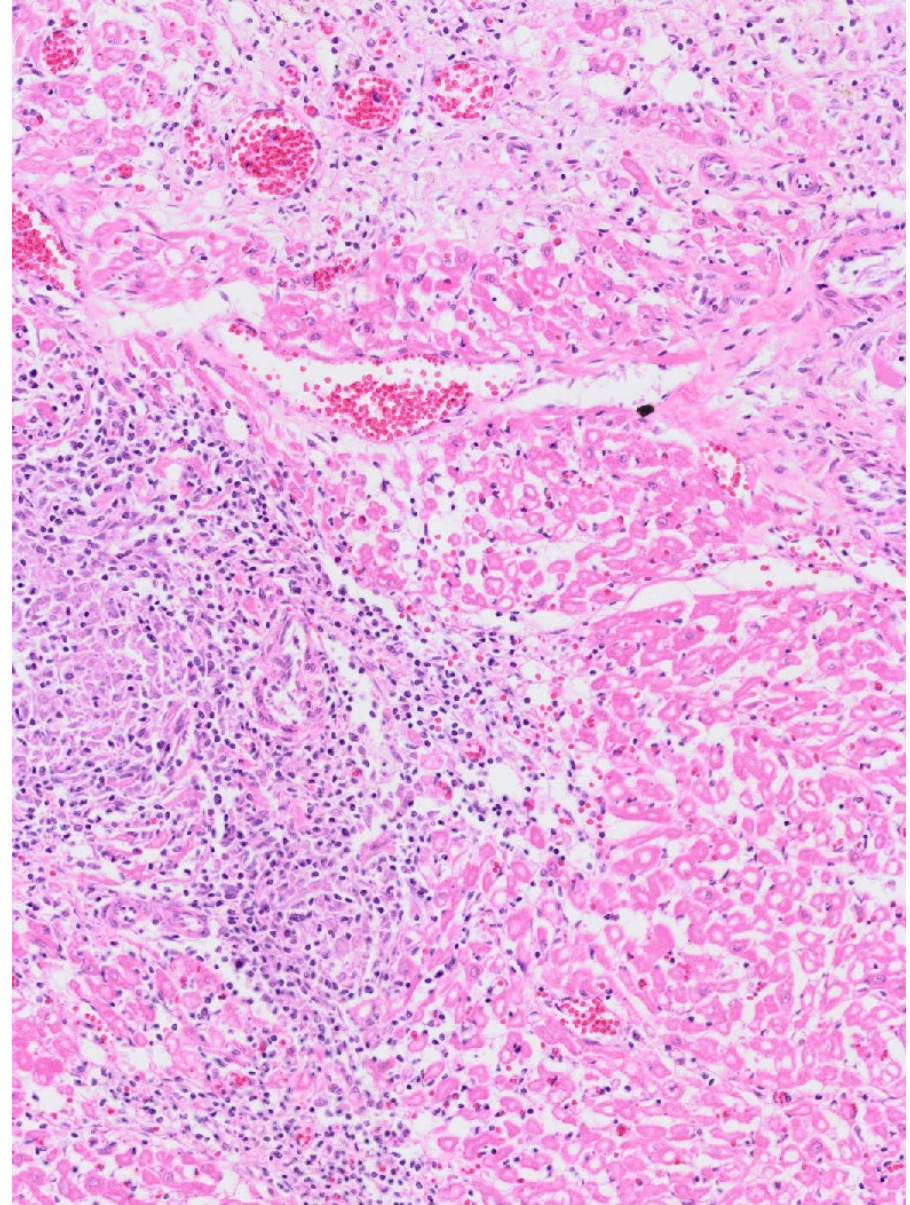
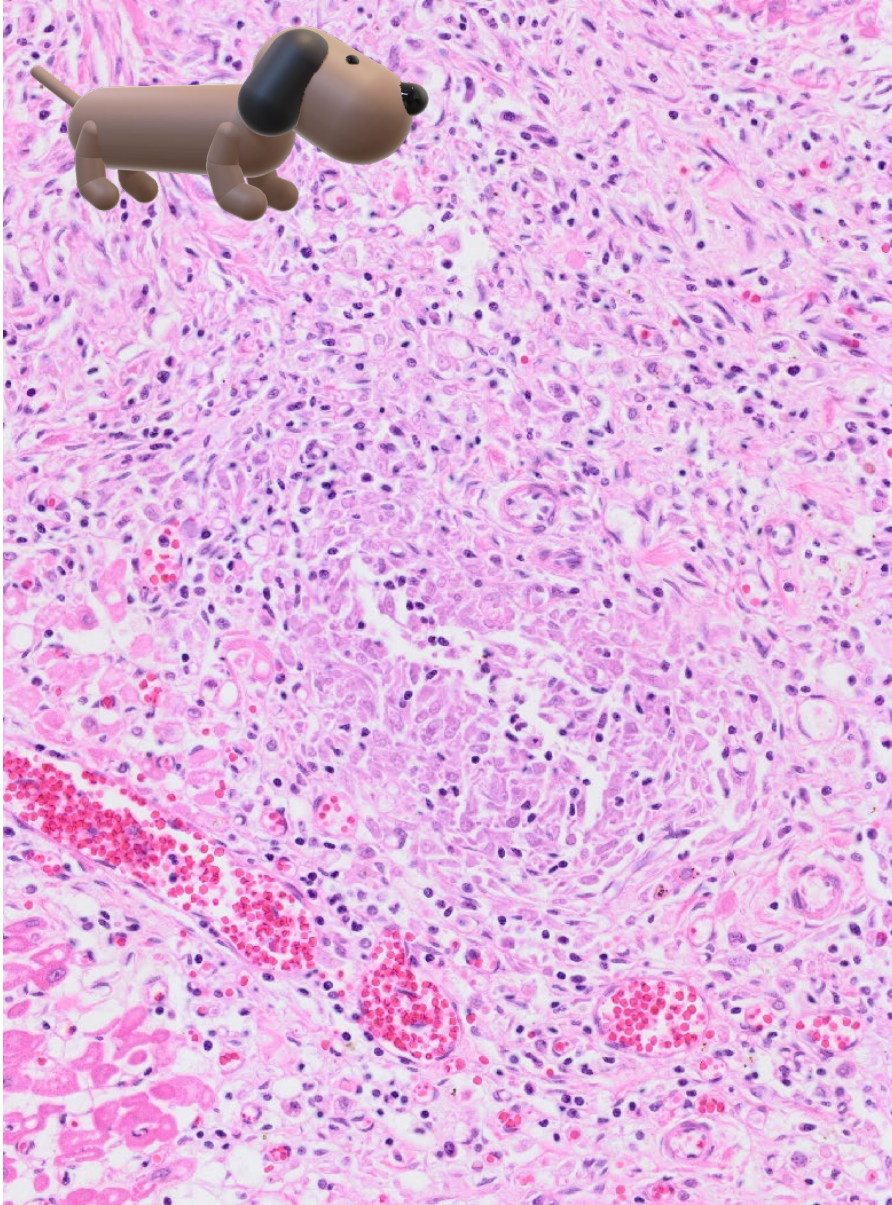
GMS



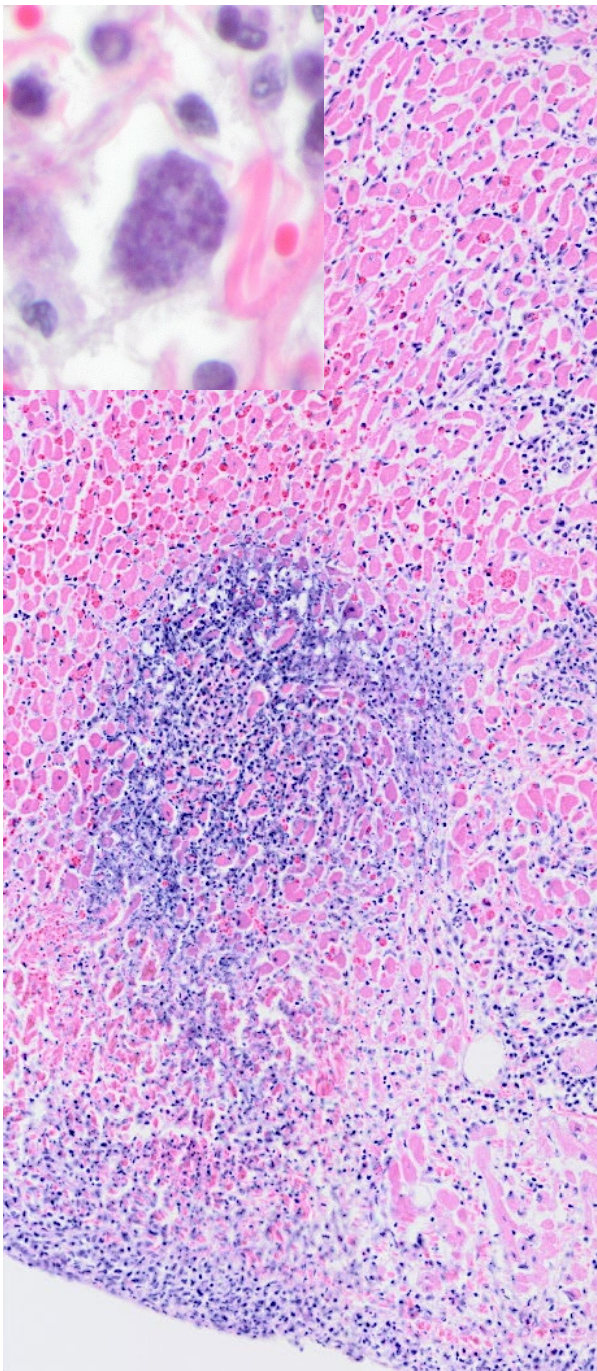
Hyphe are septate, parallel-walled, with dichotomous branching

***Brucella* spp. (PCR)**

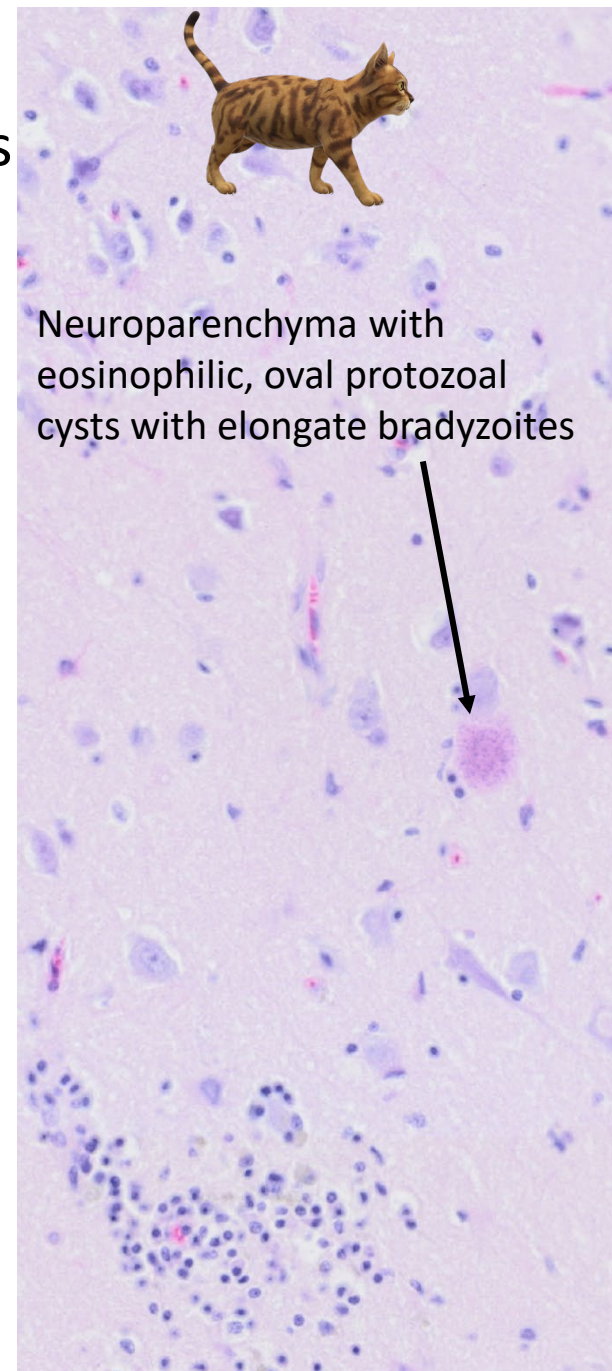
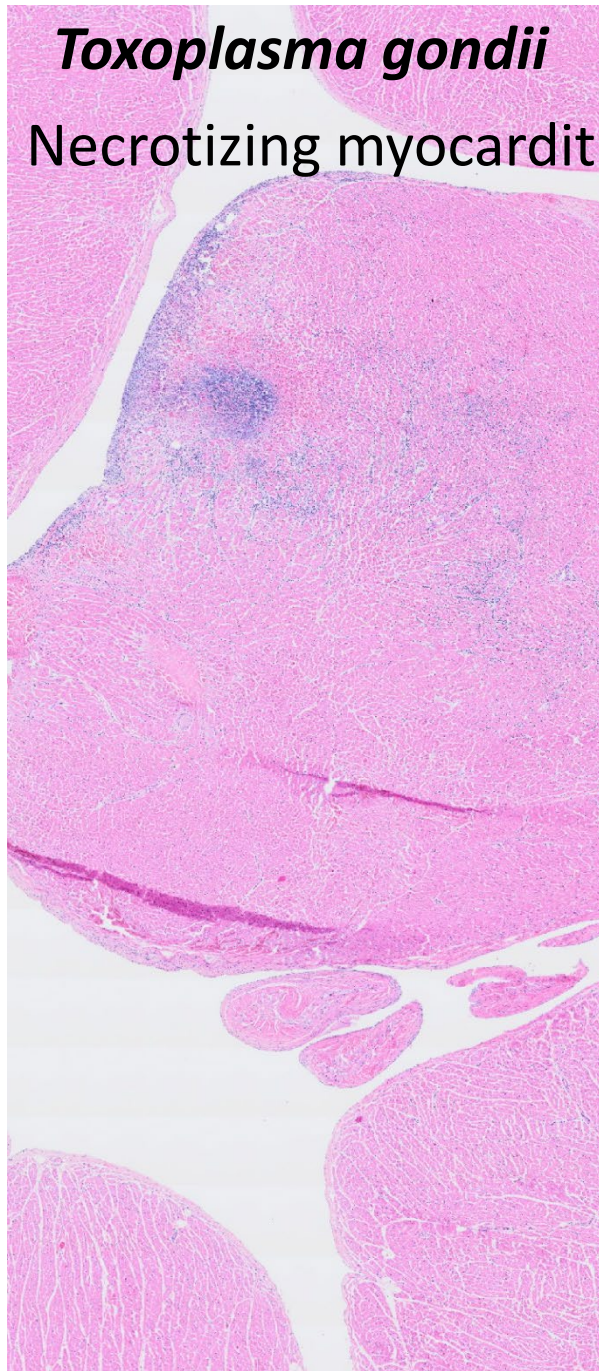
OFFICIAL
Myocarditis granulomatous multifocal



OFFICIAL



Toxoplasma gondii
Necrotizing myocarditis



Toxoplasma gondii/cysts

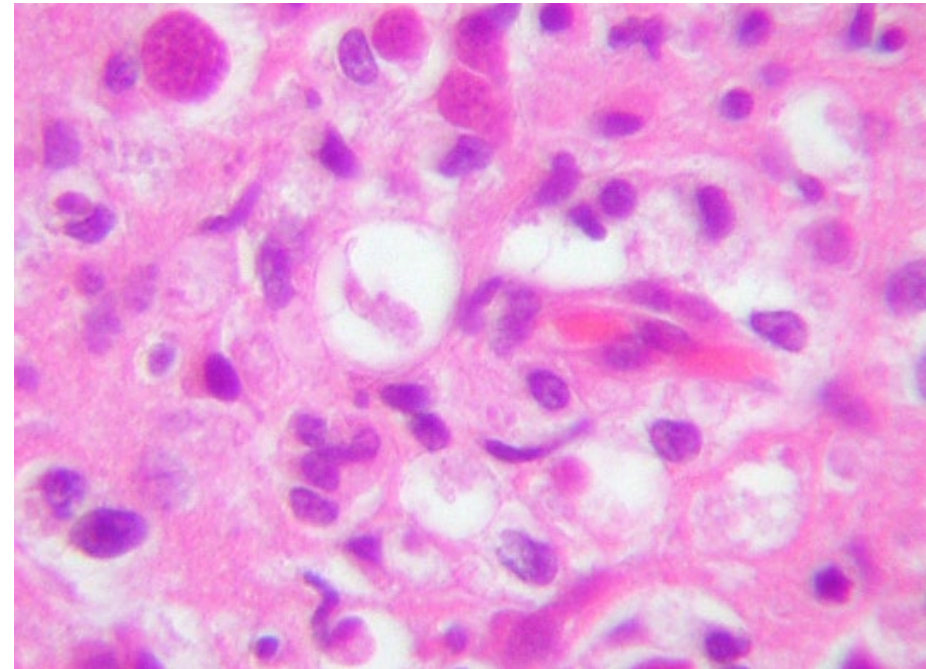


Neospora caninum

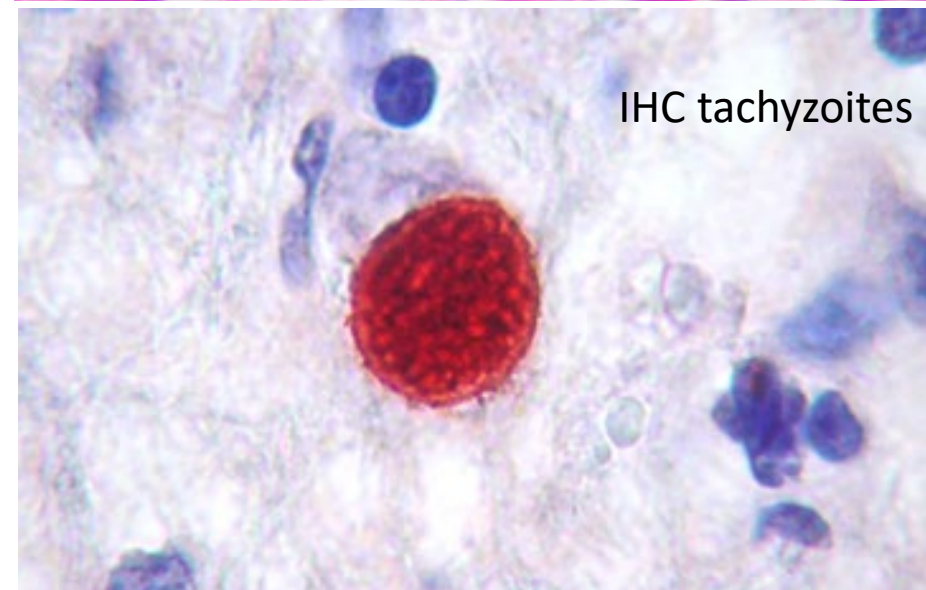
Lymphoplasmacytic/necrotizing myocarditis



brain



brain

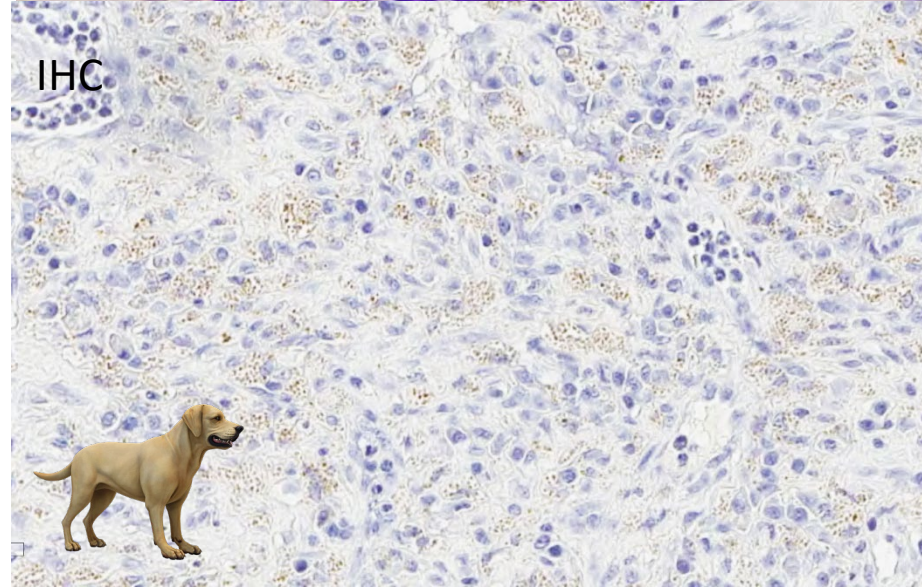
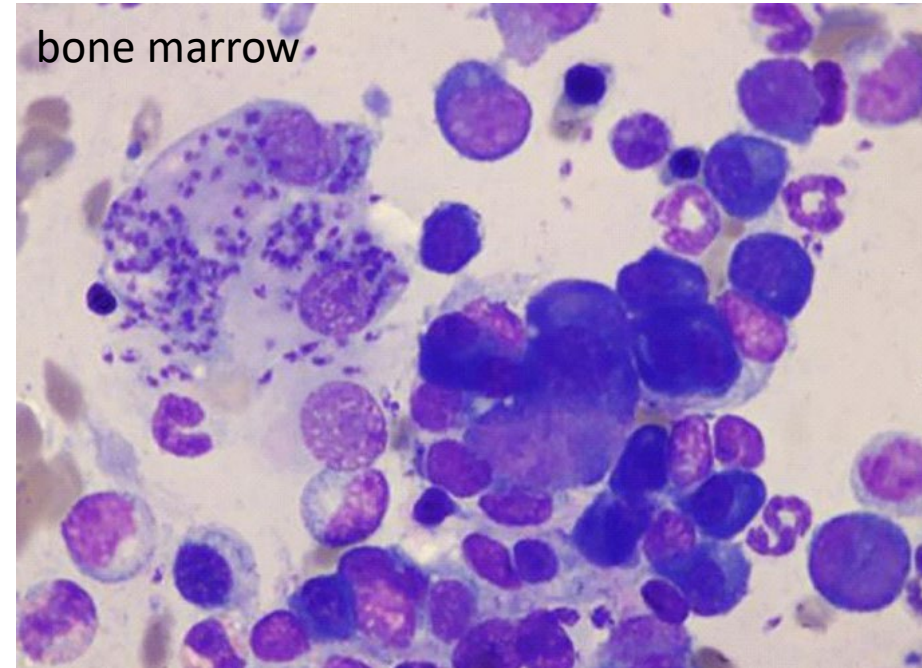
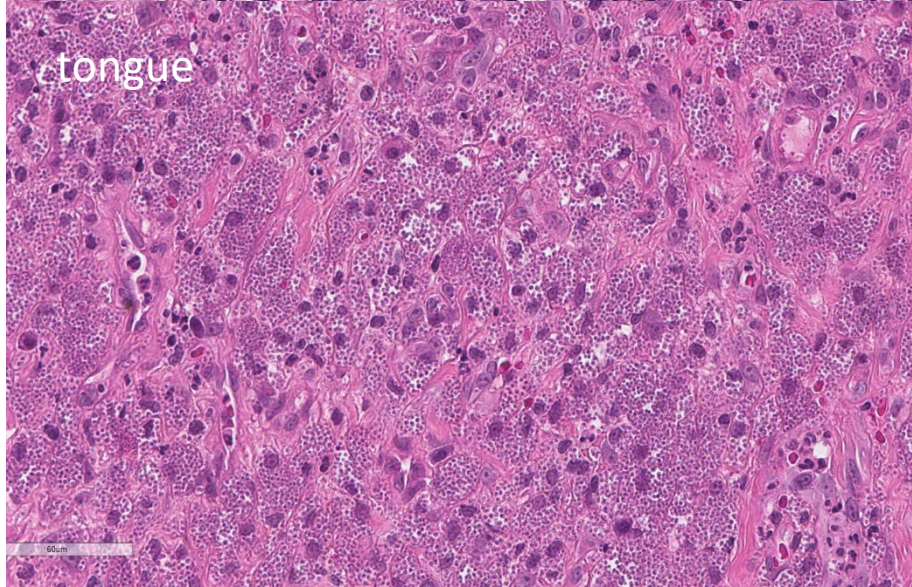
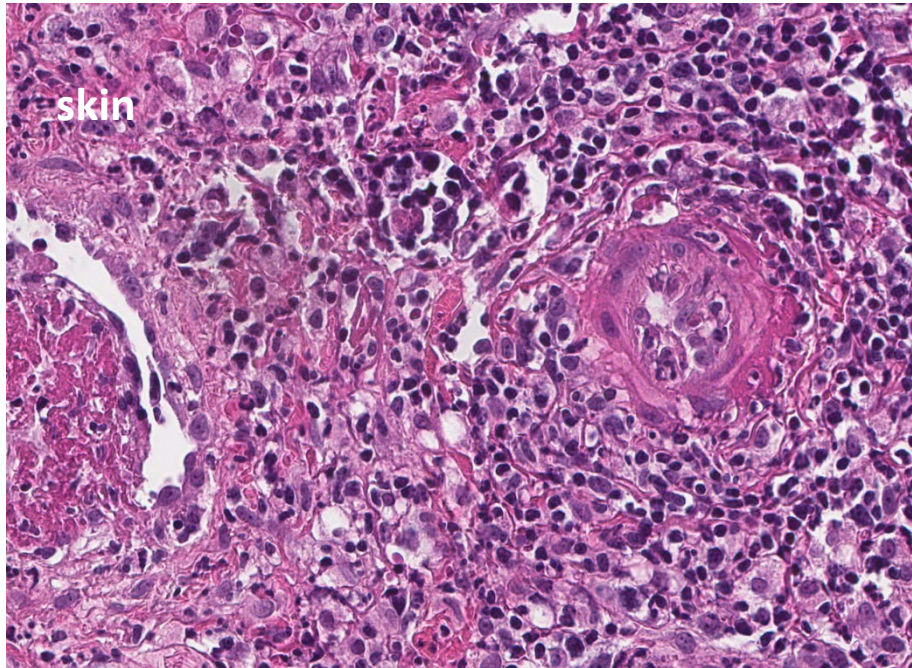


IHC tachyzoites

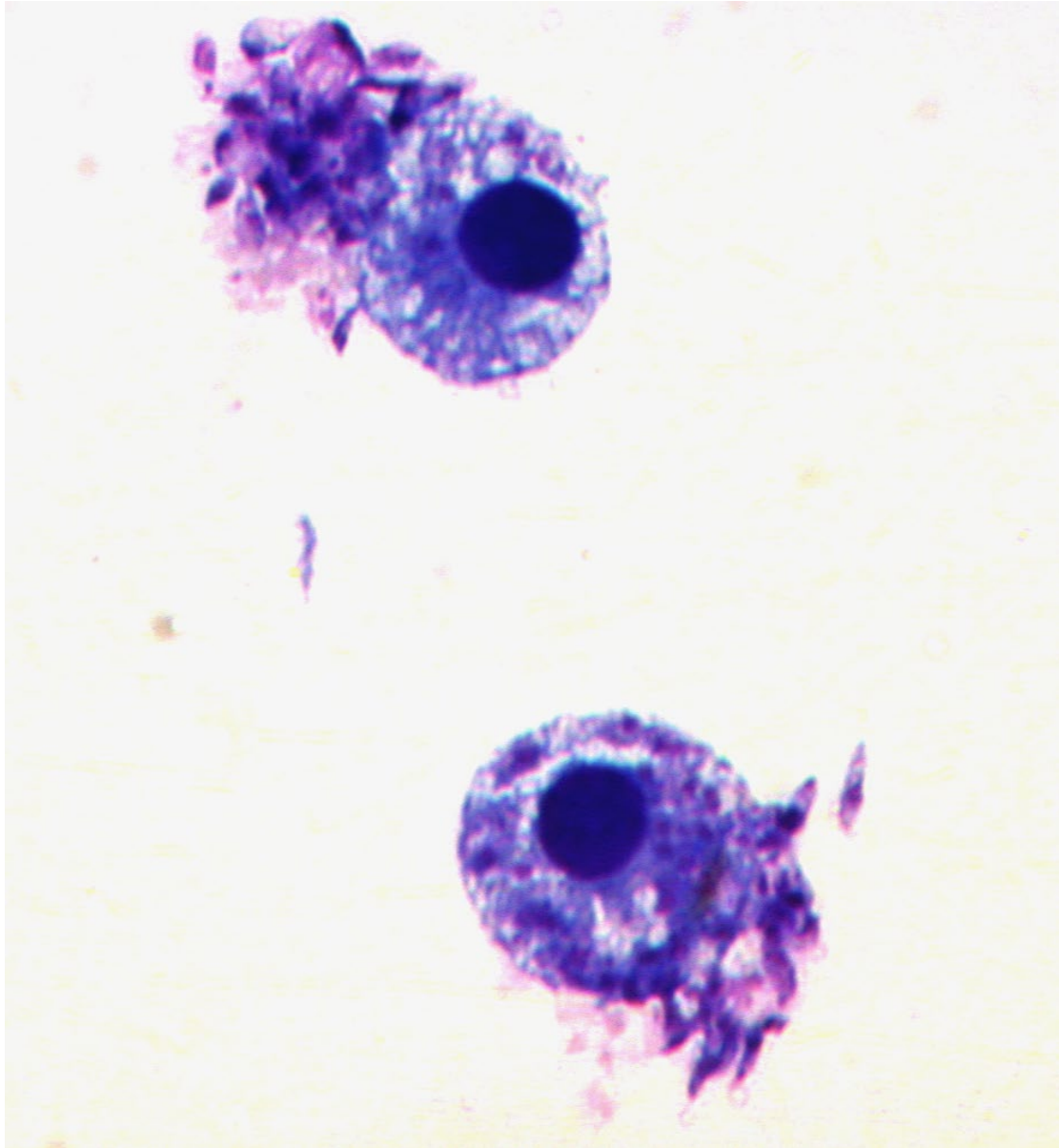
***Leishmania* spp.**

Leishmania infantum

Lymphoplasmacytic/granulomatous/necrotizing myocarditis
with fibrinoid vasculitis



Macrophages with amastigotes (experimental infection)



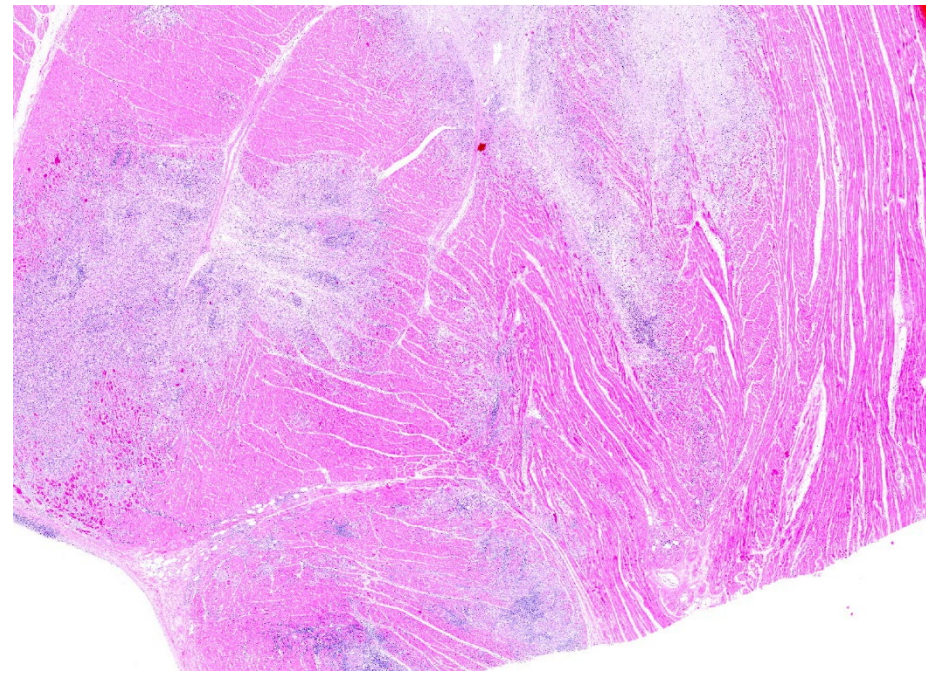
Leishmania mexicana

The principal vector is *Lutzomyia olmeca olmeca*, a sand fly that is highly attracted to rodents but is also anthropophilic, biting during the day. Cutaneous/mucocutaneous disease

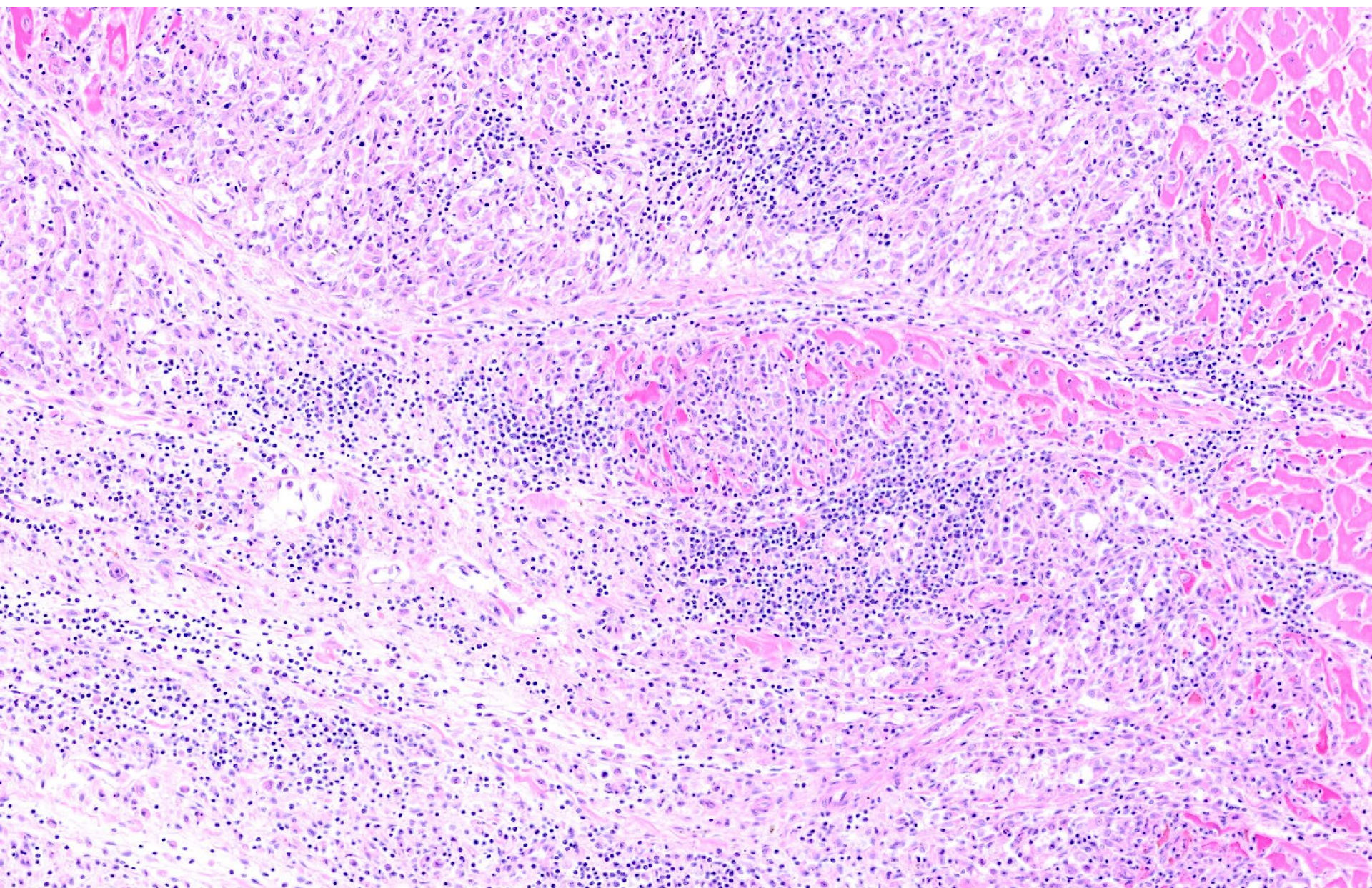
Granulomatous/lymphoplasmacytic myocarditis in dogs

In many instances, the etiological agent is not identified using H&E and special stains.

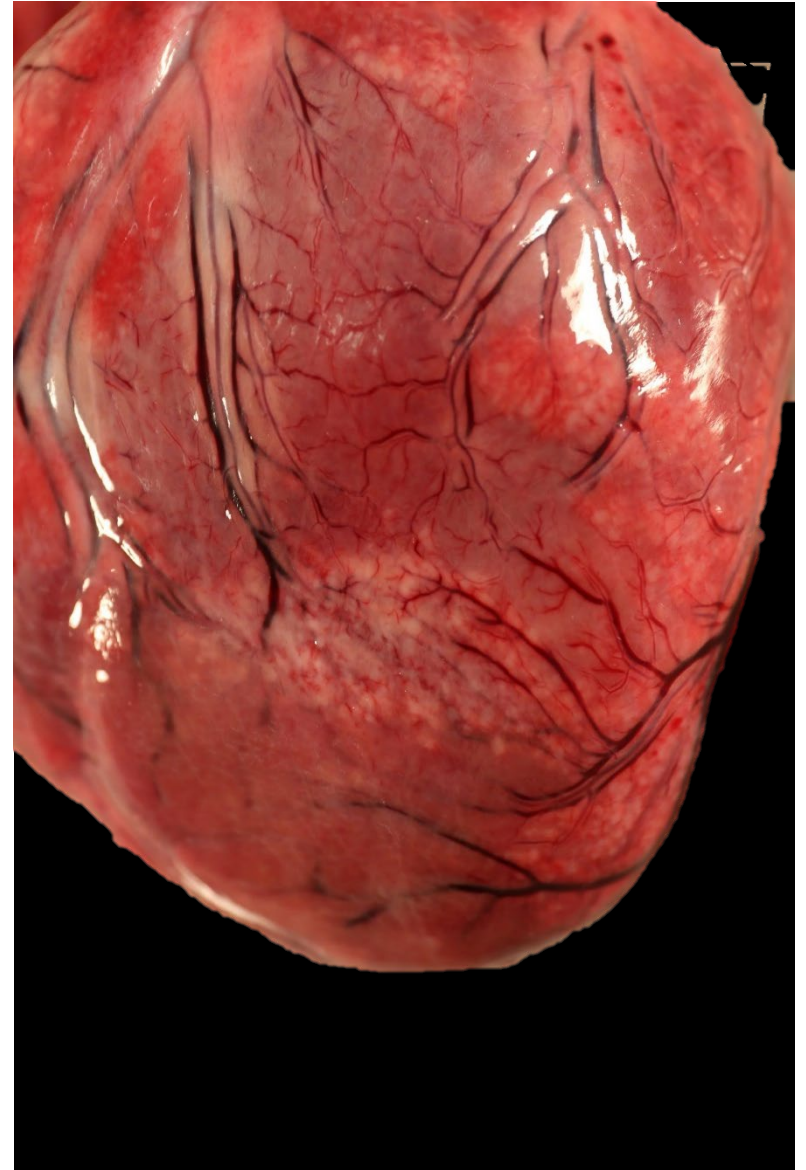
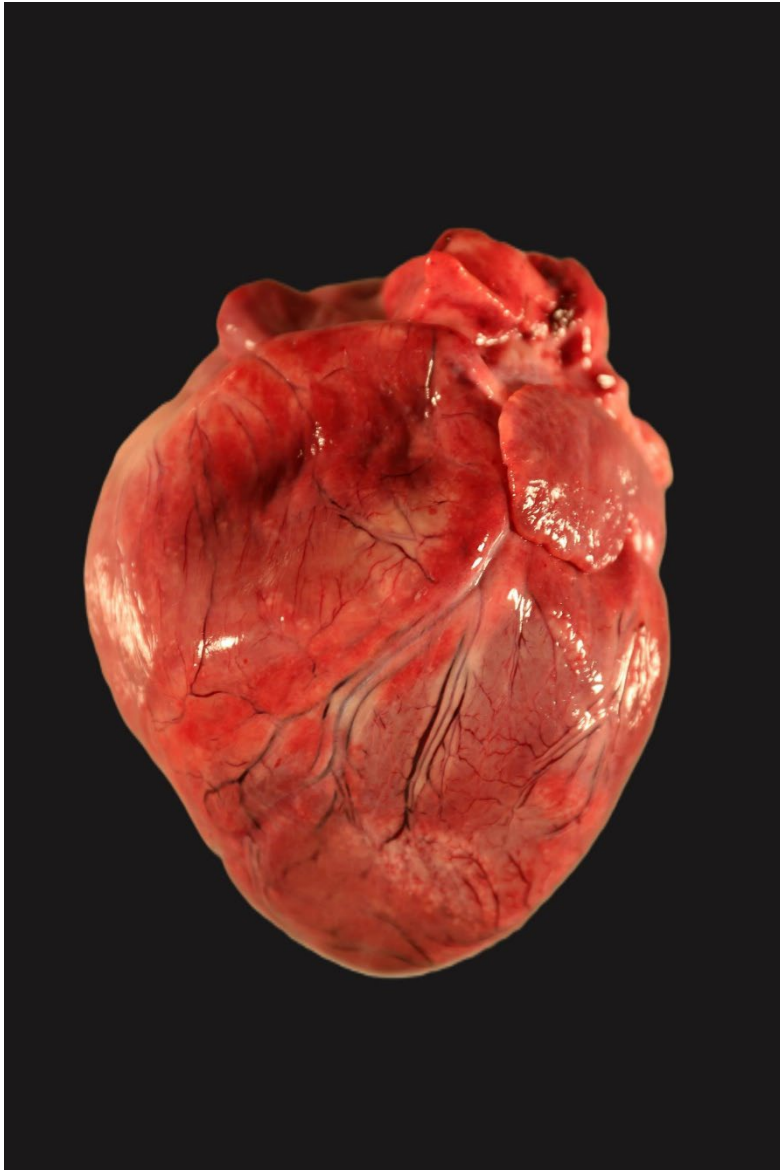
PCR screening often fails to determine the cause of myocarditis.



Granulomatous and lymphoplasmacytic myocarditis with fibrosis



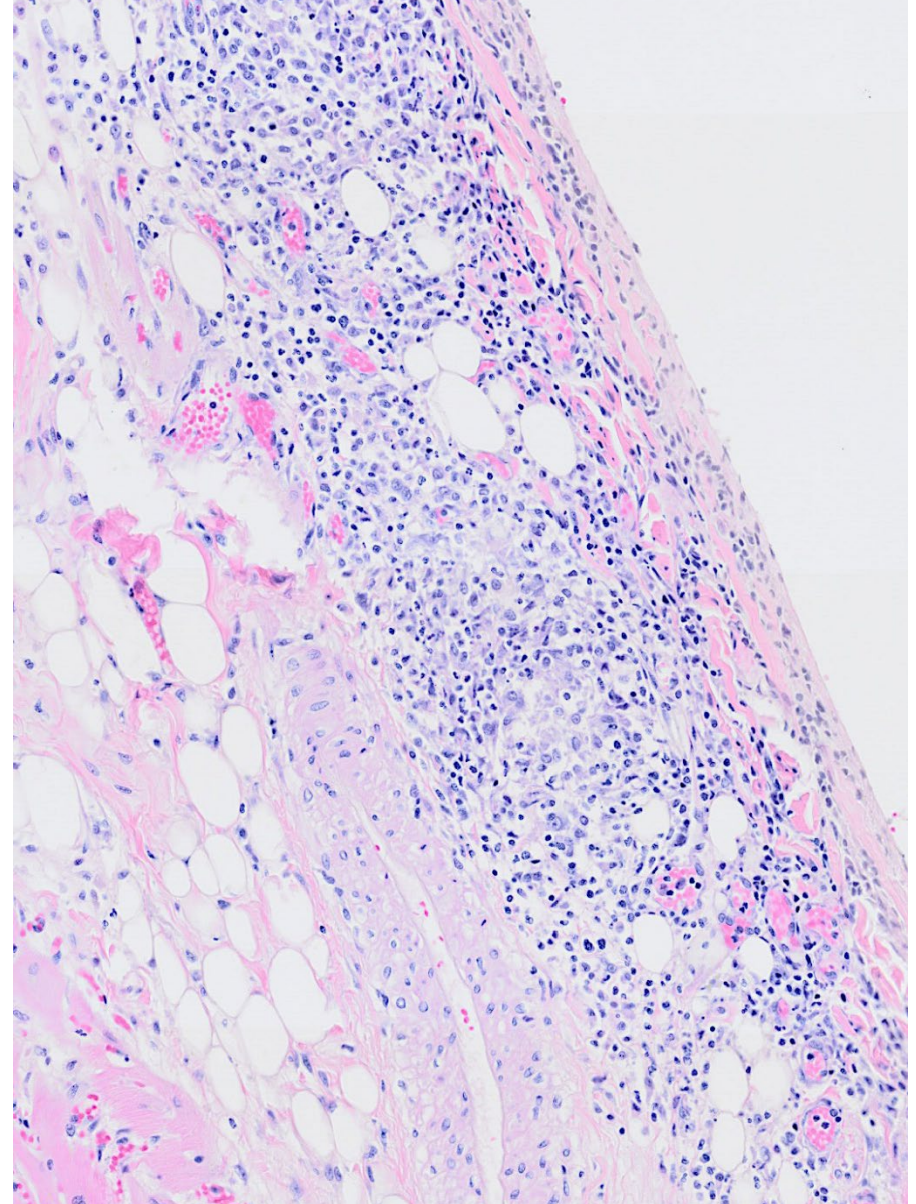
Heart with multiple to coalescing white foci
Right ventricular dilation



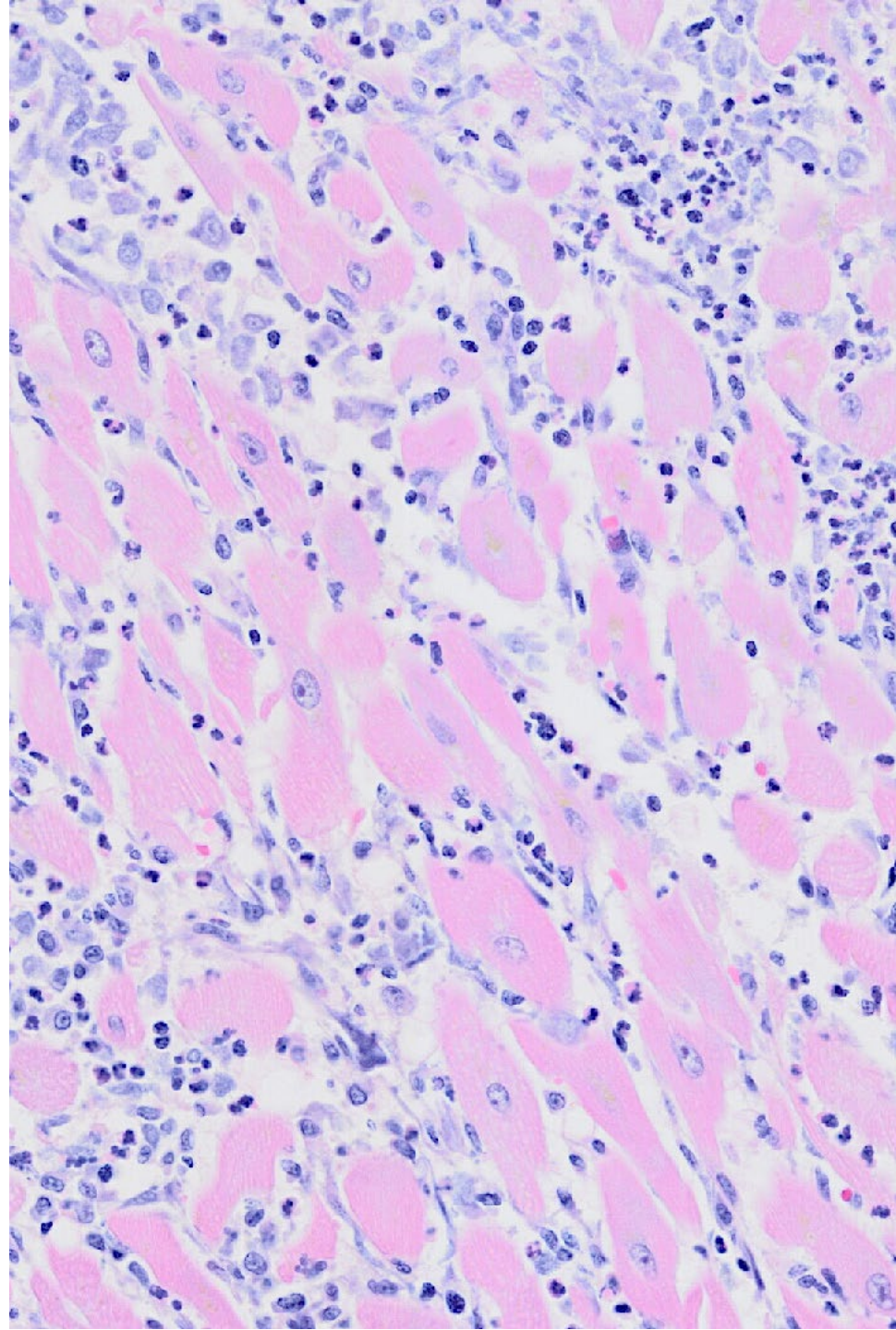
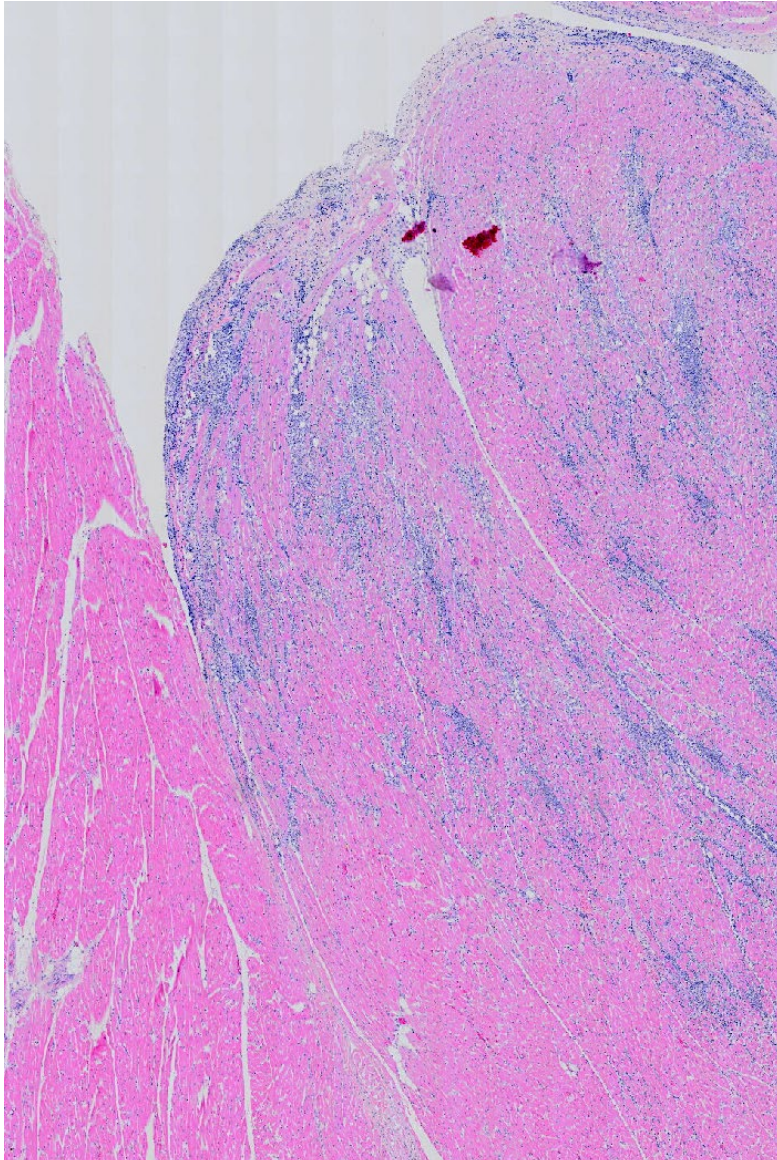
Left ventricular wall with multiple and extensive pale areas



Subepicardium with numerous lymphocytes and plasma cells

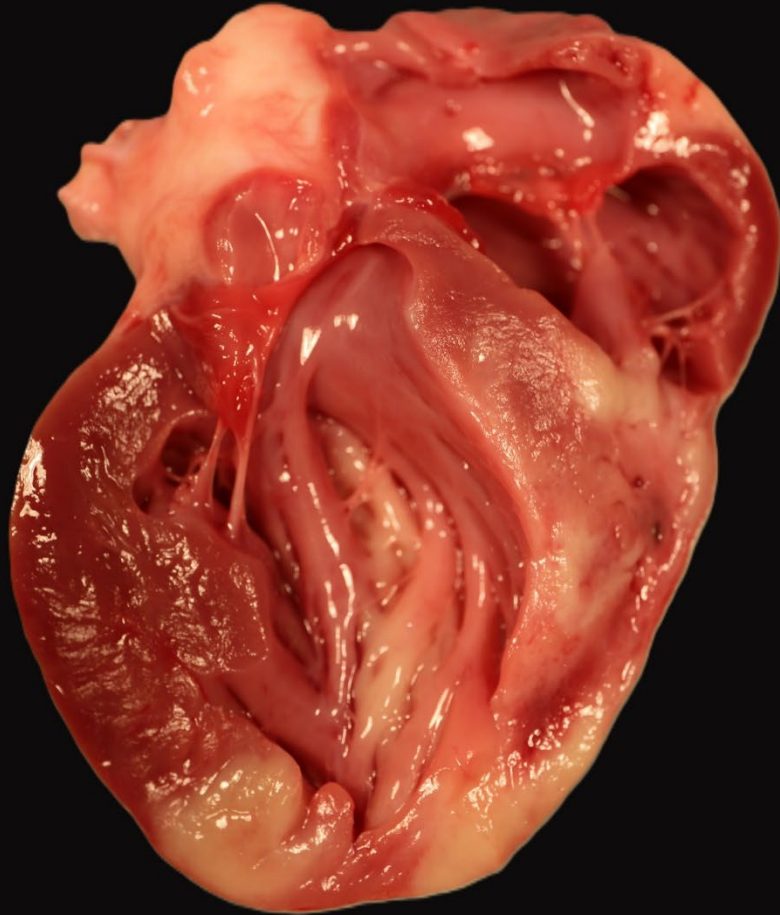


Papillary muscle
Interstitium with macrophages
and neutrophils

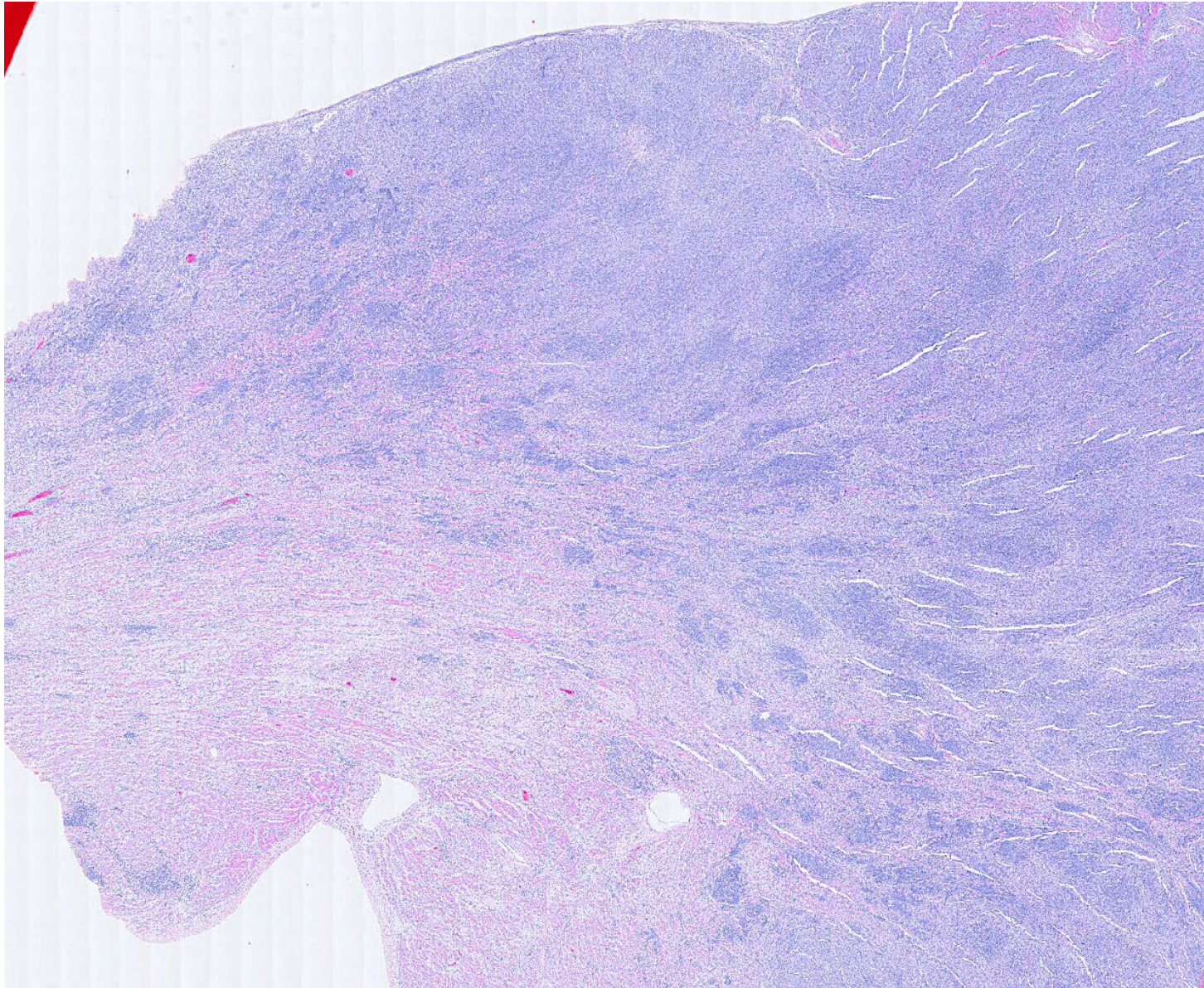


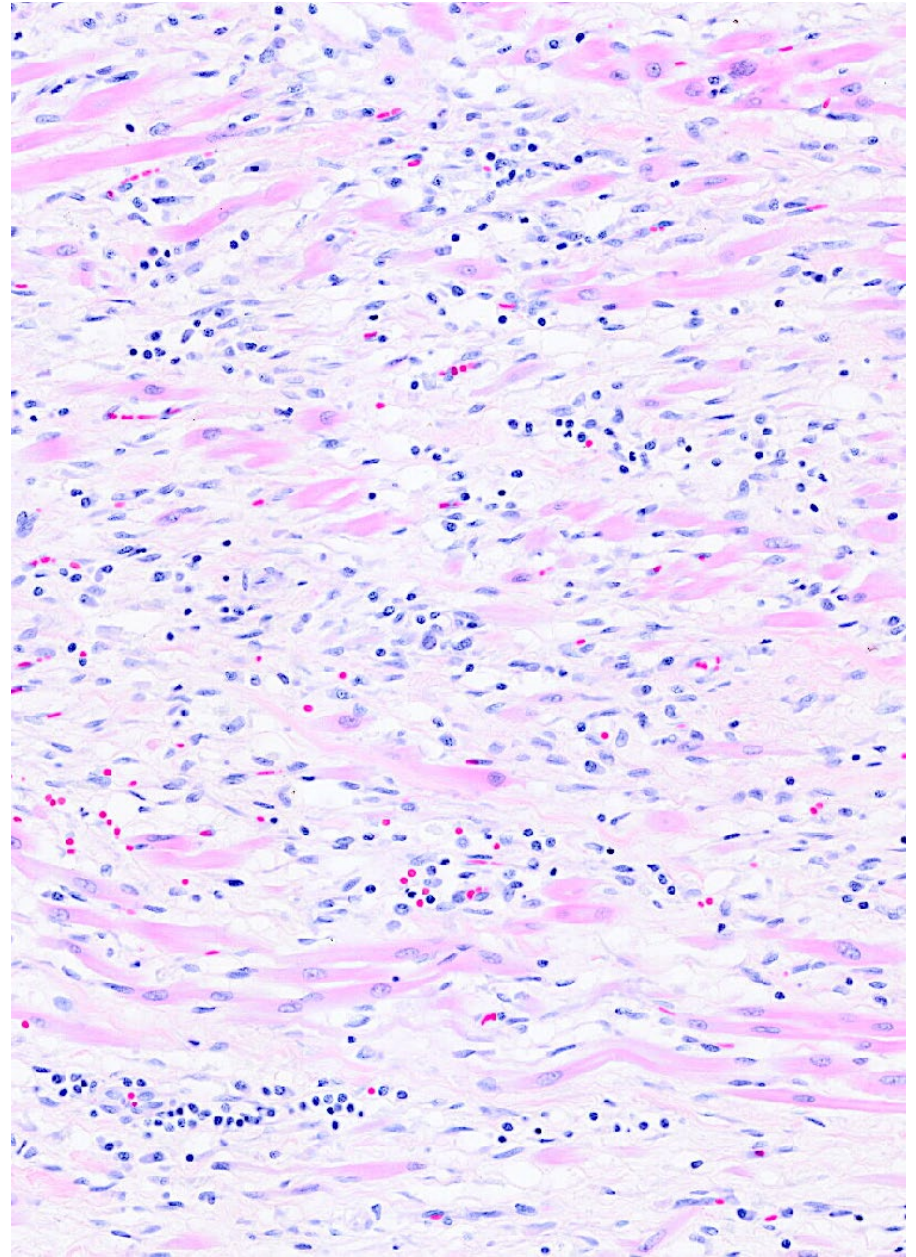
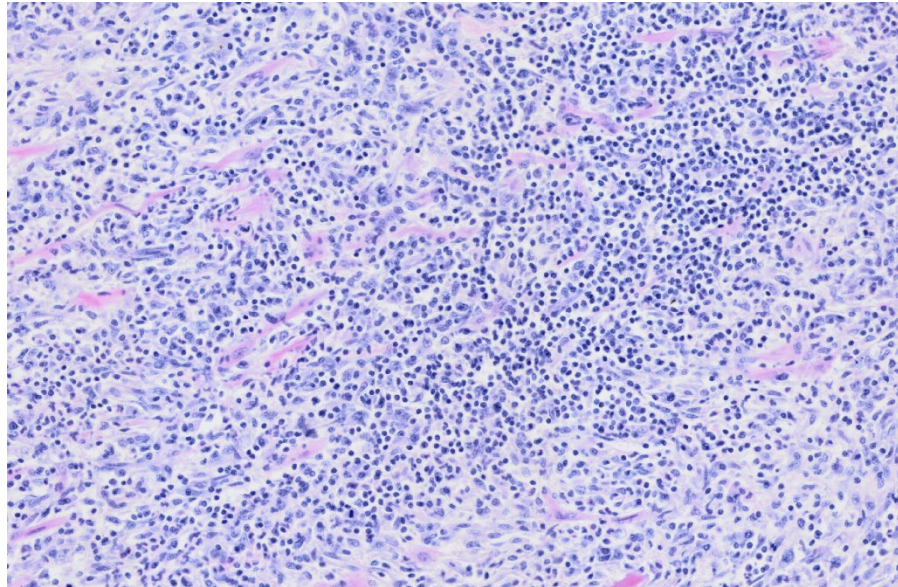
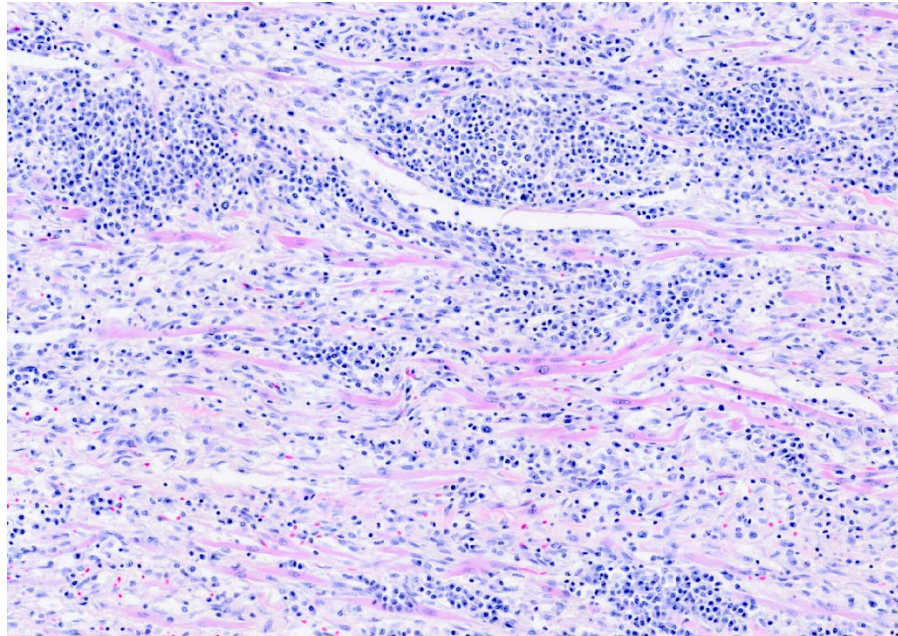
Heart

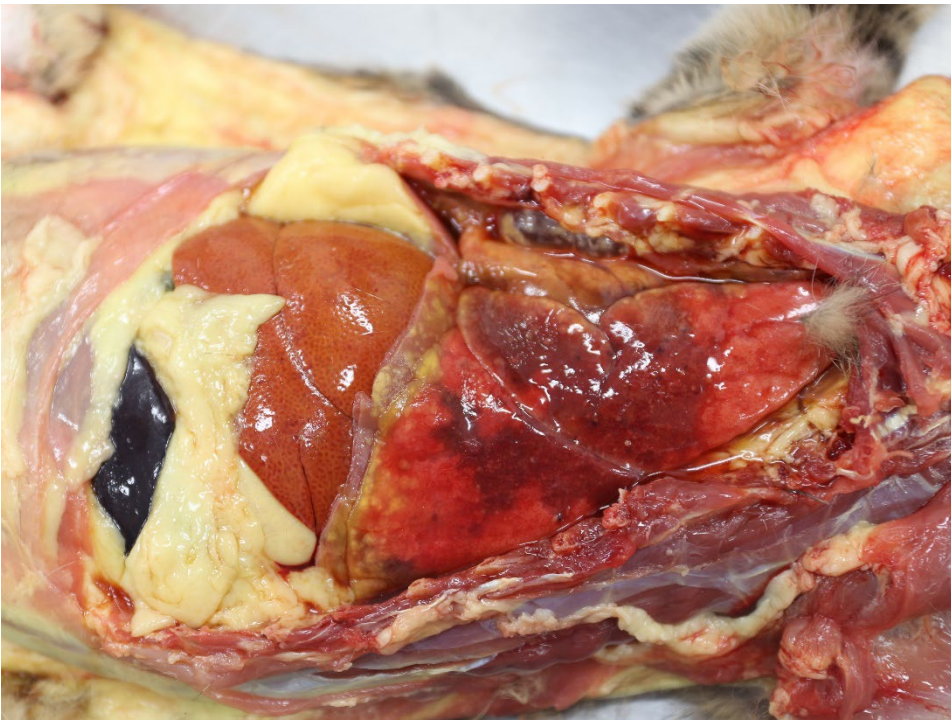
Right and left myocardium with extensive pale tan areas



The myocardium is infiltrated by numerous lymphocytes and plasma cells and replaced by fibrosis

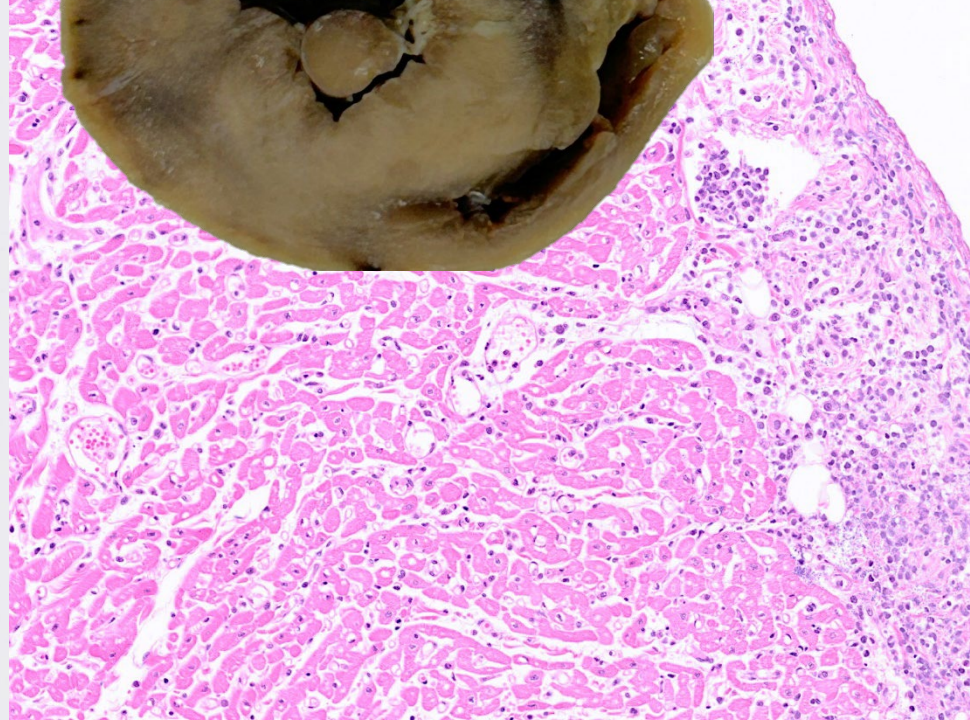
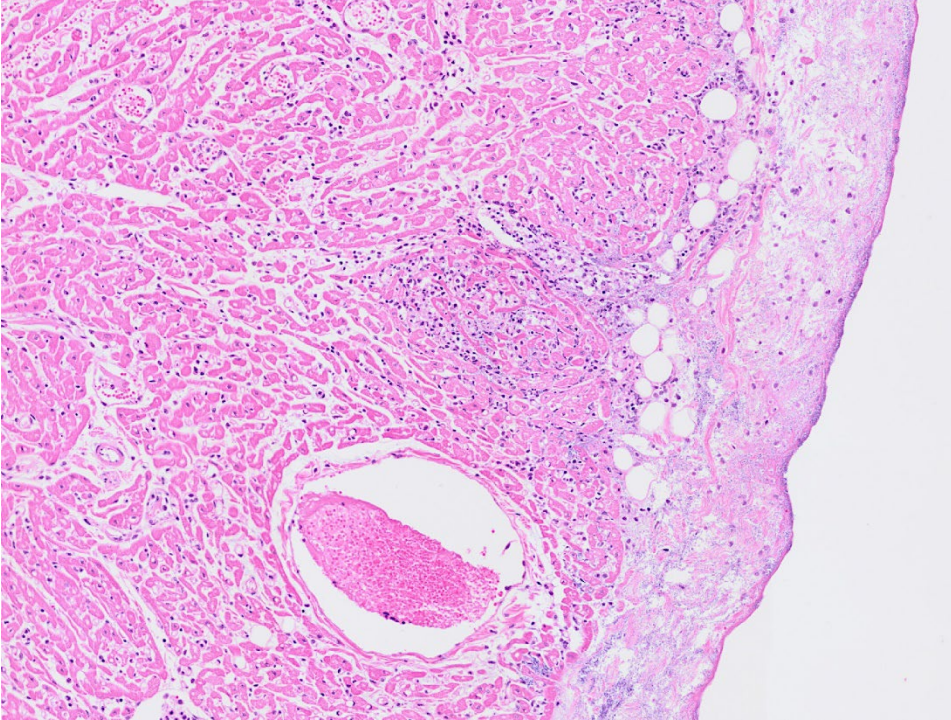






Feline infectious peritonitis
Mutated feline coronavirus

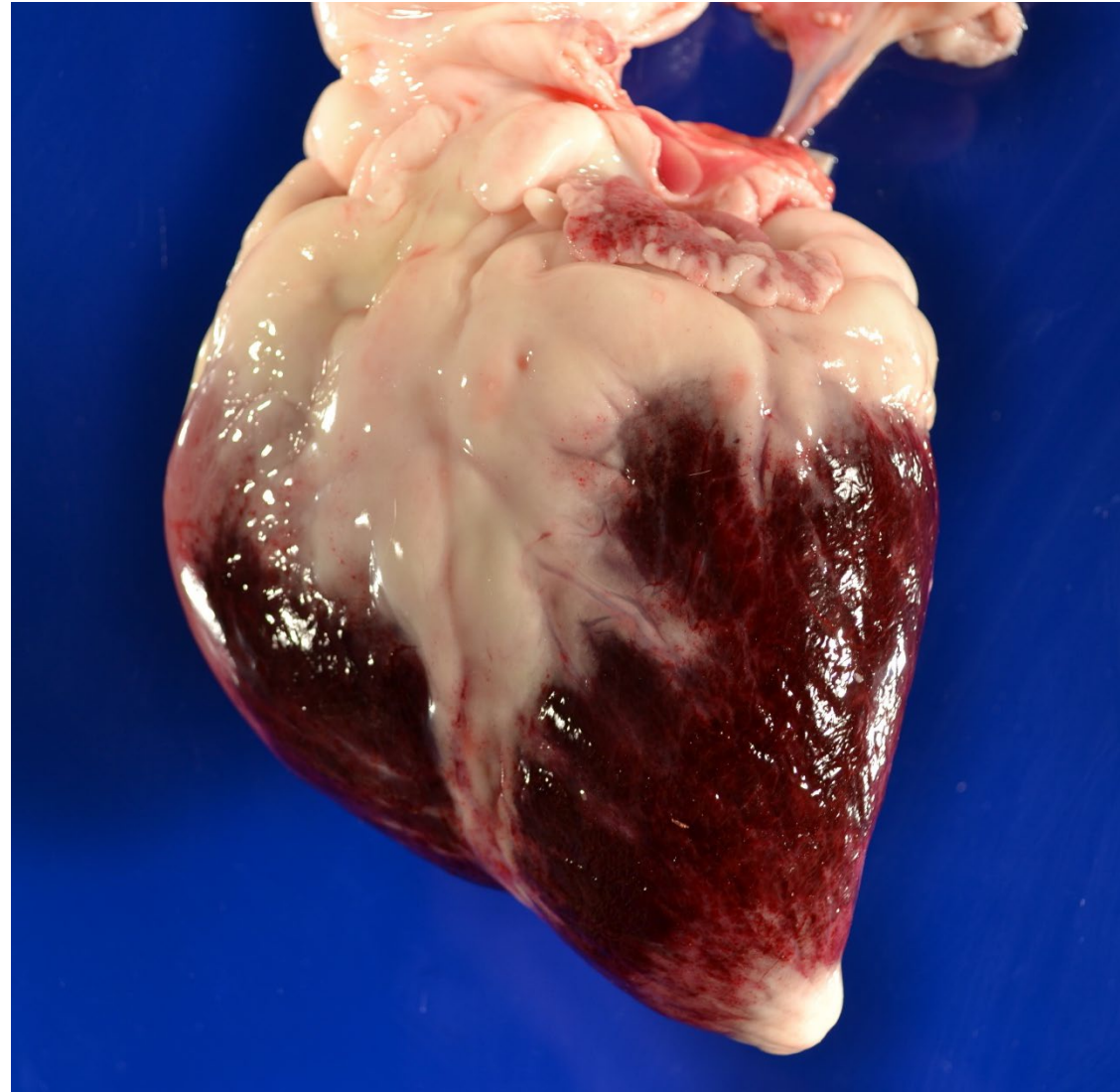
Fibrinous pericarditis



West Nile virus (arbovirus; Flaviviridae) Flaviviral myocarditis

Myocarditis lymphoplasmacytic
with necrosis

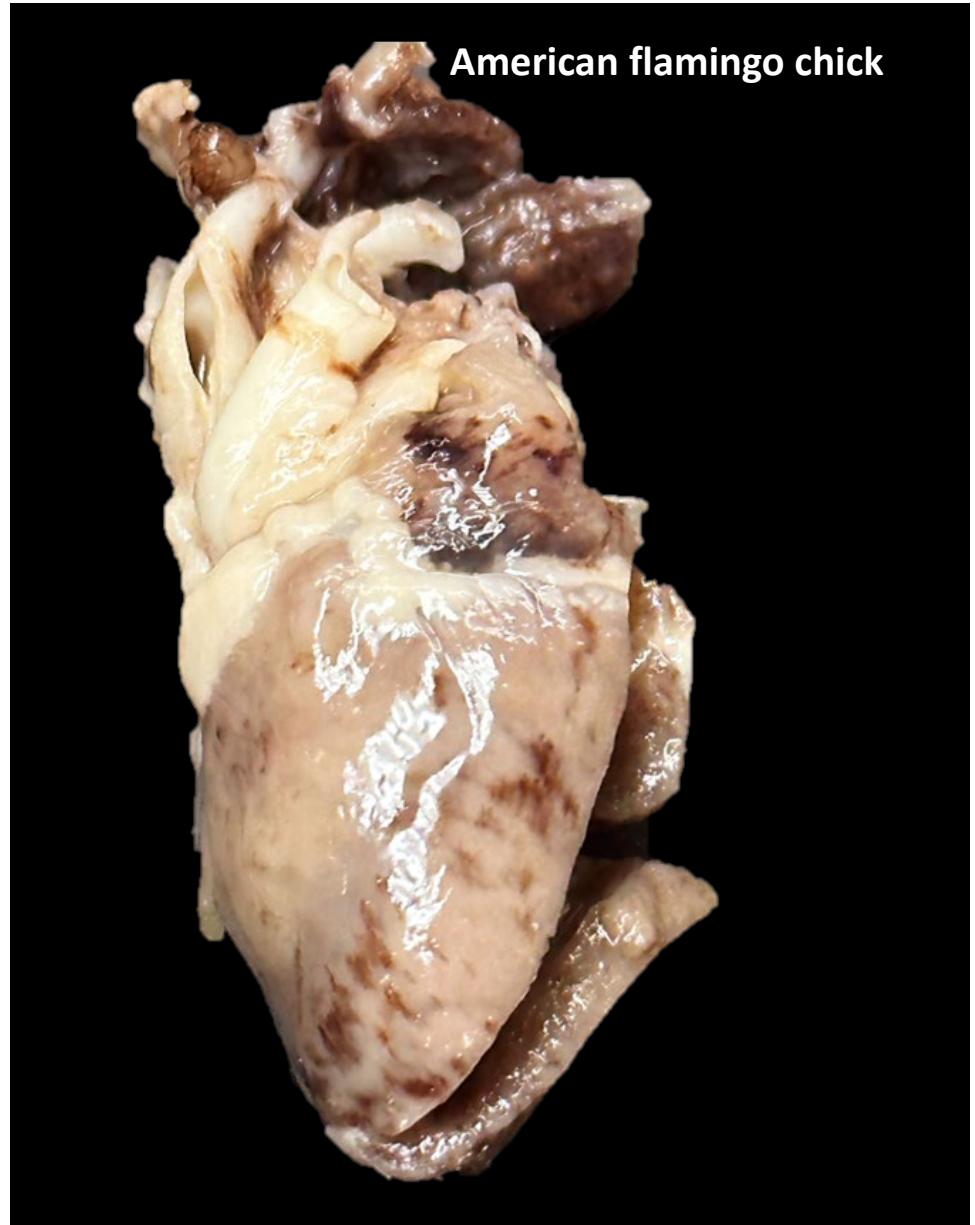
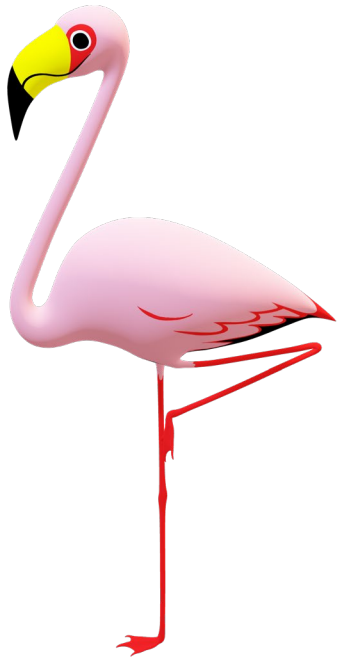
Myocardial hemorrhage



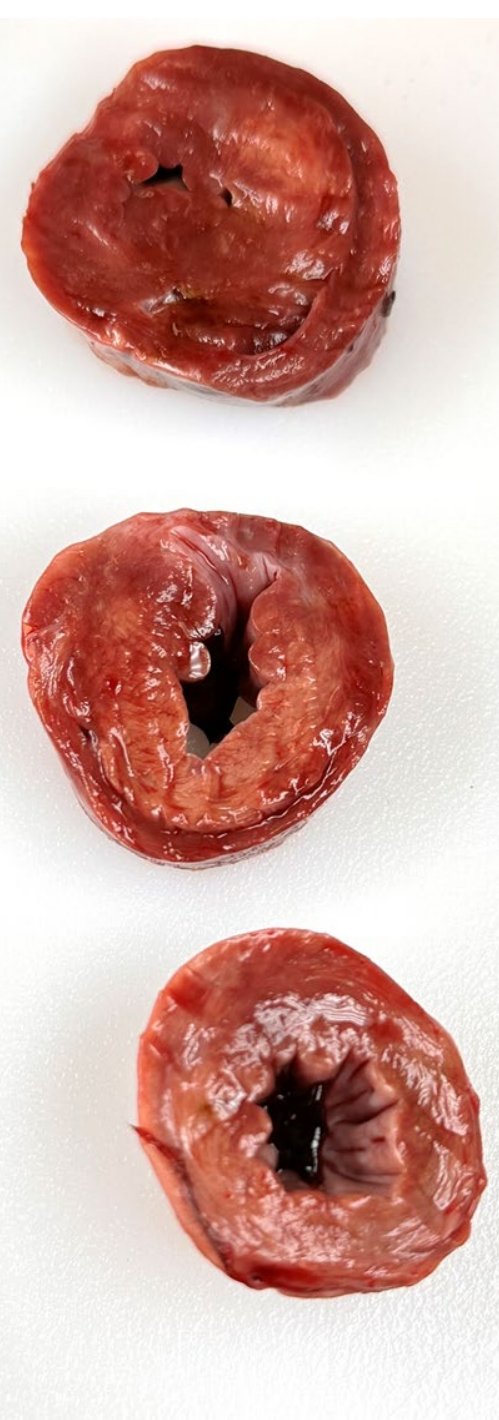
West Nile virus (arbovirus; Flaviviridae) Flaviviral myocarditis

Flamingos are vulnerable to WNV

Severe illness and death



American flamingo chick



OFFICIAL

Bald eagle with chronic active myocarditis from long-term sepsis

No underlying viral etiology



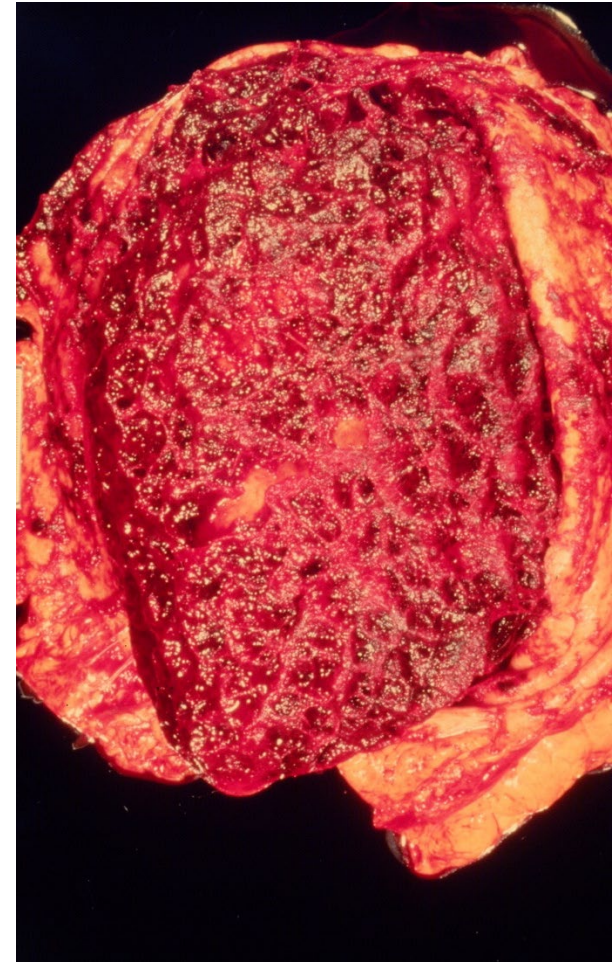
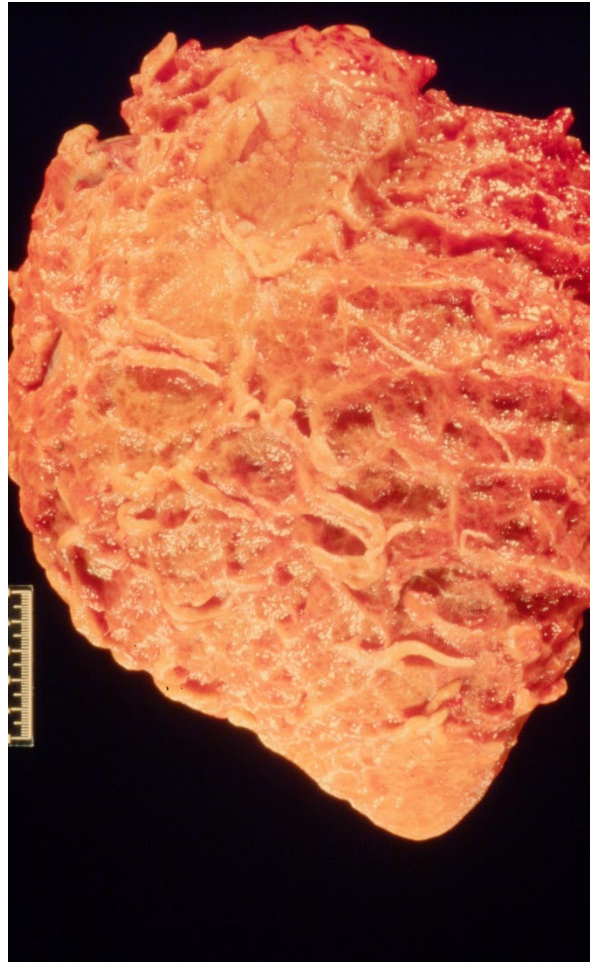
Bacterial infections: wound infections, septic arthritis
Predisposing factors: weakened immune system

OFFICIAL



Equine pericarditis

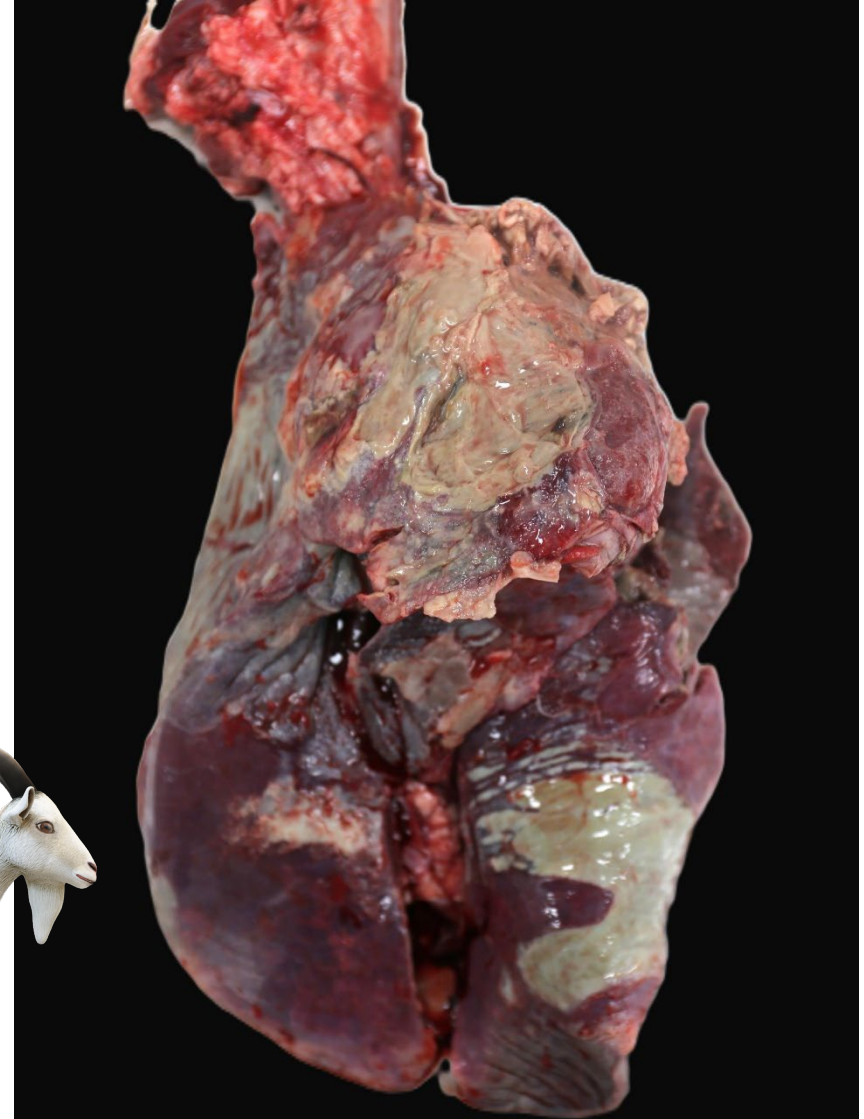
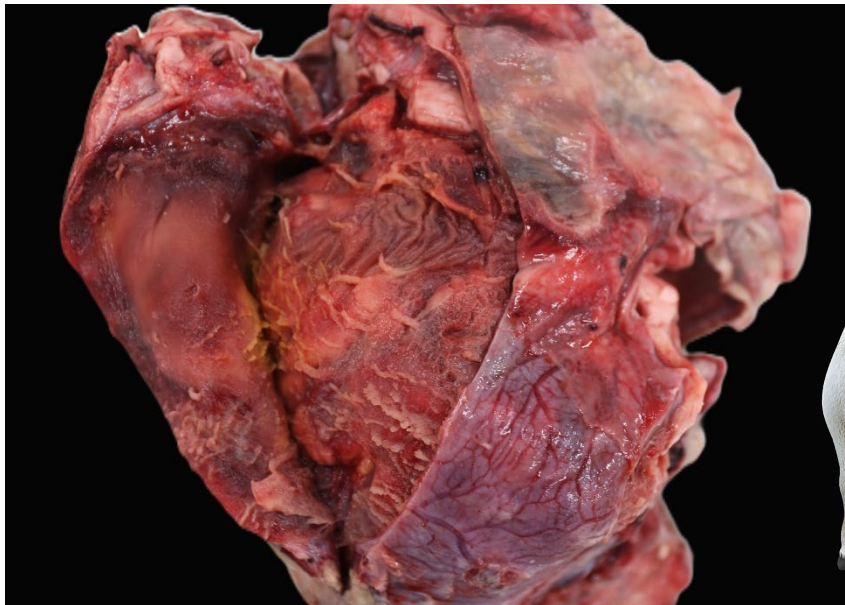
- *Actinobacillus equuli*
 - *Streptococcus* spp.
 - *Pasturella multocida*
 - *Staphylococcus aureus*
 - *Pseudomonas* spp.
 - *Acinetobacter*
 - *Salmonella*
 - *Klebsiella pneumoniae*
- Hematogenous infection
- Septicemia



Fibrinous pericarditis

Aspiration pneumonia

Inflammation extend to the pericardium-----fibrinous pericarditis/constrictive pericarditis

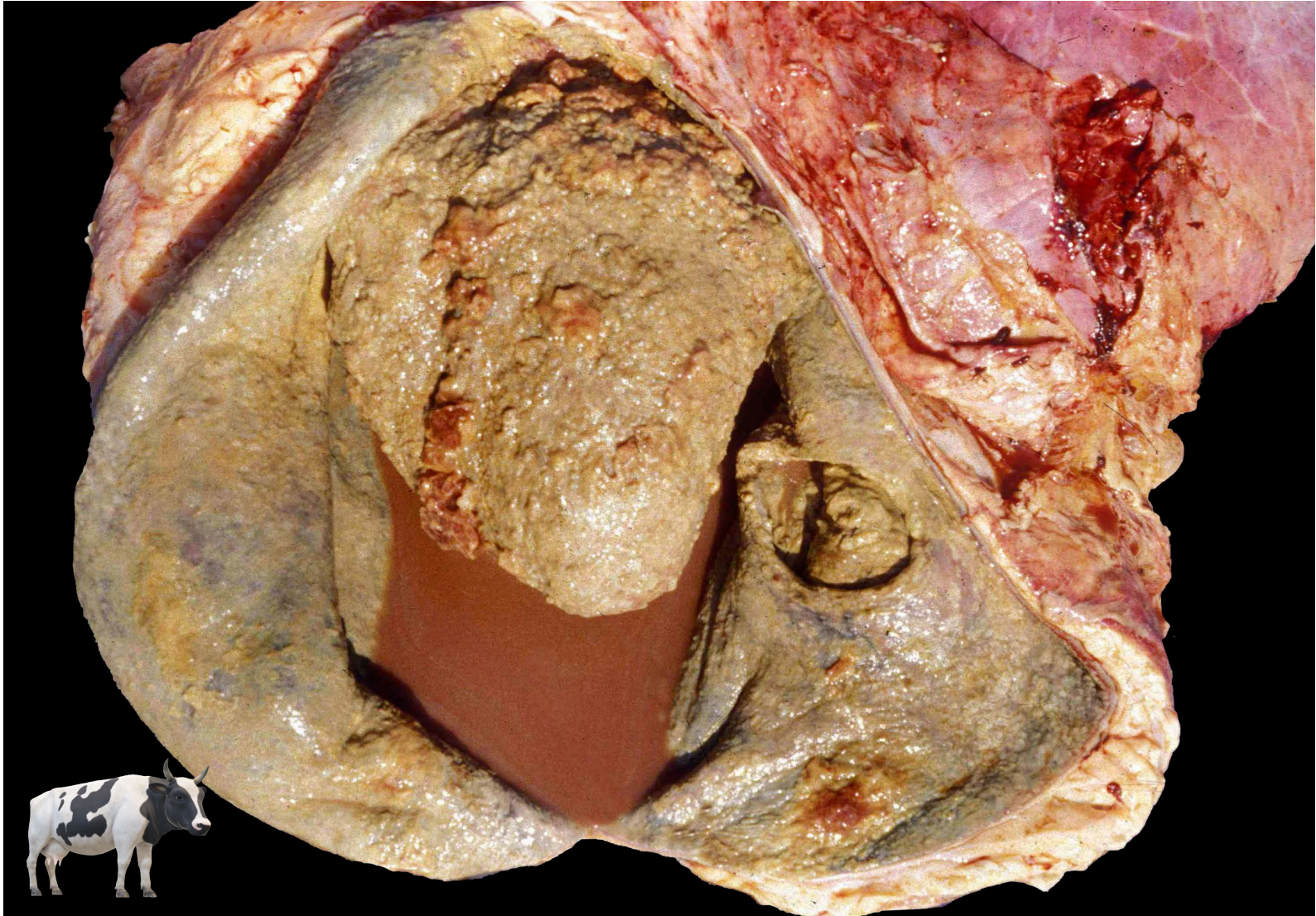


Traumatic reticulopericarditis

Trueperella pyogenes

Fusobacterium necrophorum

Pericarditis and epicarditis, fibrinosuppurative



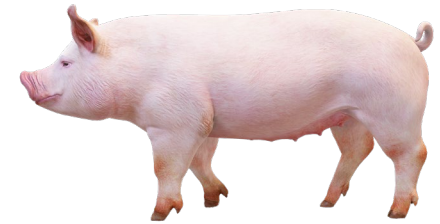
Glaesserella parasuis

OFFICIAL

Meningoencephalitis

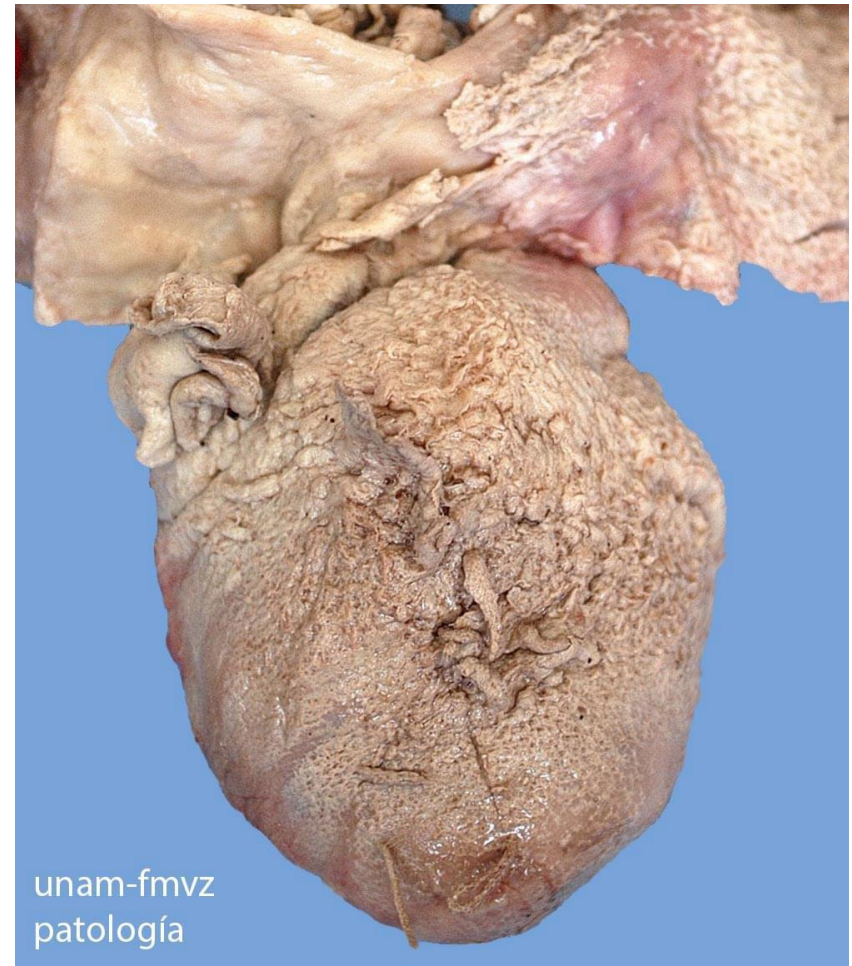
Polyserositis

Polyarthritis



Vasculitis

Serofibrinous/fibrinopurulent exudate



unam-fmvz
patología

OFFICIAL



Pleural emphyema Pleuropneumonia

Streptococcus equi subsp. *zooepidemicus*

Pasteurella

Klebsiella

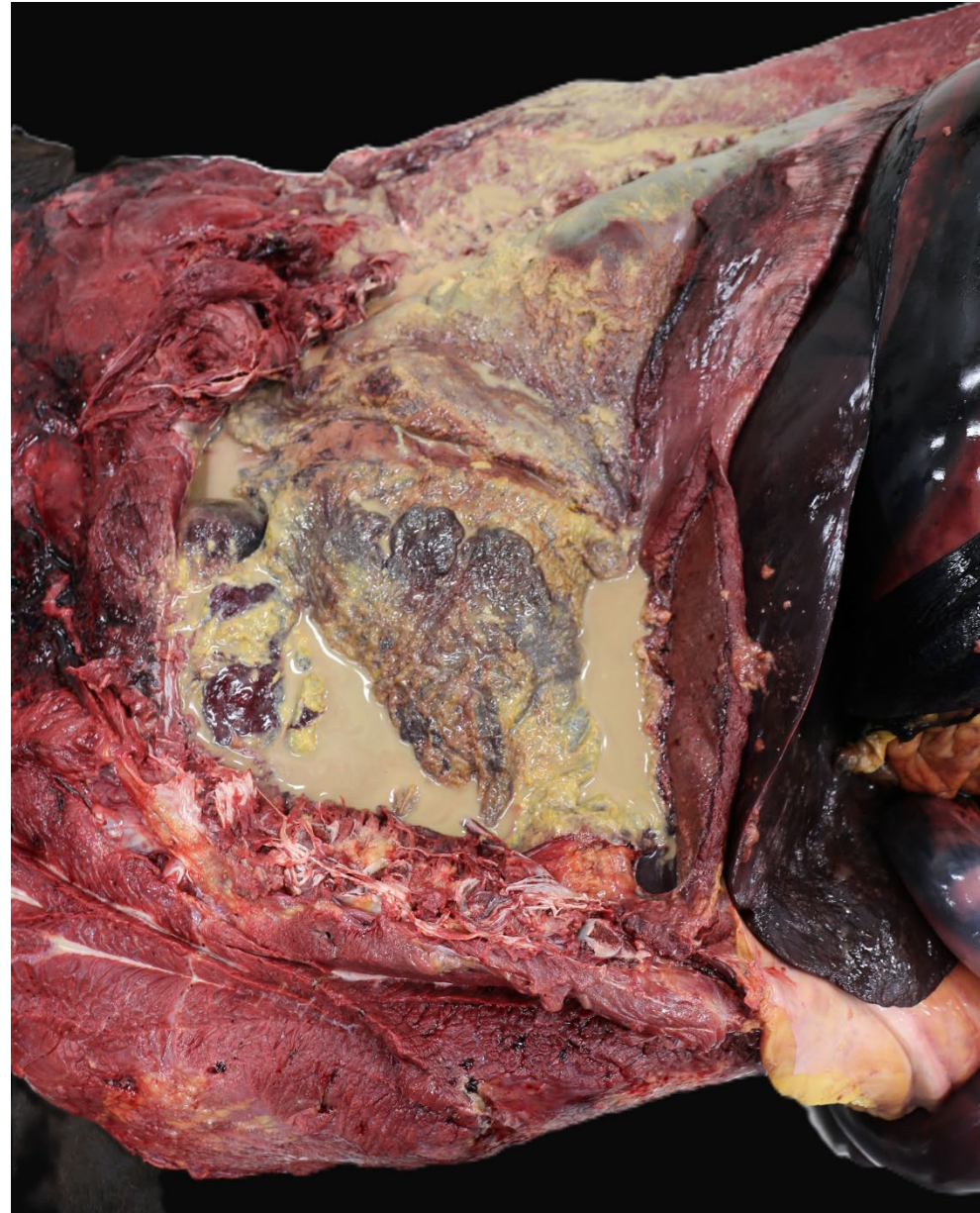
Enterobacter

Actinobacillus

Bacterioides

Fusobacterium

- Extension of bacterial pneumonia
- Lung abscesses
- Penetrating thoracic wounds
- Migrating foreign bodies

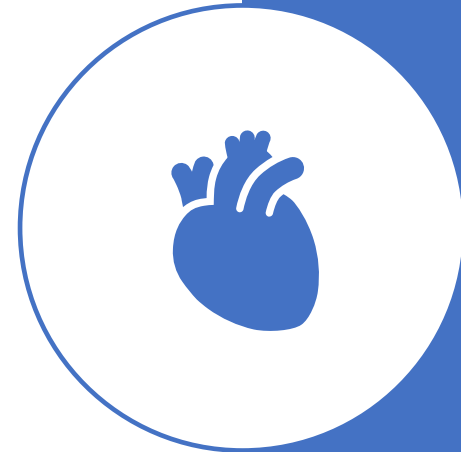


Non-infectious myocardial disease/dysfunction

Myocardium necrosis

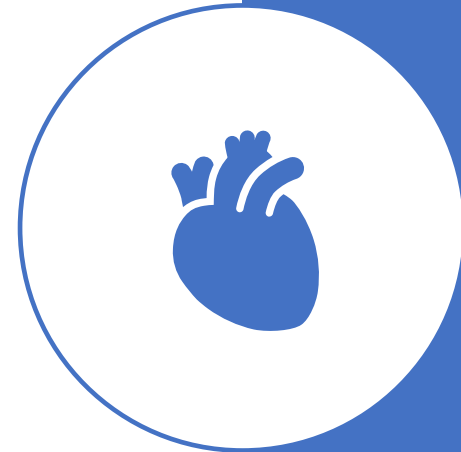
Cardiotoxins:

- Ionophores
- Catecholamines
- Antineoplastic meds:
 - Doxorubicin
 - Cyclophosphamide
- Doxycycline
- Gossypol
- Toxic plants:
 - *Lantana camara*
 - *Nerium oleander*
 - *Cassia occidentalis*
 - *Vicia villosa*
- Cantharidin (blister beetle)



Non-infectious myocardial disease/dysfunction

- Metabolic: hyperthyroidism
- Nutritional deficiency: Vitamin E-selenium, taurine, thiamine
- Genetic: Porcine stress syndrome
- Neuromuscular: Muscular dystrophy
- Storage diseases: Glycogen storage diseases, amyloidosis



Nutritional myopathy

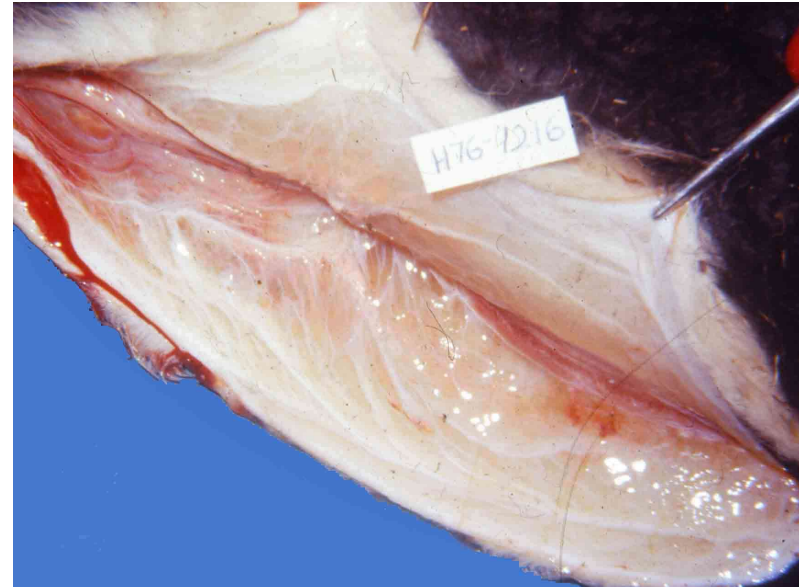
Selenium deficiency

Vitamin E deficiency without a deficiency in selenium is uncommon in mammals

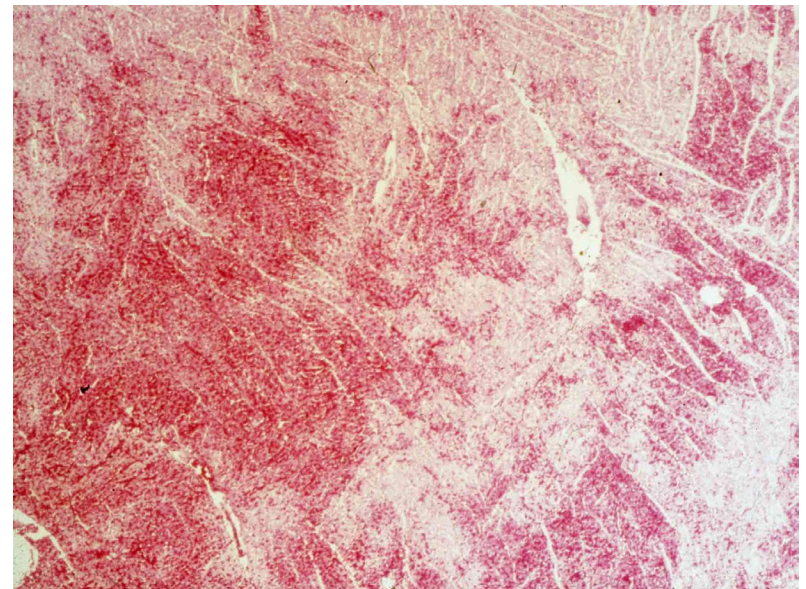


Myonecrosis, myodegeneration

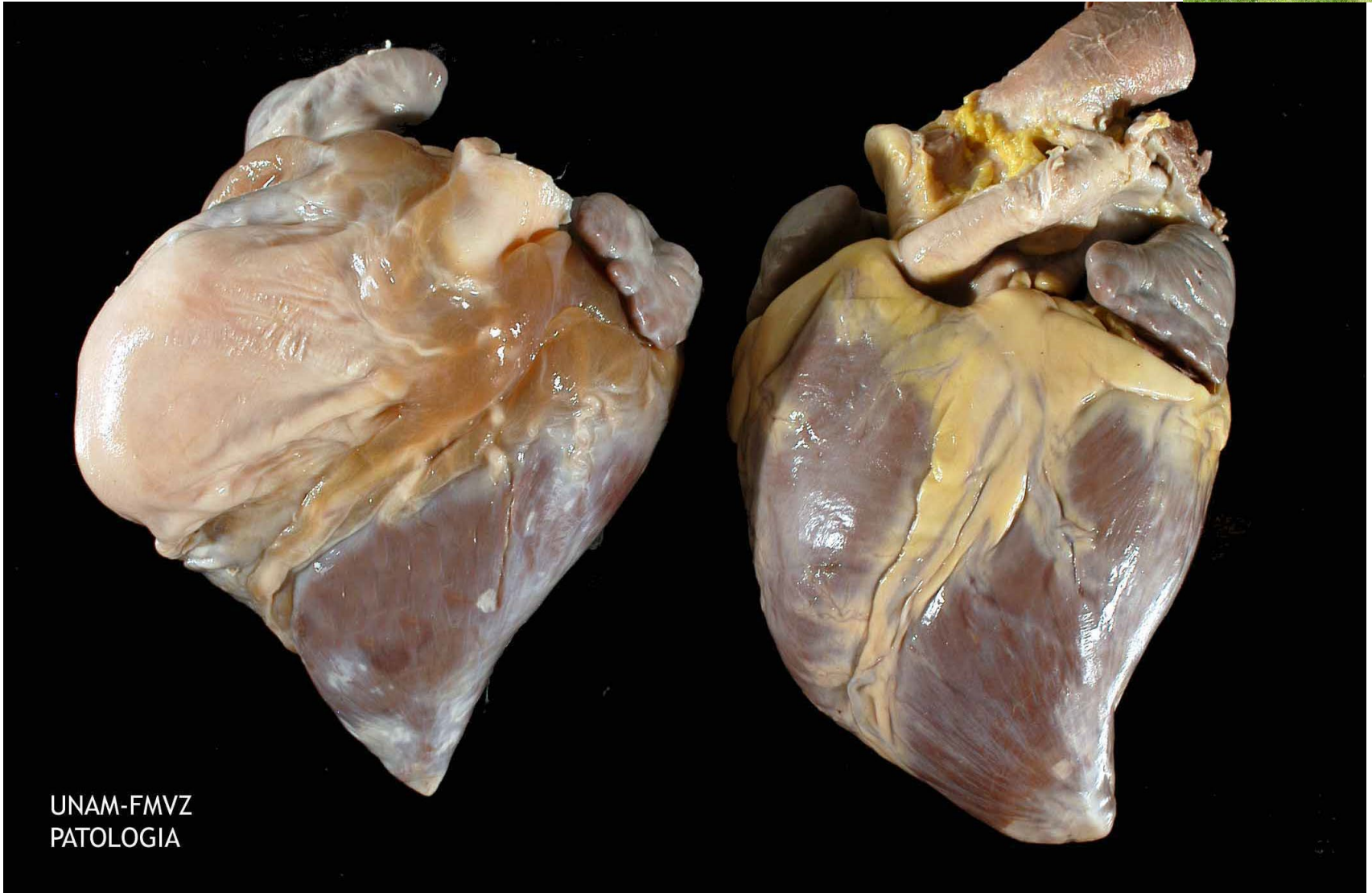
Mineralization



Skeletal muscle



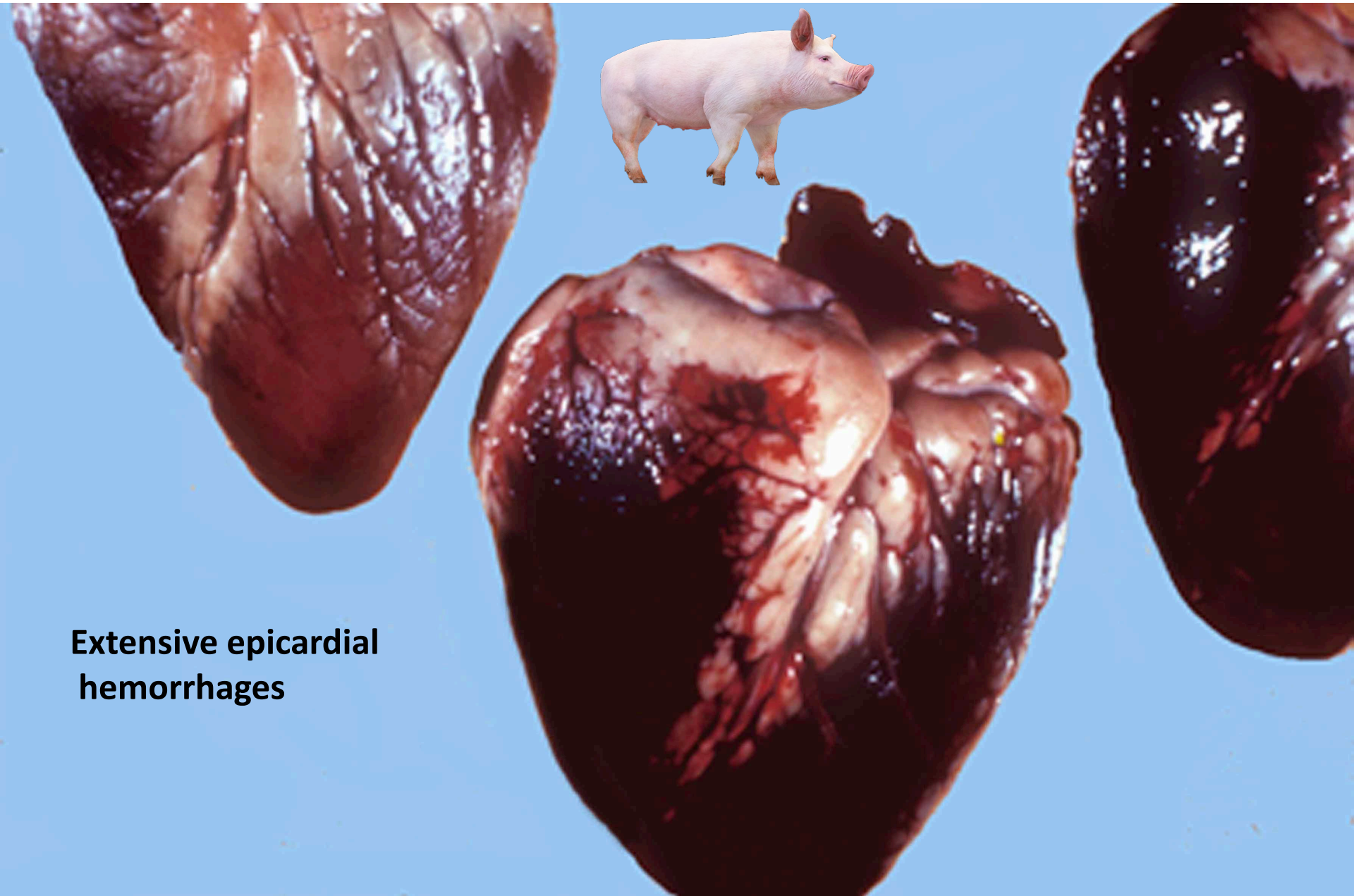
Vitamin E/selenium deficiency

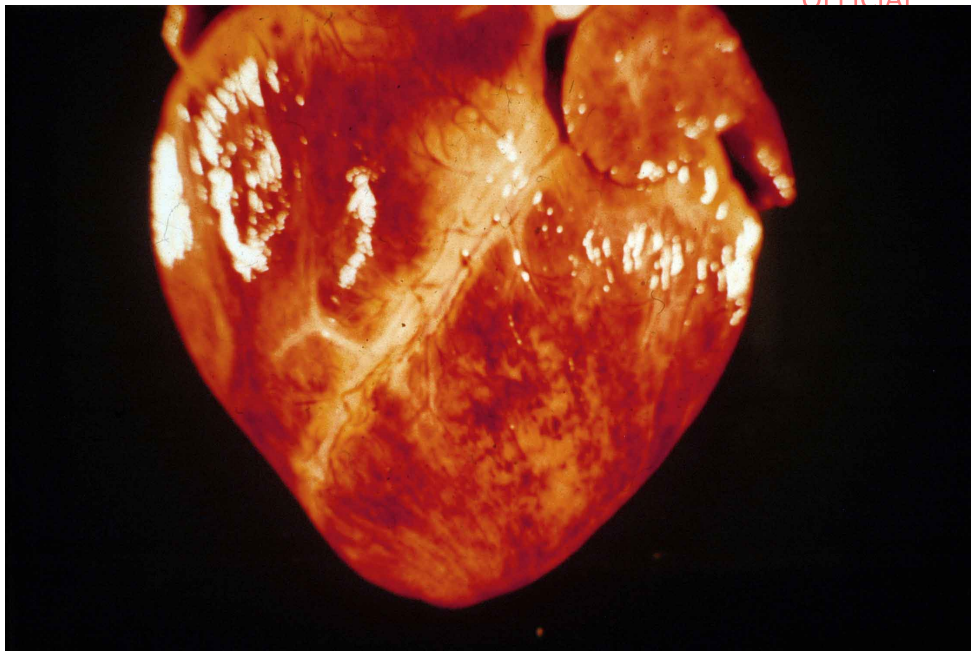


Vitamin E/selenium deficiency

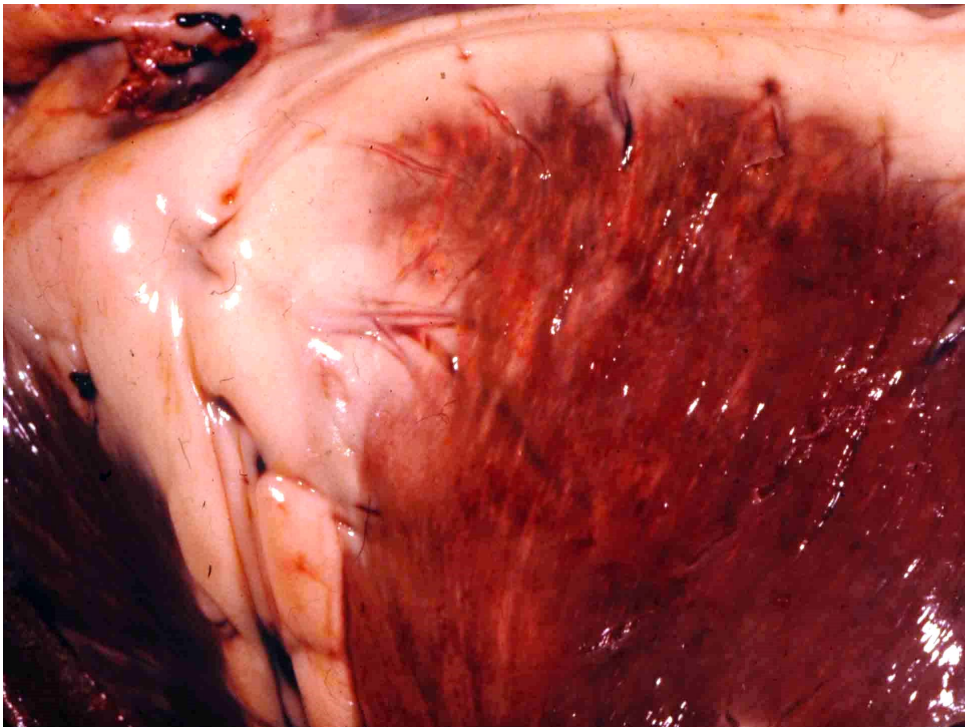
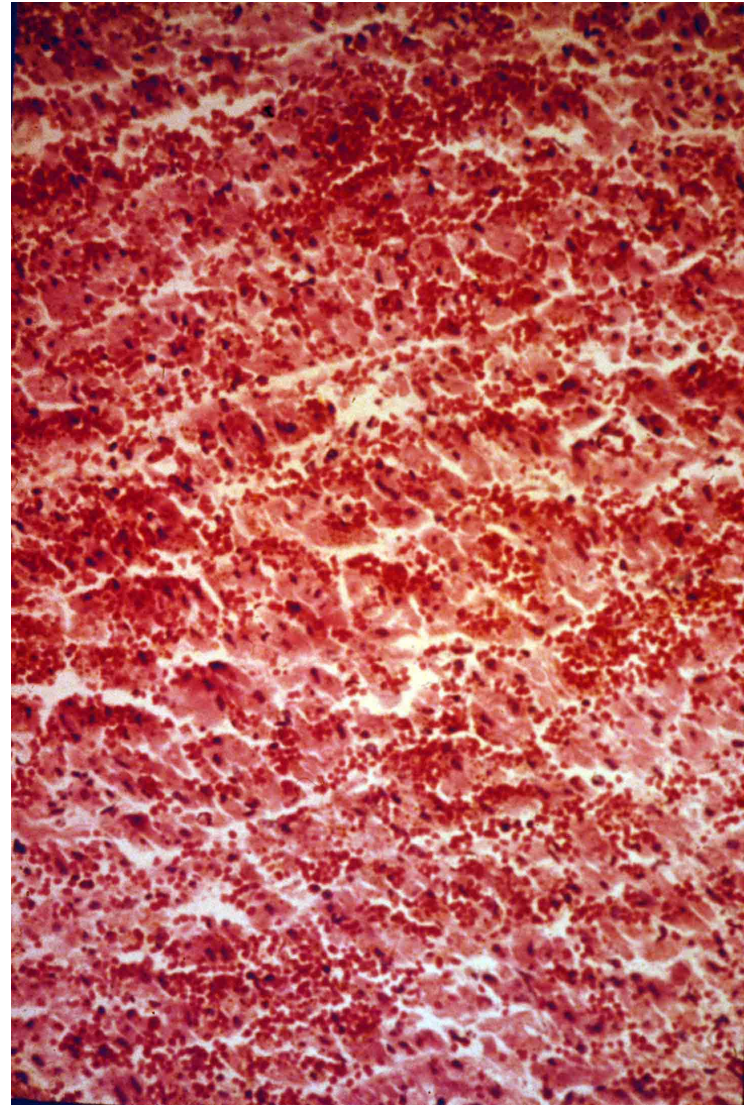


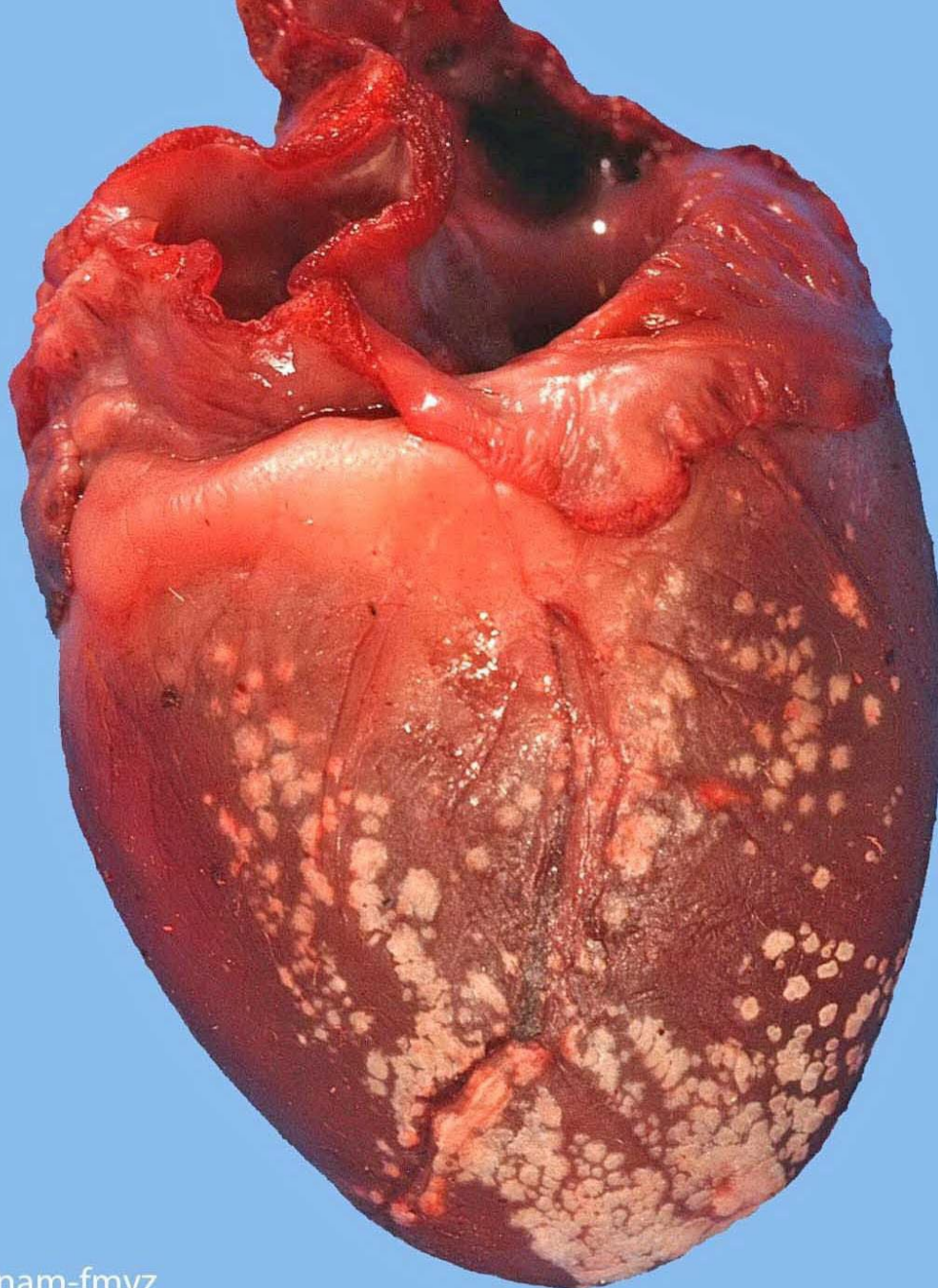
**Extensive epicardial
hemorrhages**





Hemorrhages and pale streaks and patches of epicardial necrosis

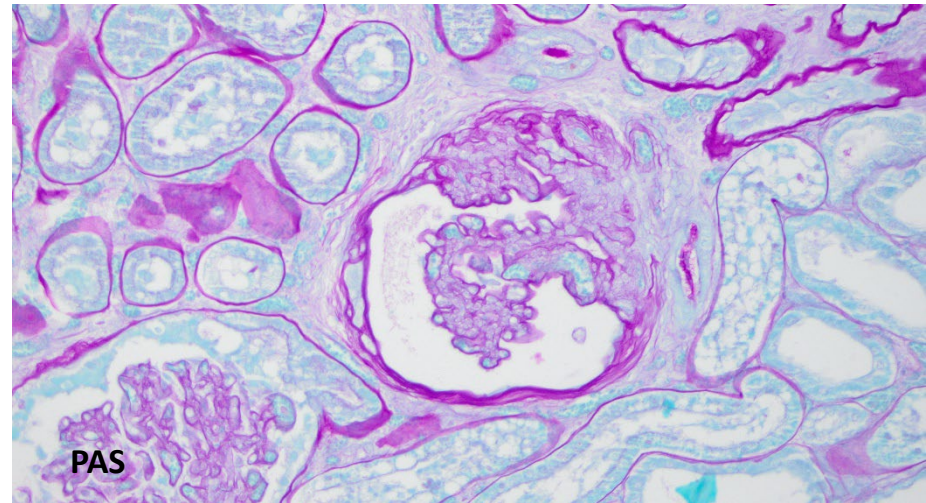
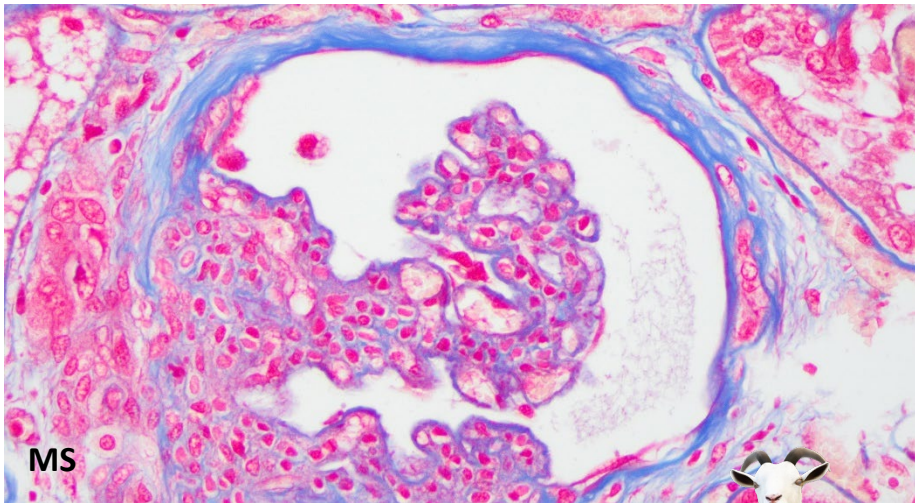
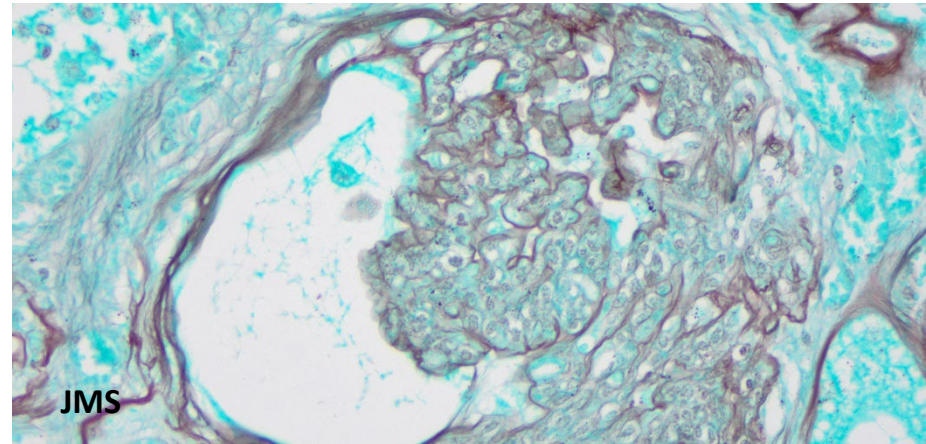
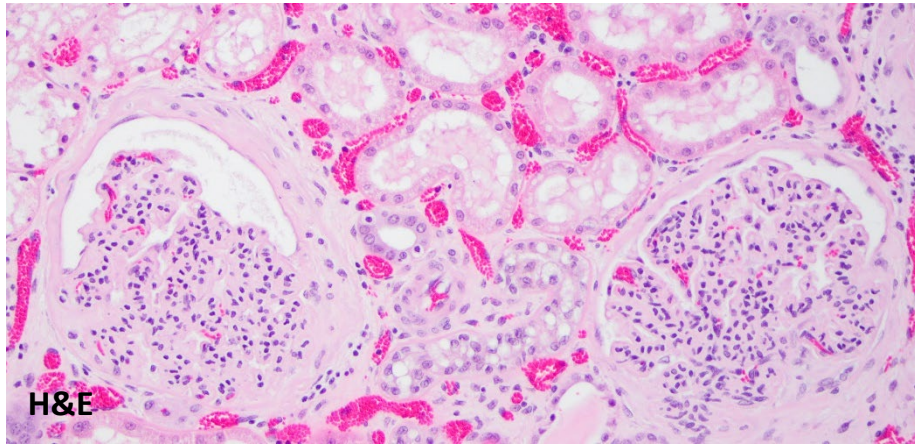


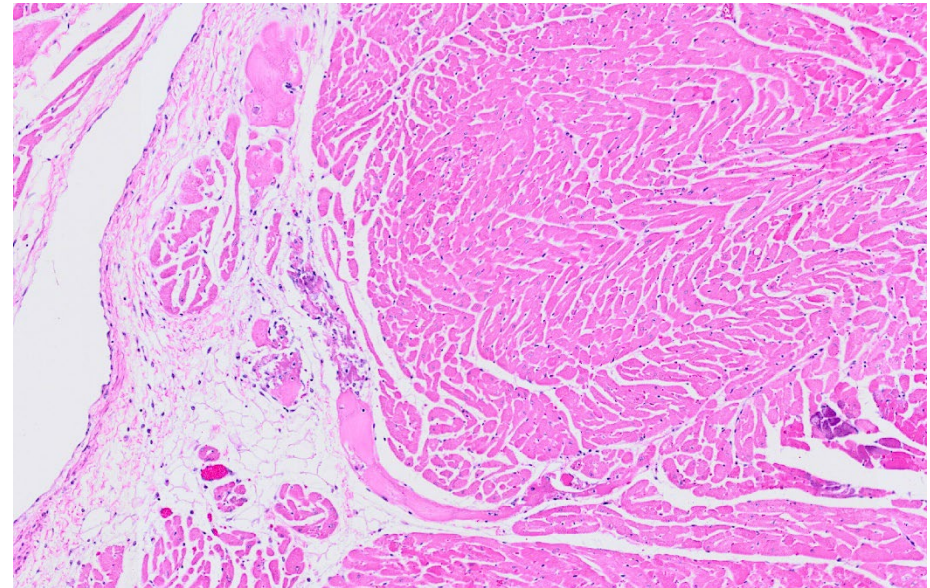
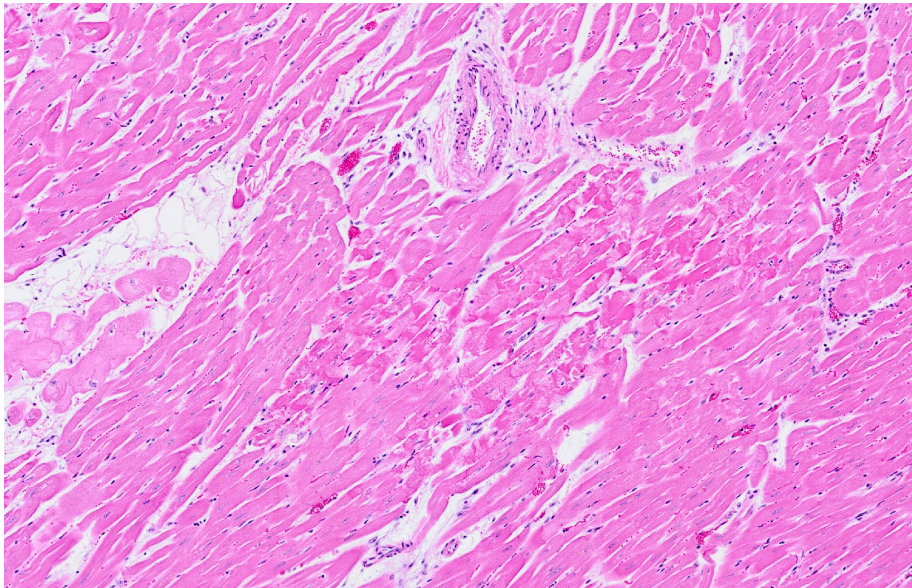
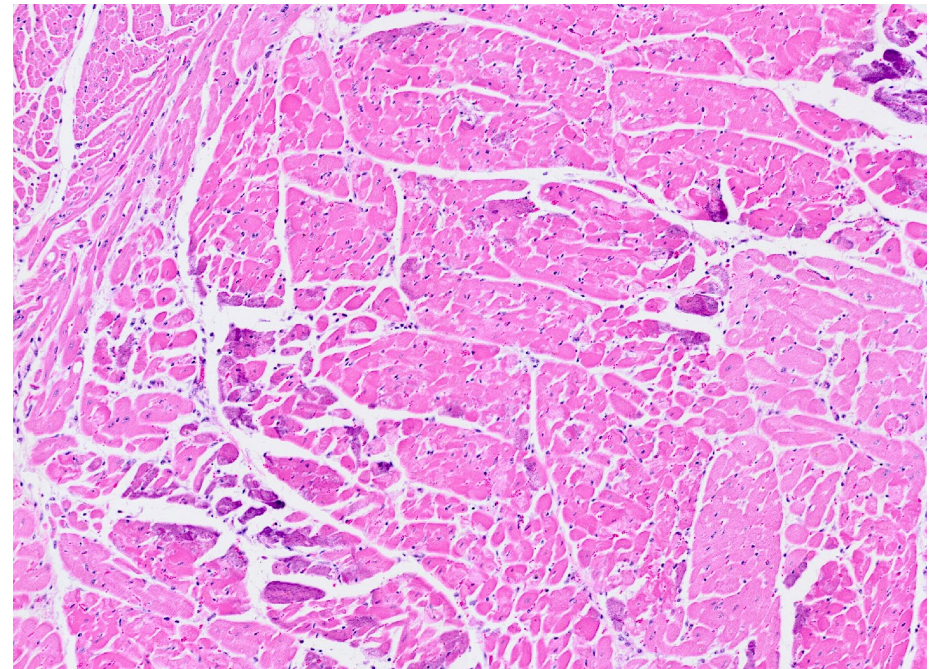
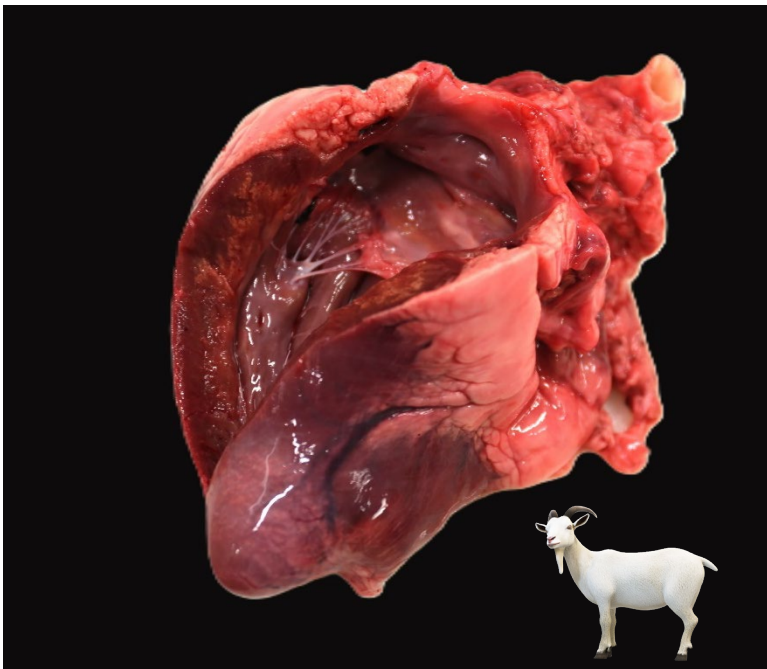


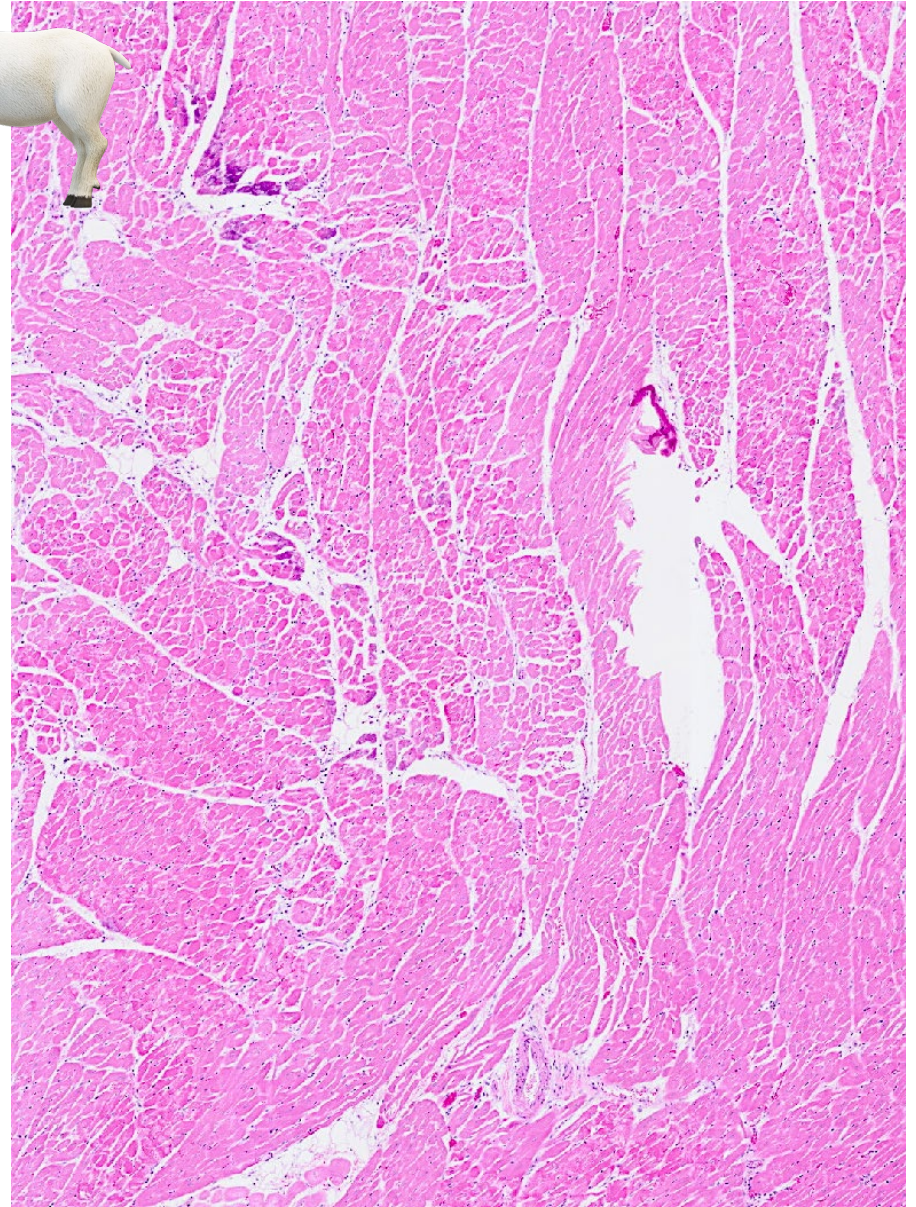
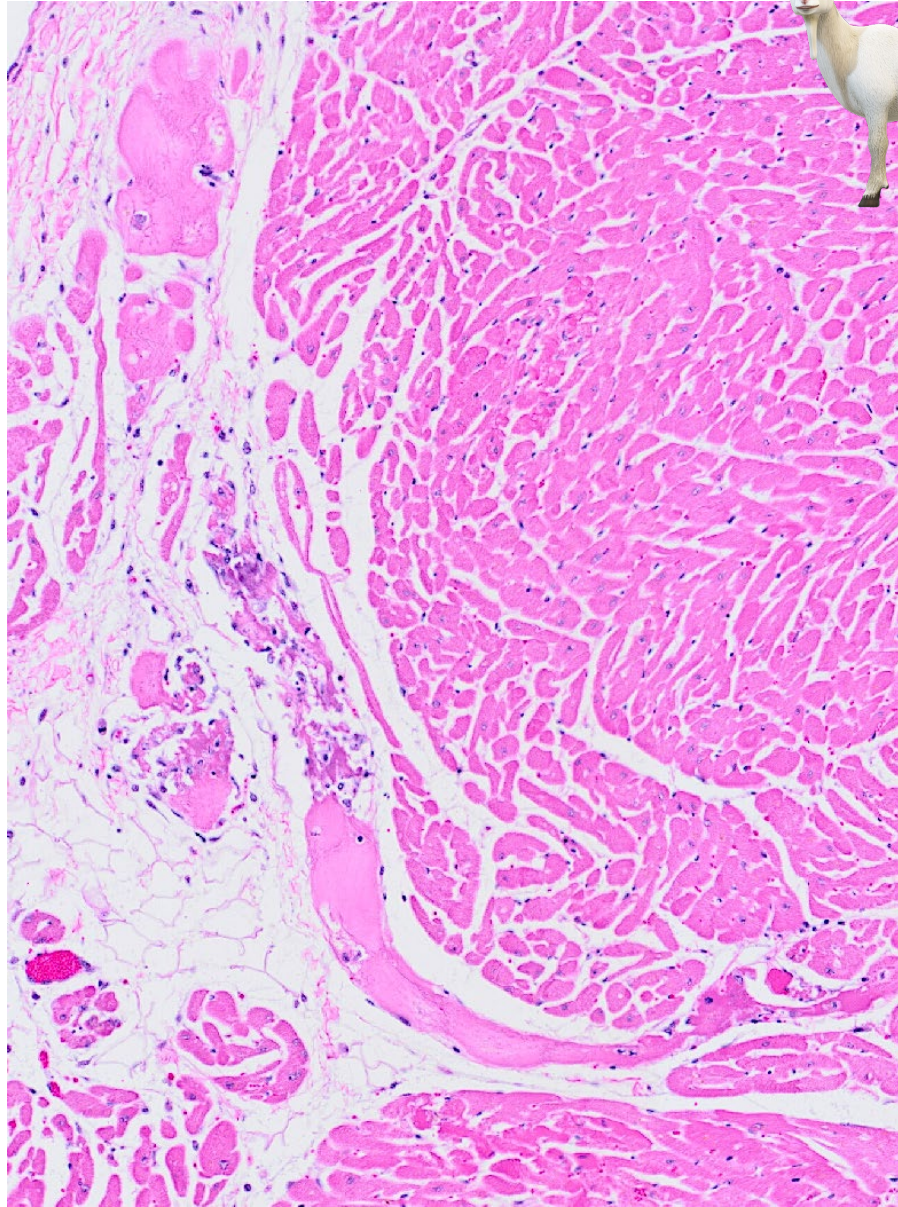
Mineralization of the heart

- Several species (cat, dog, cow)
- Idiopathic: no tissue injury
- Dystrophic
- Metastatic: chronic renal failure, hyperparathyroidism, hypervitaminosis D, bone disease

Glomerulopathy membranoproliferative

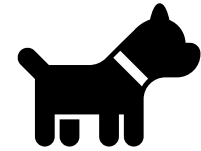






Myocardial necrosis

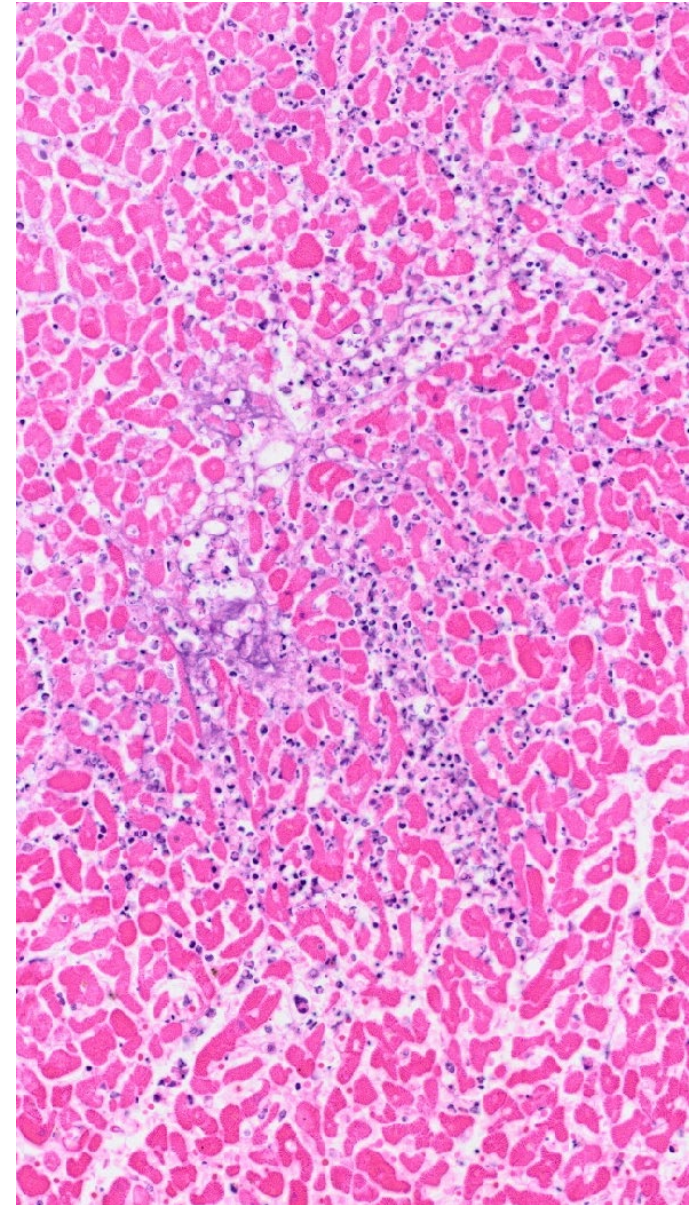
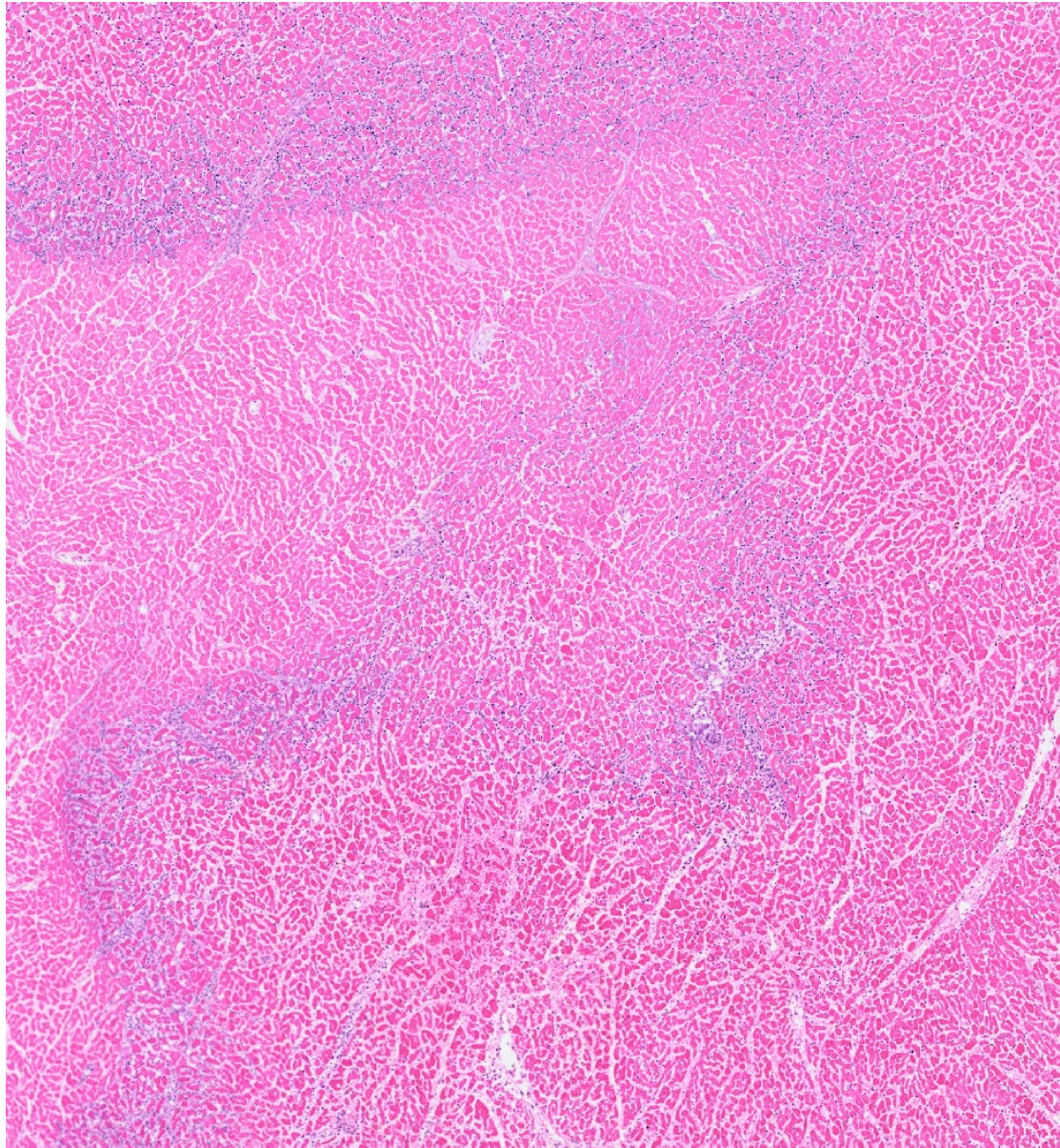
Immunomediated thrombocytopenia

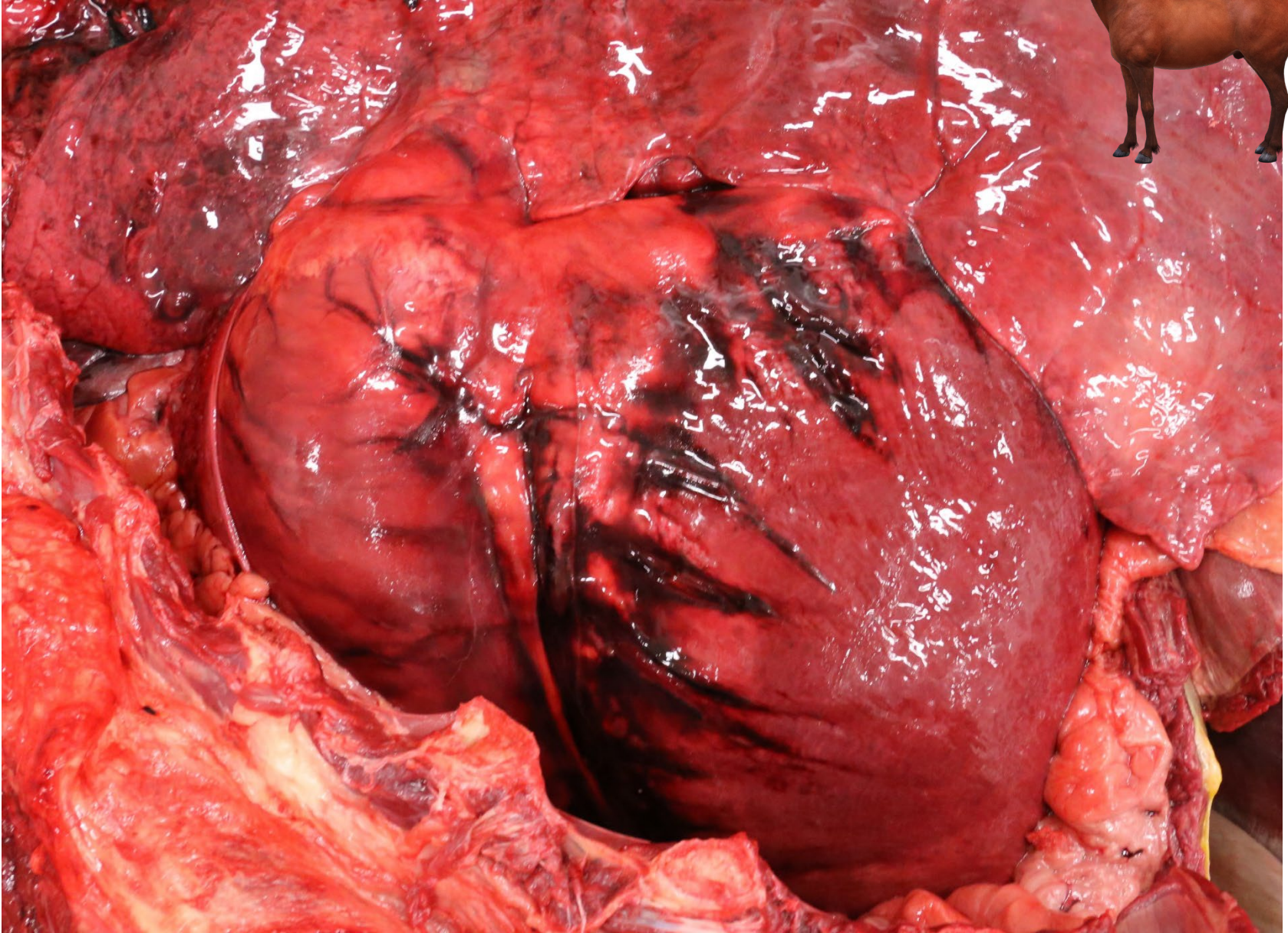


Endothelial damage induced by autoantibodies directed against antigens present on both platelets and coronary endothelial cells

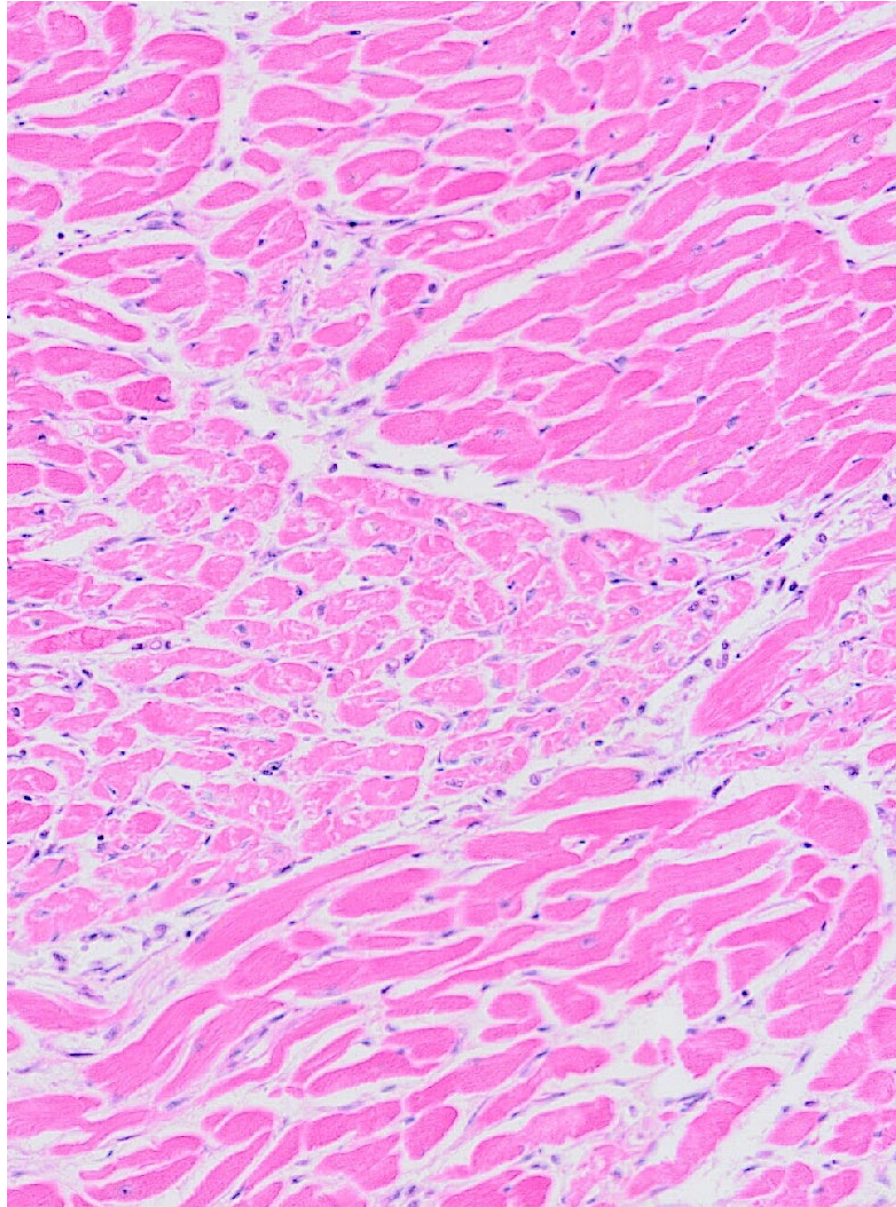


Myocardial necrosis
Immunomediated thrombocytopenia



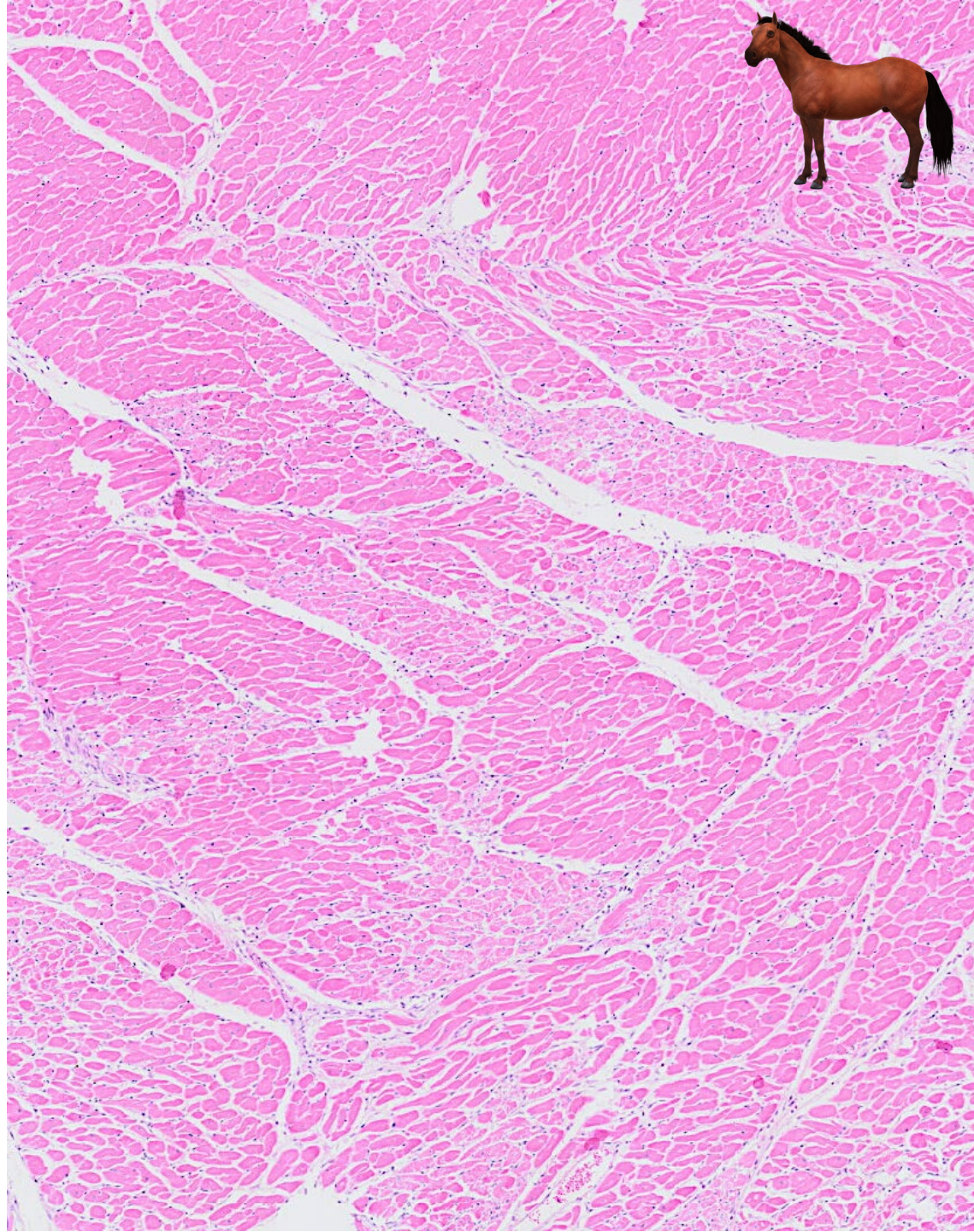


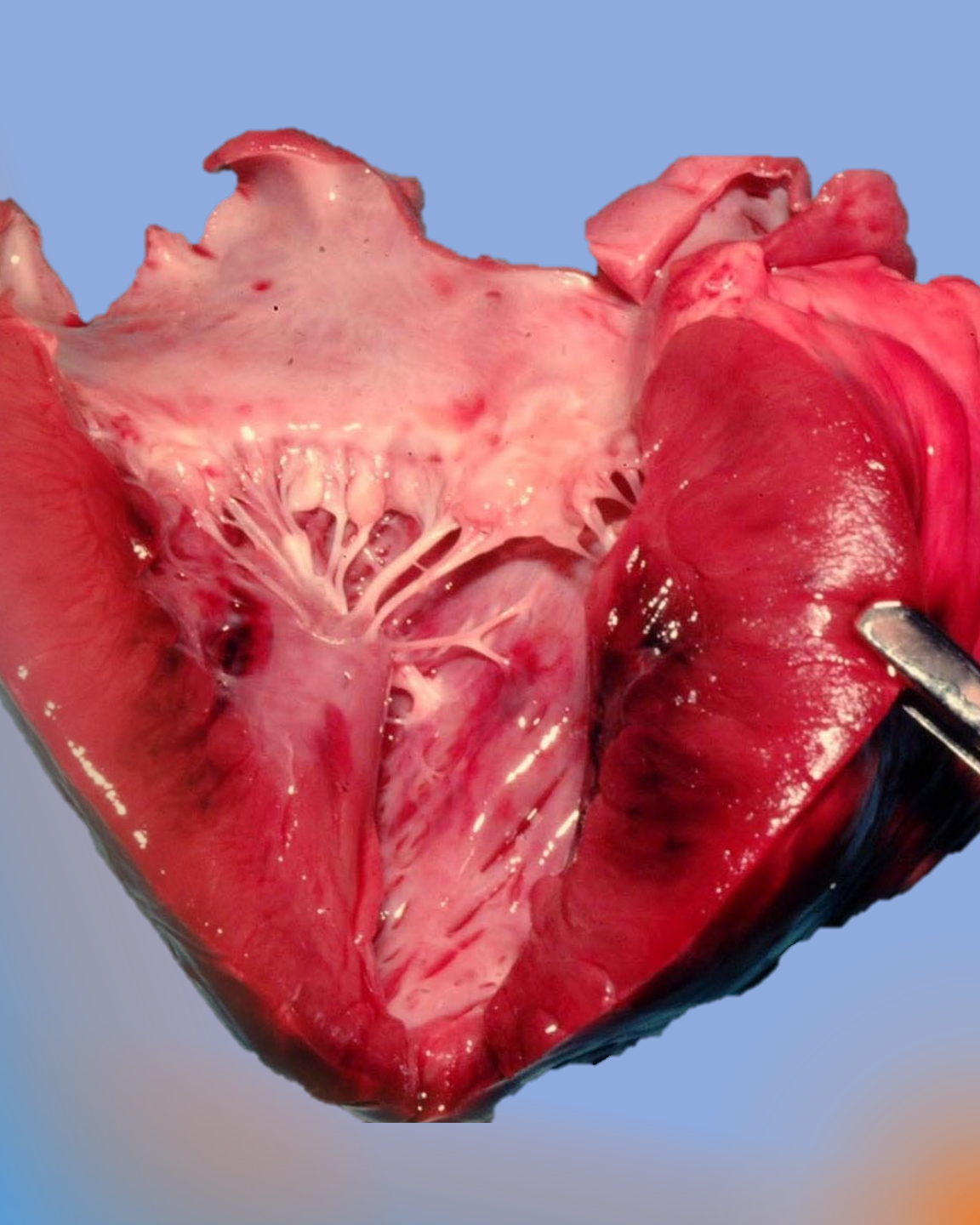
Myocardial necrosis



Ionophore (monensin) toxicosis

- Monensin: fermentation product of *Streptomyces cinnamonensis*
- Feed supplement- toxicity is usually due to mixing errors.
- Function: alters membrane permeability to electrolytes that facilitate the transport of Na^+ and K^+ across cell membranes.
- Influx Na^+ leads to abnormalities in Ca channels----
-Ca overload---cell death.
- Atrial fibrillation, tachycardia
- Myodegeneration and necrosis

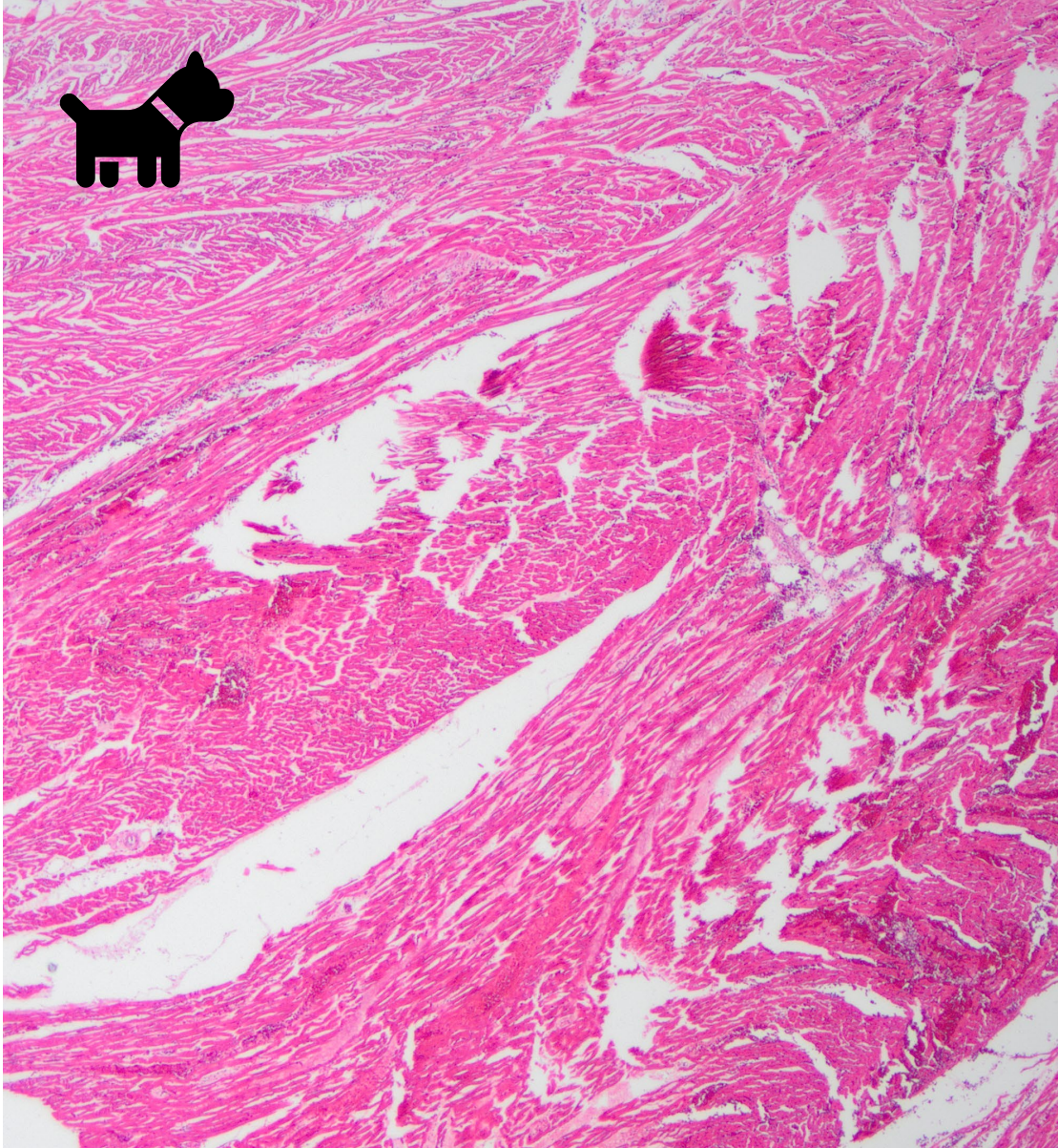




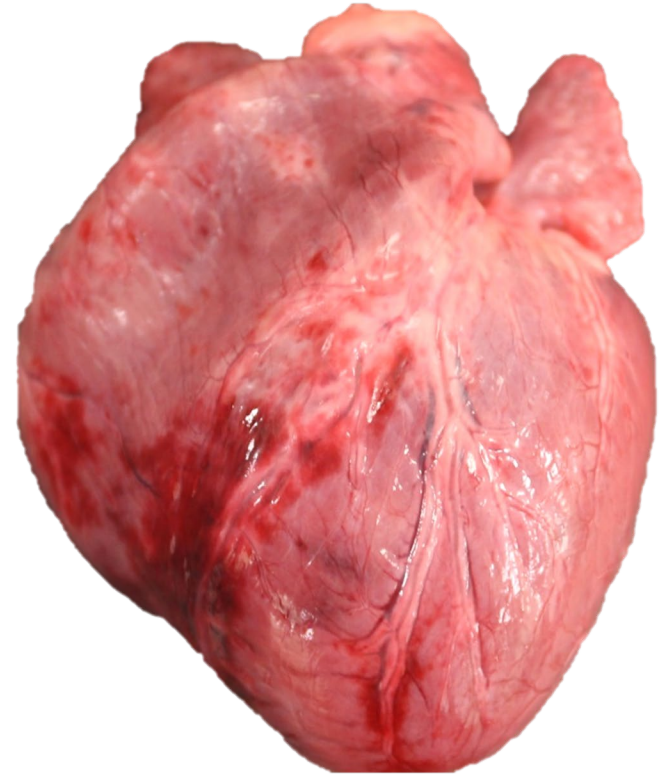
Catecholamine cardiotoxicity

- Massive release of catecholamines
 - Pheochromocytoma
 - Adrenergic stress
- Catecholamines produce a direct toxic effect on the myocardium by increasing the sarcolemmal permeability and cellular calcium influx.
- Myocardial necrosis (contraction band necrosis-hypercontracted sarcomeres)
- Cardiac arrhythmias
- Hemorrhage
- CHF

Contraction band necrosis

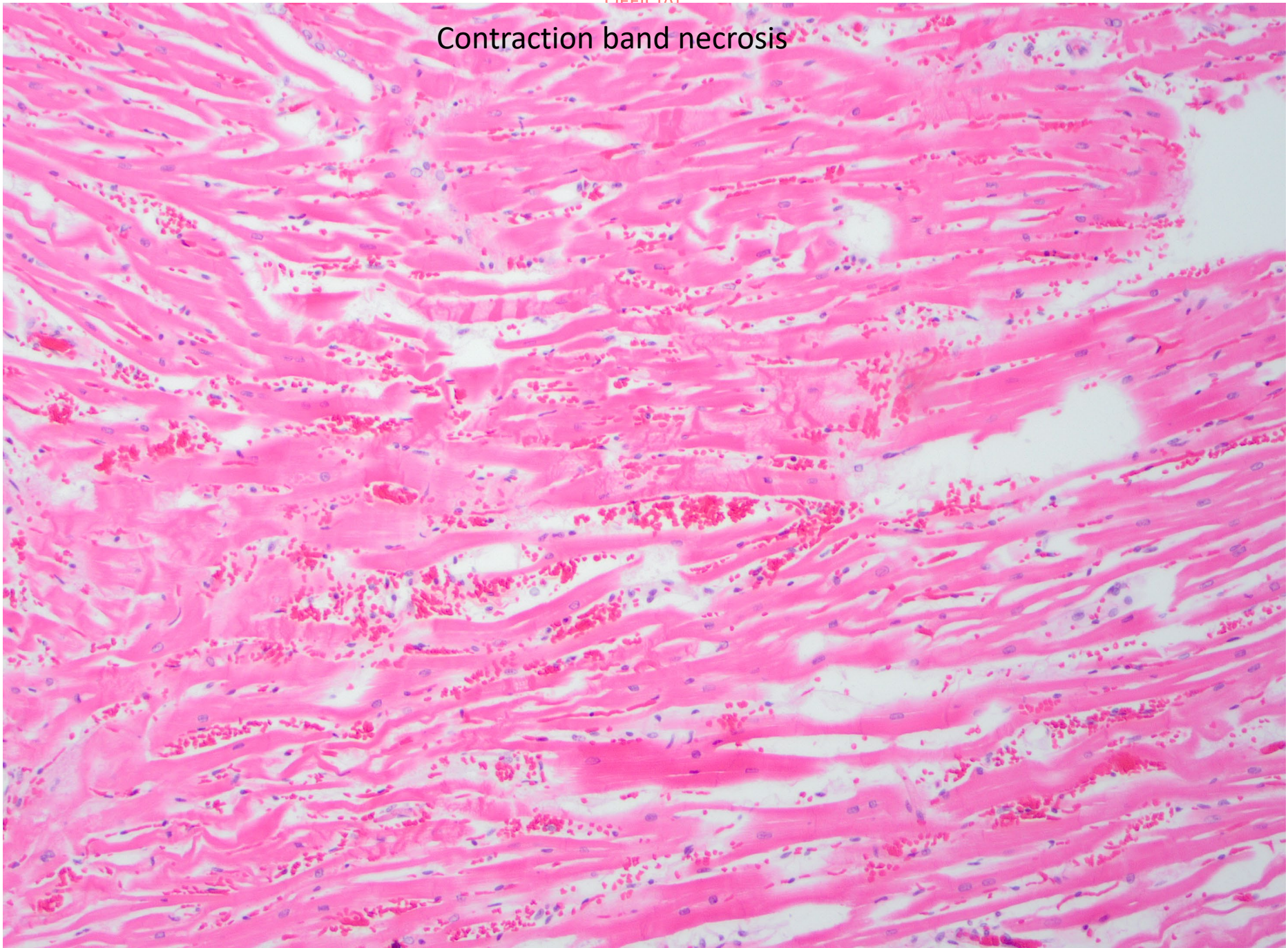


Heart with extensive hemorrhages

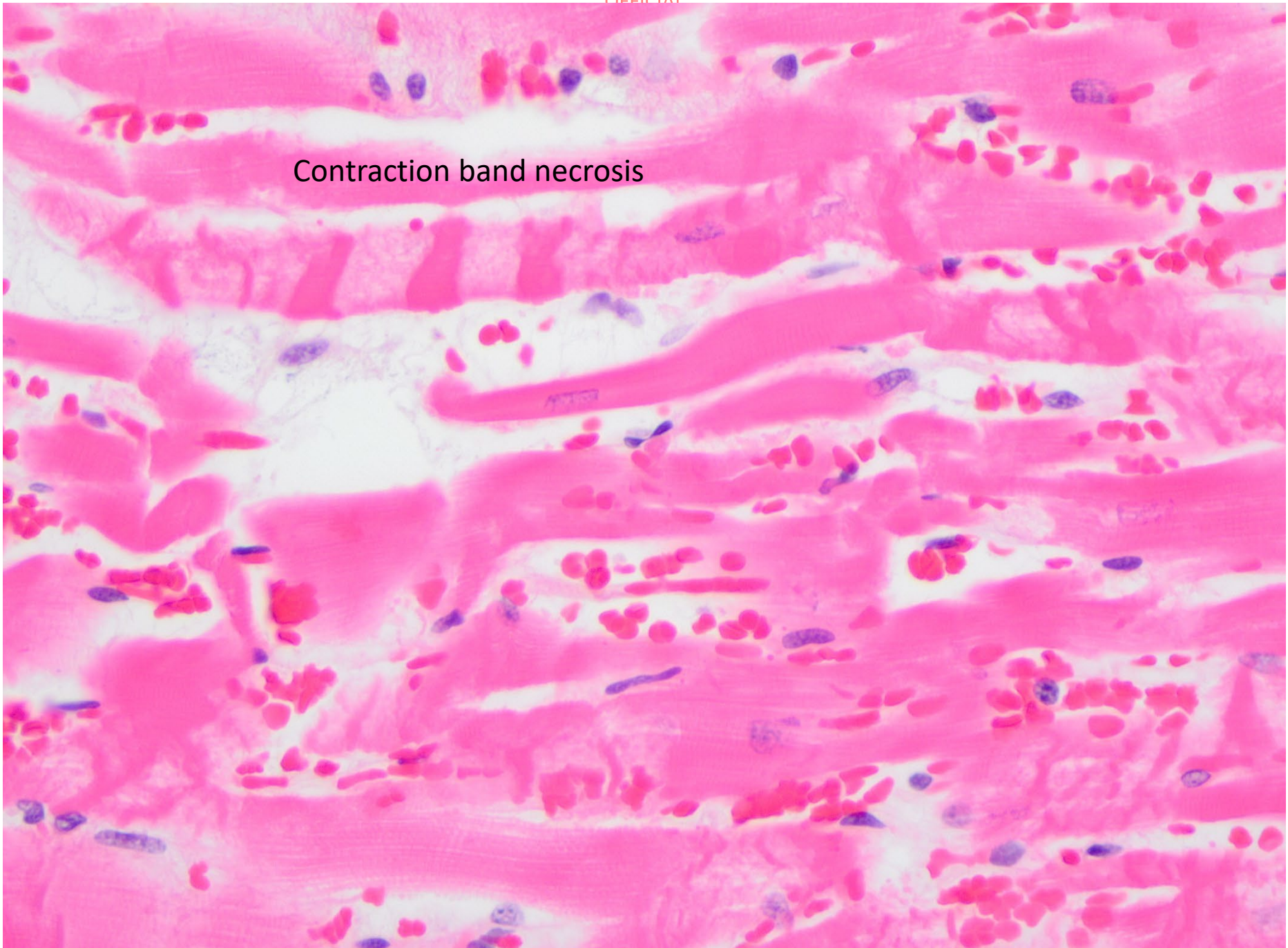


- Pneumonia
- Fever
- Diarrhea
- Tachycardia

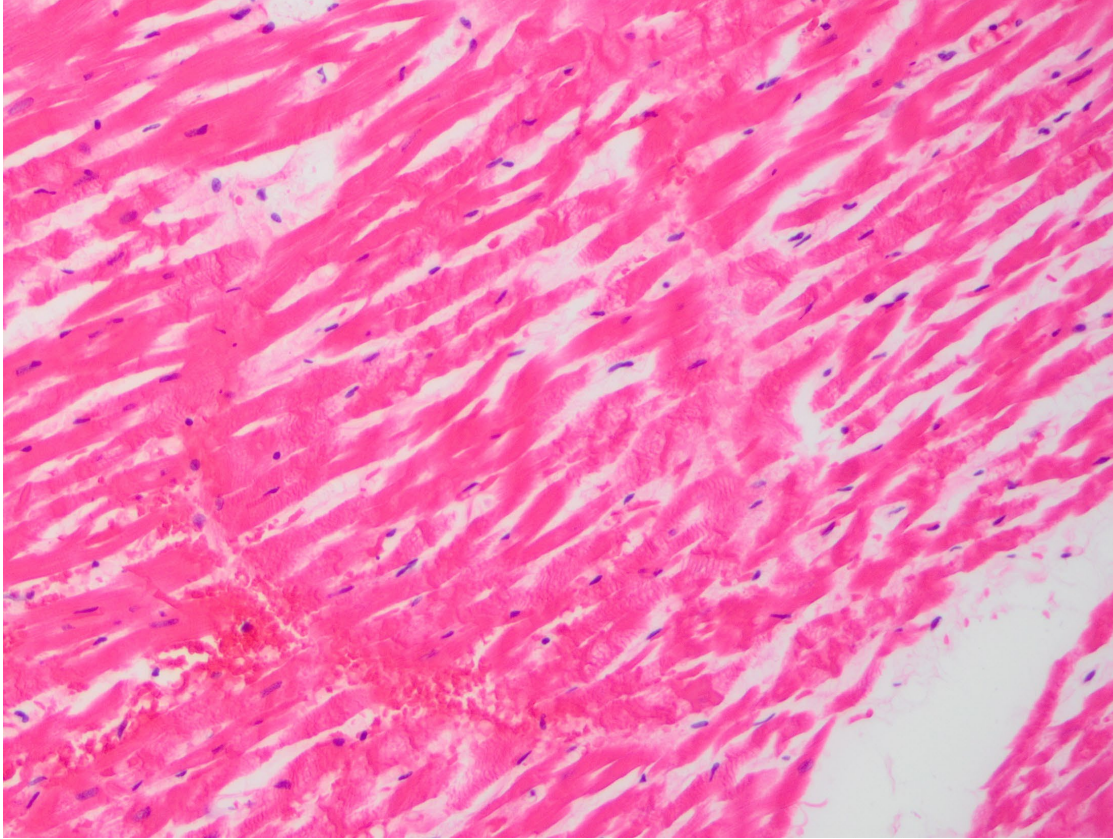
Contraction band necrosis



Contraction band necrosis



Contraction band necrosis



Severe hyponatremia

Hyperosmolar state associated w/hyponatremia contributes to metabolic, neurological and cardiovascular complications.

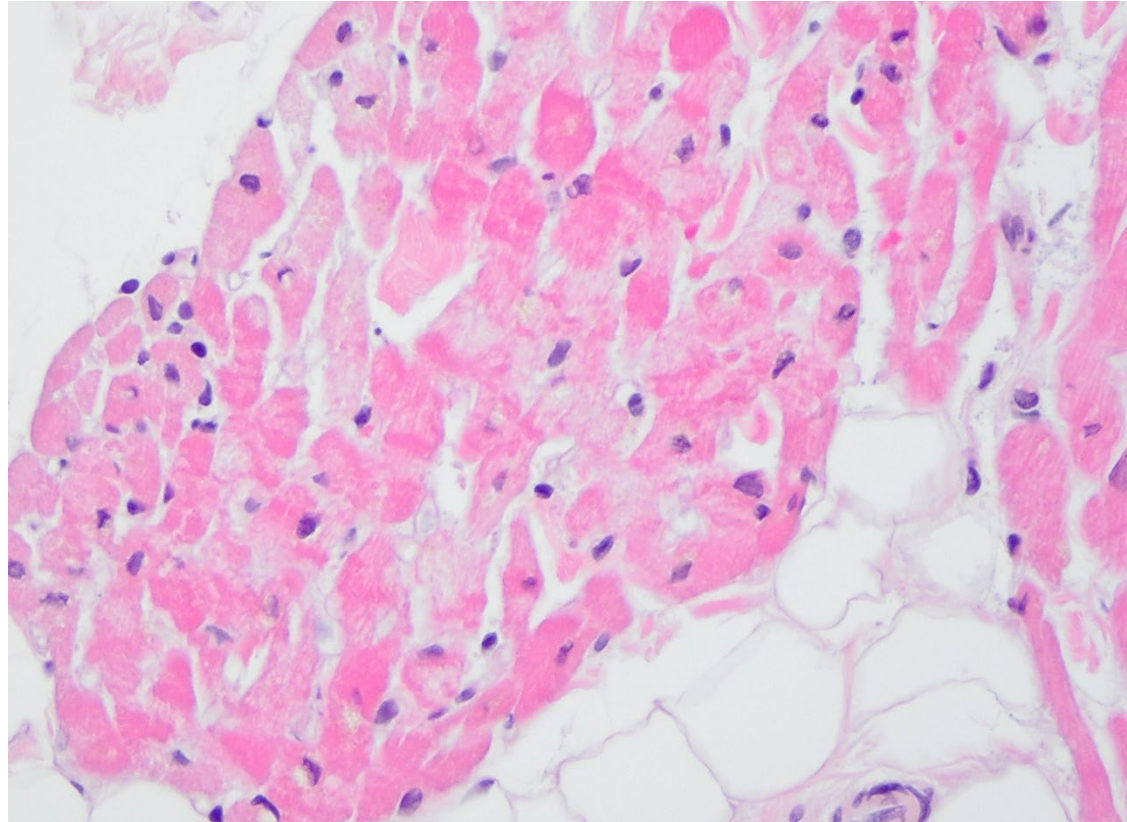
- Cortical laminar necrosis (hyponatremic encephalopathy)
- Extremely high sodium levels can disrupt the electrical conduction system, leading to arrhythmias and ventricular tachycardia.
- Contraction band necrosis is associated with arrhythmias.

Remember!



Contraction band necrosis-like changes:

- Tissue handling and processing
- Cardiac massage



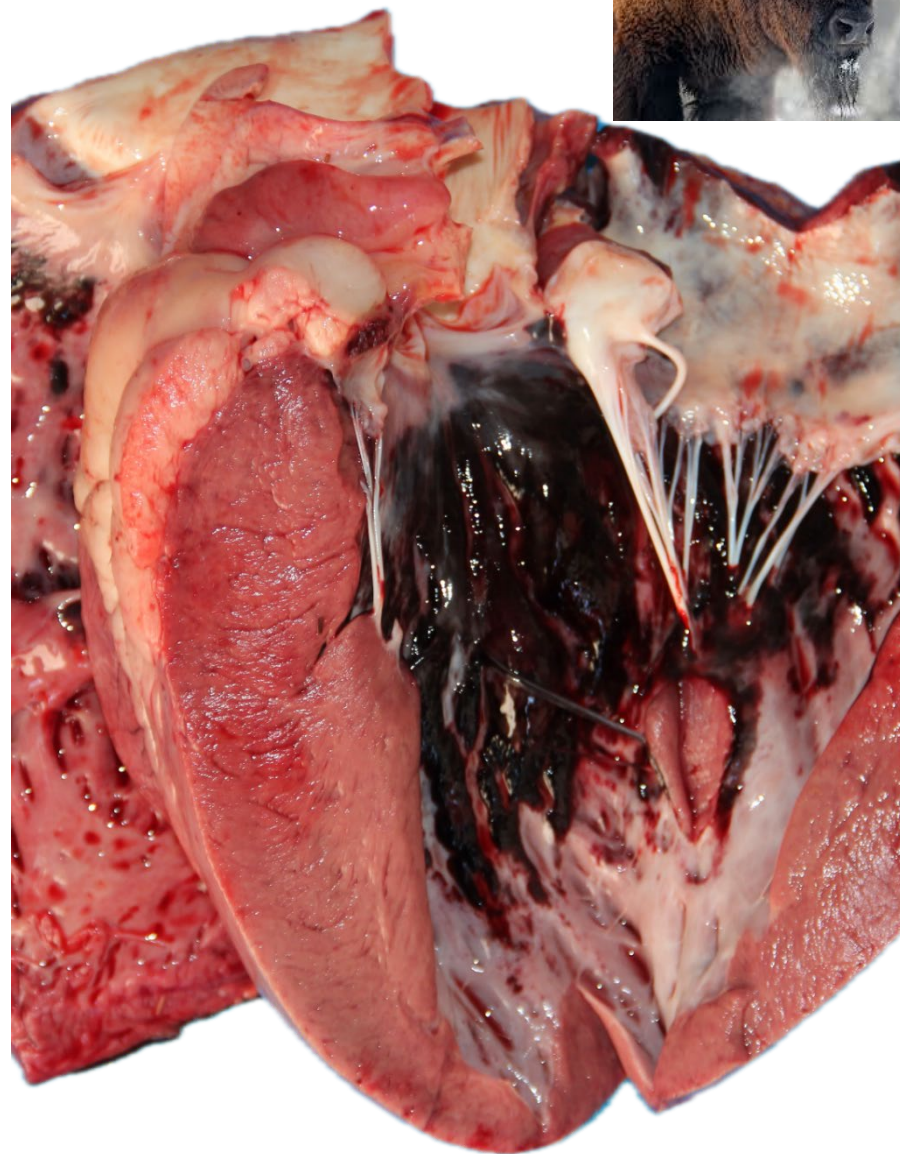


TOXIC PLANTS

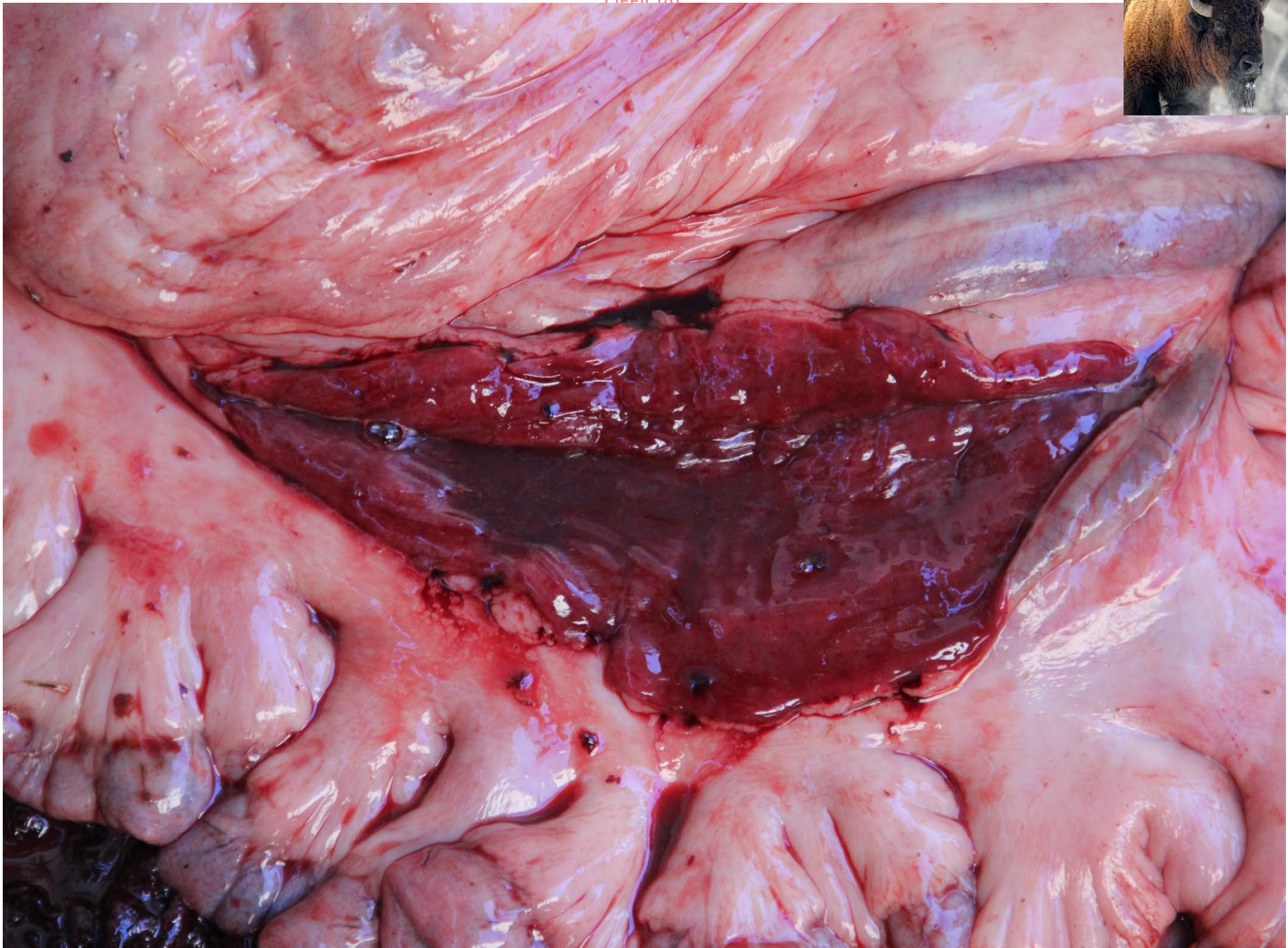
Oleander toxicity

- Perennial, evergreen shrub
- Cattle, horses, sheep, goats, llamas, humans
- Red-flowered varieties appear to be more toxic
- Cardiac glycosides (cardenolides): all parts of the plant are toxic
- Oleandrin and other cardiac glycosides inhibit Na^+/K^+ ATPase---leads to accumulation of sodium----changes the shift of $\text{Na}^+-\text{Ca}^{2+}$ channels-----increased intracellular Ca^{2+} -----arrhythmias. Also, there is an increase of serum K^+
- Decrease electrical conductivity
- Block cardiac activity and death



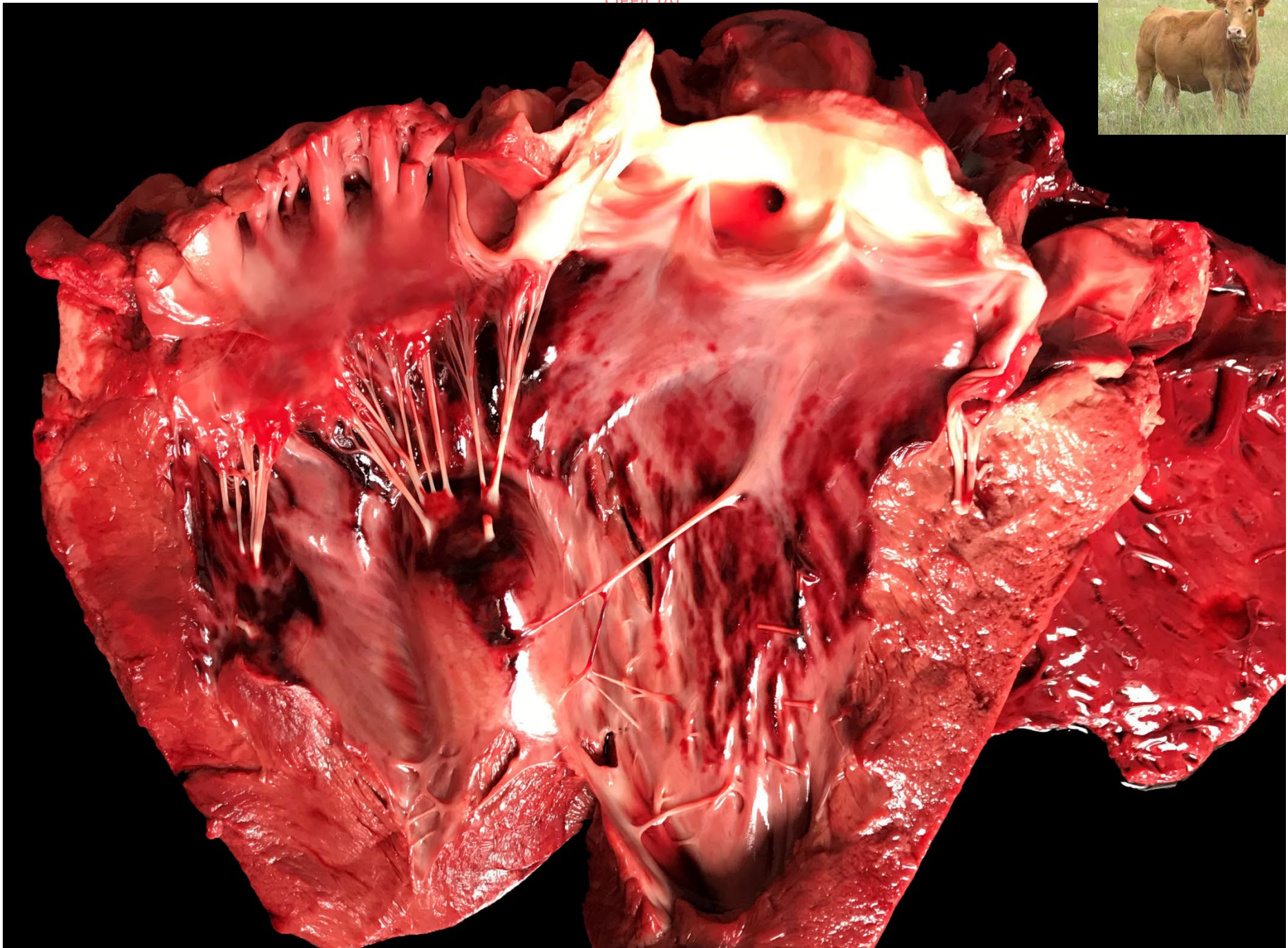


OFFICIAL



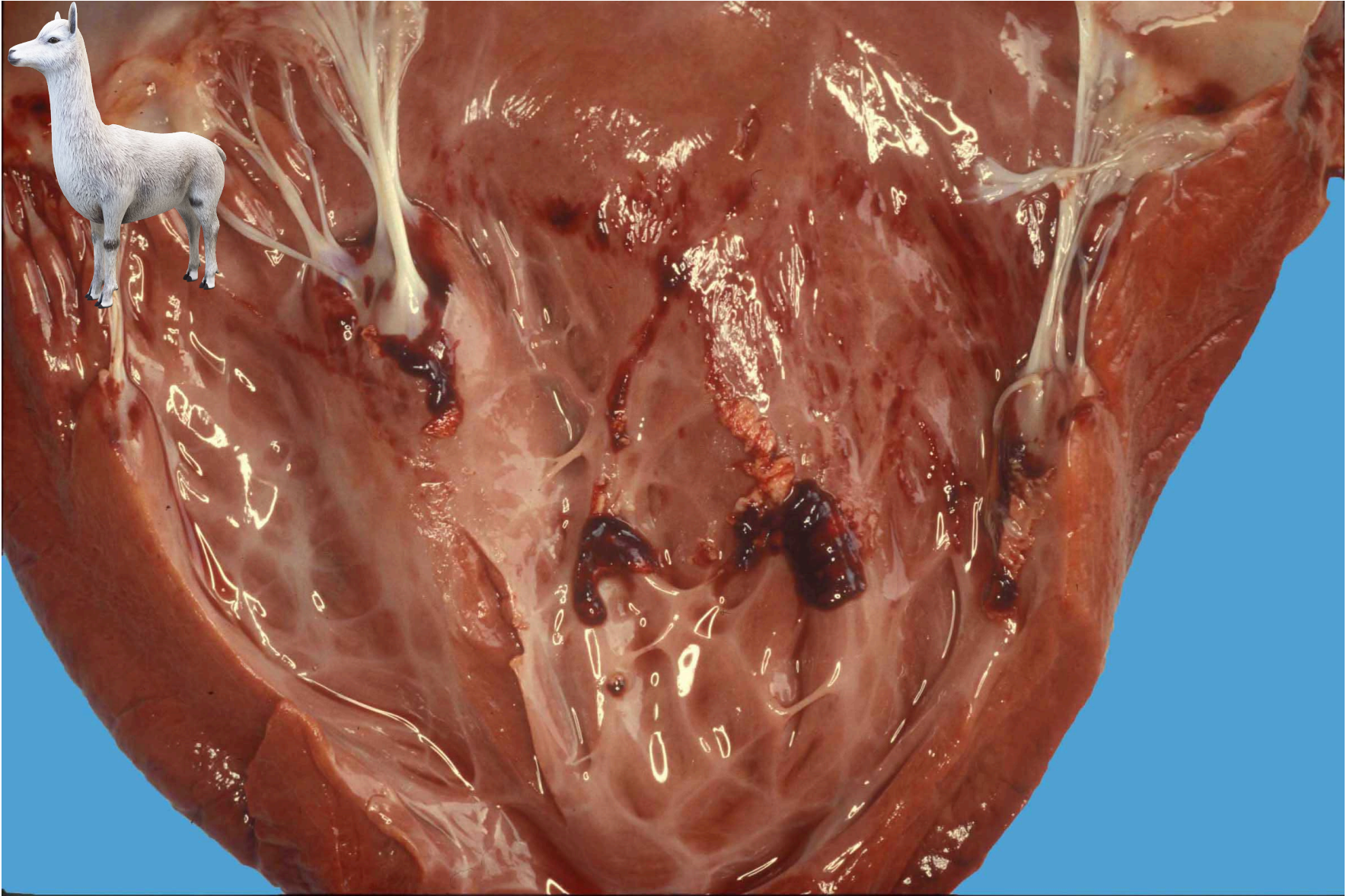
OFFICIAL

OFFICIAL



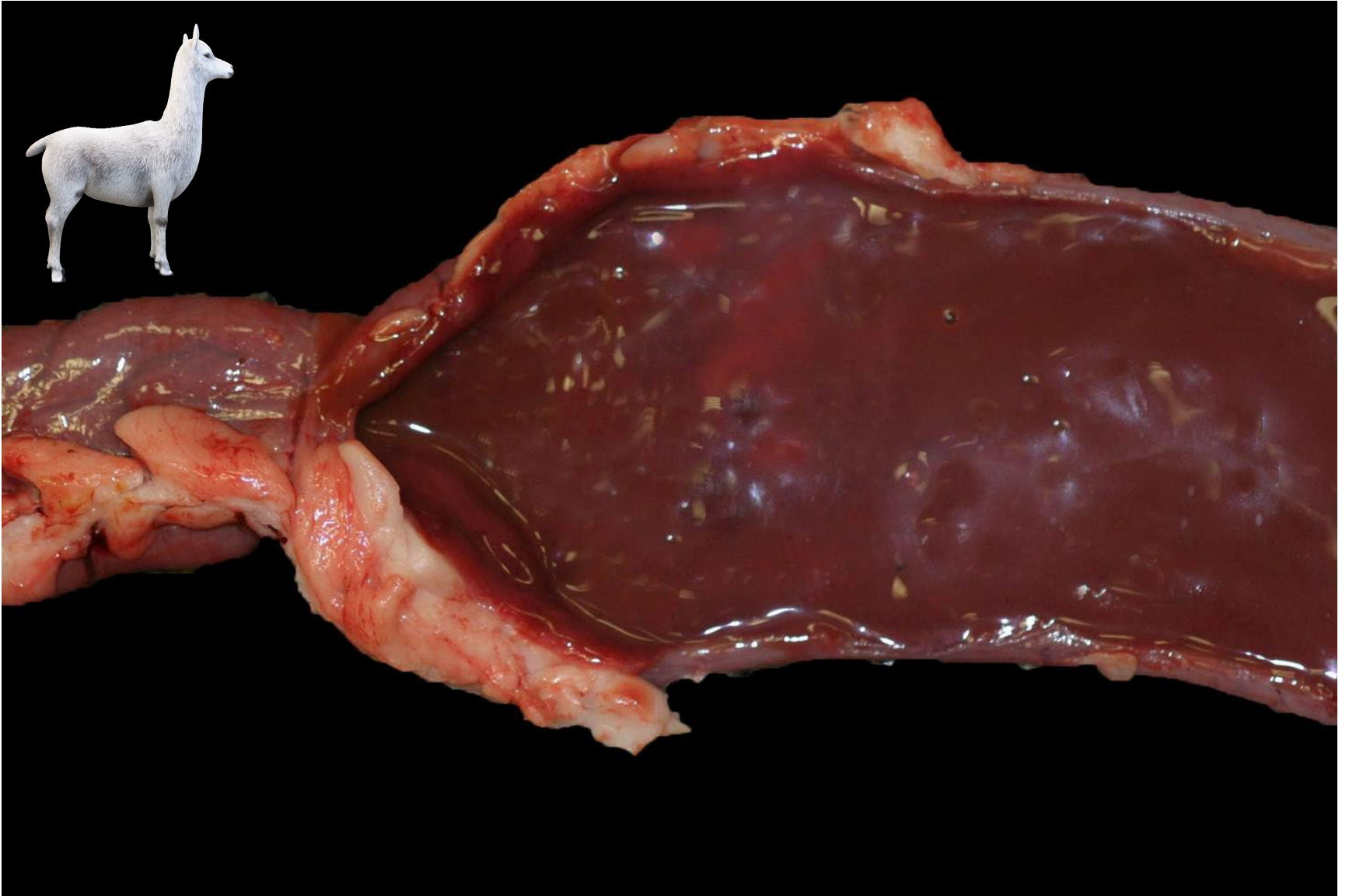
OFFICIAL

OFFICIAL

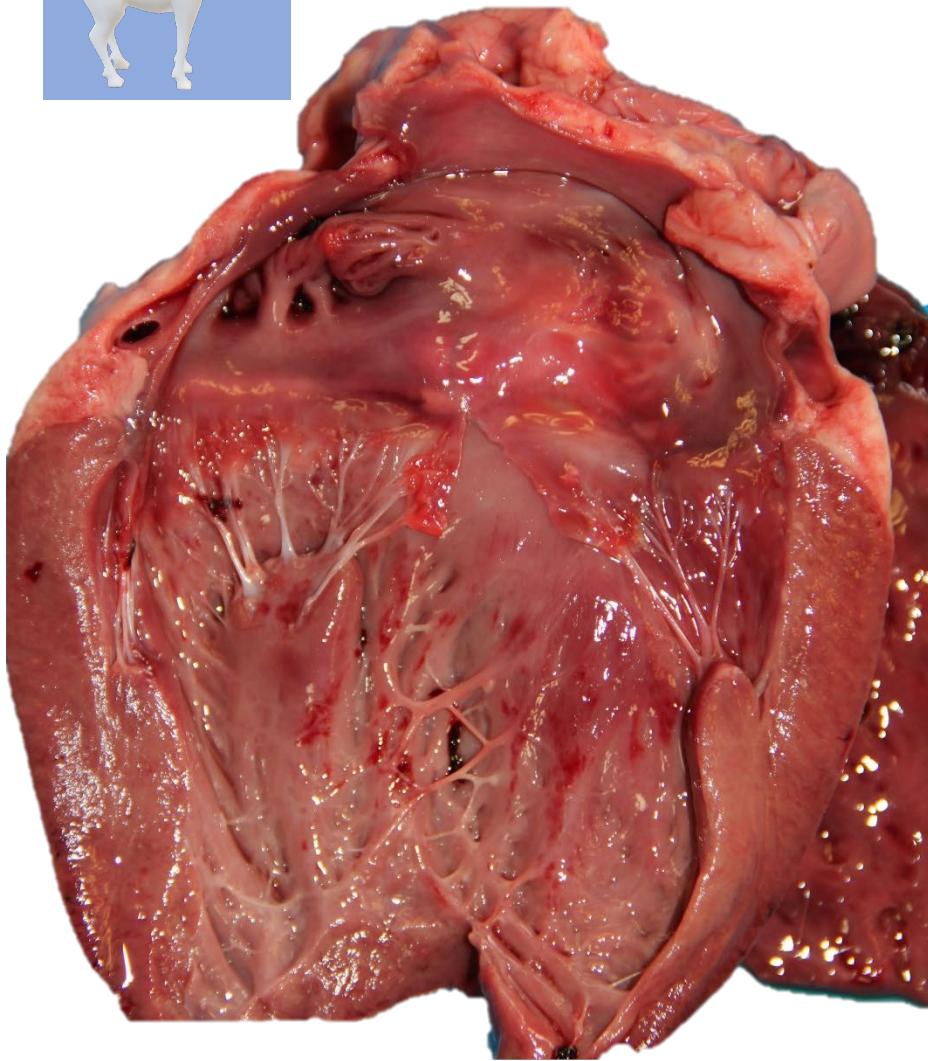


OFFICIAL

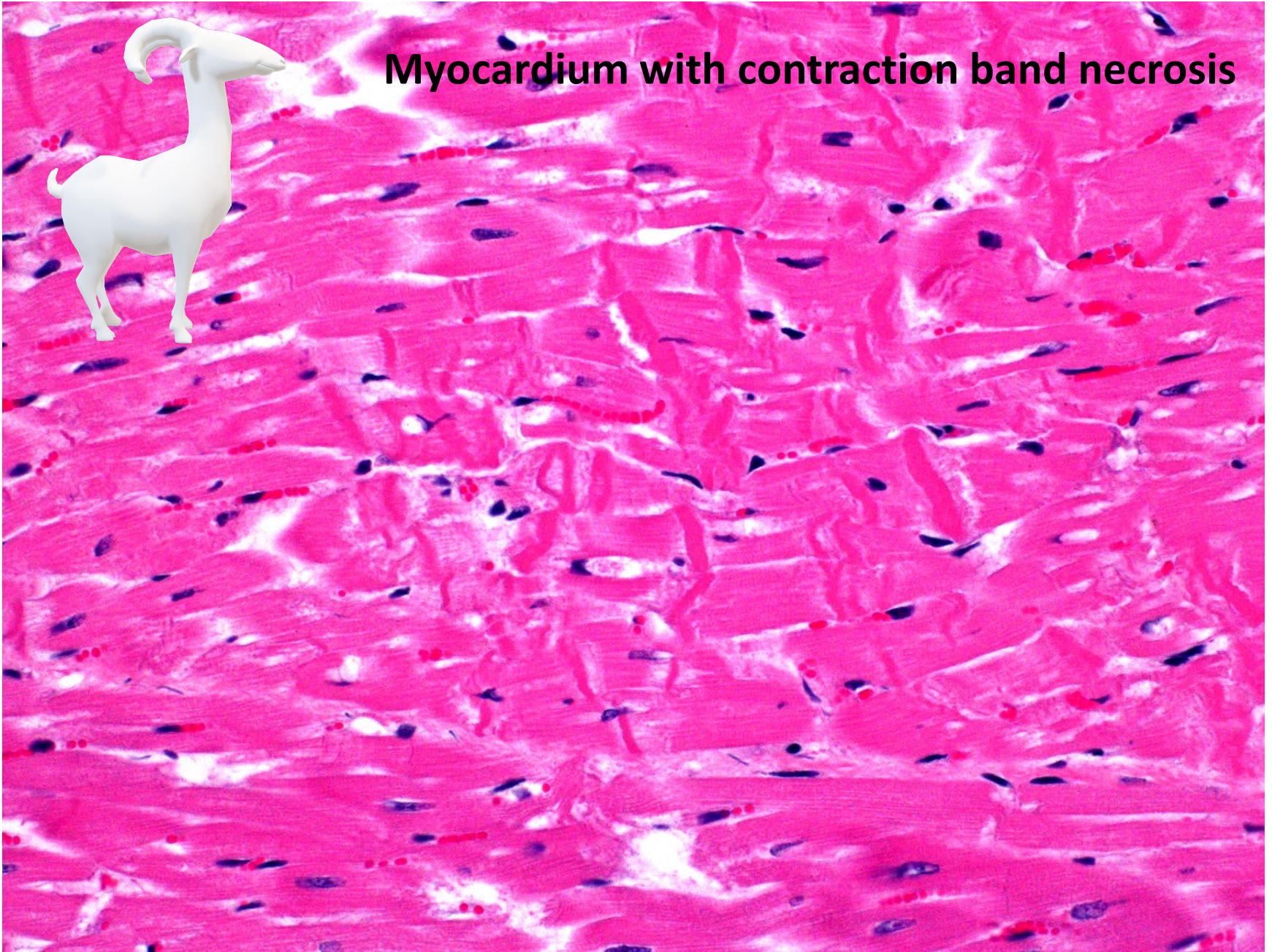
OFFICIAL

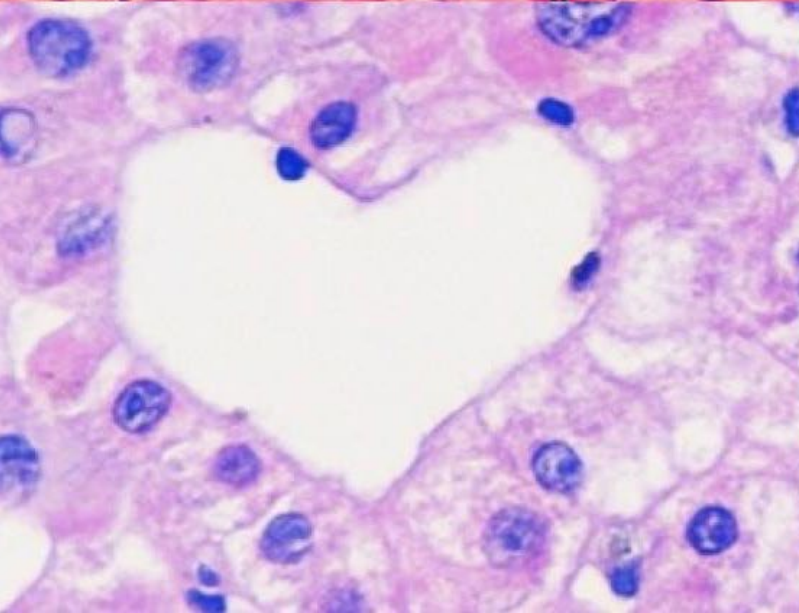


OFFICIAL



Myocardium with contraction band necrosis





Acknowledgments

Thank you for all the photos!

Cummings Veterinary School of Veterinary Medicine-Tufts University

Dr. Emily Brinker- Department of Pathobiology
Dr. Francisco Conrado- Department of Pathobiology
All Anatomic Pathologists

Dr. John Rush- Department of Clinical Sciences
Dr. Emily Karlin- Department of Clinical Sciences
Dr. Lisa Freeman- Department of Clinical Sciences

Great Ape Heart Project

Dr. Sushan Han- Denver Zoo, GAHP Pathology Advisor
Dr. Linda Lowenstein- UC Davis, Emeritus Professor, GAHP Pathology Advisor
Dr. Ritha McManamon- University of Georgia, GAHP Pathology Advisor
Dr. Karen Terio- University of Illinois, GAHP Lead Pathology Advisor
Dr. Marieta Dindo Danforth- GAHP director

Dr. Francisco Carvallo- Virginia-Maryland College of Veterinary Medicine
Dr. Francisco Uzal- UC Davis School of Veterinary Medicine
Dr. Laura Nordio, Division of Pathology, San Marco Veterinary Clinic and Laboratory, Veggiano, Italy

Facultad de Medicina Veterinaria y Zootecnia-UNAM Mexico

Dr. Feliz Sanchez Godoy- Departamento de Aves
Dr. Elizabeth Morales Salinas- Departamento de Patologia
Dr. Gerardo Salas Garrido- Departamento de Patologia

