Diseases of the aorta

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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

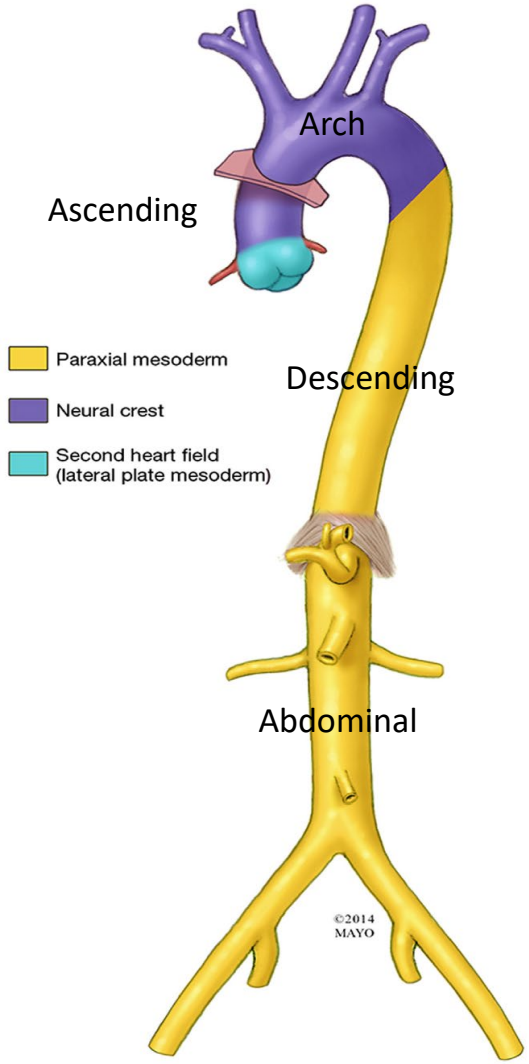
Dr. John Rush- Department of Clinical Sciences
Dr. Emily Karlin- Department of Clinical Sciences
Dr. Lisa Freeman- Department of Clinical Sciences

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

Facultad de Medicina Veterinaria y Zootencia-UNAM Mexico
Dr. Feliz Sanchez Godoy- Departamento de Aves
Dr. Elizabeth Morales Salinas- Departamento de Patologia
Dr. Gerardo Salas Garrido- Departamento de Patologia

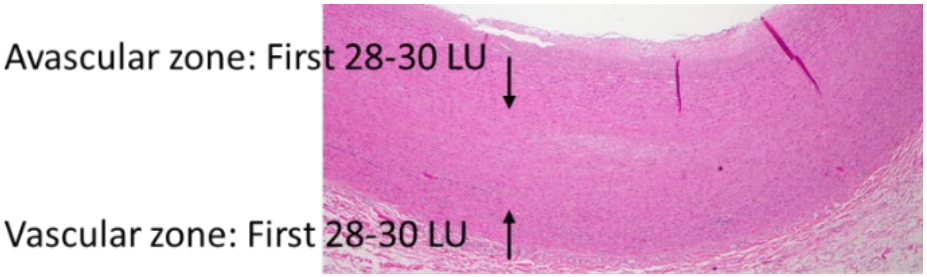
Regional Heterogeneity within the Aorta



J Thoracic Cardiovasc Surg. 2015.

Variable	Thoracic Aorta	Abdominal Aorta
Embryology	Derived from neural crest	Derived from mesoderm
Structure	Vascular outer media 55-60 lamellar units Grows by synthesizing additional lamellar units Greater elastin & collagen content	Avascular medial layer 28-32 lamellar units Grows by increasing lamellar unit thickness Lower elastin & collagen content
Mechanics	Greater distensibility	Increased stiffness
Atherosclerosis	Low likelihood of lesion progression from fatty streak to atheroma	Site of most severe atherosclerosis High likelihood of lesion progression from fatty streak to atheroma
Matrix Metalloproteinases (MMPs)	Inconsistent role for MMP-2 MMP-9 produced by synthetically active SMCs and fibroblasts Lack of MMP-9 attenuated aneurysm development	Early aneurysm growth driven by MMP-2 MMP-9 produced by macrophages MMP-9 proportional to aneurysm diameter Lack of MMP-9 prevented aneurysm development
TGF-β Response	Increased signaling contributes to aneurysm disease	Overexpression attenuated proteolytic state

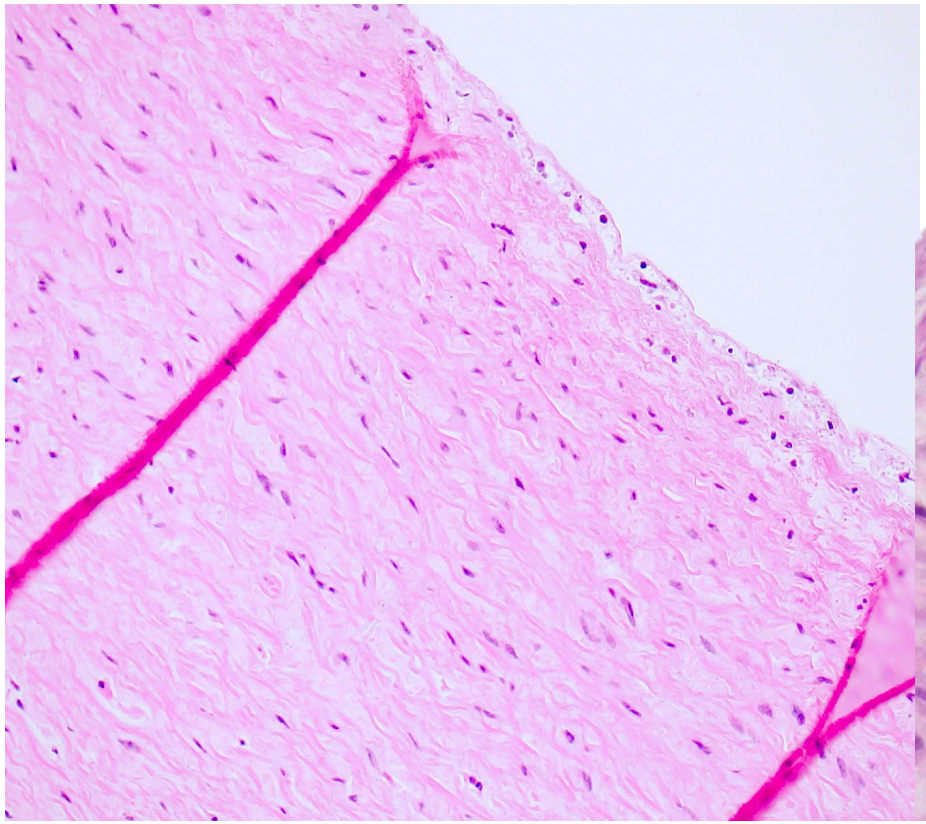
J Thorac Cardiovasc Surg. 2008.

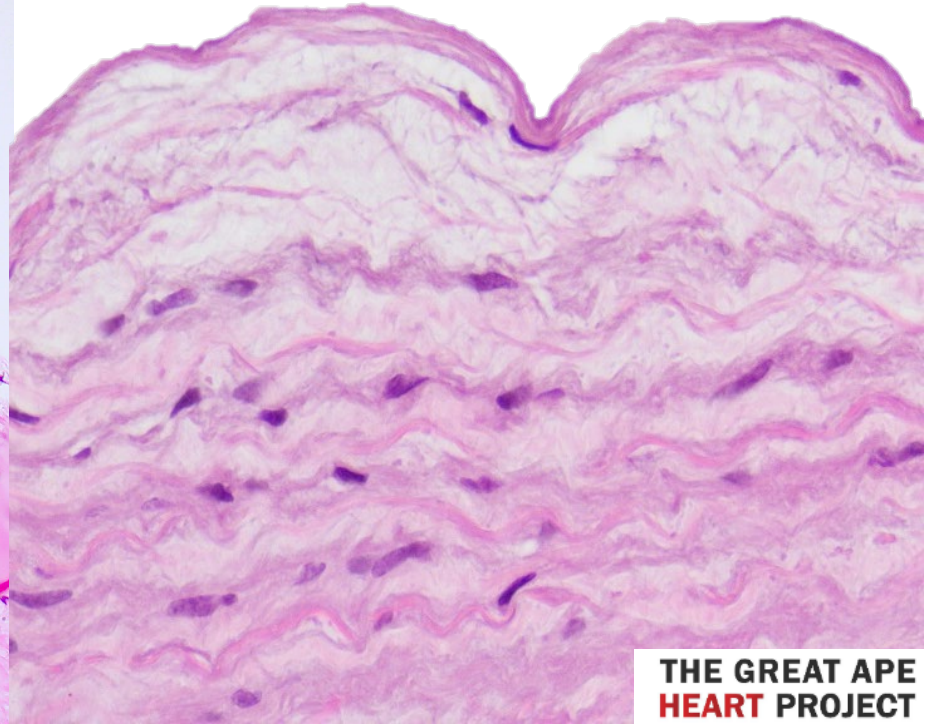


Aorta

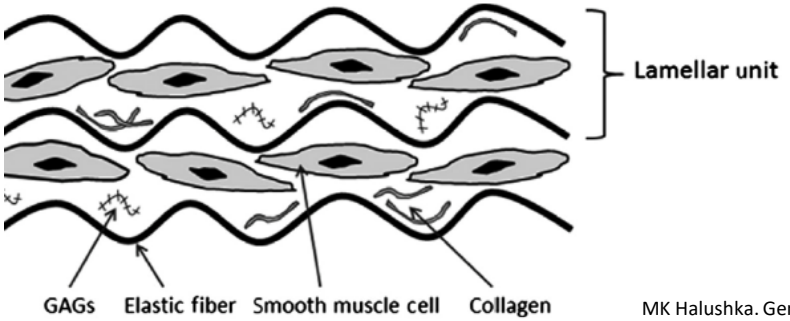
INTIMA

- Single layer of ECs
- Basement membrane (ECM: laminin, collagen IV, fibronectin, perlecan, heparan sulfate PGs)
- Internal elastic lamina

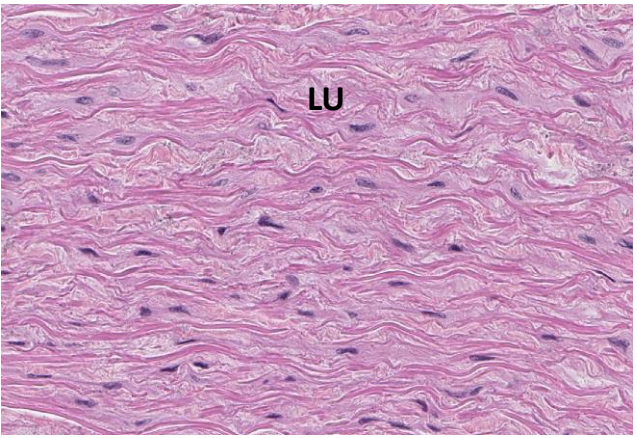




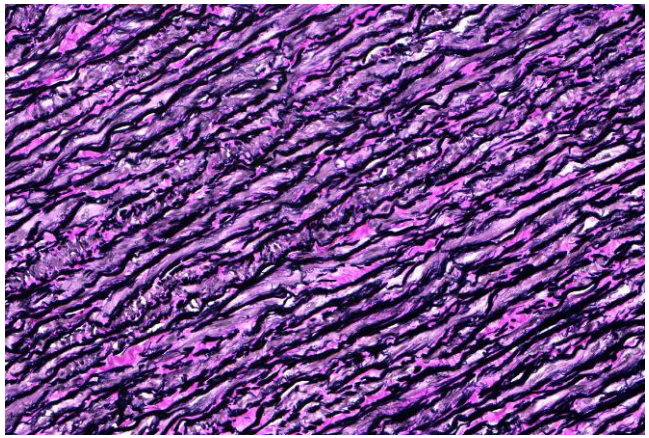
MEDIA



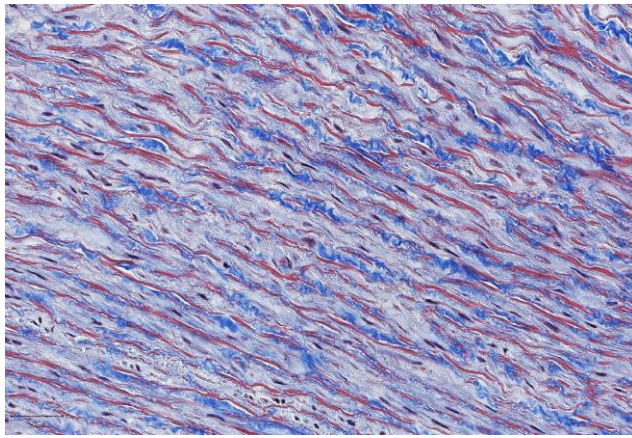
MK Halushka. Genetic Diseases of the Aorta. 2014.



H&E

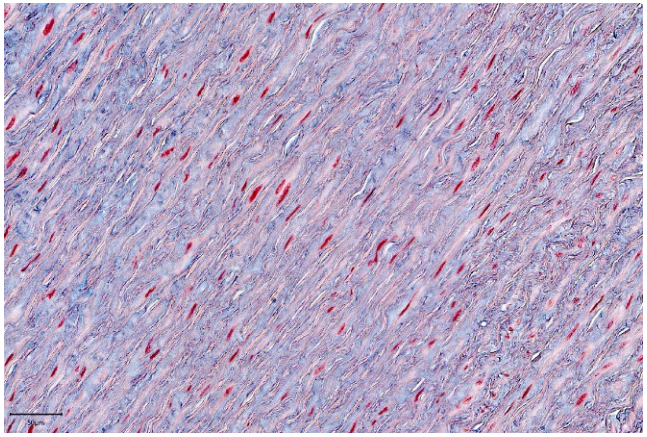


Van Gieson's stain

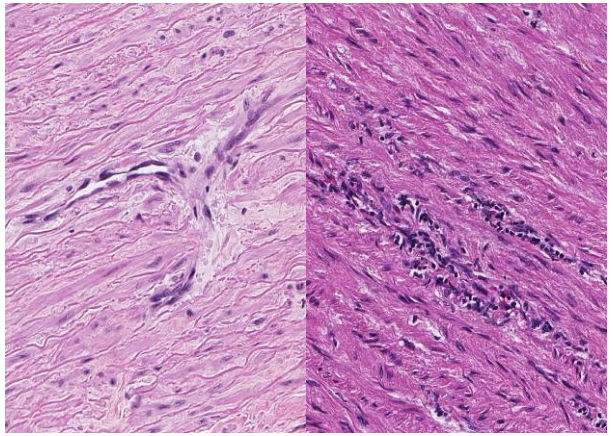


Trichrome

SMA



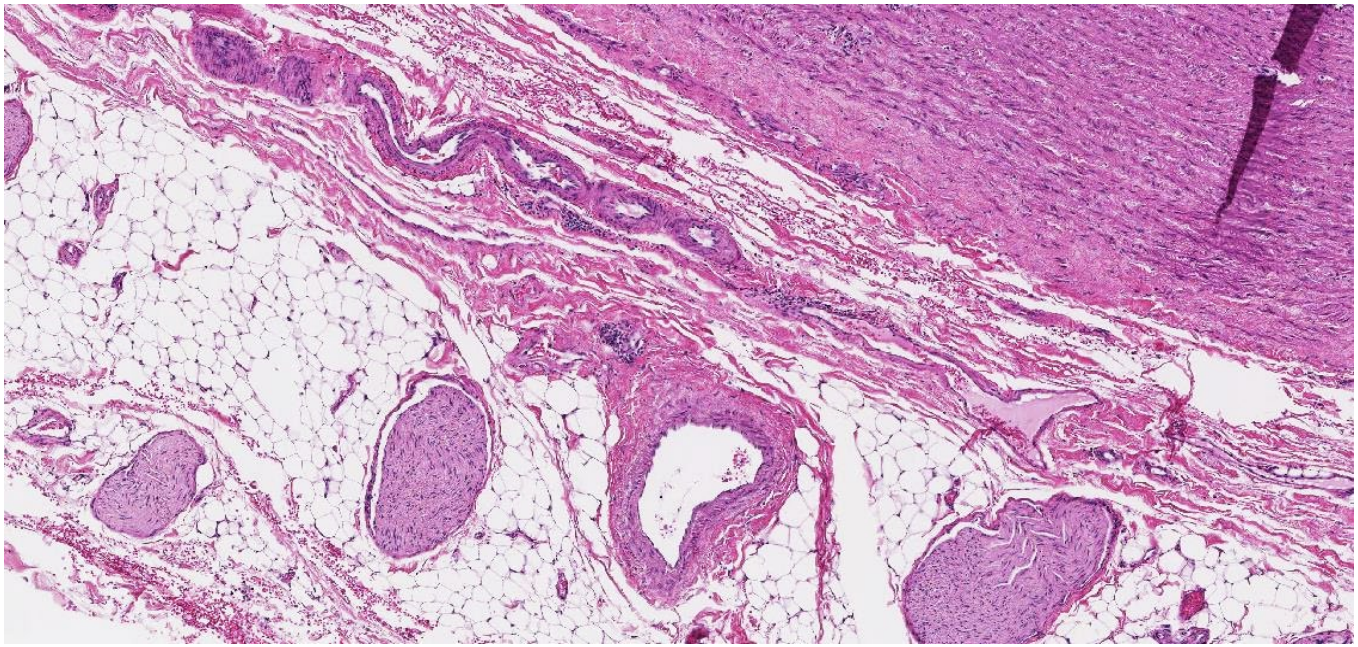
Alcian blue

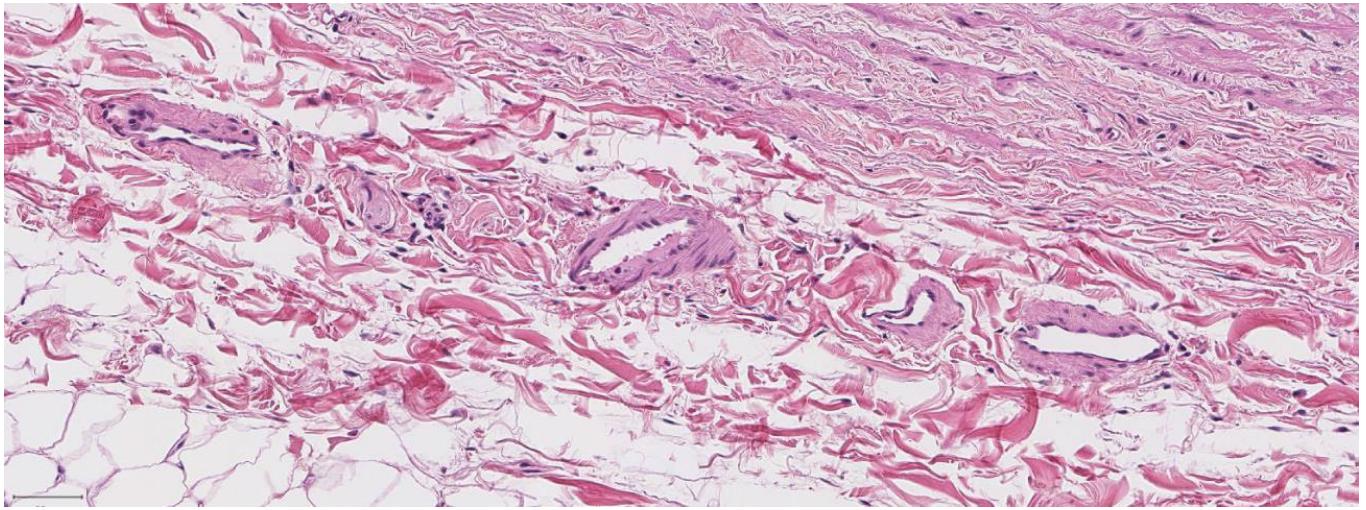


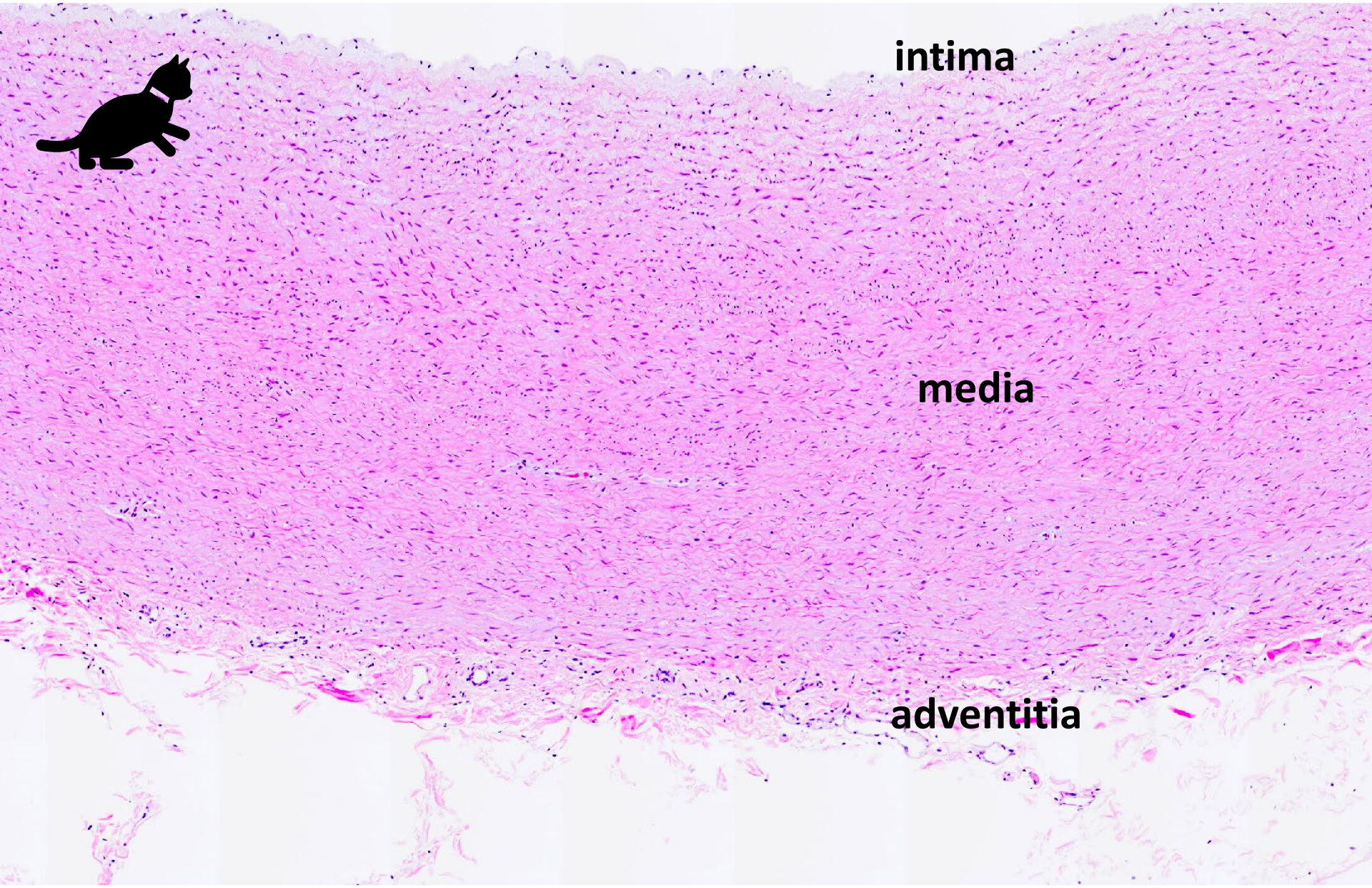
H&E

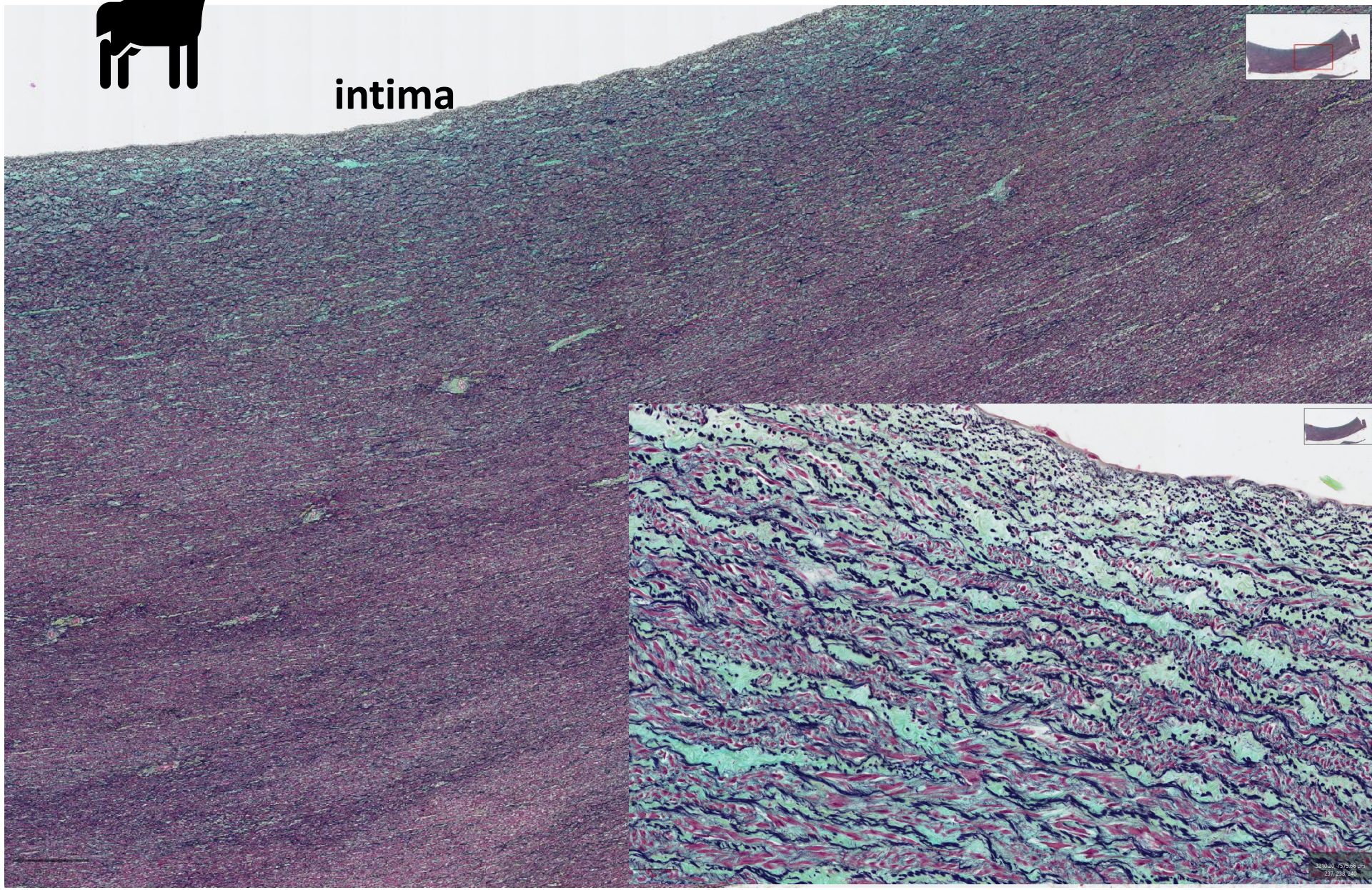
ADVENTITIA

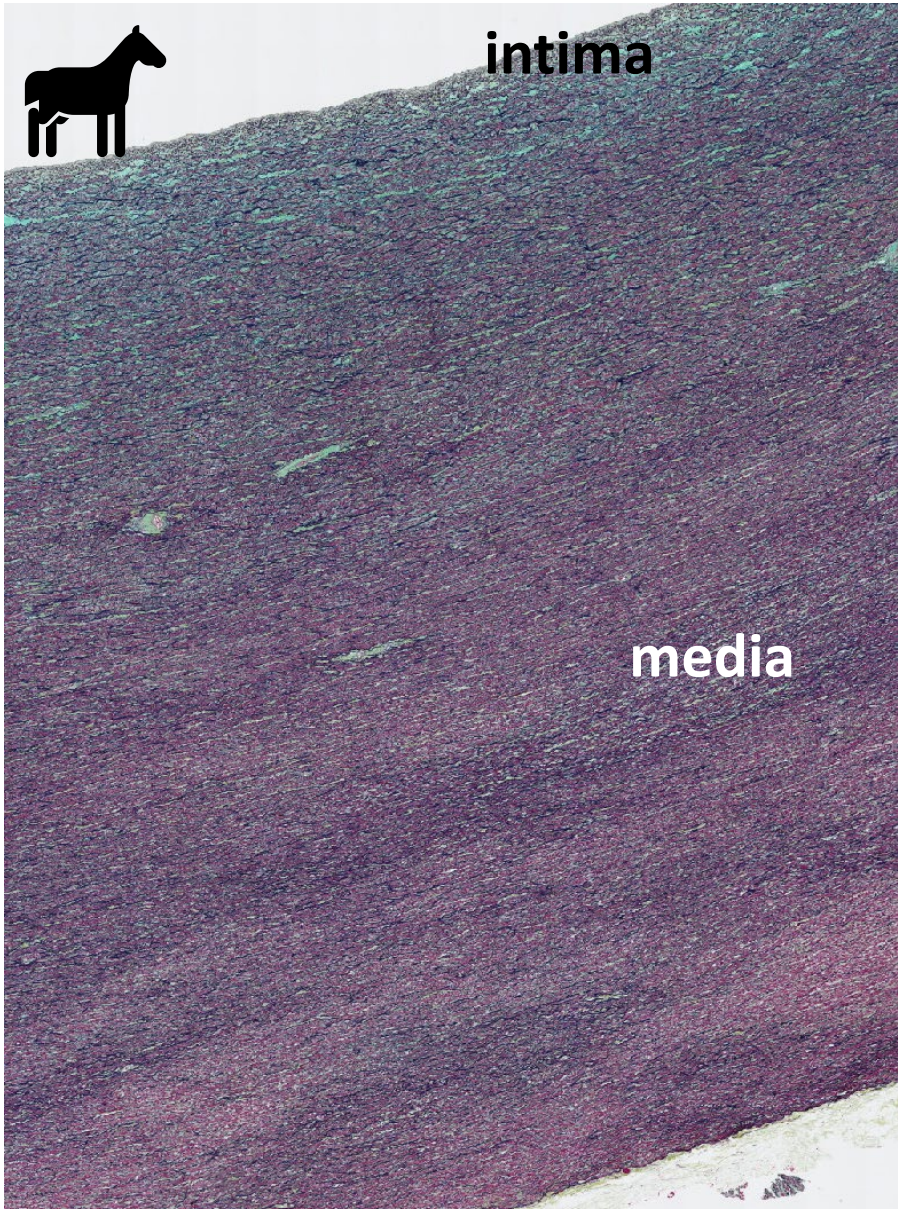
- Vasa vasorum
- Nerves
- Loose/dense connective tissue
- Adipocytes
- Fibroblasts
- Pericytes
- Progenitor cells
- Lymphatics
- Lymphocytes
- Macrophages

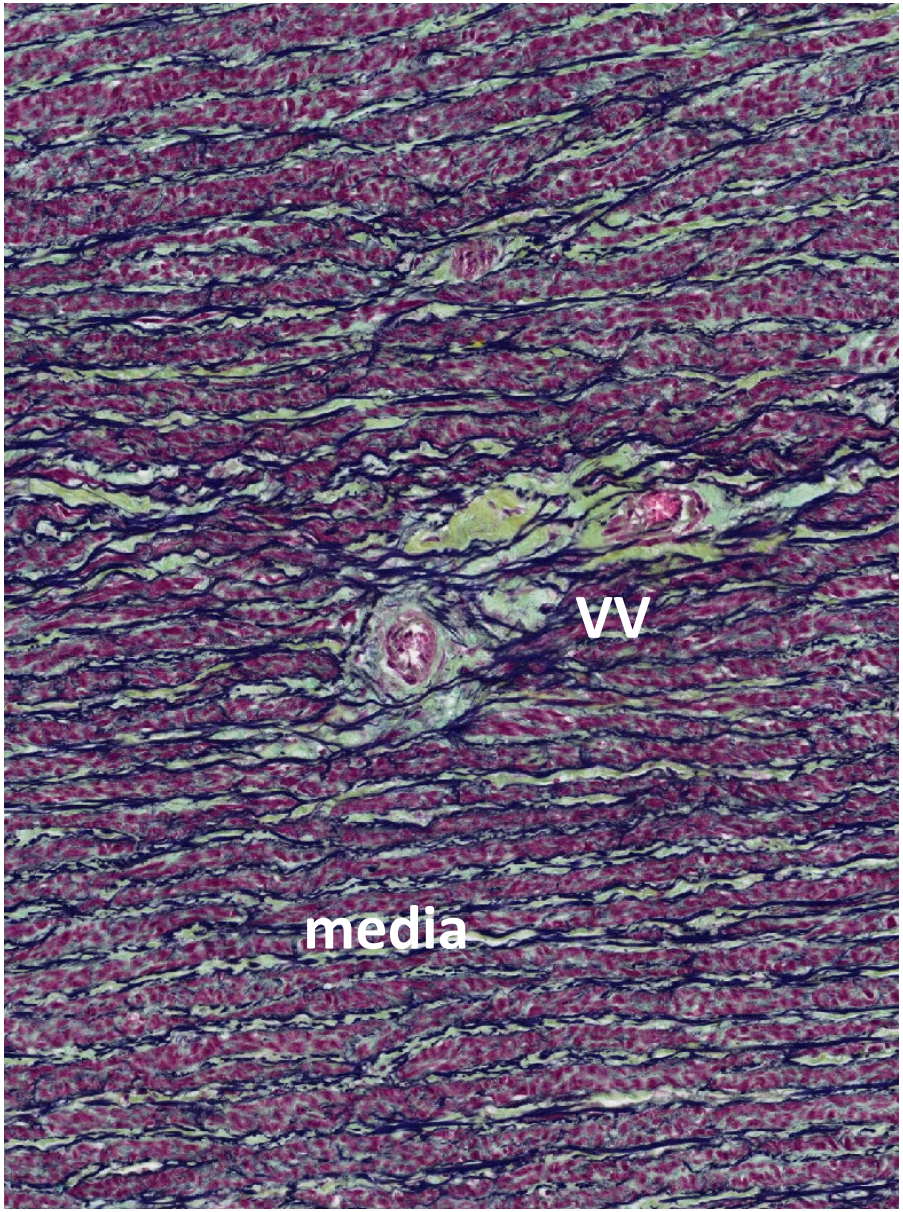







intima





Pentachrome stain

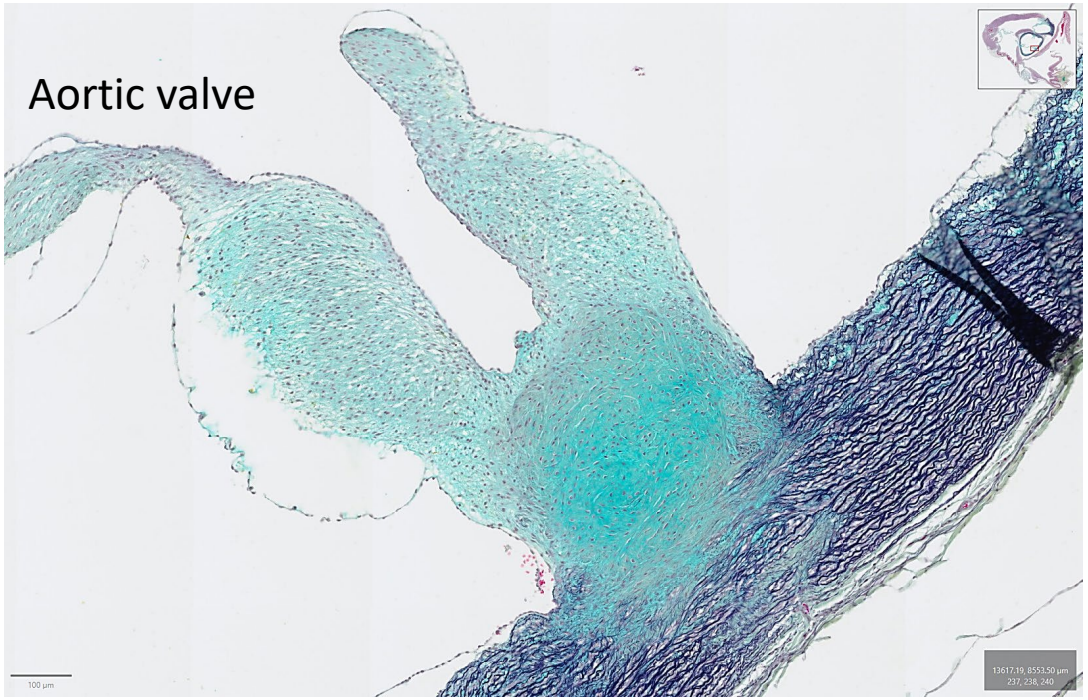
Aortic valve

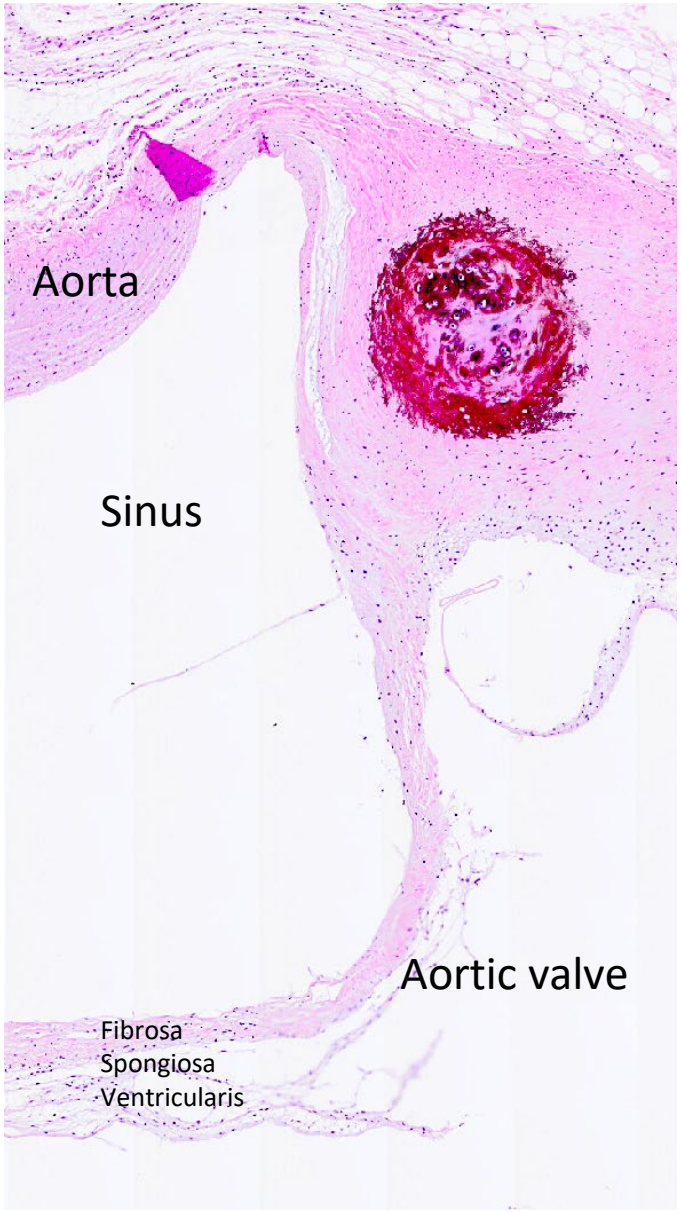
Core of connective tissue of three layers:

- Ventricularis: elastic fibers and collagen
- Spongiosa: proteoglycans, glycosaminoglycans
- Fibrosa: collagen and interstitial cells

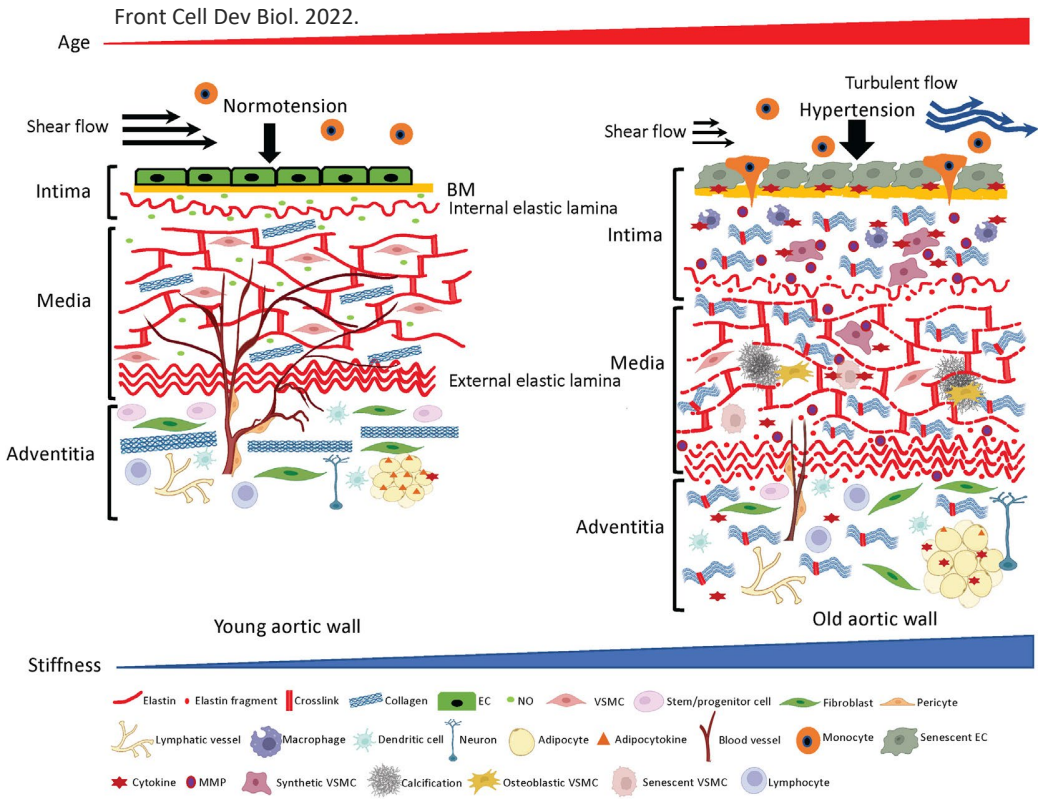
ALL THREE LAYERS ARE POPULATED WITH VALVE INTERSTITIAL CELLS

Core is covered by endothelium





Remodeling of the Extracellular matrix



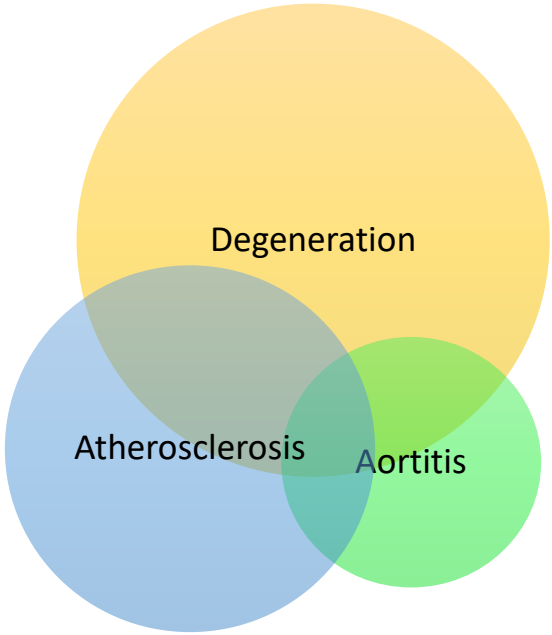
Intima	Media	Adventitia
Endothelial apoptosis	Proliferation VSMC	Calcification
Endothelial senescence	Migration of VSMC	Myofibroblasts
ECM production	Increase MMPs	Fibroblasts
Collagen deposition	Collagen deposition	Modified ECM
Deposition VSMCs infiltrate into the subendothelial space	Elastin fragmentation	
	Calcification	
	Increased inflammatory cells	
	Collagen/elastin ratio increased	

New Approaches to Aortic Diseases from Valve to Abdominal Bifurcation. Chapter 1. 2018.

Histopathologic changes to the aorta

Overlapping changes

- Atherosclerotic plaques
  - Cause of aortic aneurysm
- Inflammation
  - Granulomatous (giant cells)
  - Lymphoplasmacytic
  - Mixed
  - Suppurative
- Medial degeneration
  - Aging
  - Abnormal post-valvular hemodynamics
  - Connective tissue disorders



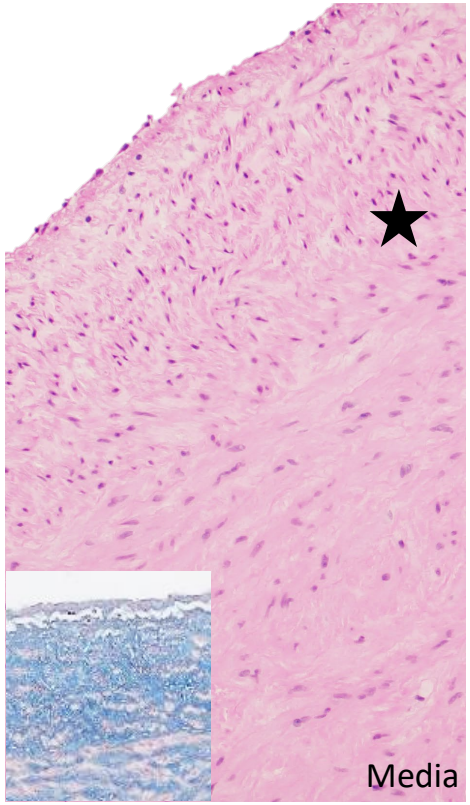
Aortic histopathology

MEDIA	INTIMA	ADVENTITIA
• Mucoid extracellular matrix accumulation • Elastic fiber fragmentation/loss • Elastic fiber thinning • Elastic fiber disorganization • Smooth muscle cell nuclei loss • Laminar medial collapse • Smooth muscle cell disorganization • Medial fibrosis • Calcification	• Intimal thickening • Intimal fibrosis • Atherosclerosis	• Perivascular lymphocytes • Medial hypertrophy VV

Cardiovascular Pathology. 2016. Vol 25-3, 247-257.

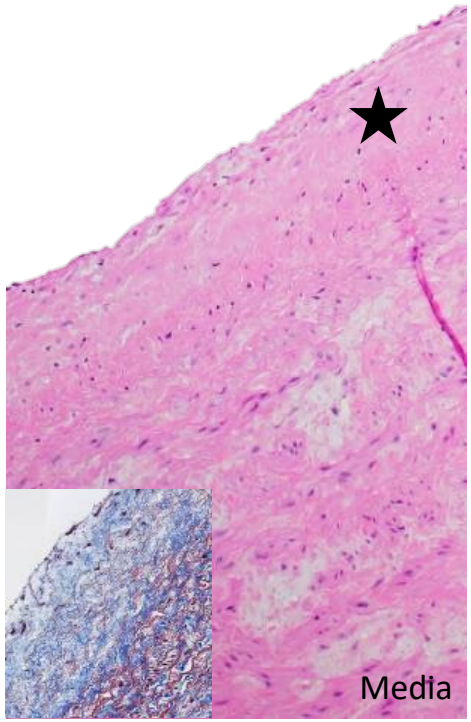
HISTOLOGIC CHANGES IN THE ASCENDING AORTA/INTIMA

Intimal thickening



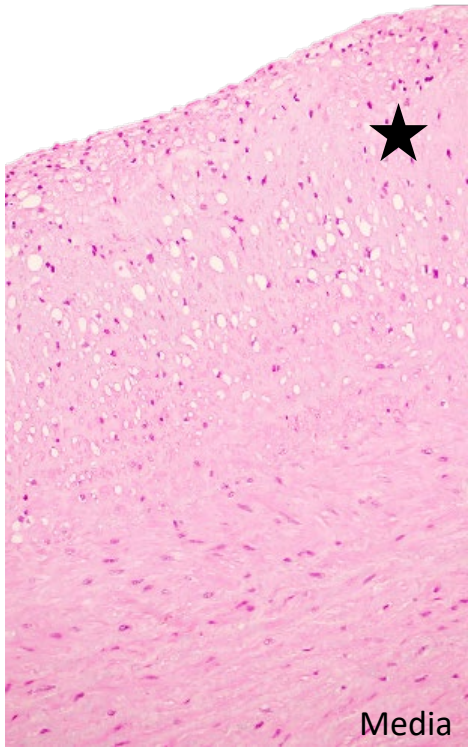
Alcian Blue

Intimal fibrosis

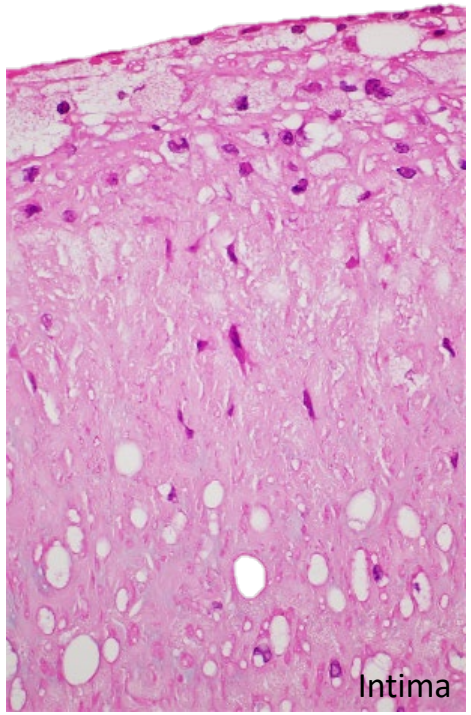


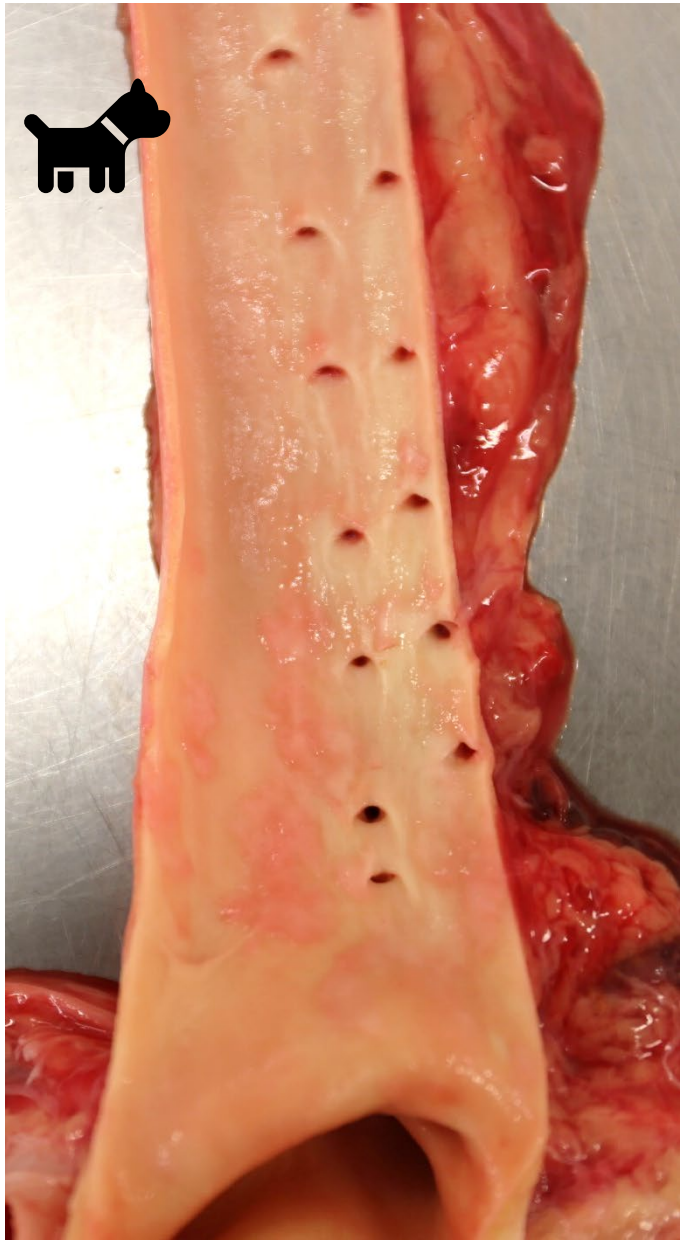
Masson trichrome stain

Atherosclerosis

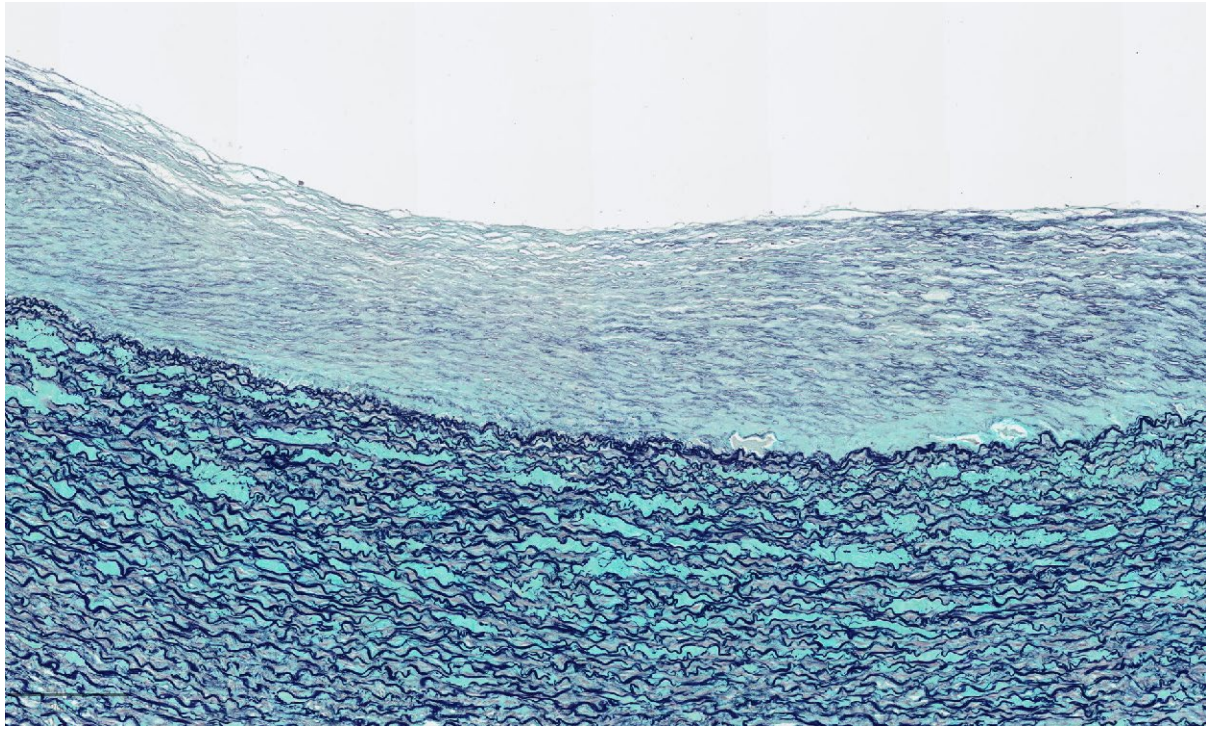


Atherosclerosis

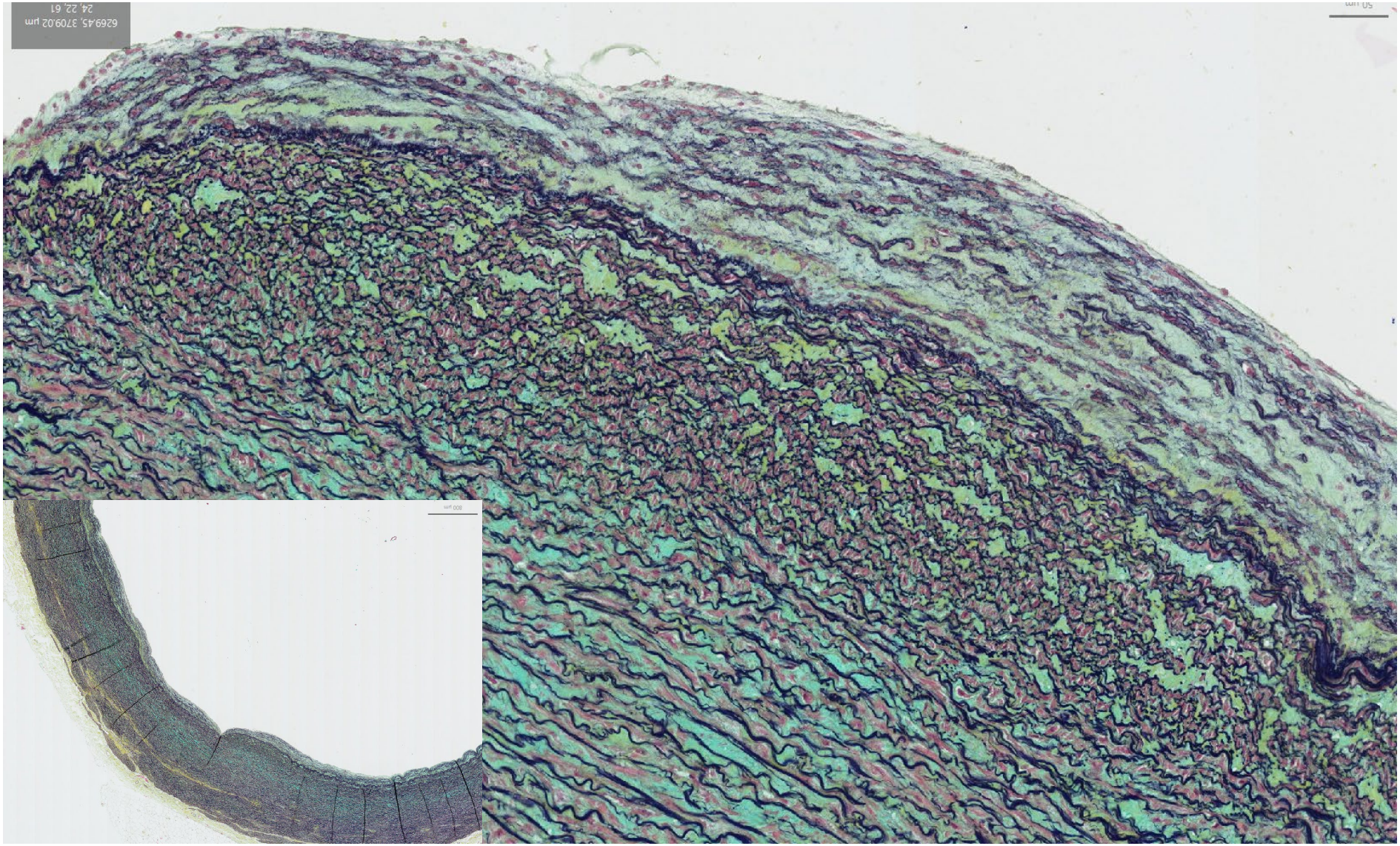




Intimal thickening



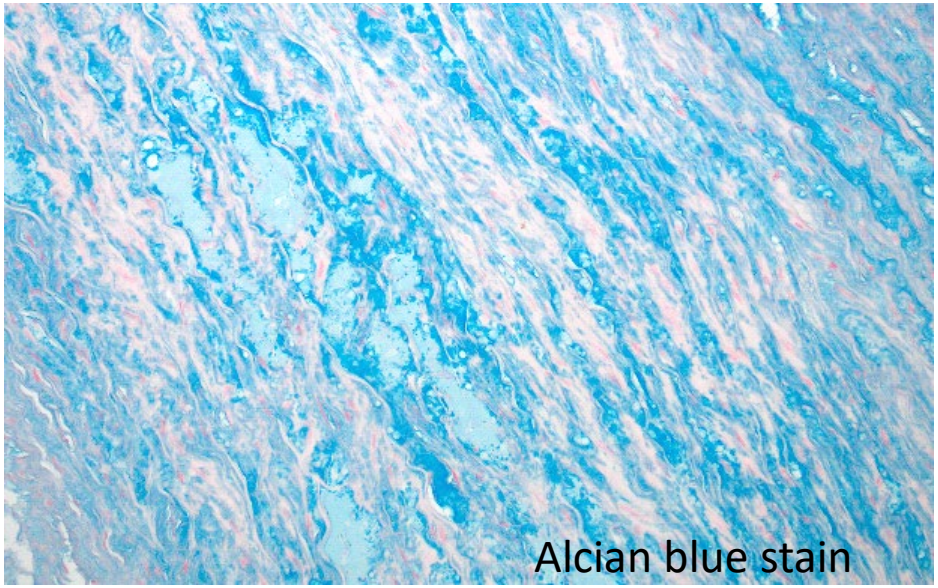
Intimal thickening



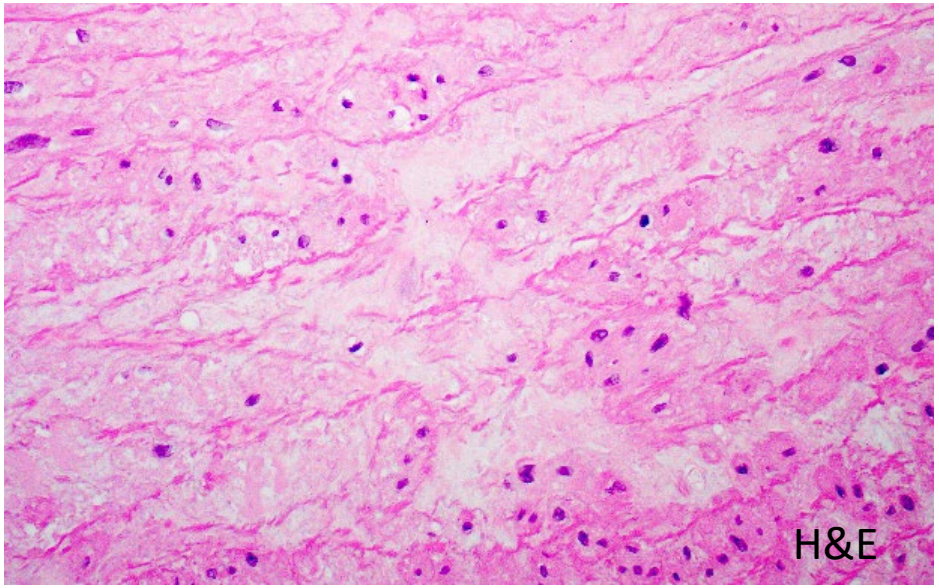
Pentachrome stain

HISTOLOGIC CHANGES IN THE ASCENDING AORTA/MEDIA

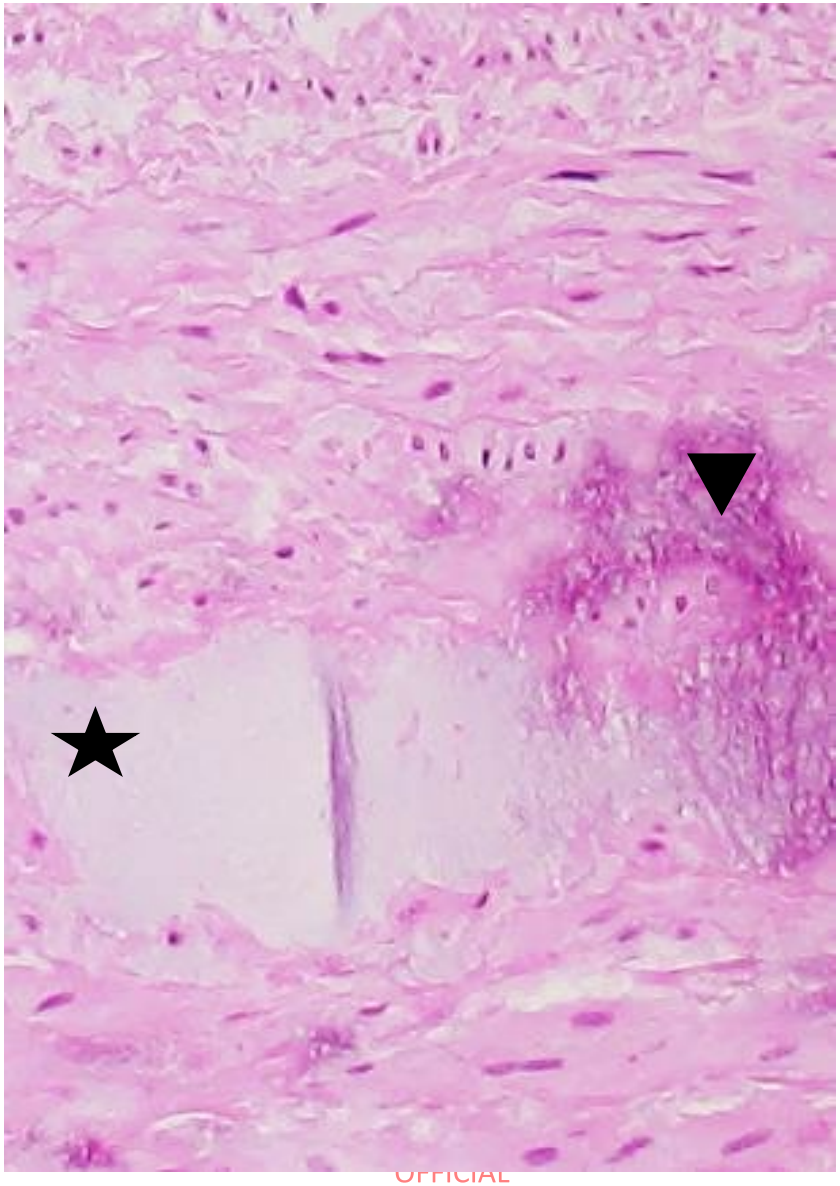
Intralamellar mucoid extracellular matrix accumulation



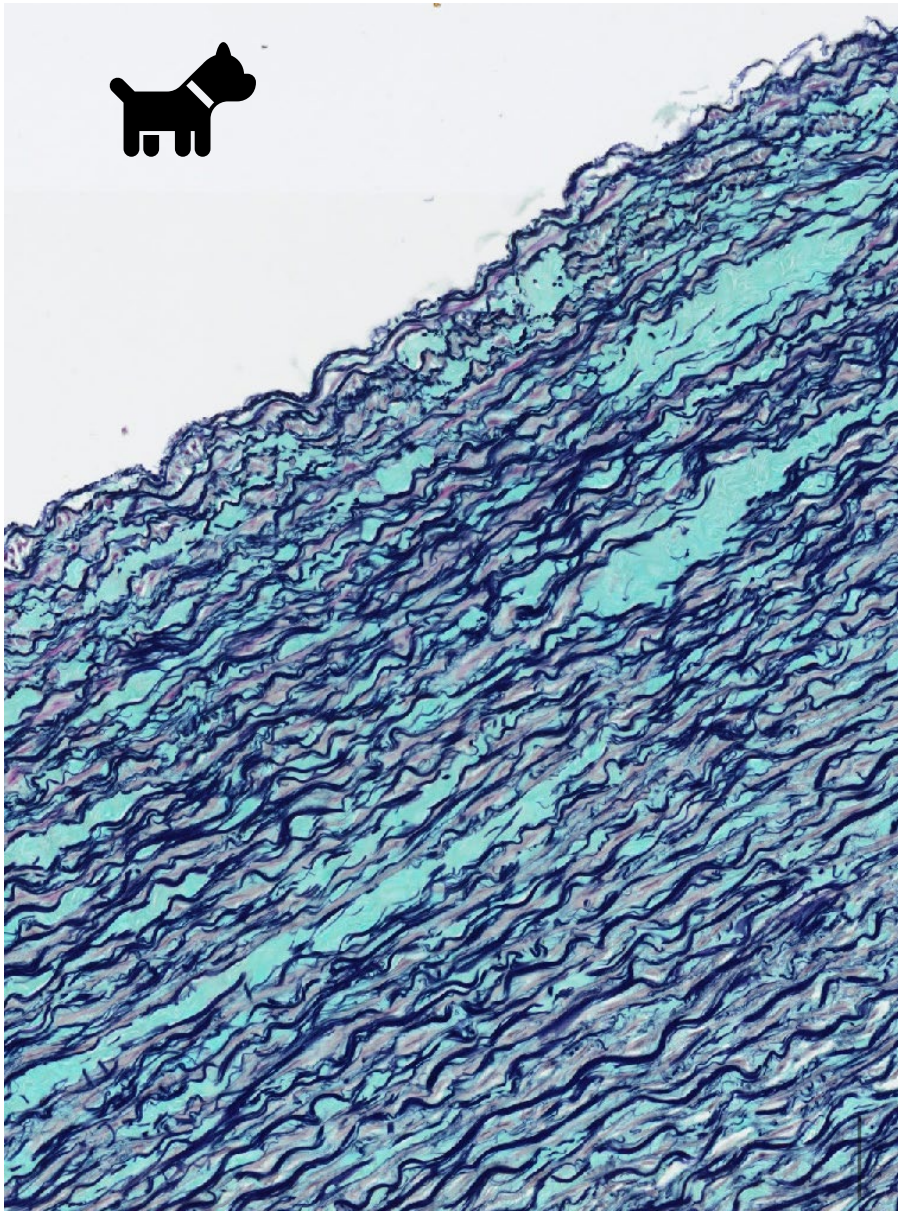
Translamellar mucoid extracellular matrix accumulation

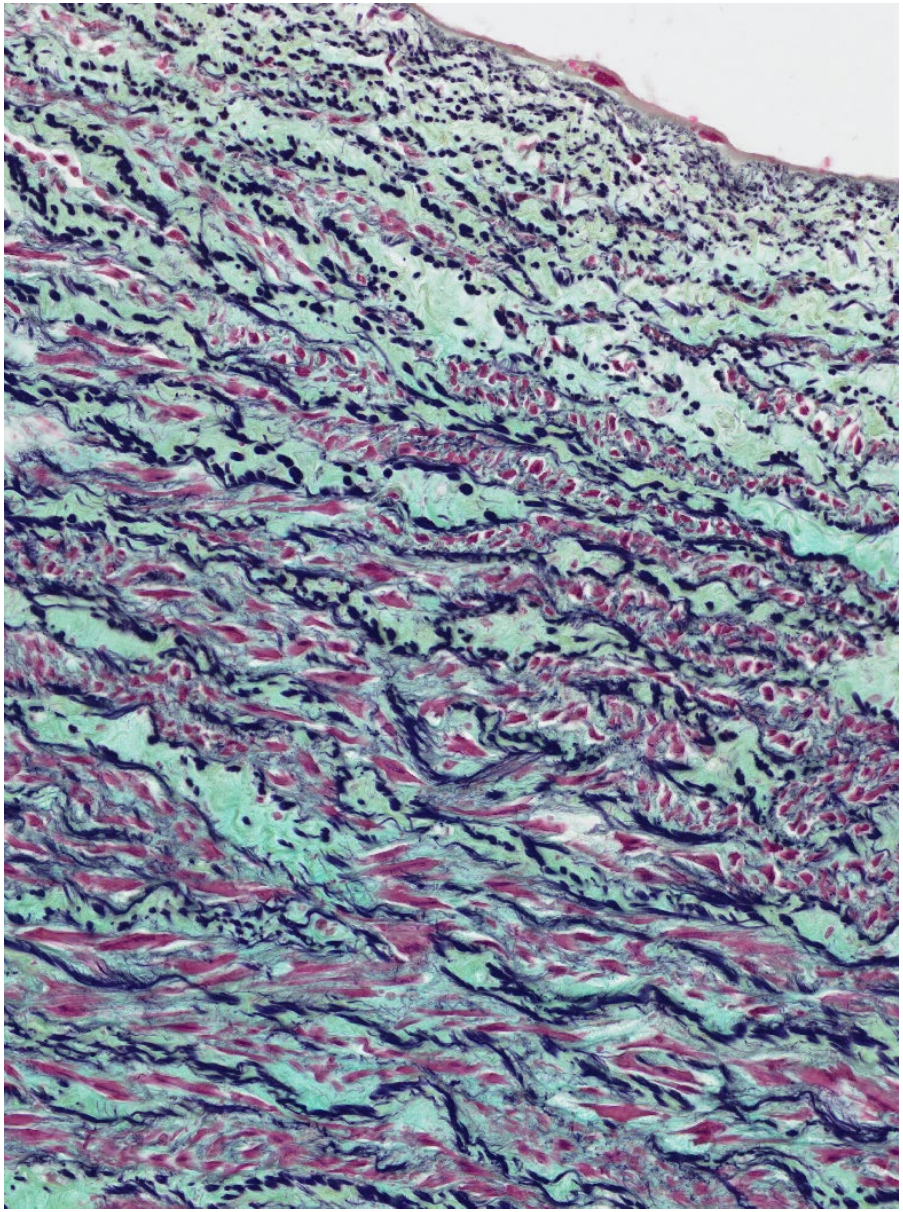


Intralamellar mucoid extracellular matrix accumulation and mineralization



Intralamellar MEMA

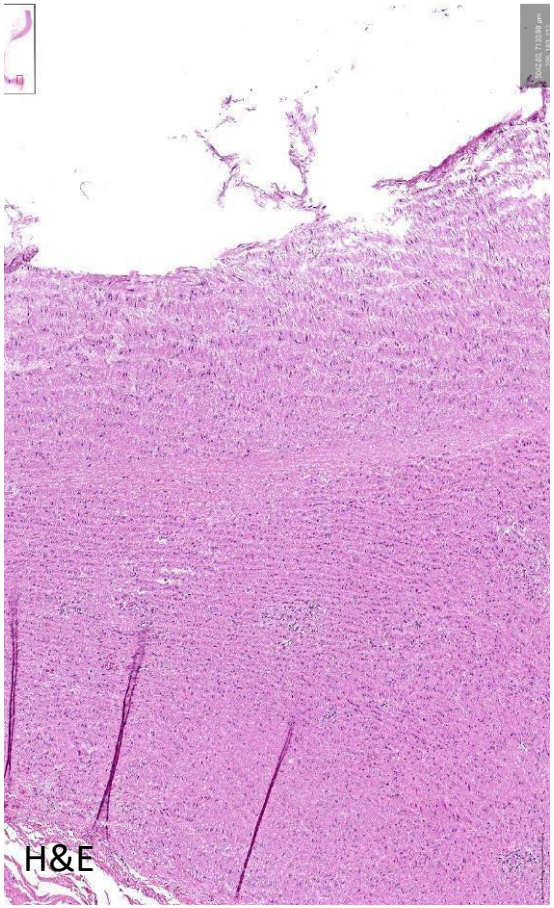


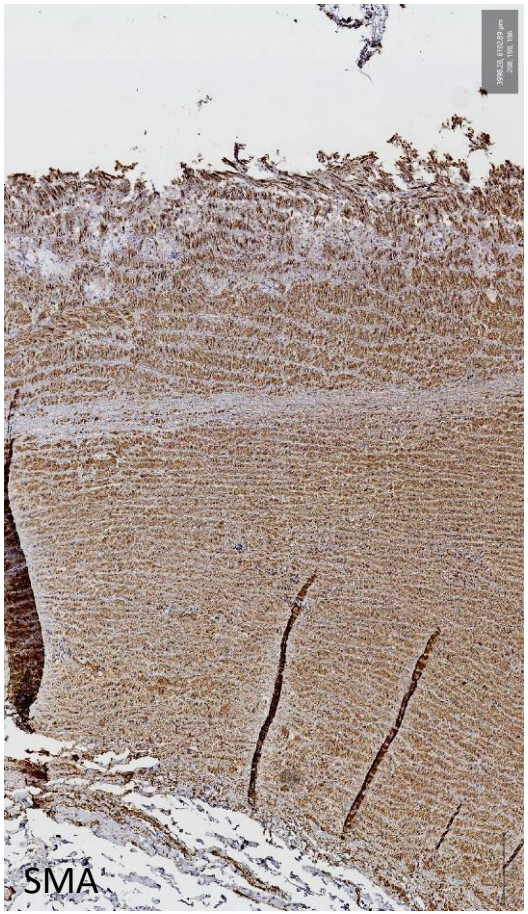


Pentachrome stain

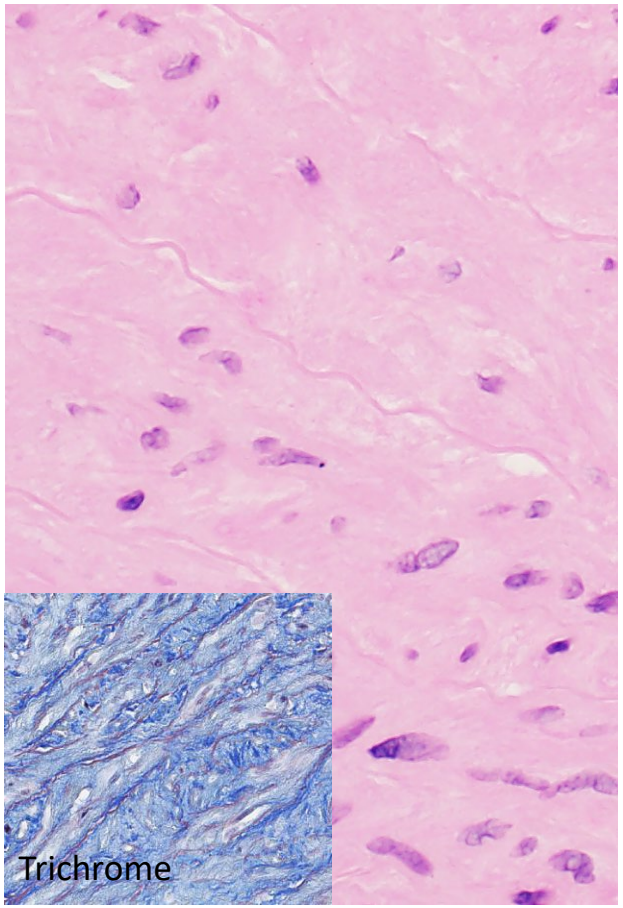
HISTOLOGIC CHANGES IN THE ASCENDING AORTA/MEDIA

Smooth muscle cell nuclei loss

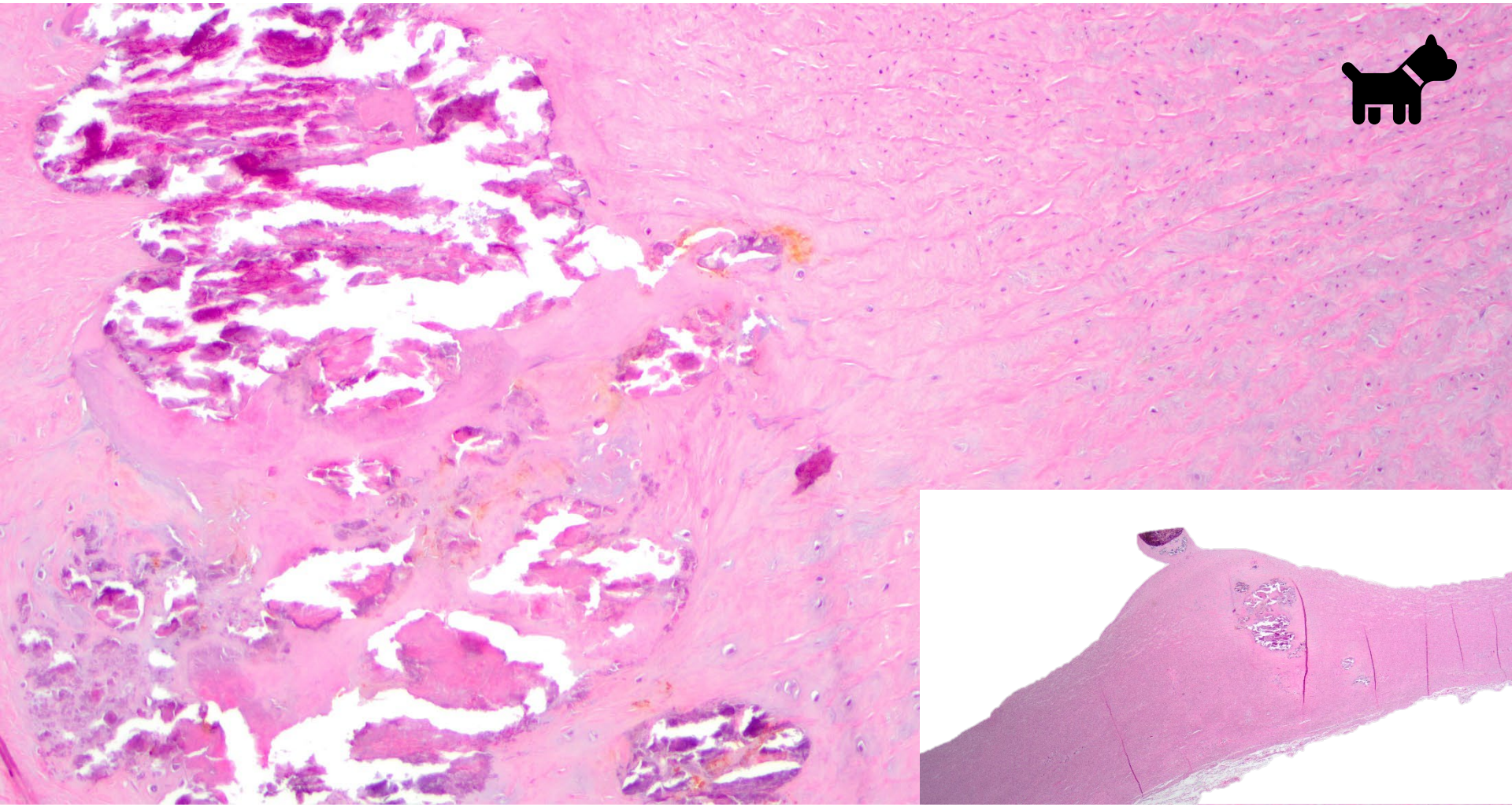




Fibrosis



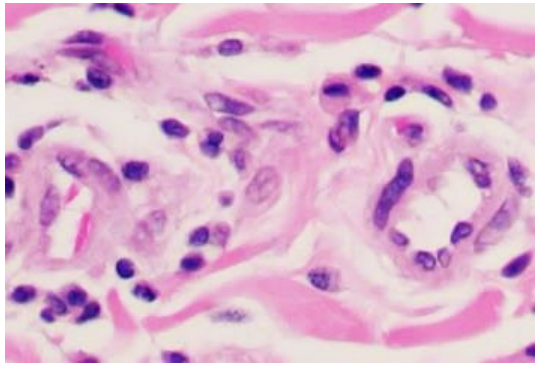
Medial calcification



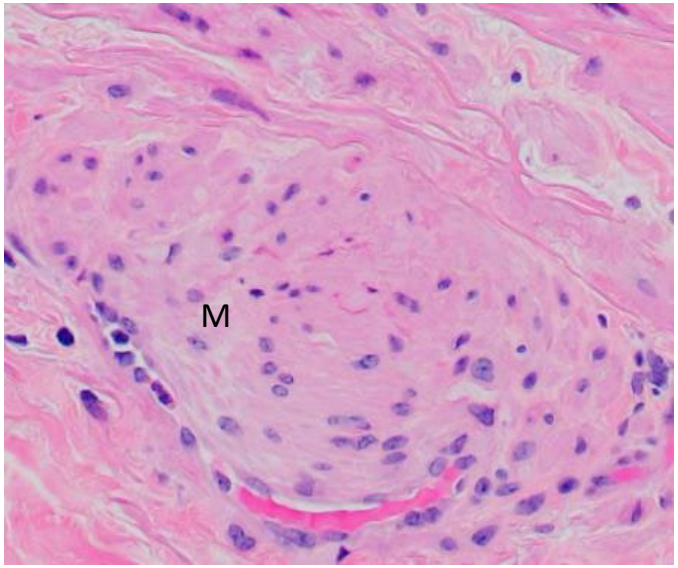
HISTOLOGIC CHANGES IN THE ASCENDING AORTA/ADVENTITIA (*vasa vasorum*)

Hypertension

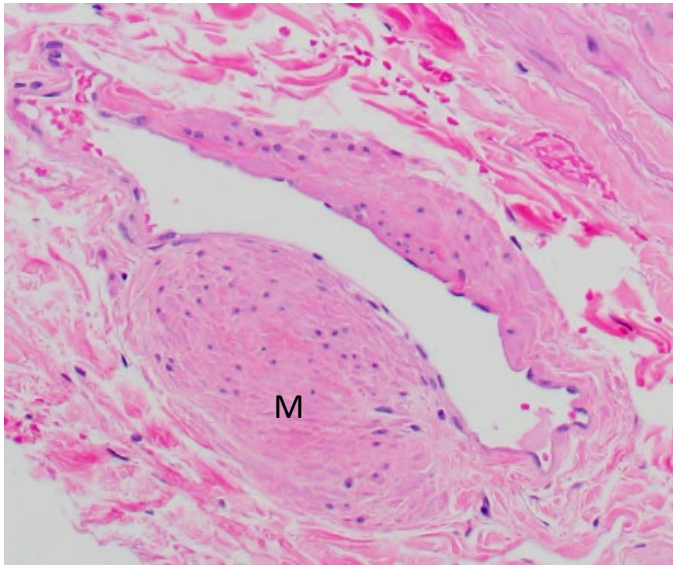
Normal *vasa vasorum*



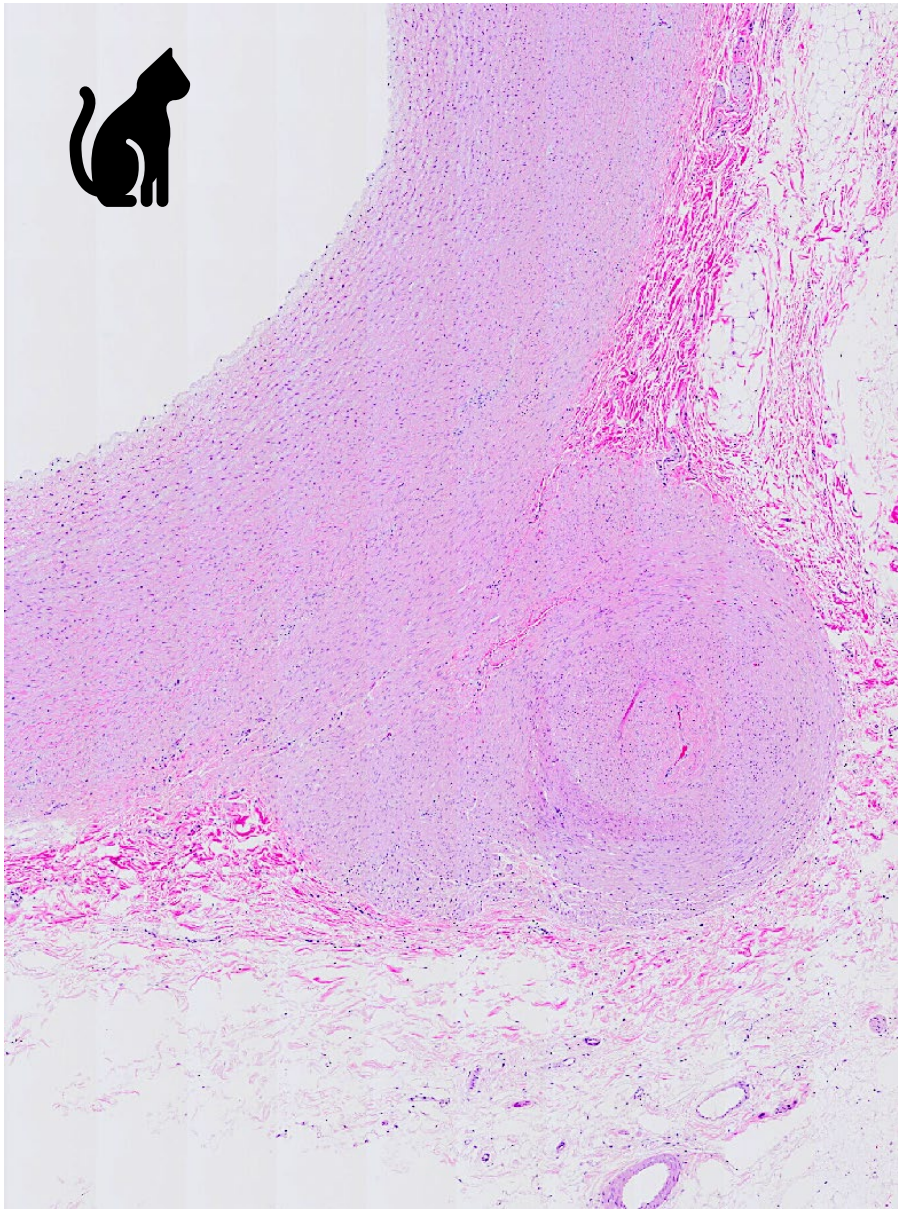
Vasa vasorum with medial hypertrophy/complete occlusion

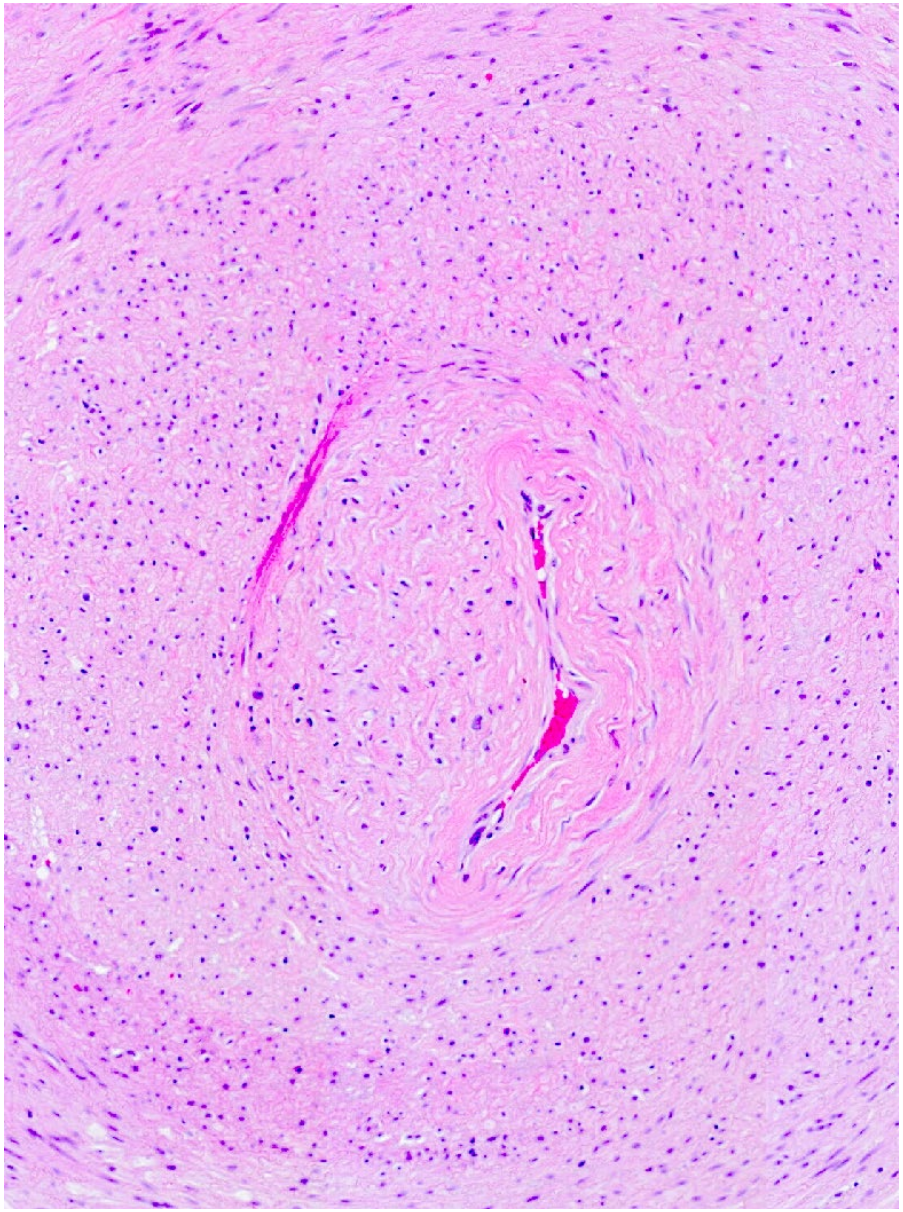


Vasa vasorum with medial hypertrophy/partial occlusion



Vasa vasorum with medial hypertrophy



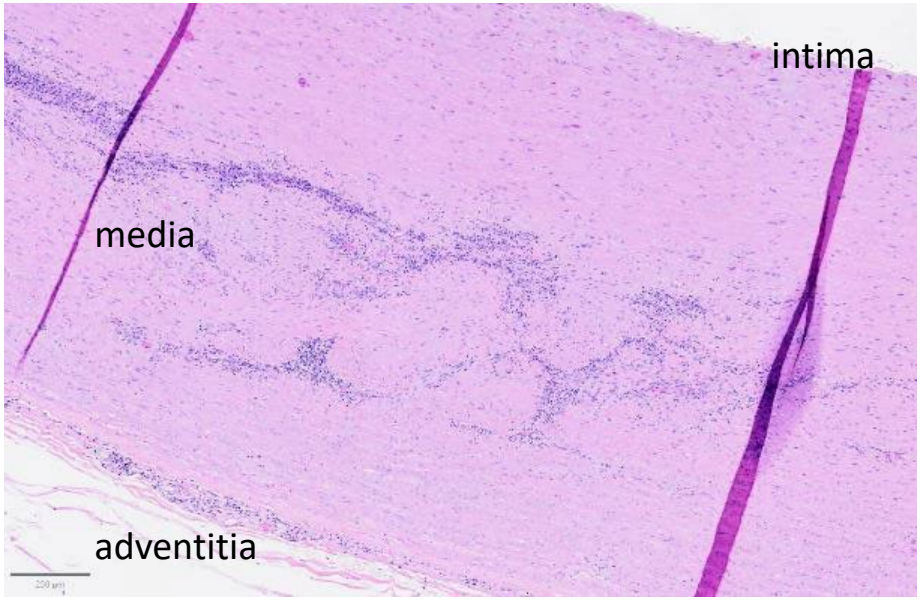


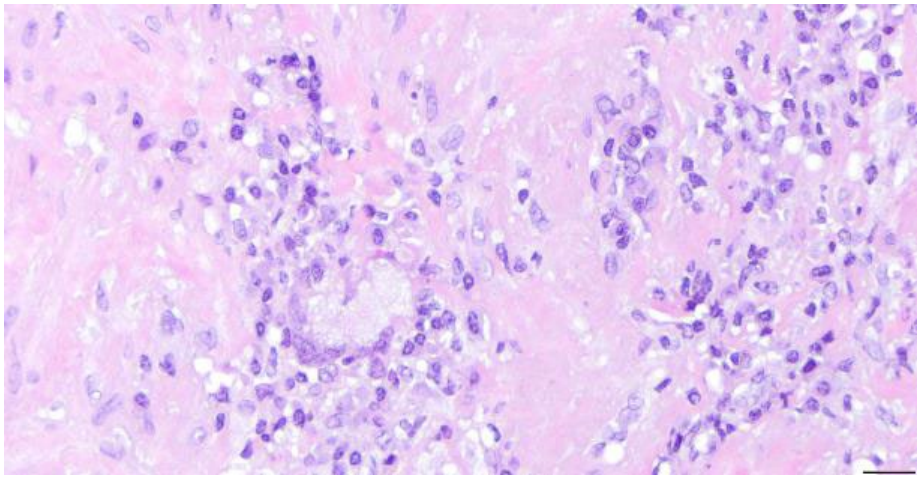
AORTITIS

Non-infectious (human)
- Giant cell arteritis
- Takayasu arteritis
- IgG4-related disease
- etc….

Infectious
- Fungi
- *M. tuberculosis*

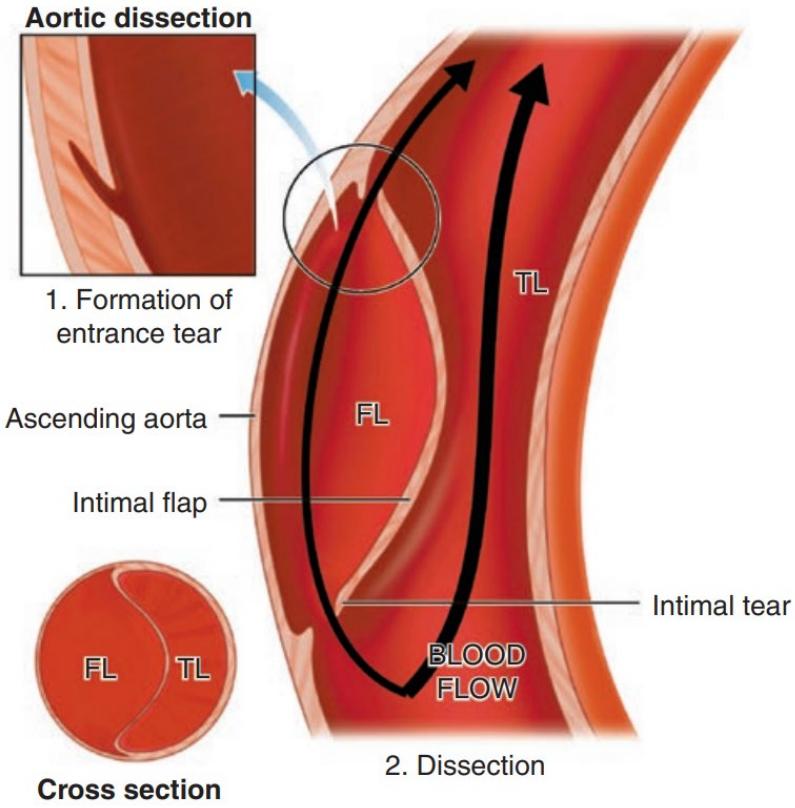
tree-bark appearance





Great ape

Aortic dissection

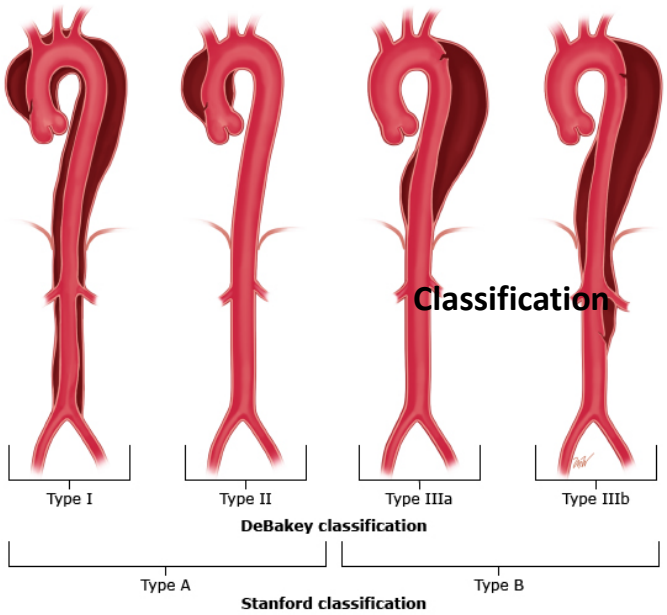


Diseases of the Aorta. Springer Nature Switzerland. 2019

Risk factors

- Hypertension
- Abrupt/transient/severe increase in blood pressure
- Genetic diseases
- Congenital diseases
- Pre-existing aortic aneurysm
- Atherosclerosis
- Family history
- Trauma, blunt, or iatrogenic
- Inflammatory/infectious diseases
- Pregnancy

Classification of aortic dissection



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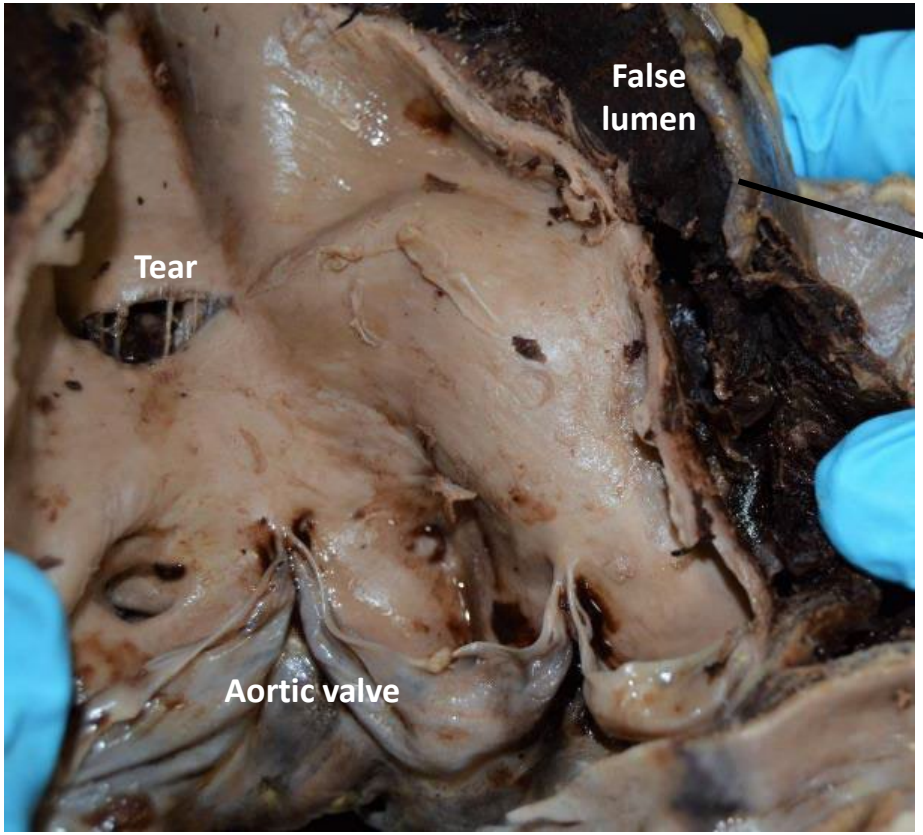
DeBakey classification

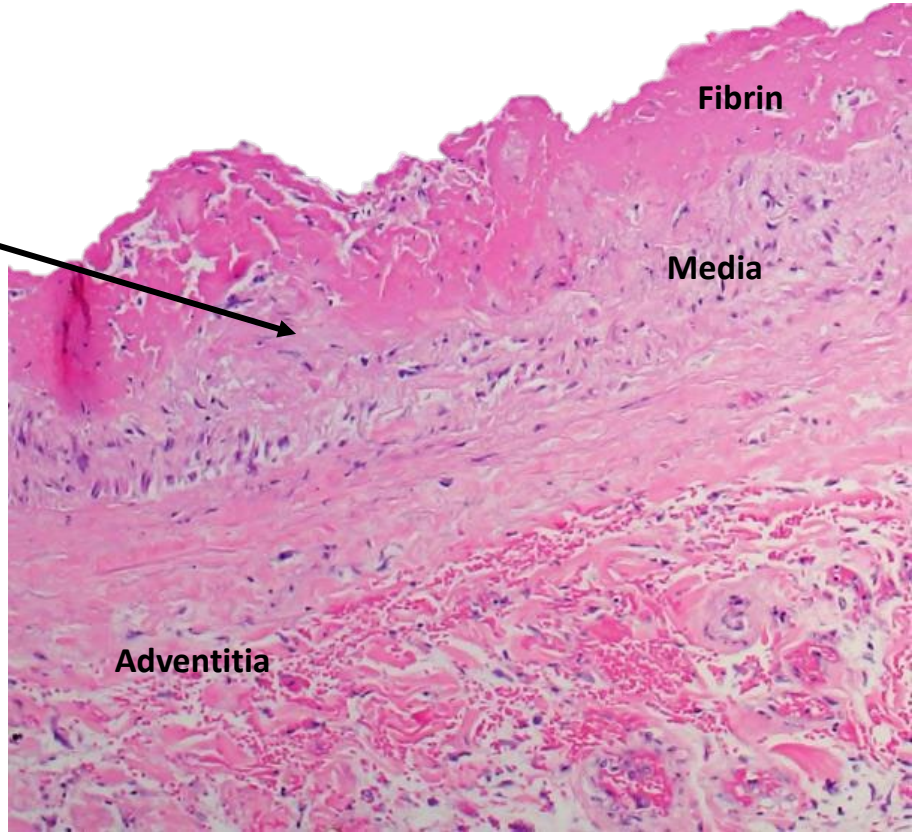
- Type I: ascending aorta/arch/descending thoracic aorta/ progress to involve the abdominal aorta
- Type II: ascending aorta
- Type IIIa: descending thoracic aorta distal to the left subclavian artery and proximal to the celiac artery
- Type IIIb: thoracic and abdominal aorta distal to the left subclavian artery

Stanford classification

- Type A: ascending aorta/may progress to involve the arch and thoracoabdominal aorta
- Type B: descending thoracic or thoracoabdominal aorta distal to the left subclavian artery without involvement of ascending aorta

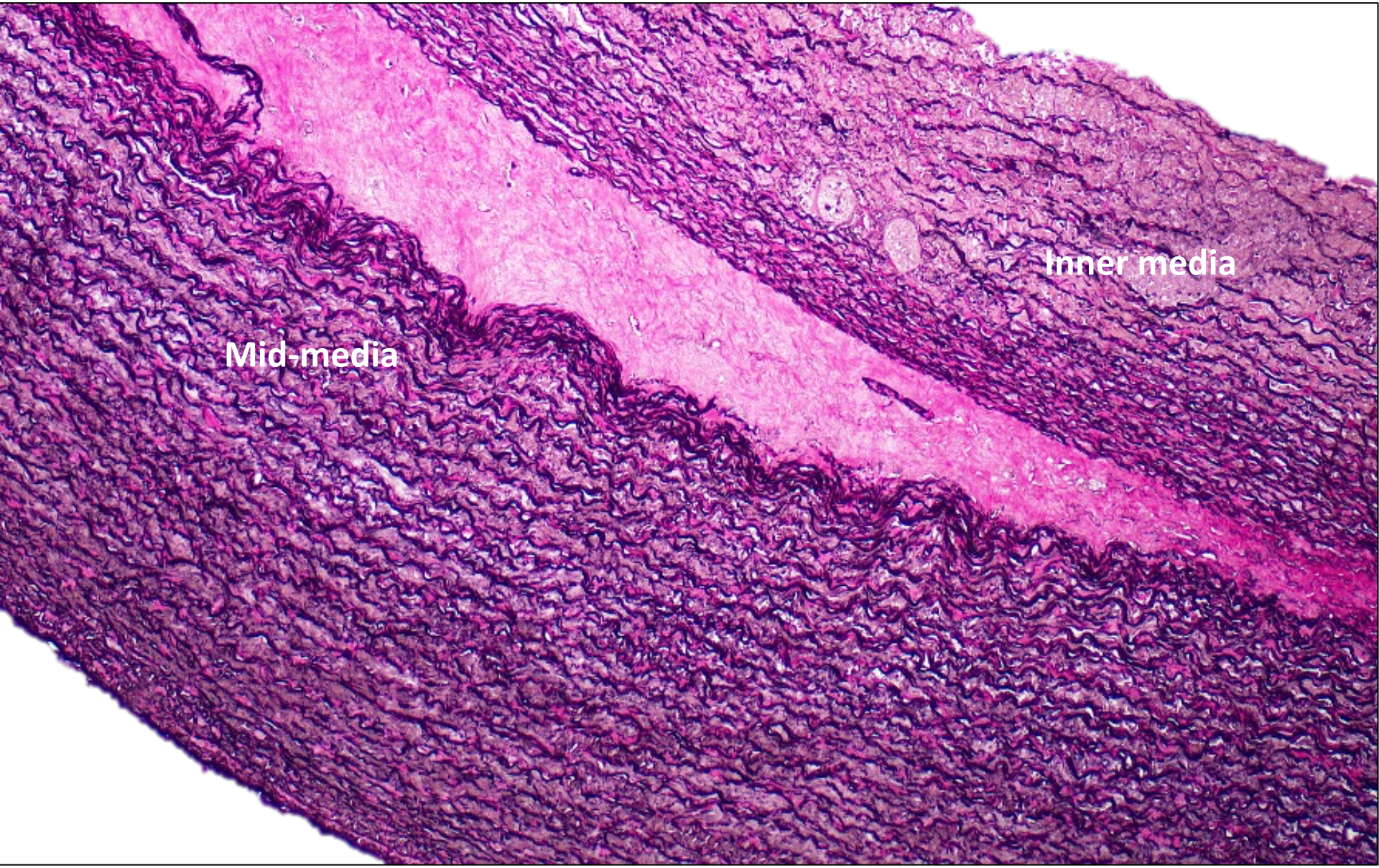
AORTIC DISSECTION





Great ape

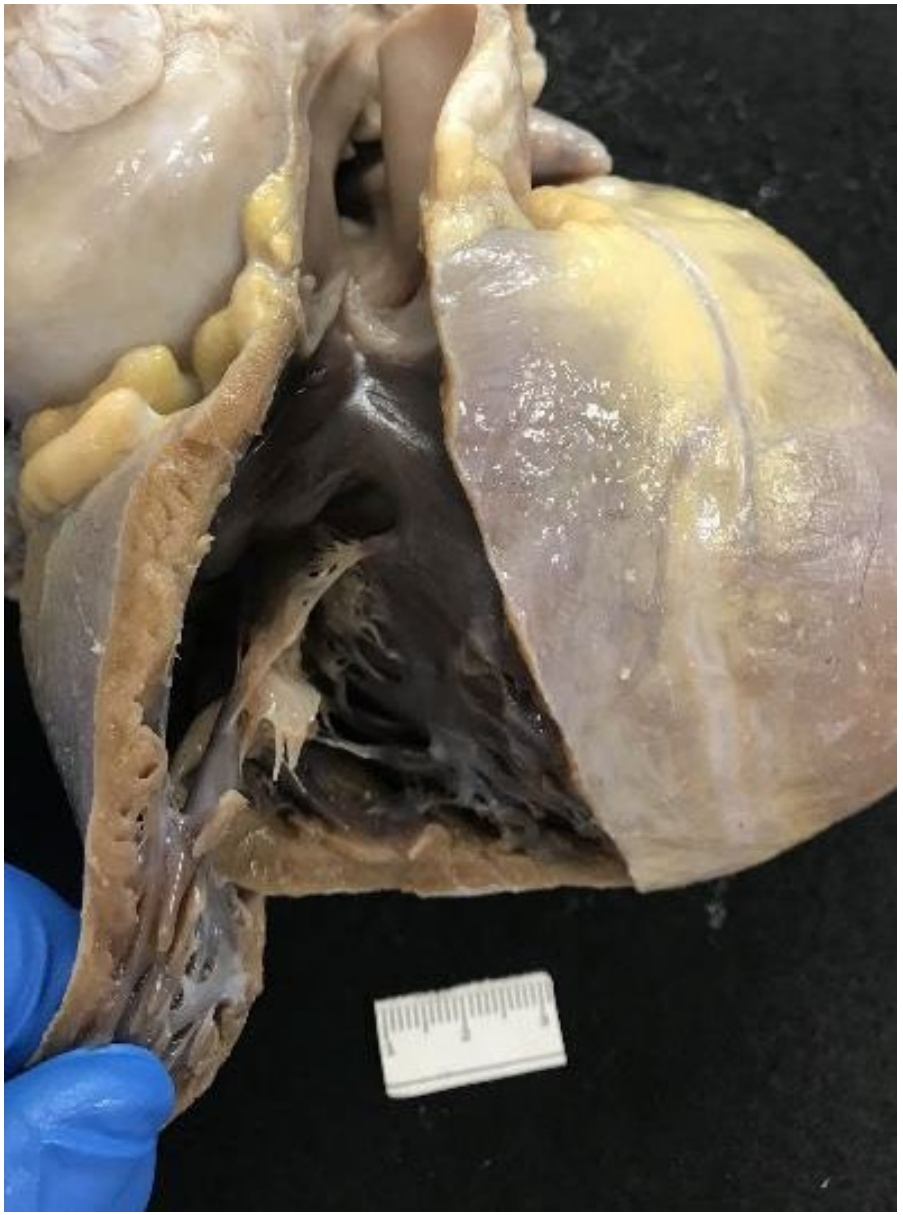
AORTIC DISSECTION



Van Gieson stain

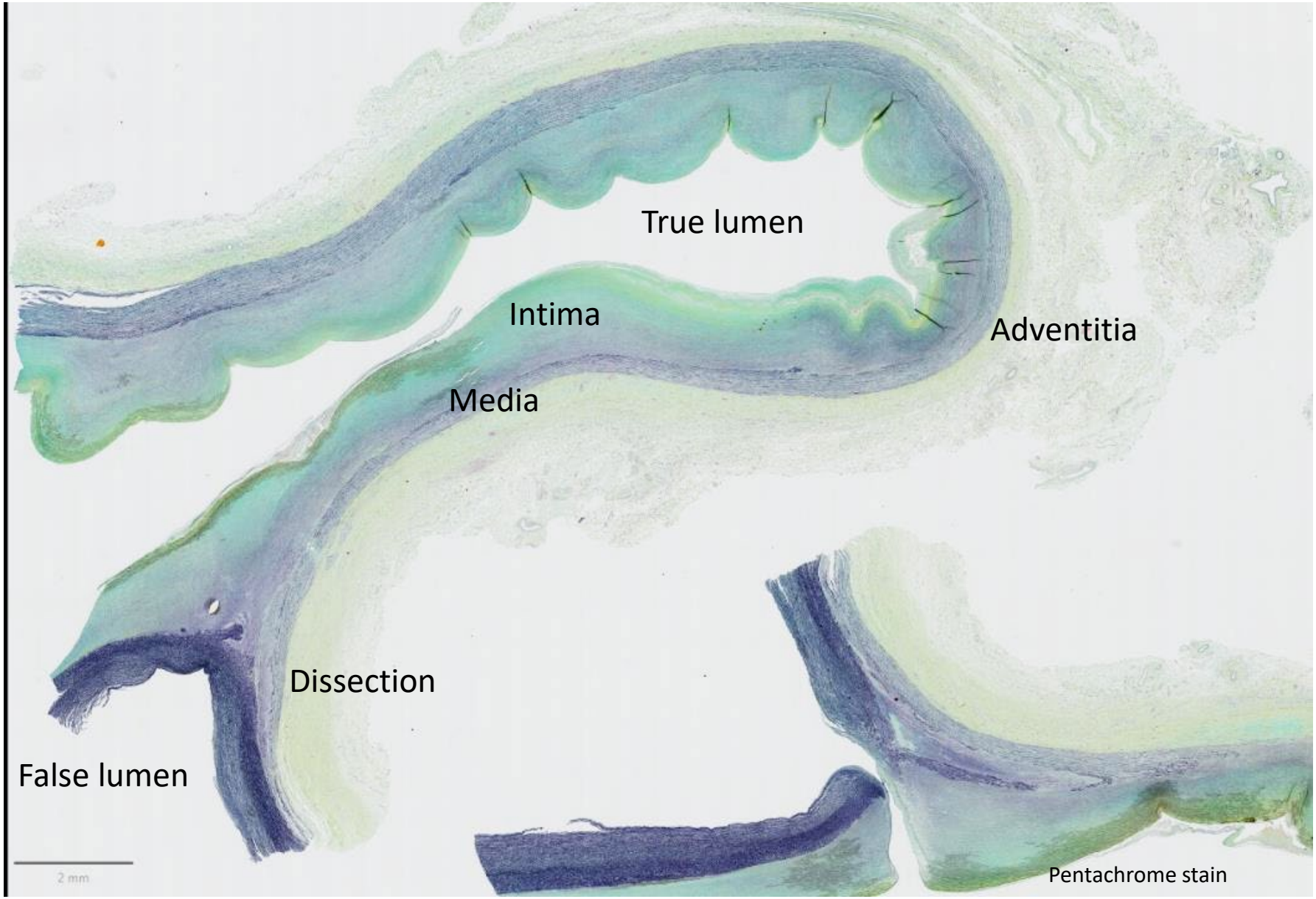
AORTIC DISSECTION

THE GREAT APE HEART PROJECT

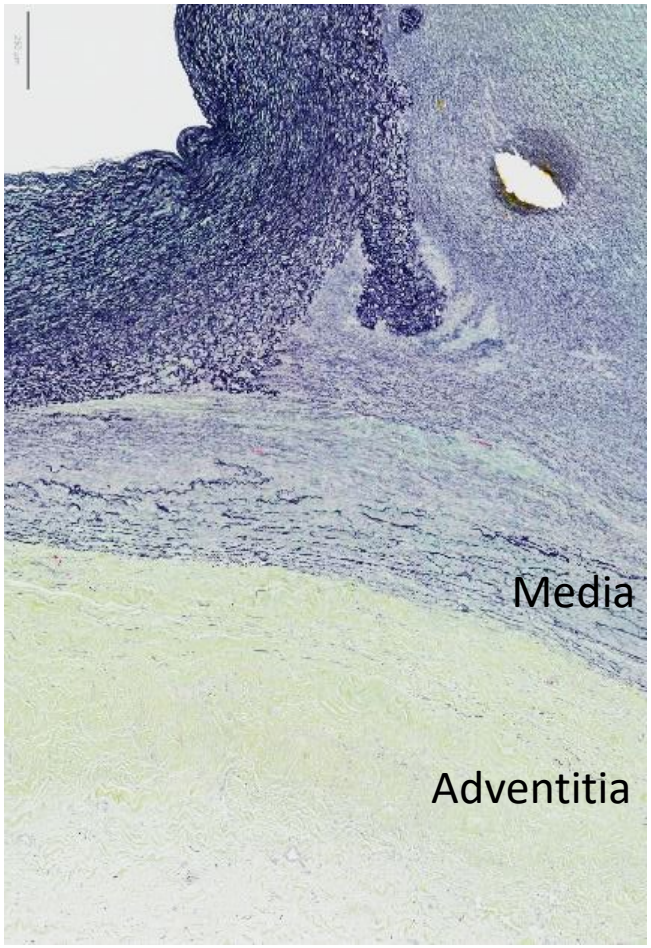


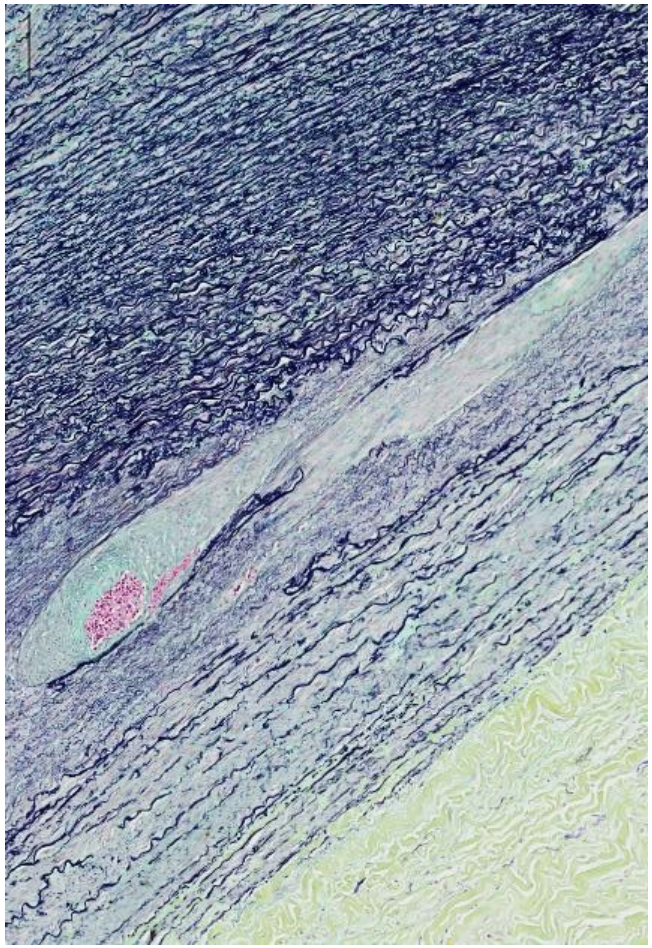
Great ape

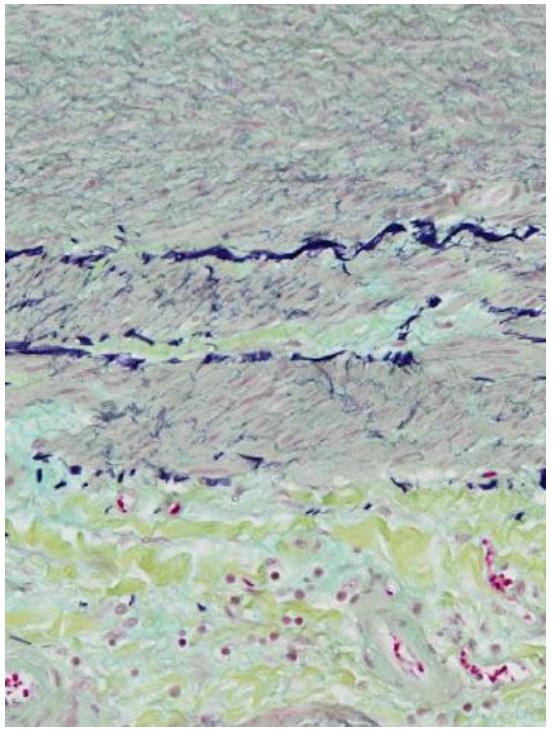
AORTIC DISSECTION



AORTIC DISSECTION



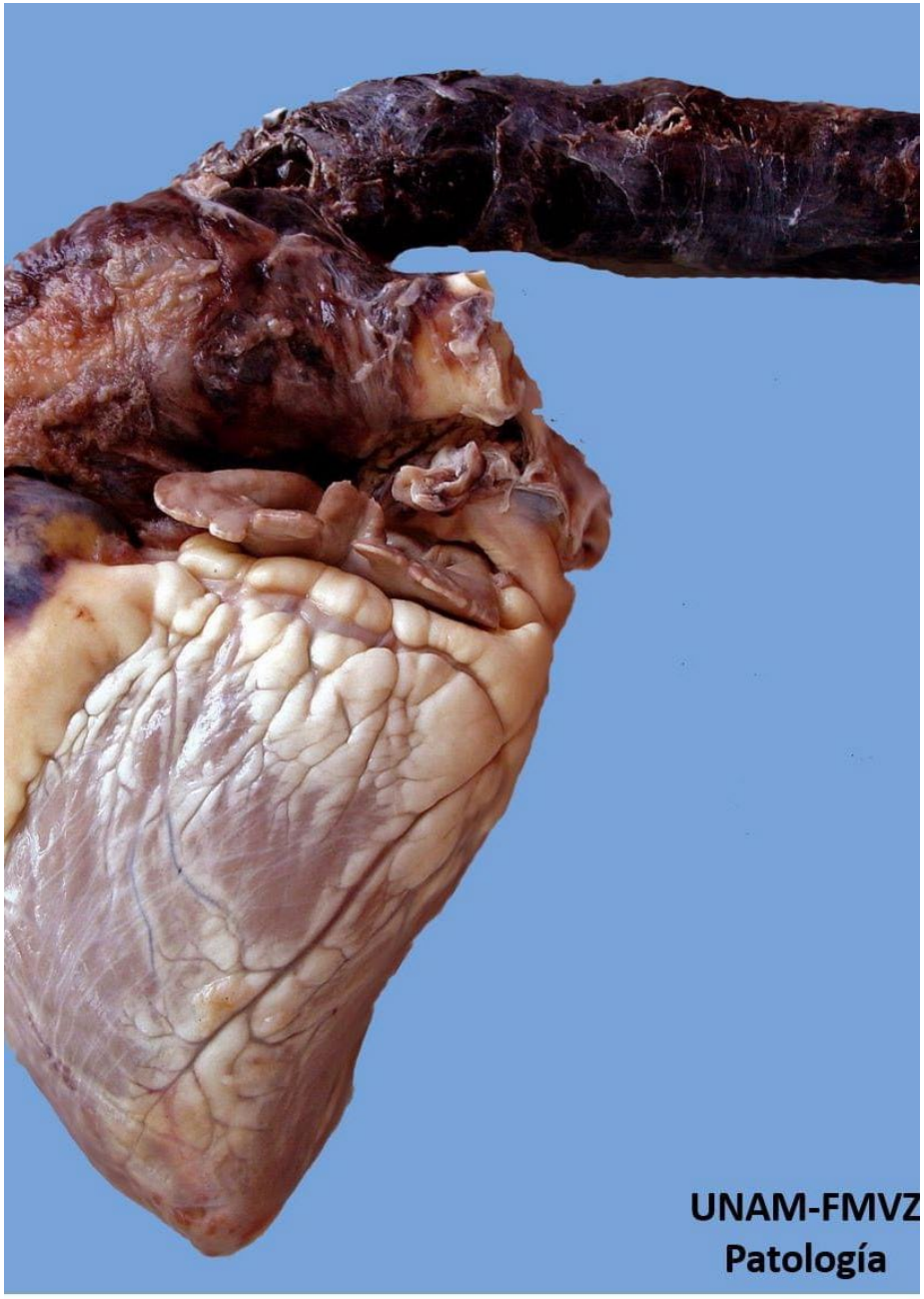




Pentachrome stain

Great ape

Descending aorta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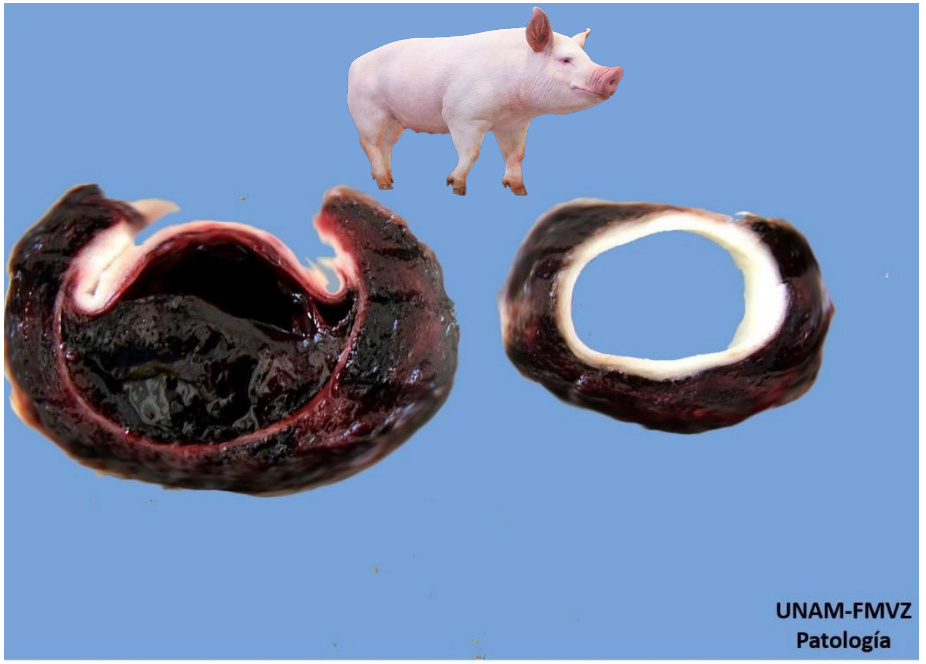
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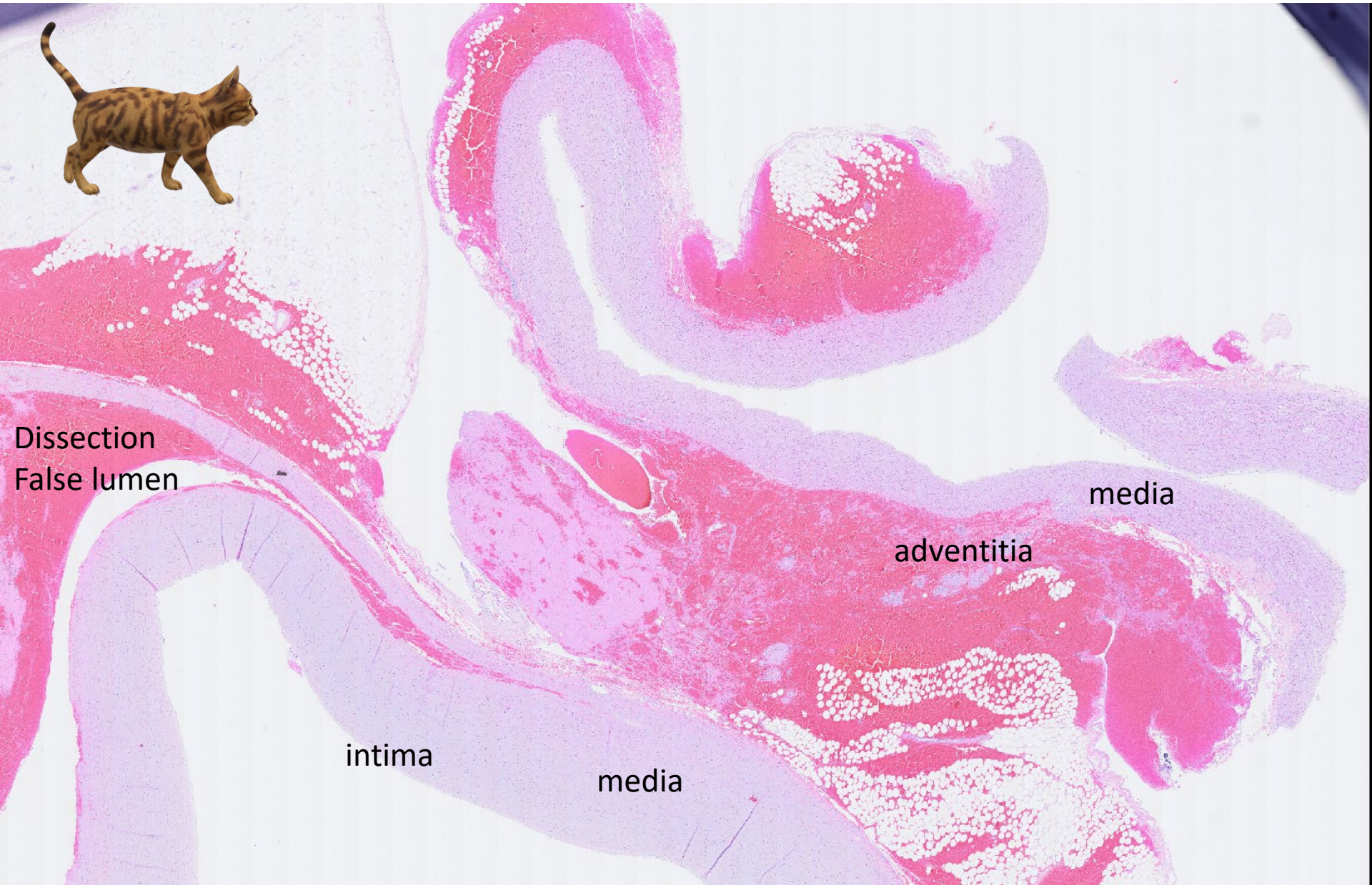
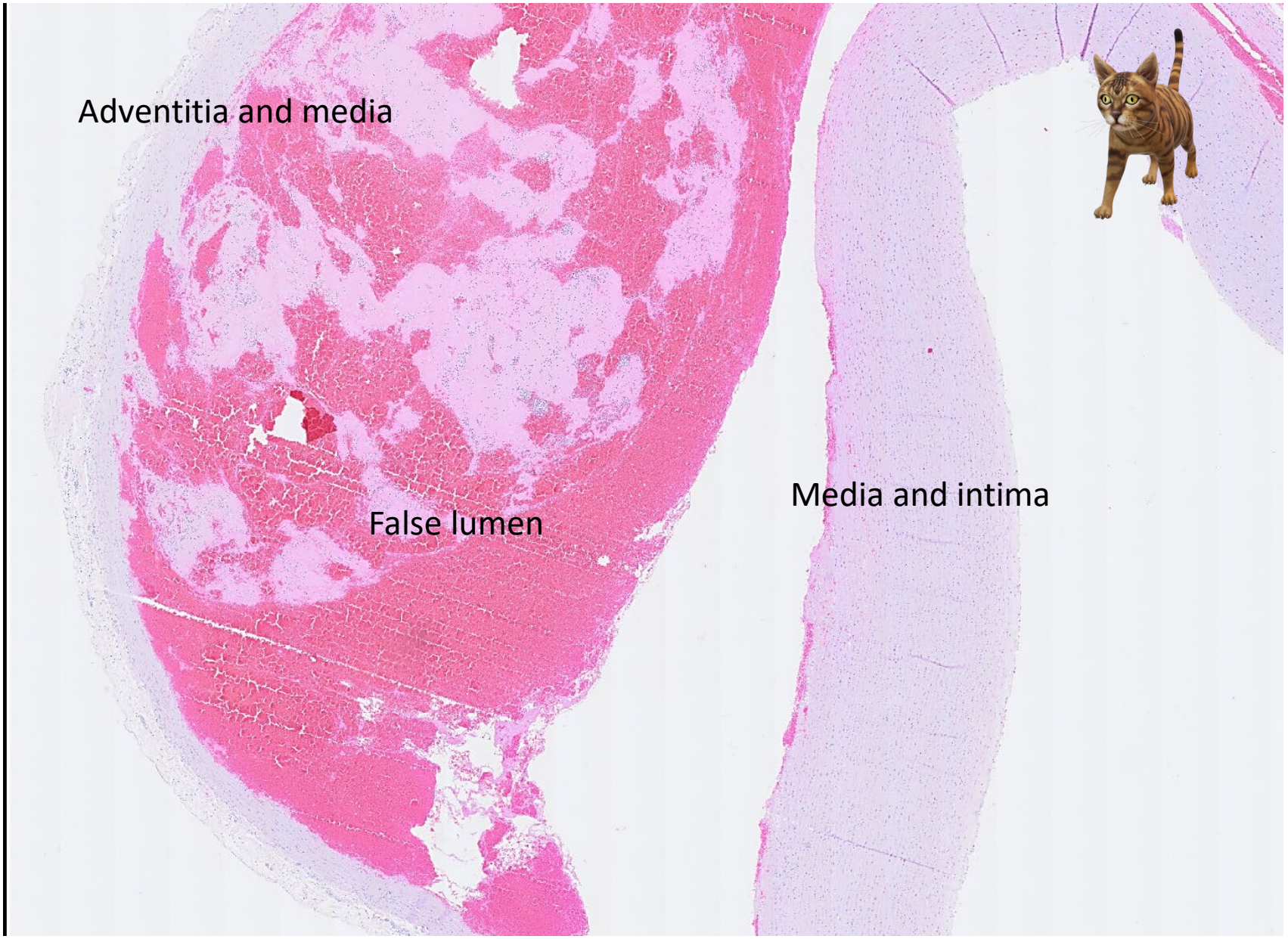
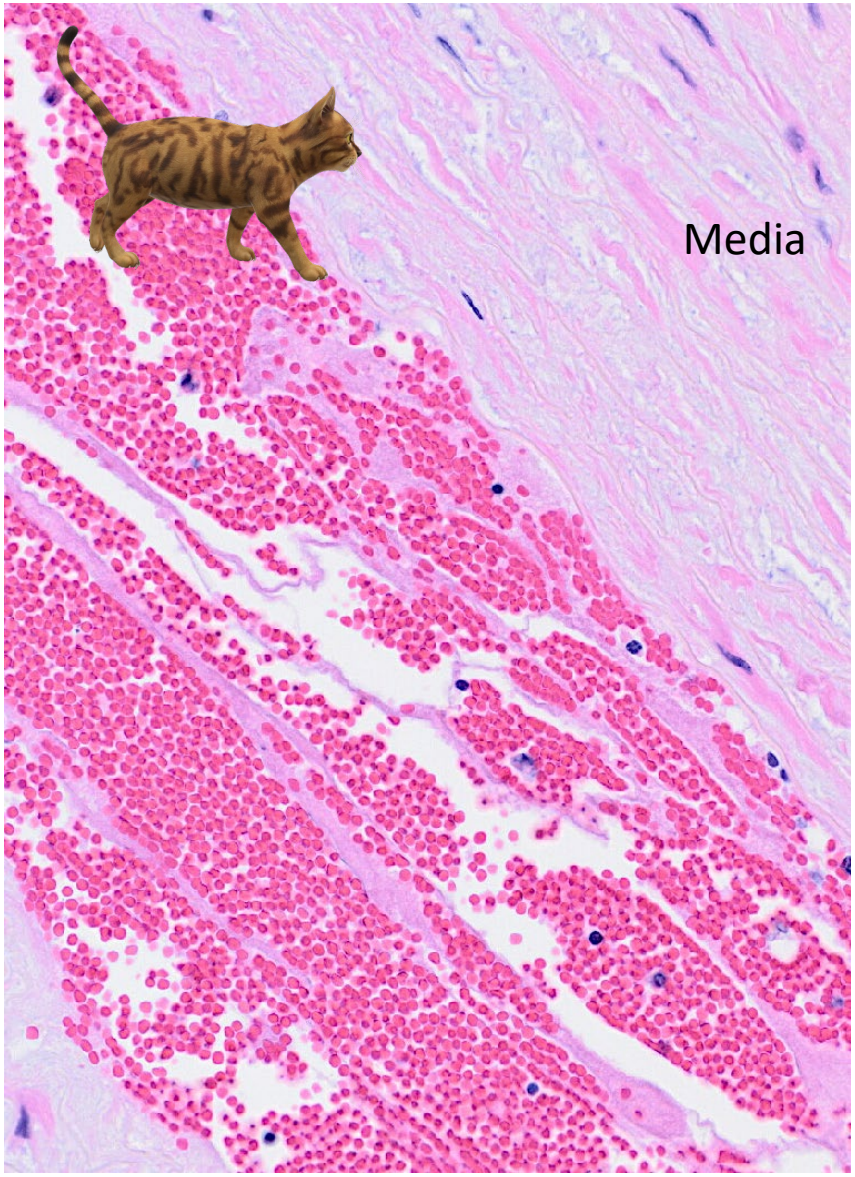
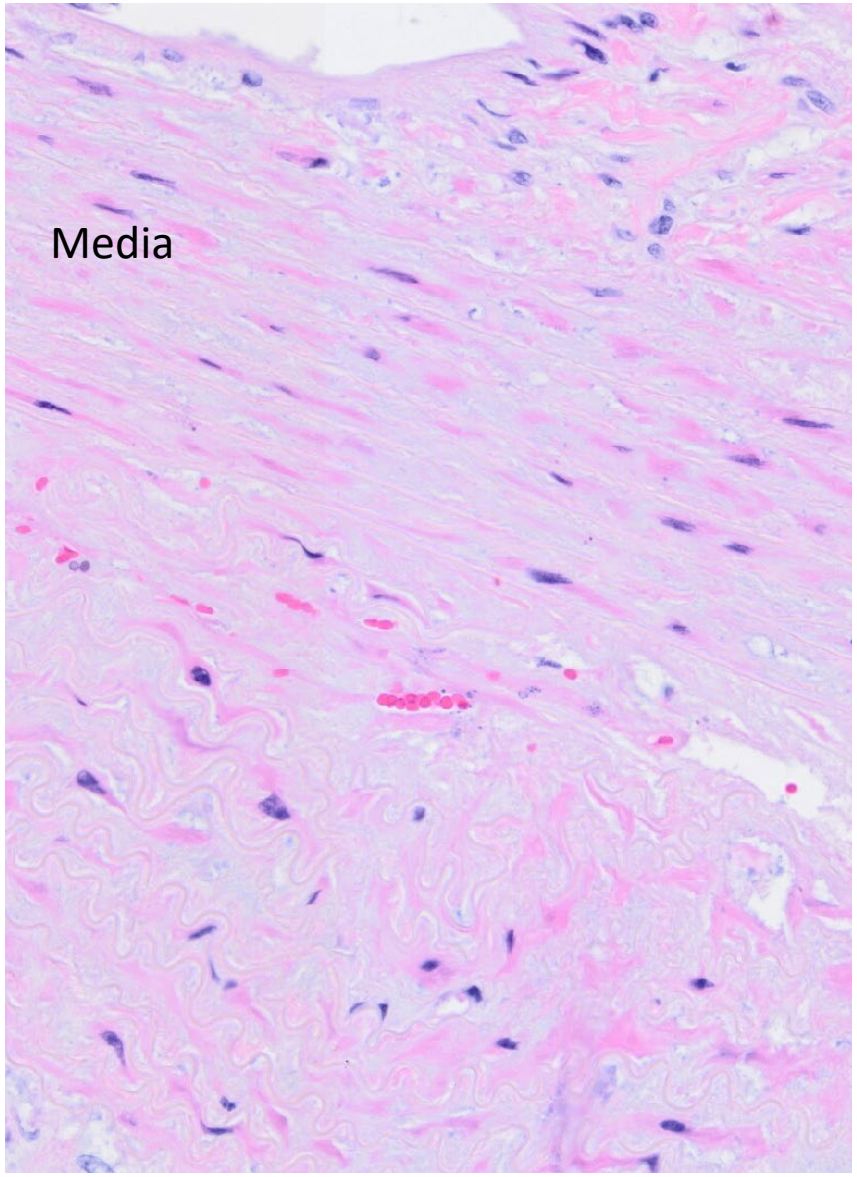
Aortic dissection

Aortic dissection


Dissection
False lumen
media
adventitia
intima
media


Adventitia and media
False lumen
Media and intima


Media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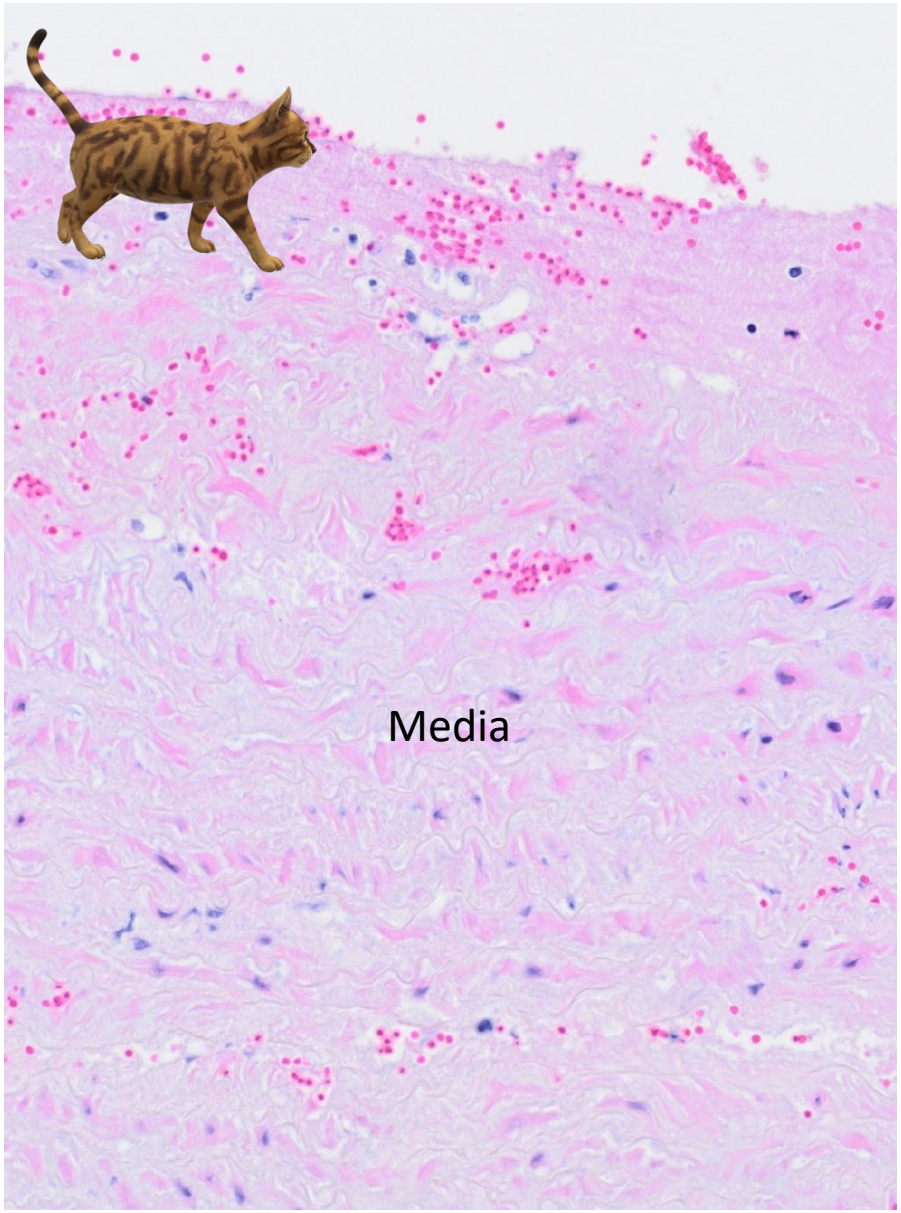
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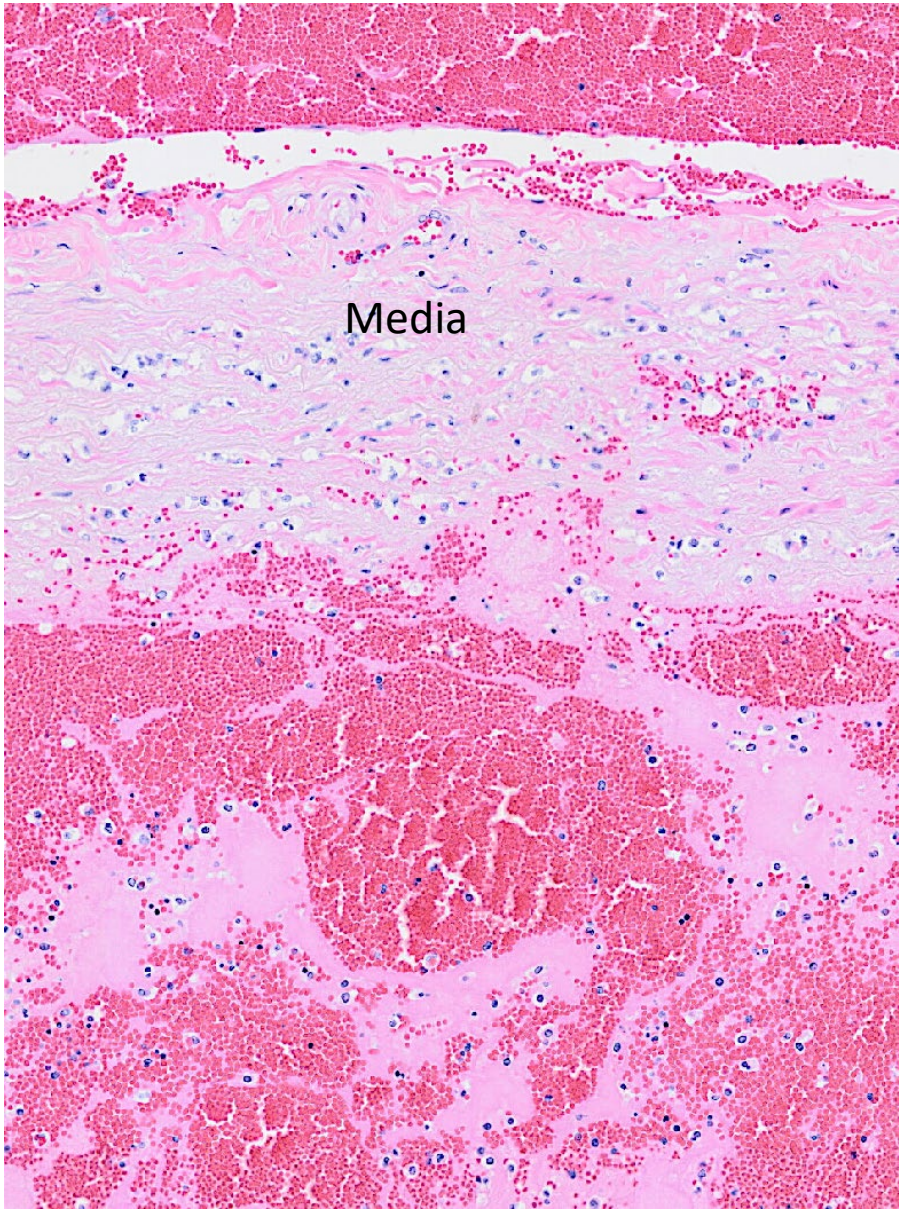
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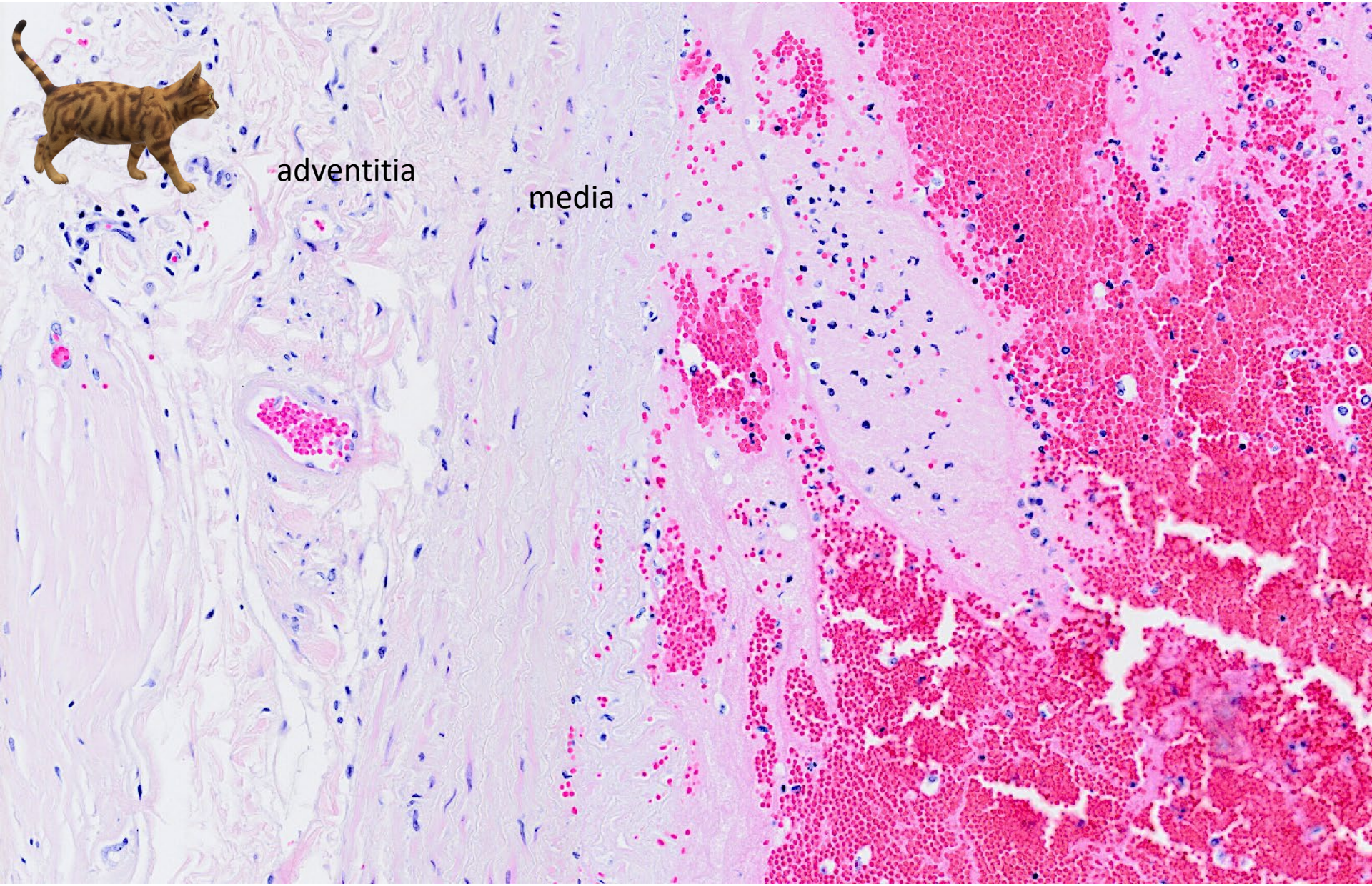
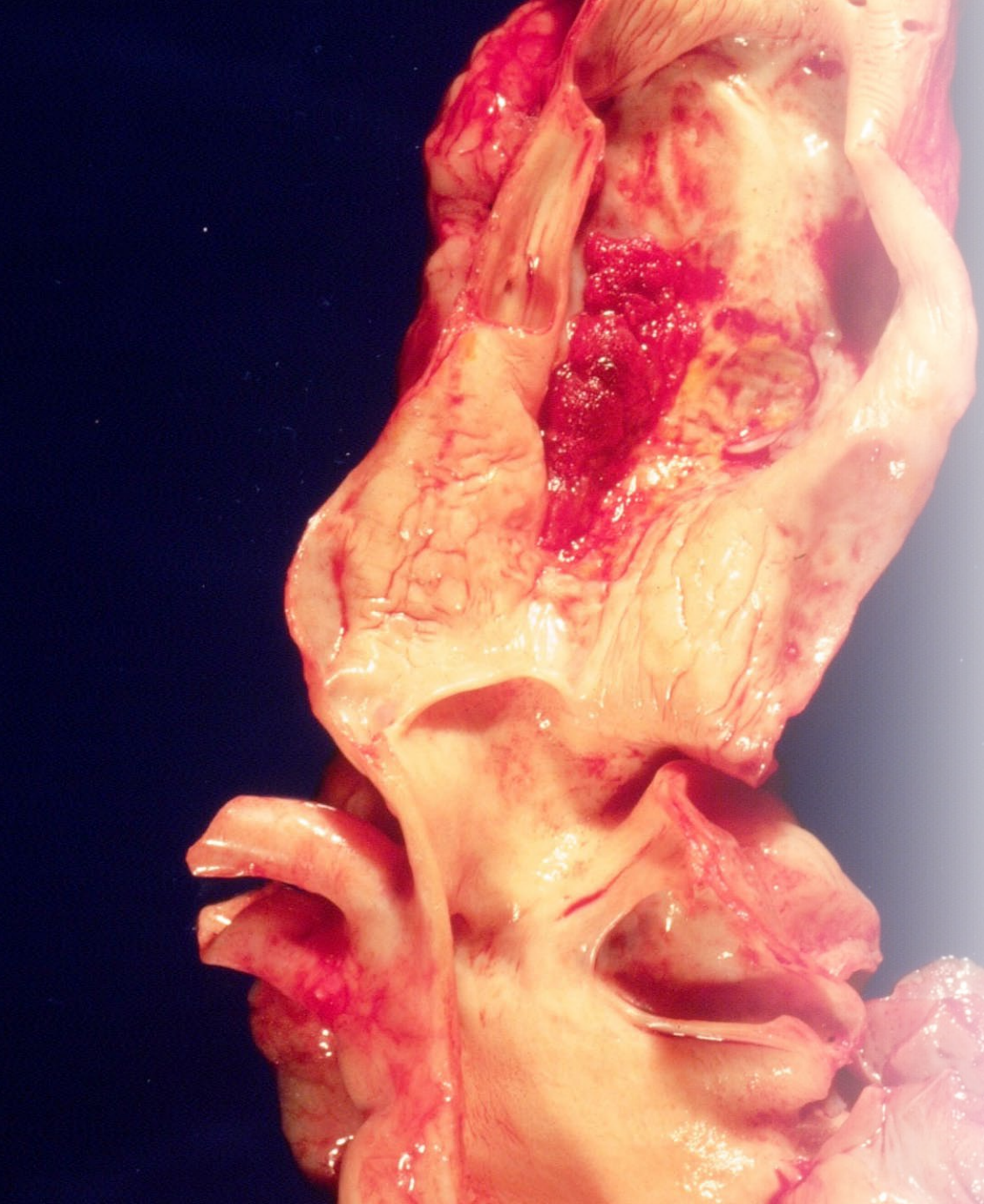
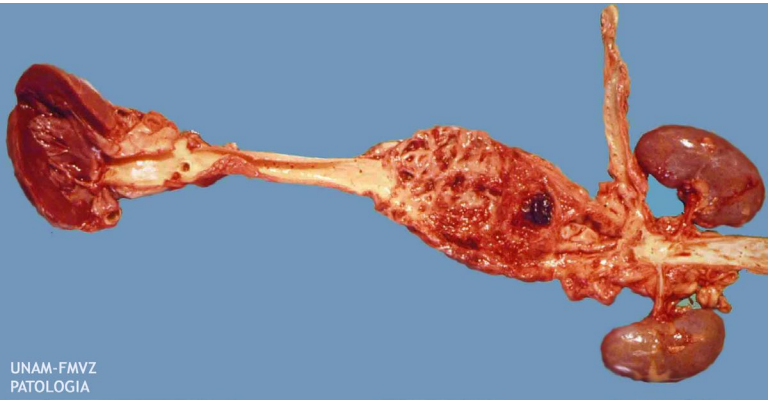




Aneurysm

Predisposing factors

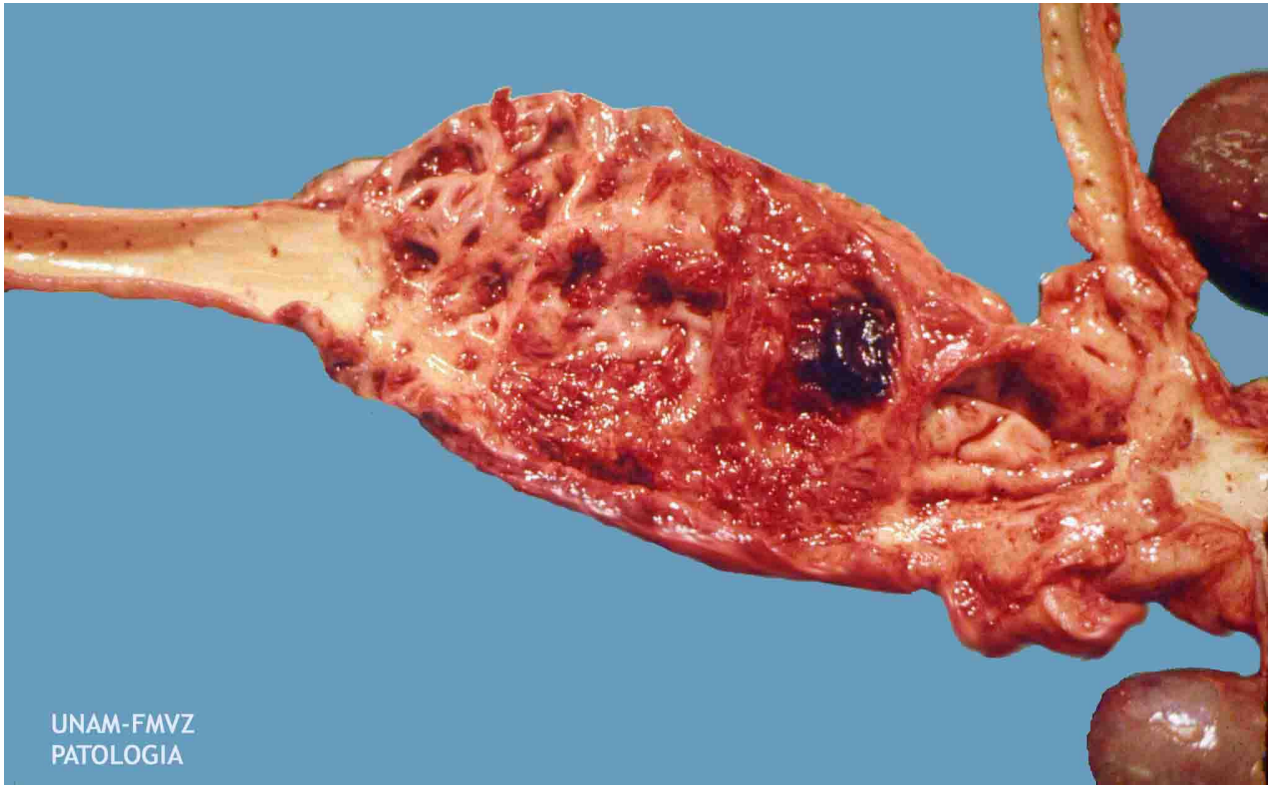
- Genetic
- Atherosclerosis
- Hypertension
- Smoking
- Infections
- Age
- Traumatic
- Iatrogenic



Aneurysm

Spirocerca lupi

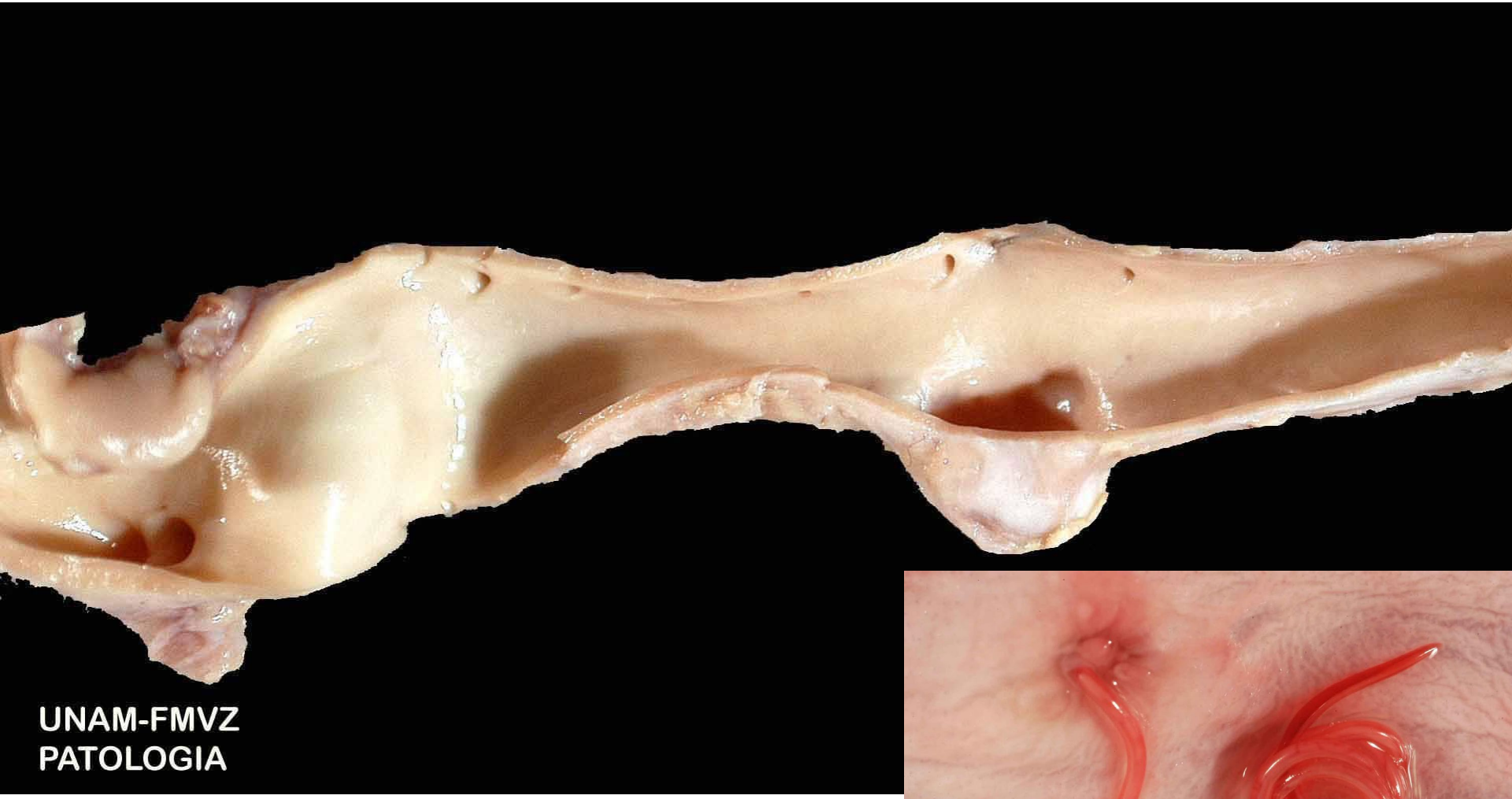
- Nematode parasitizes dogs and other carnivores
- Beetles are the intermediate hosts
- Parasitic granulomas in the thoracic aorta and esophagus



Aortitis necrotizing
Aneurysm
Aortic rupture

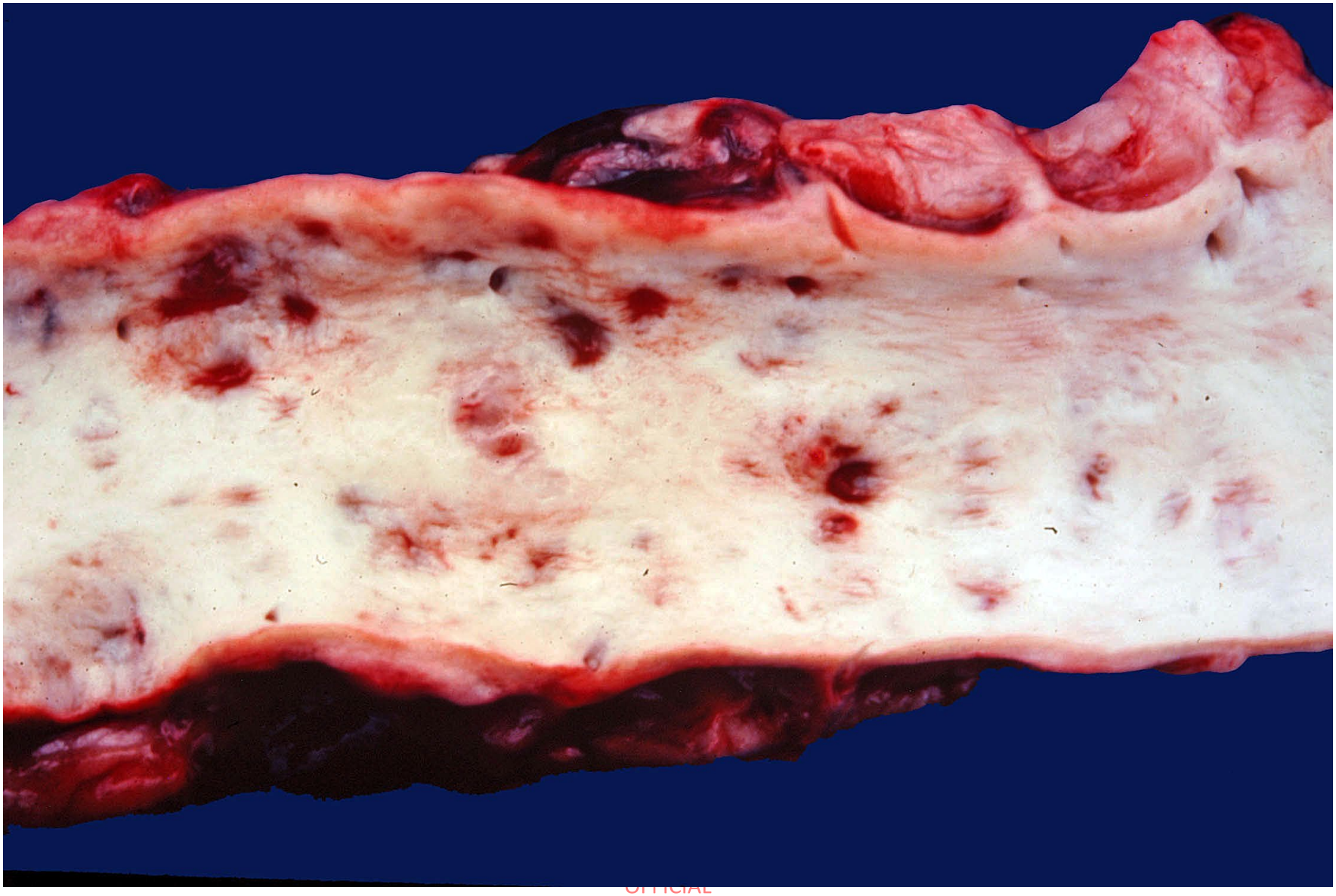
Aneurysm

Spirocerca lupi



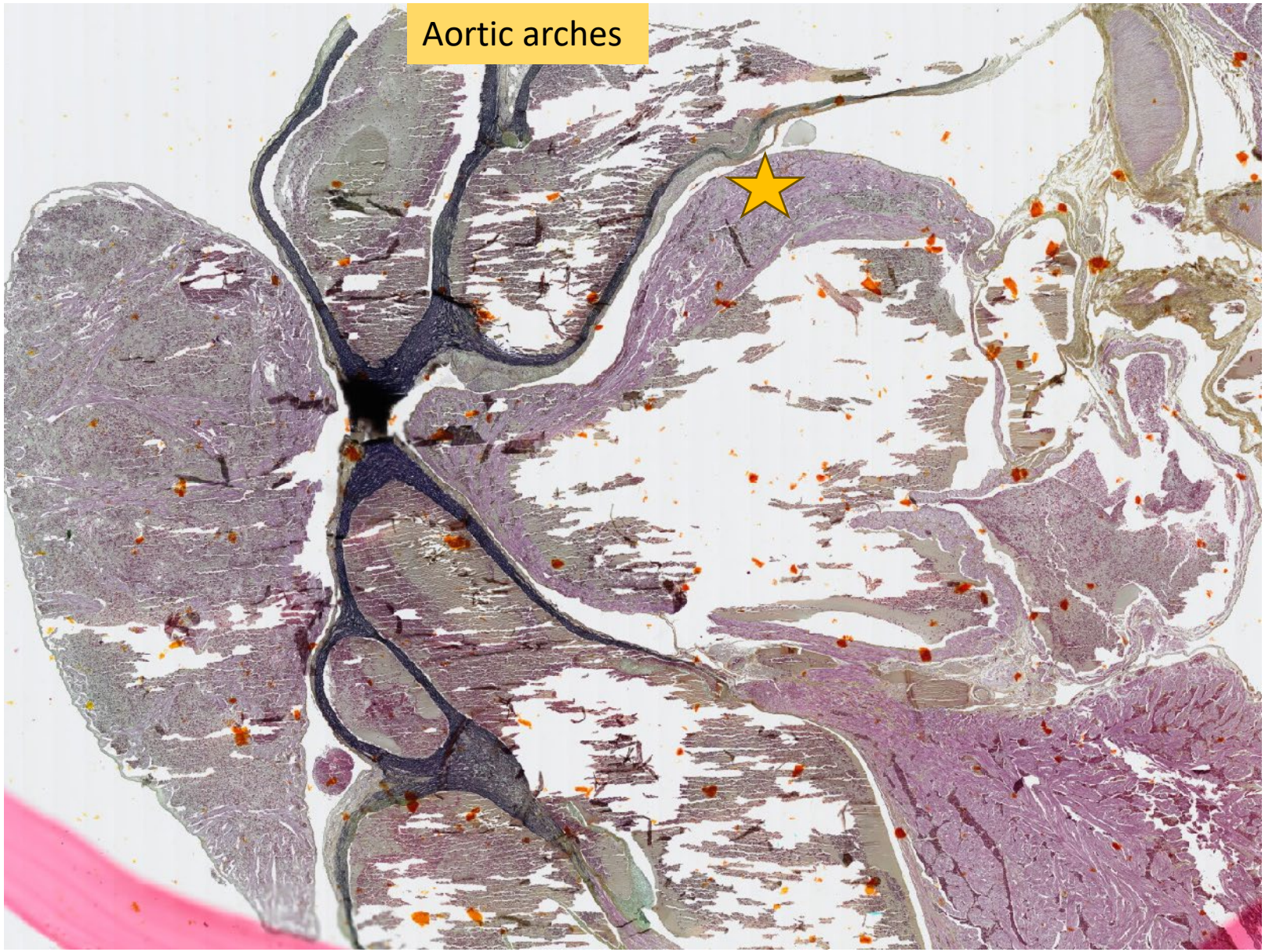
Aortitis

Spirocerca lupi

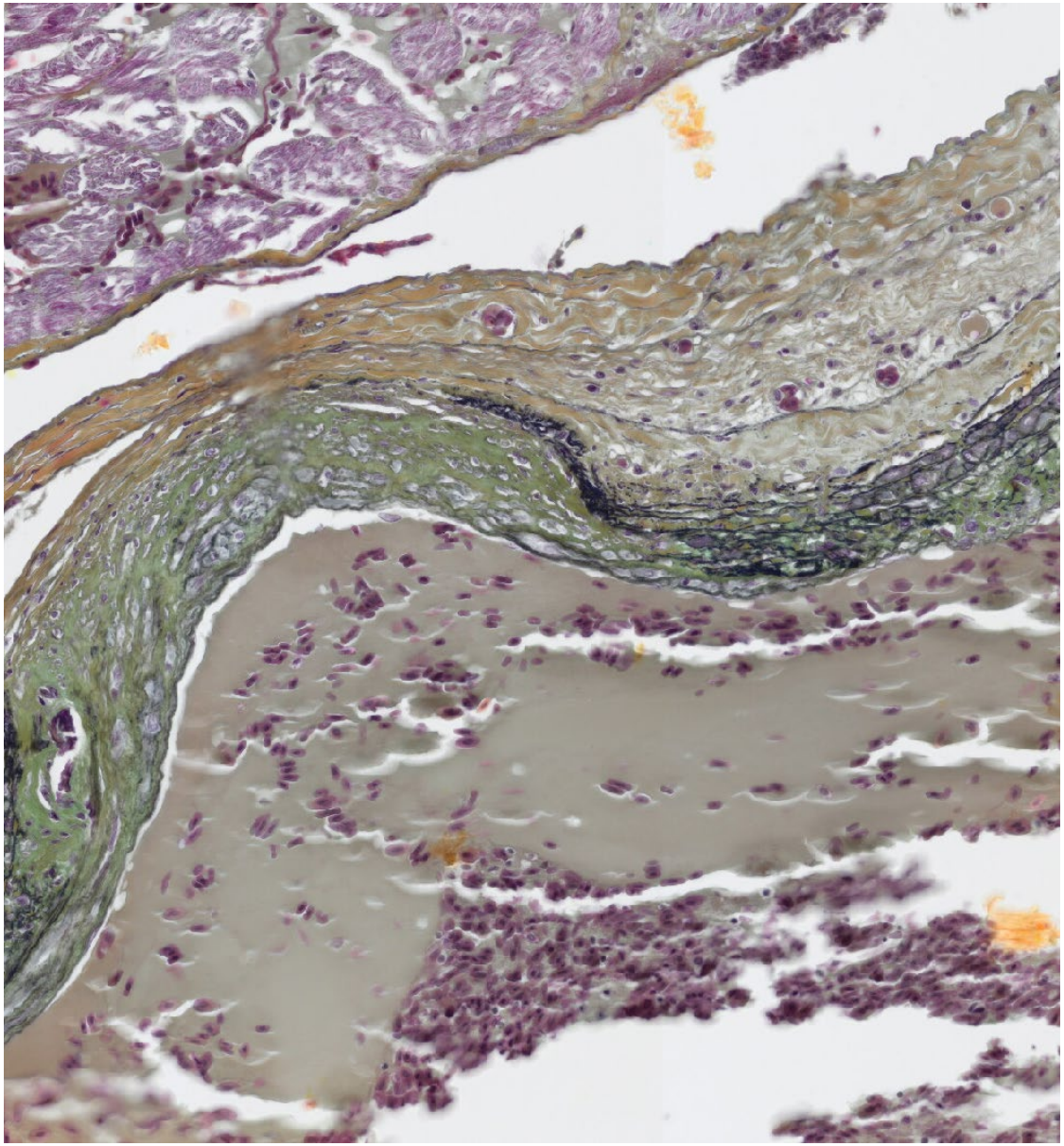


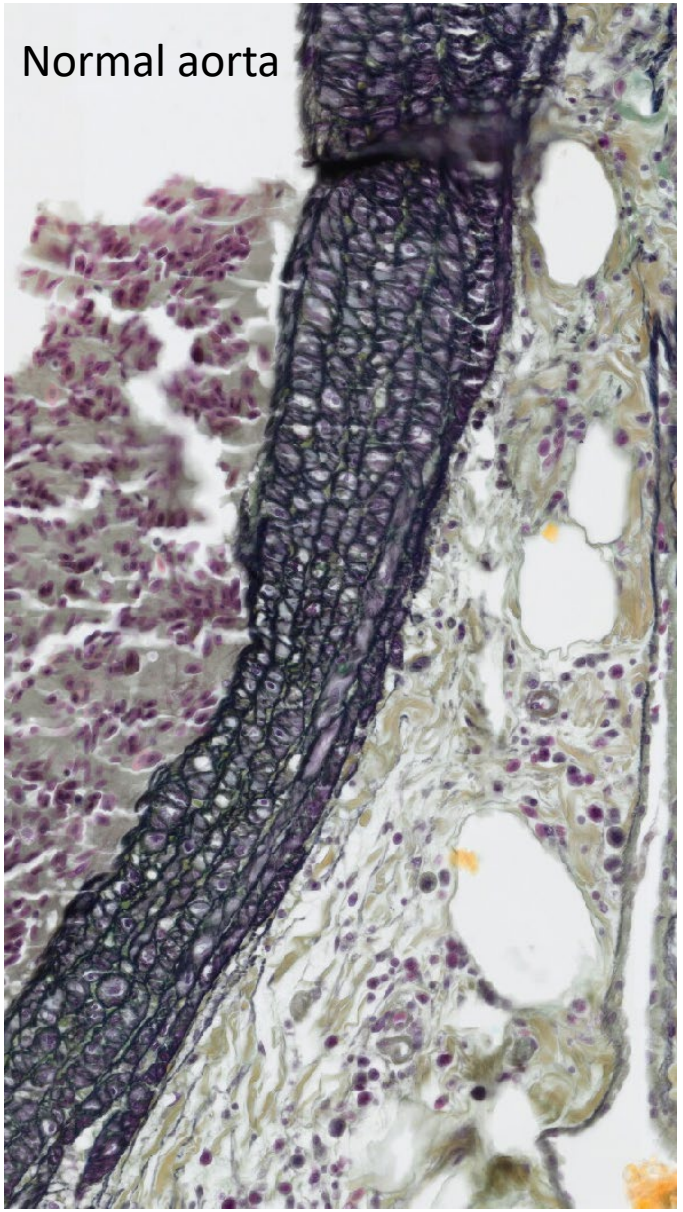
Bearded dragon

Aortic aneurysm

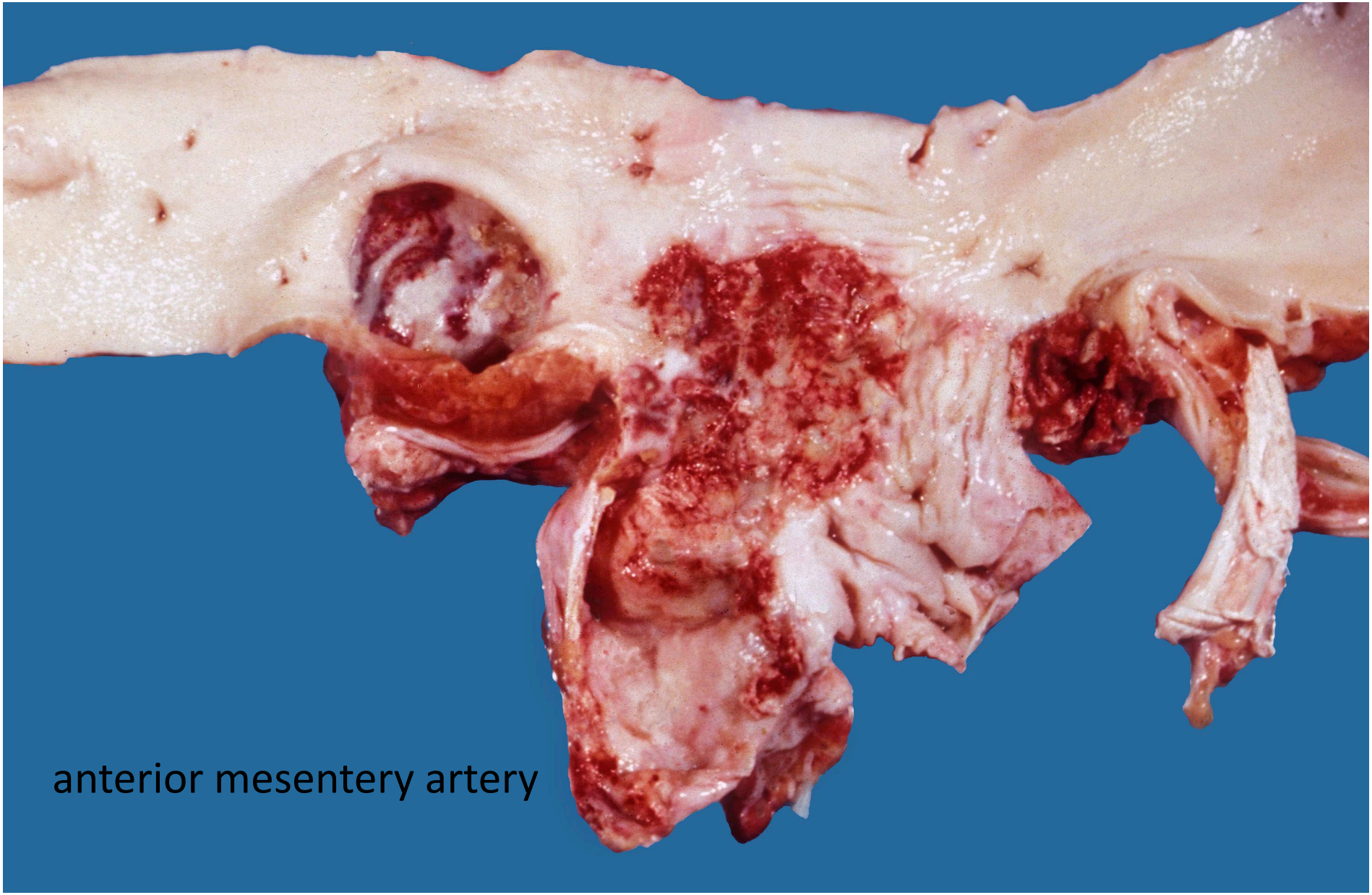


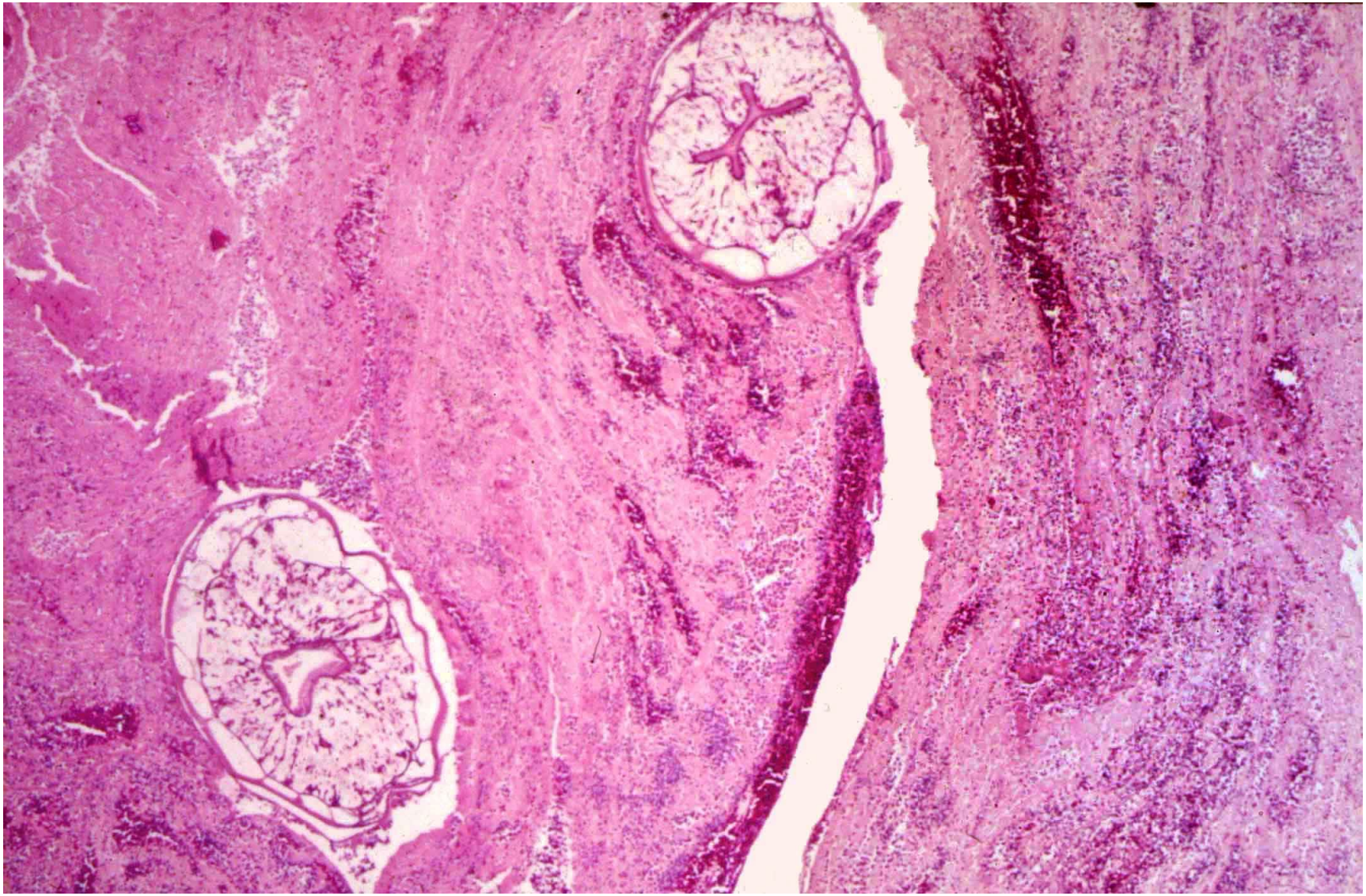
Aorta with loss and fragmentation of the elastic fibers and medial fibrosis





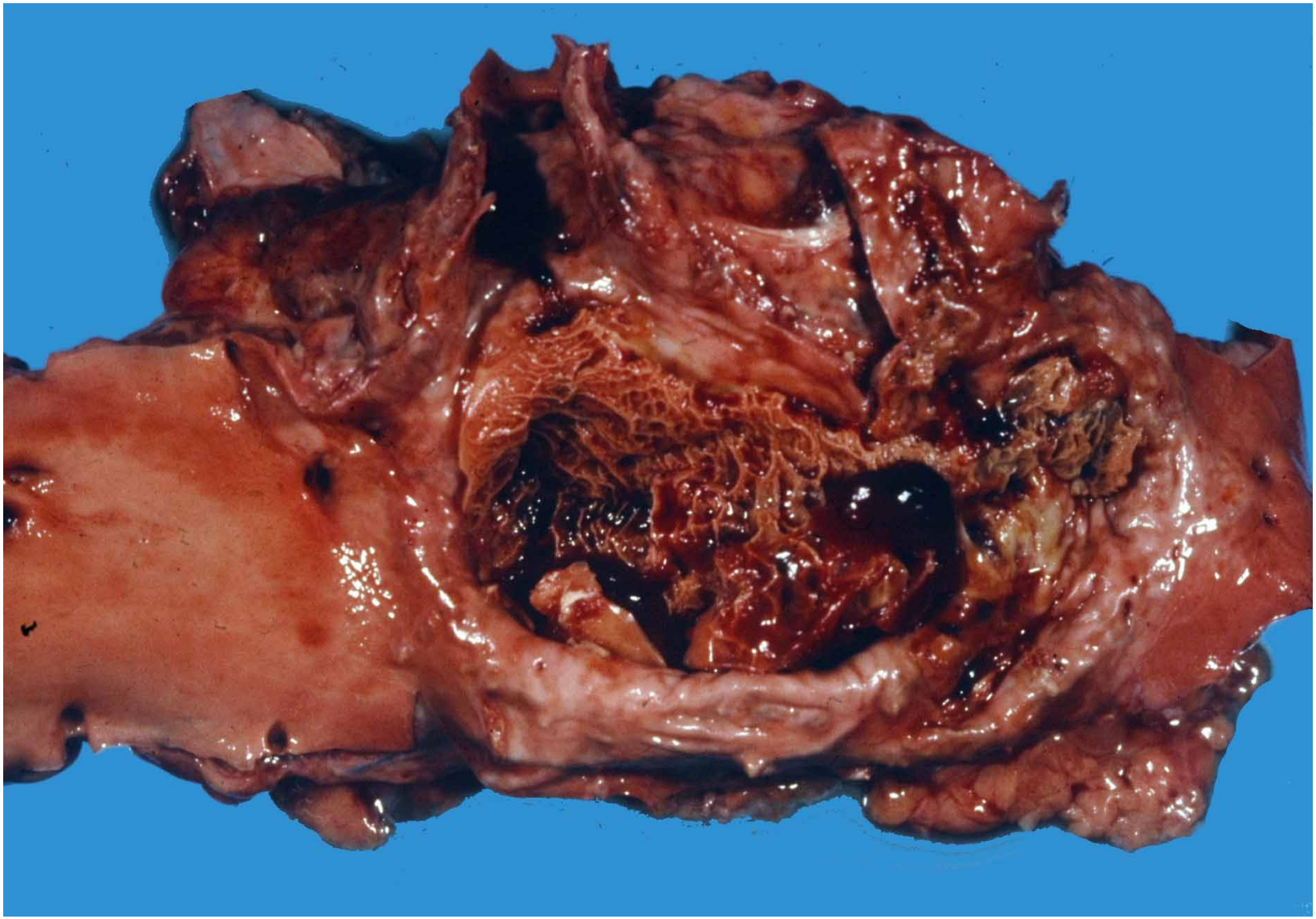
Aneurysm with thrombosis/*Strongylus vulgaris*



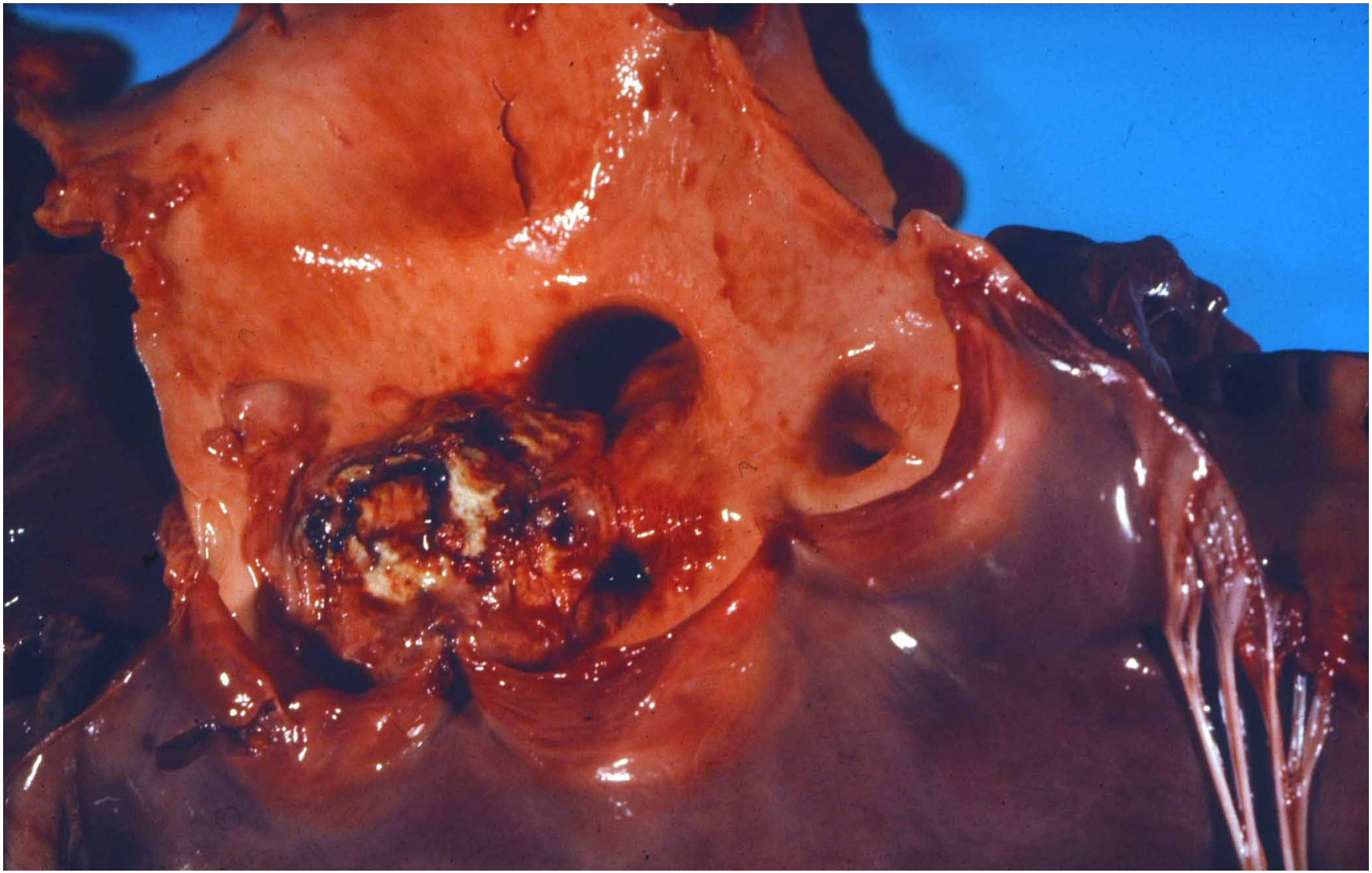


Larval nematodes: thick cuticle, a pseudocoelom, platymyarian-coelomyarian musculature, and a large intestine with multinucleate columnar epithelial cells

Aneurysm with thrombosis/*Strongylus vulgaris*



Granulomatous aortitis/*Strongylus vulgaris*

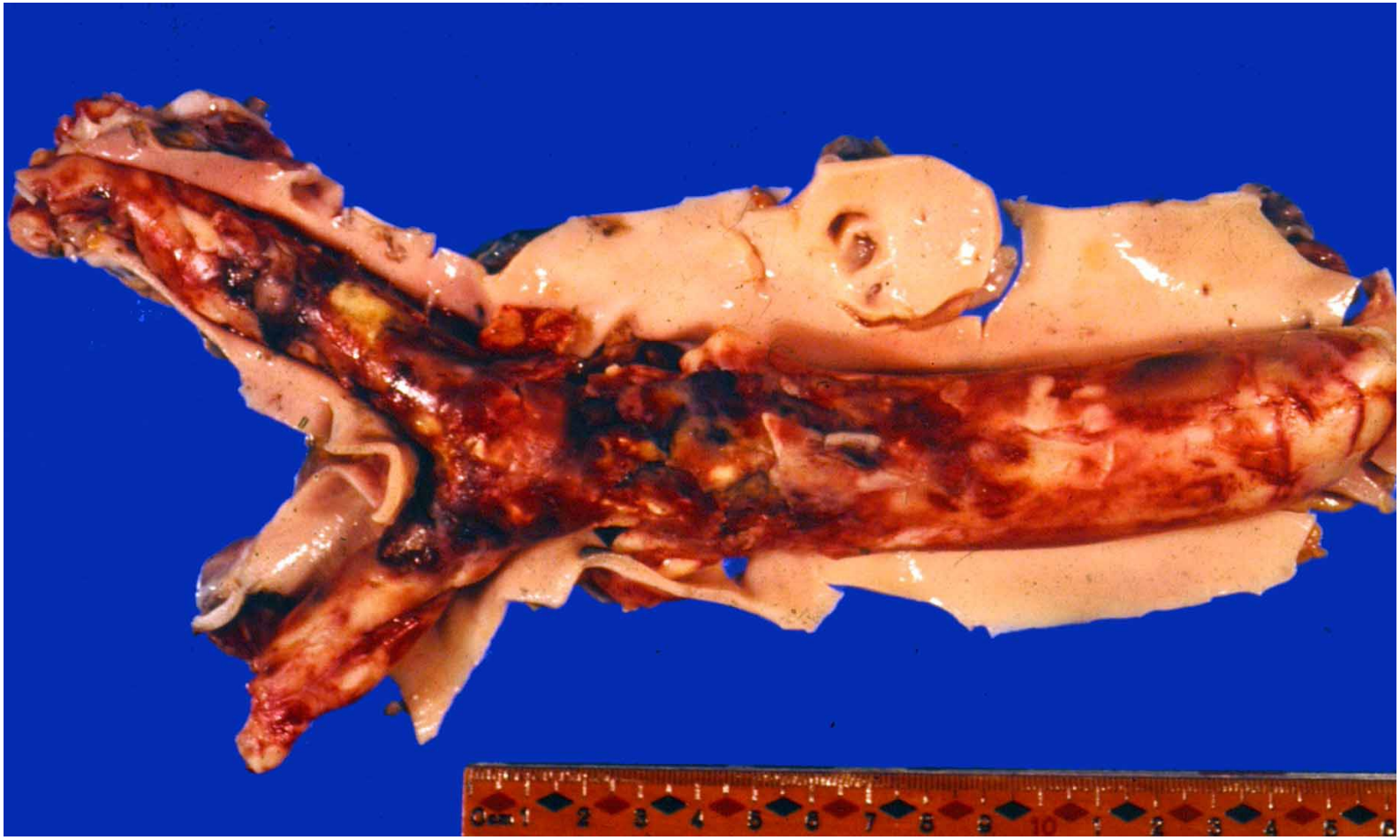


Aortoiliac thrombosis in horses

Strongyle-related thromboembolism with organization of thrombi and their incorporation into the arterial wall

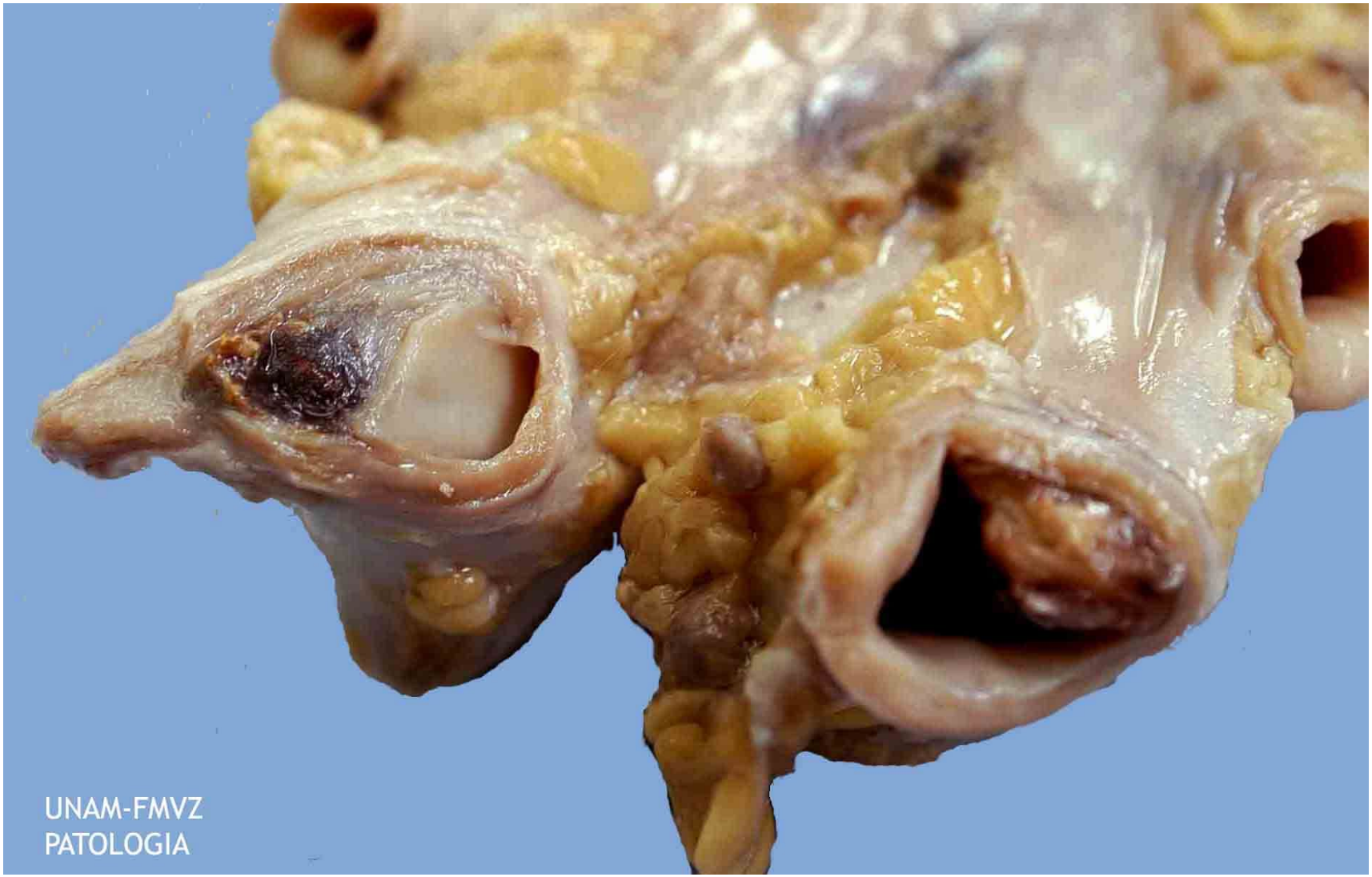
or

Spontaneous degeneration of the aorta of unknown etiology, resulting in thrombosis



Iliac thrombosis

- The exact cause of the thrombus is unknown
- This condition was previously associated with migrating strongyle larvae; however, it can still occur in horses that have been dewormed.



Aortic mineralization

Vitamin D toxicity:
Cattle, horses, pigs, birds, reptiles, rabbits

Oversuplementation of vitamin D
Ingestion of plants:

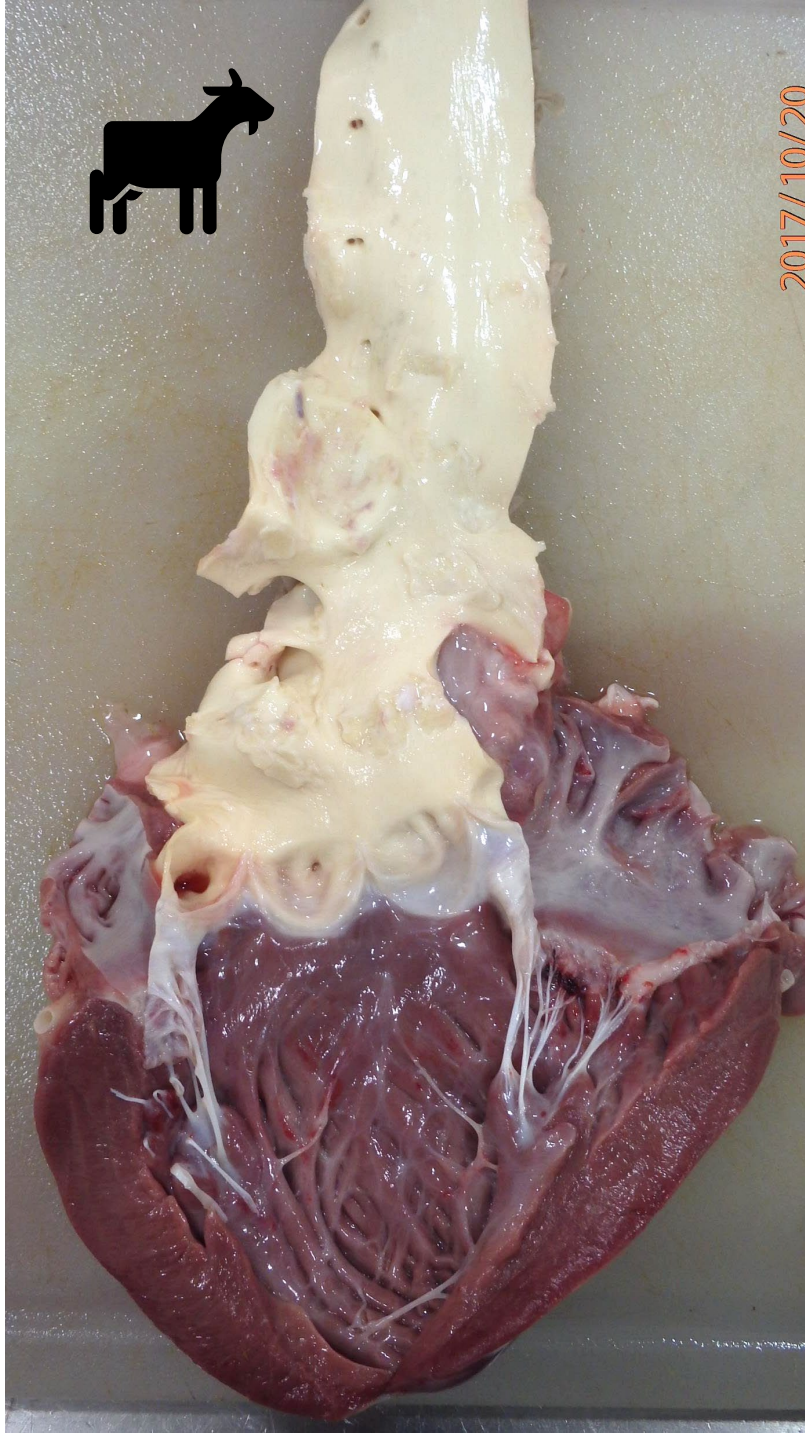
- *Solanum glaucophyllum*
- *Solanum torvum*
- *Trisetum flavescens*
- *Cestrum diurnum*

Toxic principle: 1,25-dihydroxycholecalciferol-glycoside

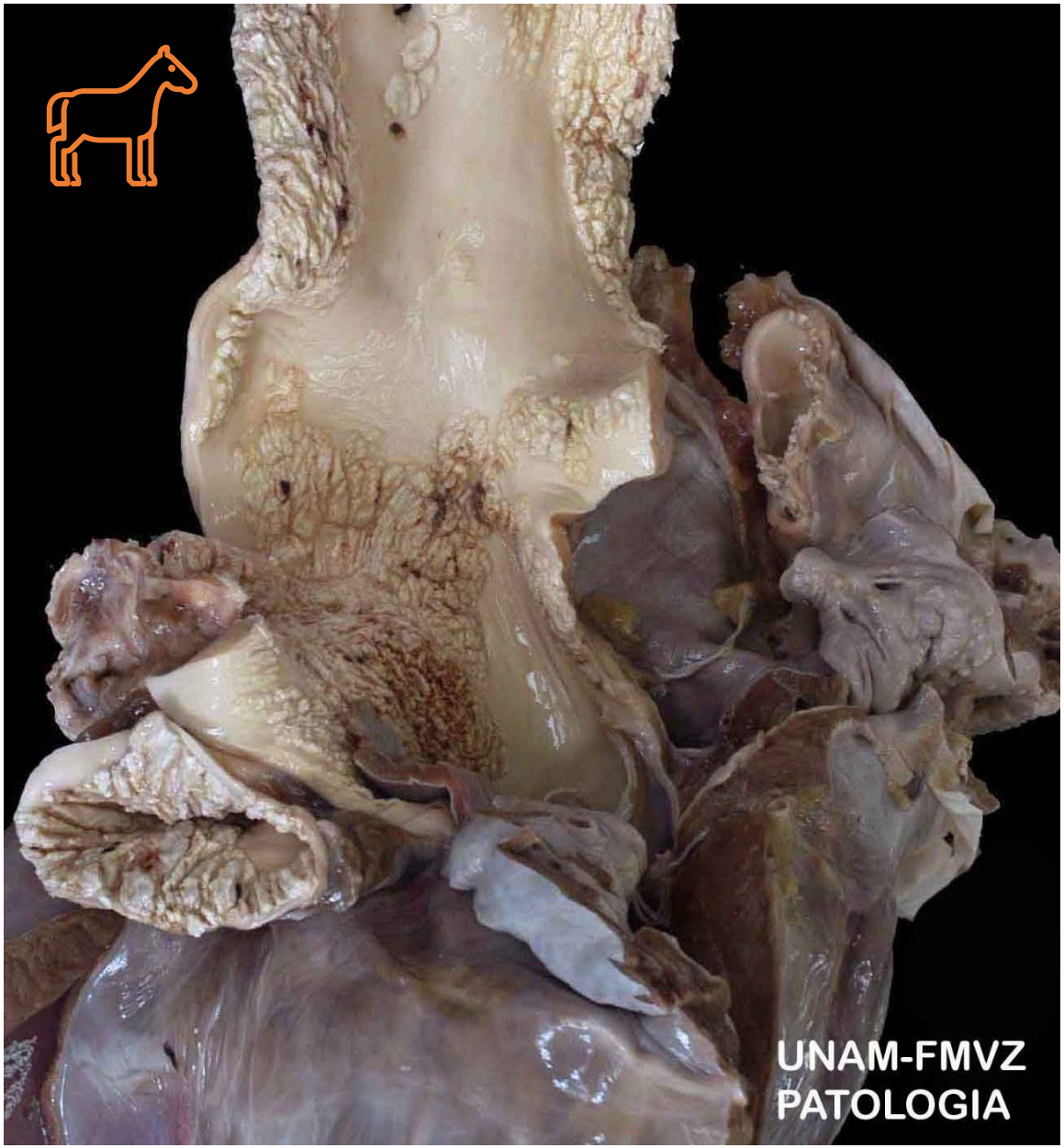
Dog and cat: rodenticides

Chronic debilitating diseases (granulomatous inflammation)
Paraneoplastic syndrome: lymphoma, apocrine gland adenocarcinoma (PTH-related protein)

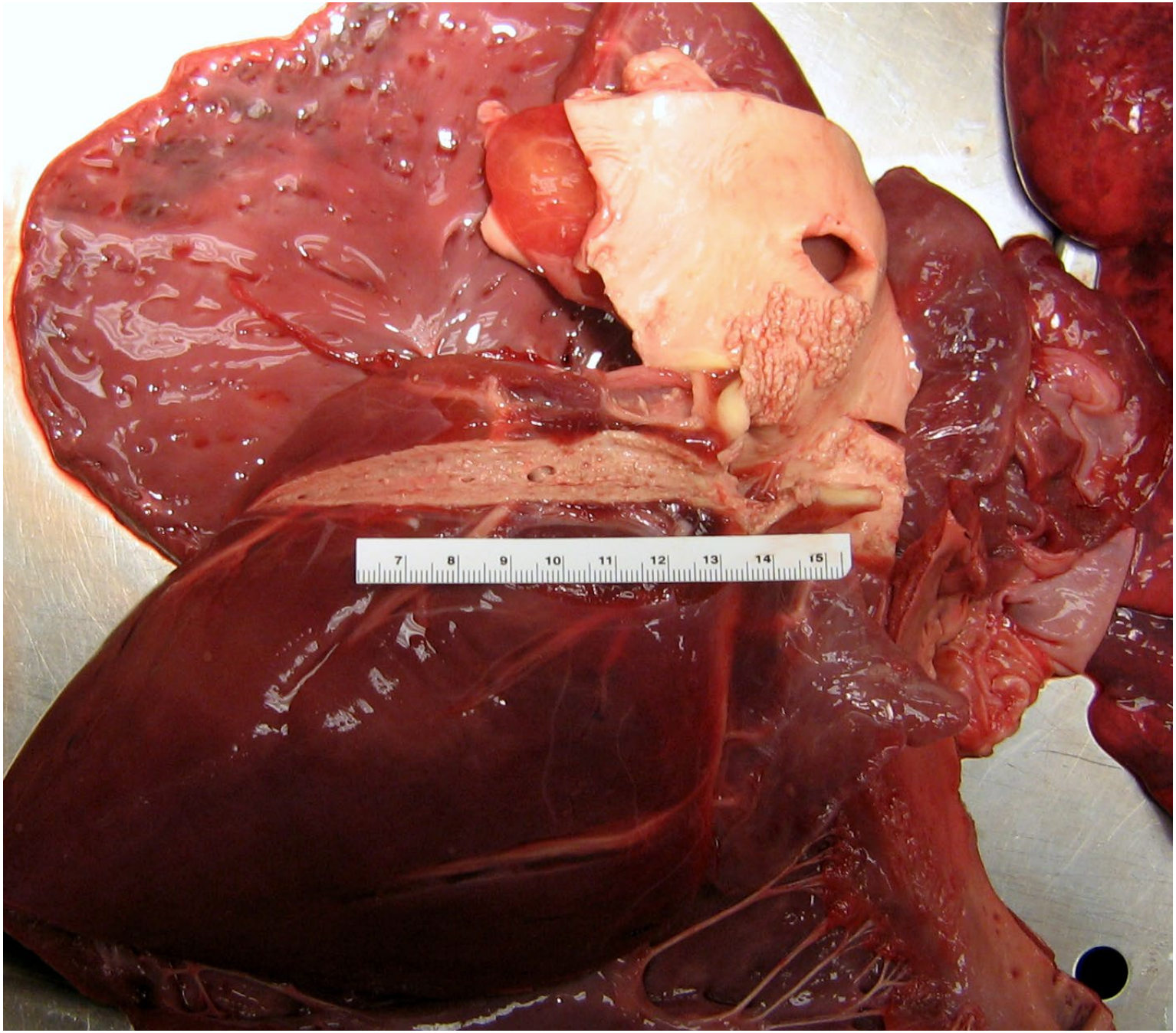
Advanced age
Unknown



Aortic mineralization



Bovine/lymphoma



Aortic rupture

- Trauma
- Spontaneous
- *Spirocerca lupi*-aneurysm

- Well-known in horses: periods of excitement and activity (racing or in stallions while breeding)
- Predisposing aortic lesion has not been identified
- Elastic fragmentation and accumulation of mucoid material- histologic findings

Tears: valvular annulus to brachiocephalic trunk

Hemopericardium

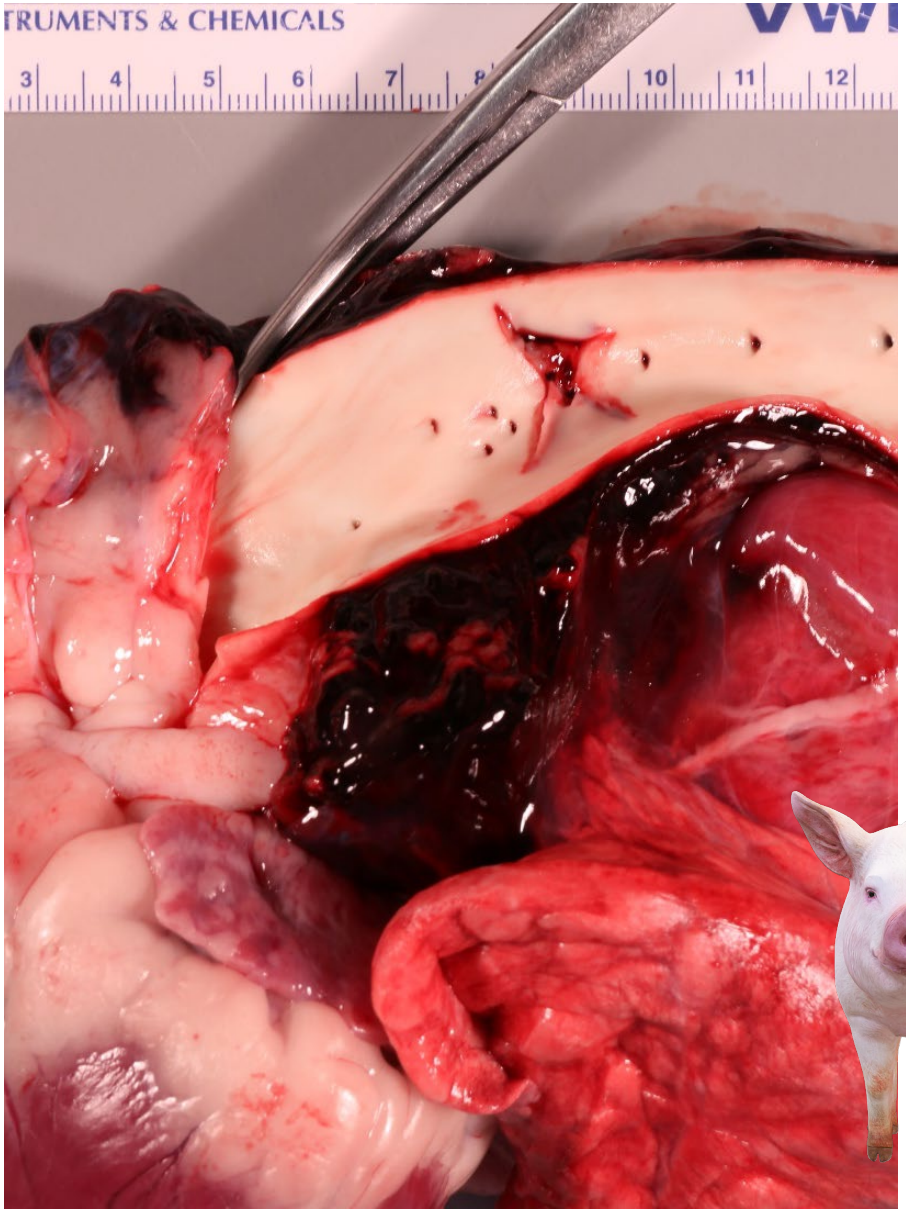
Hemorrhage extends into the AV node or bundle of His

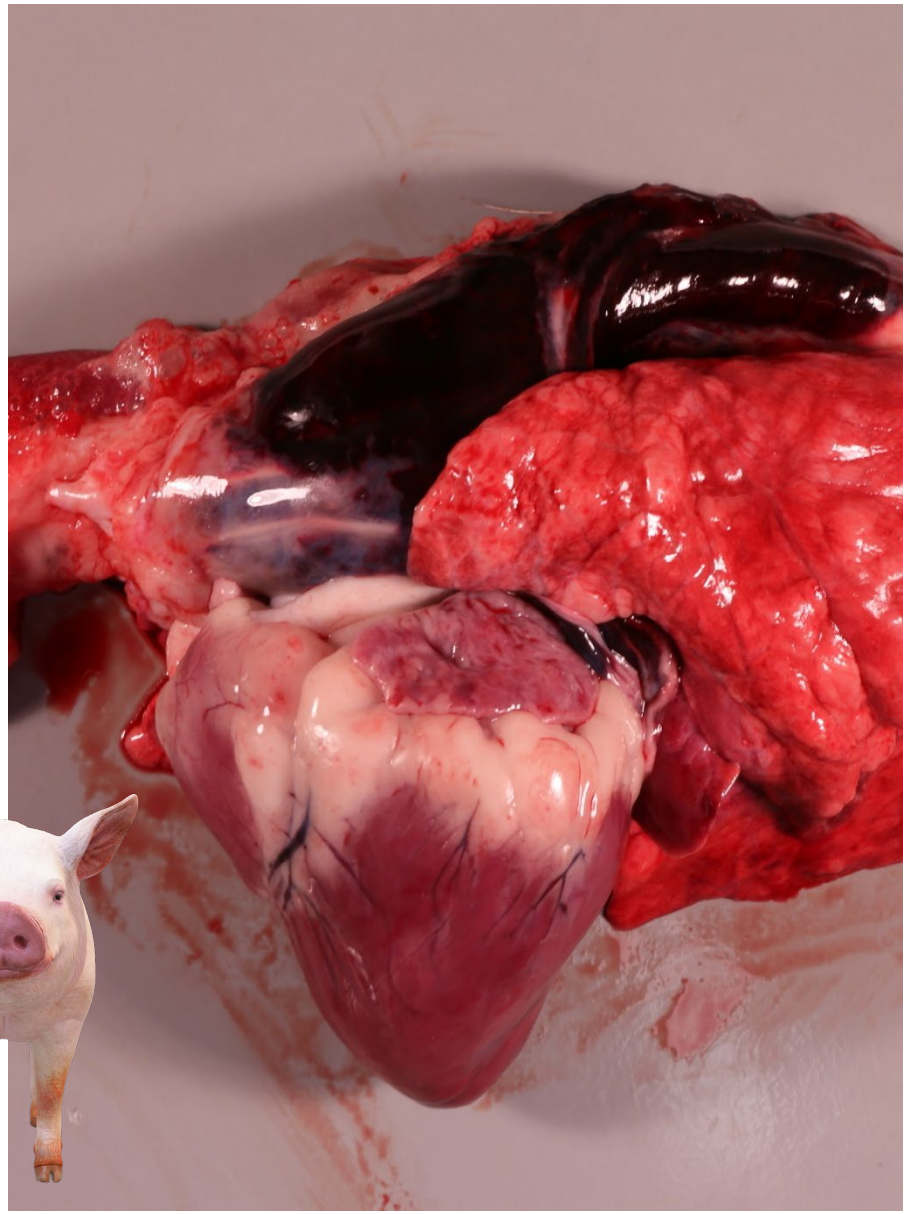
Experimental: copper-deficient pigs

Deficiency of lysyl oxidase, a copper-containing enzyme responsible for cross-linking of collagen and elastin

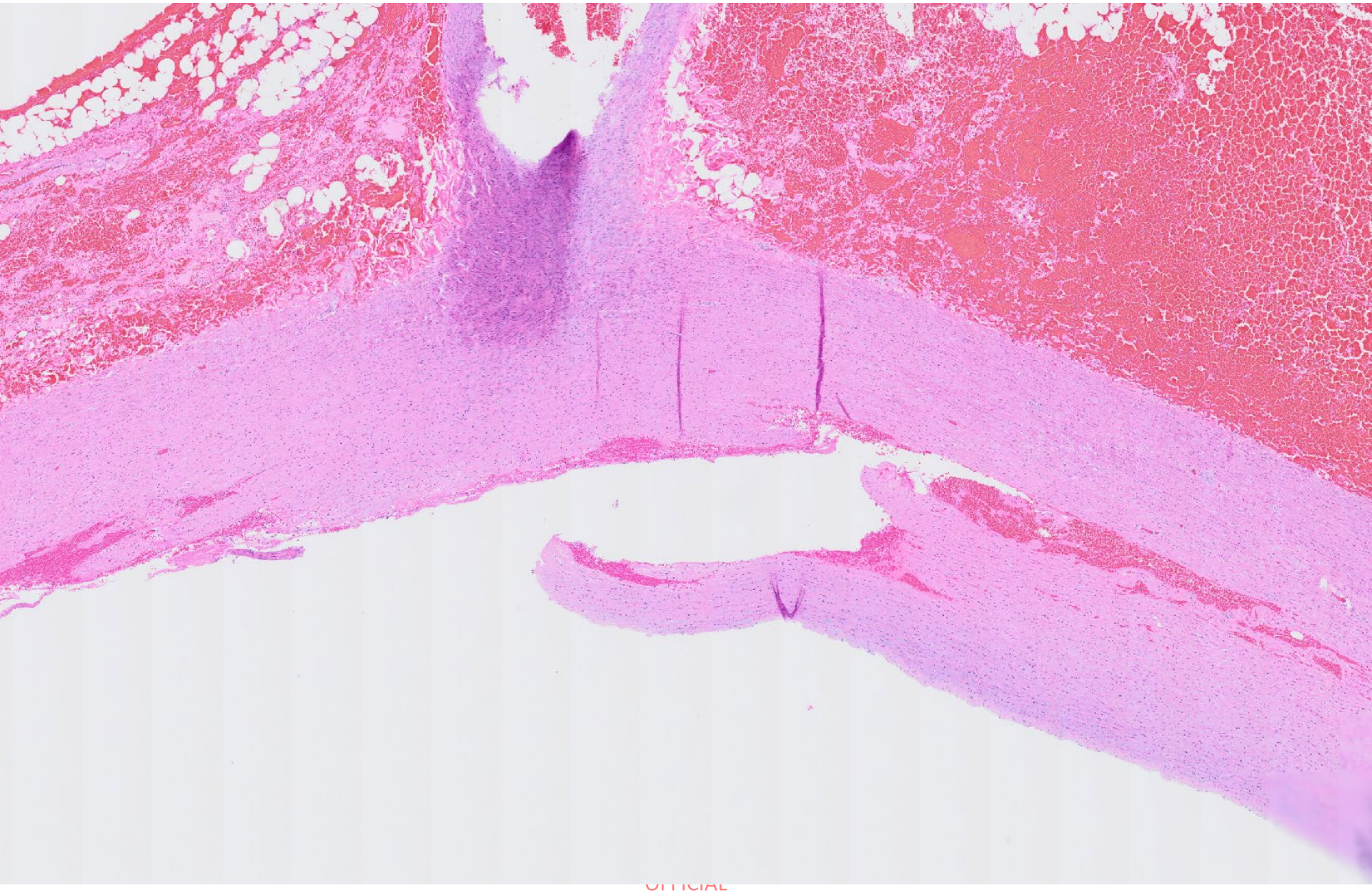
In the majority of animals, the cause is unknown.

Aortic rupture

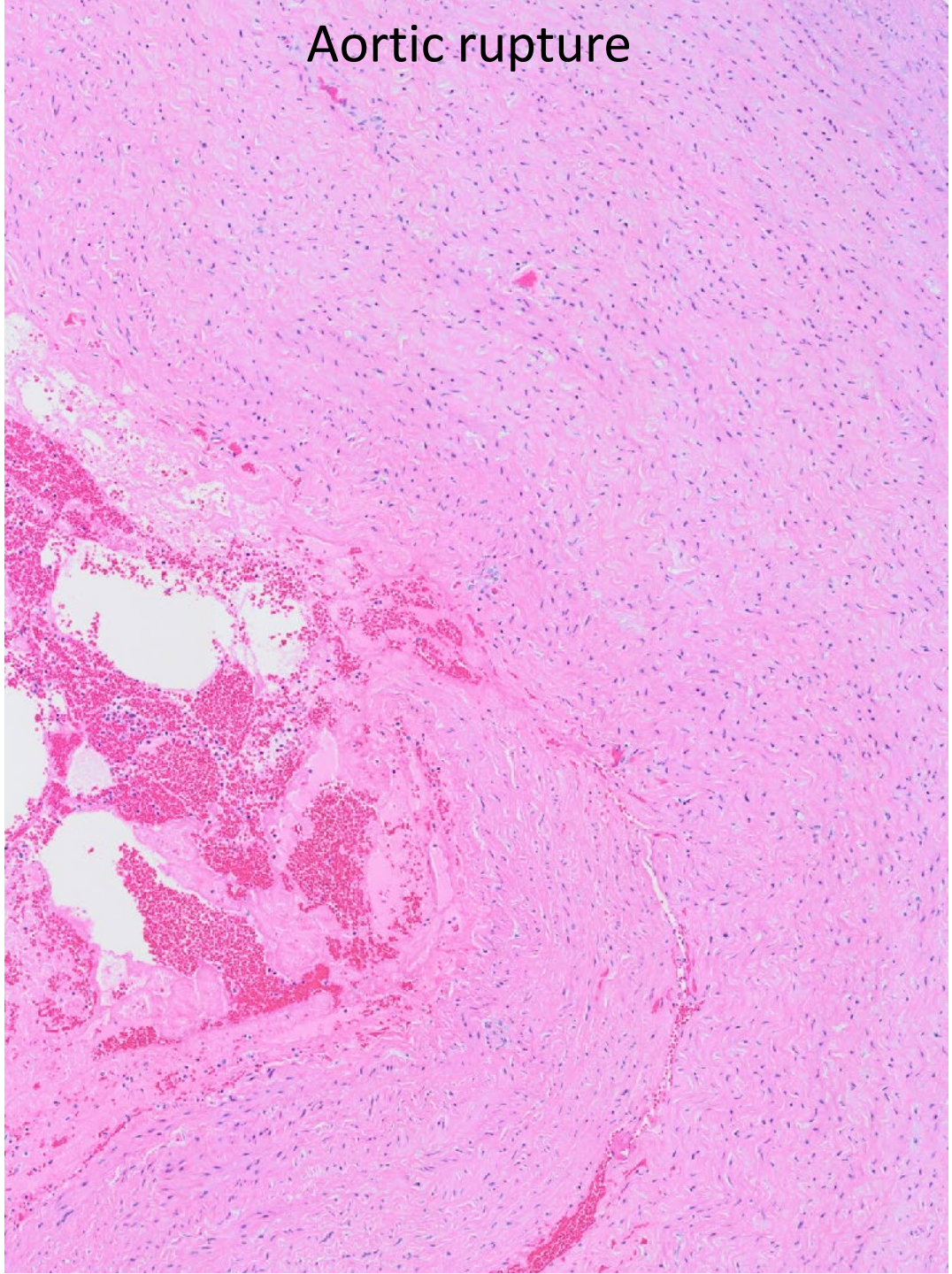




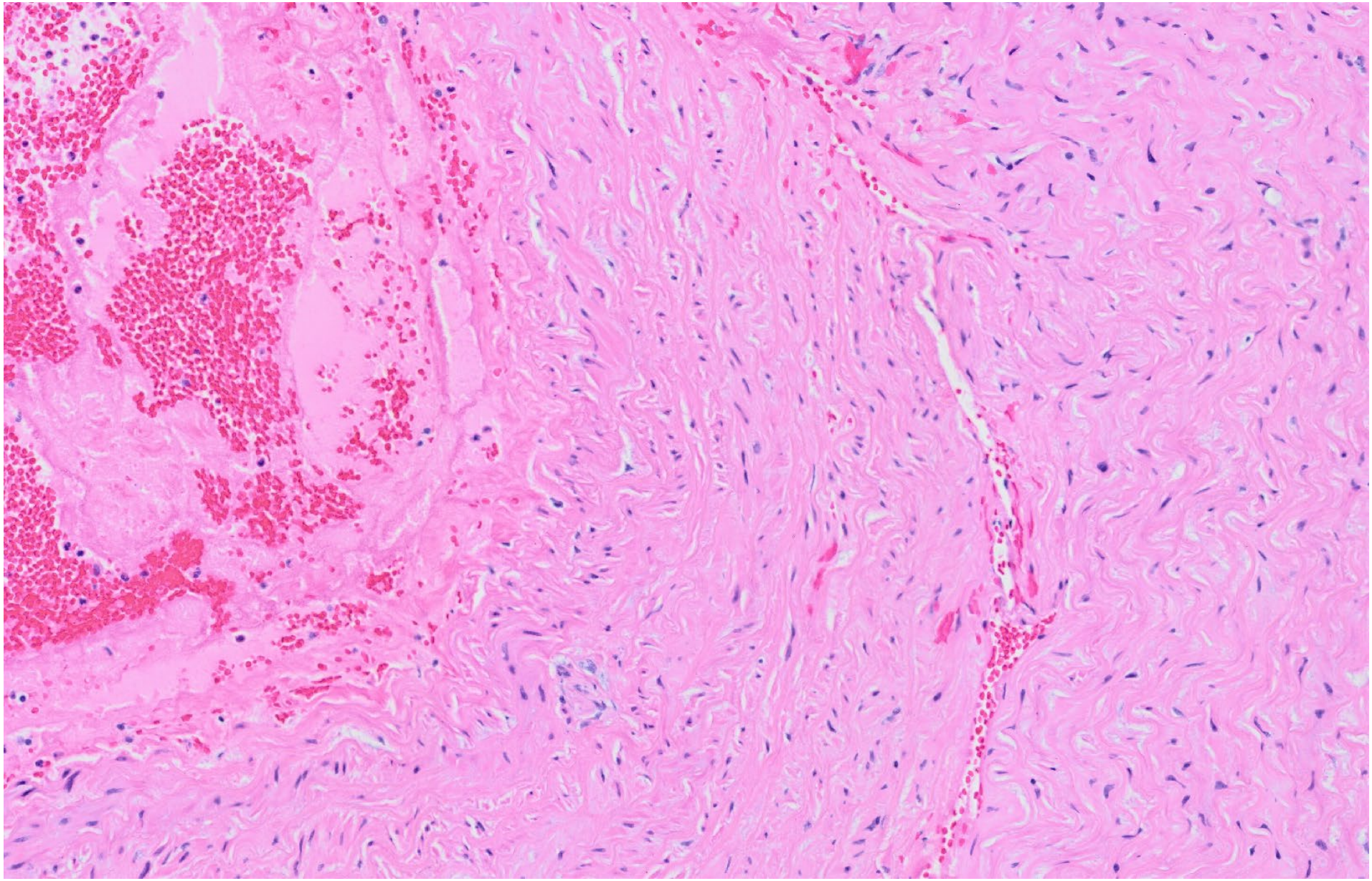
Aortic rupture



Aortic rupture



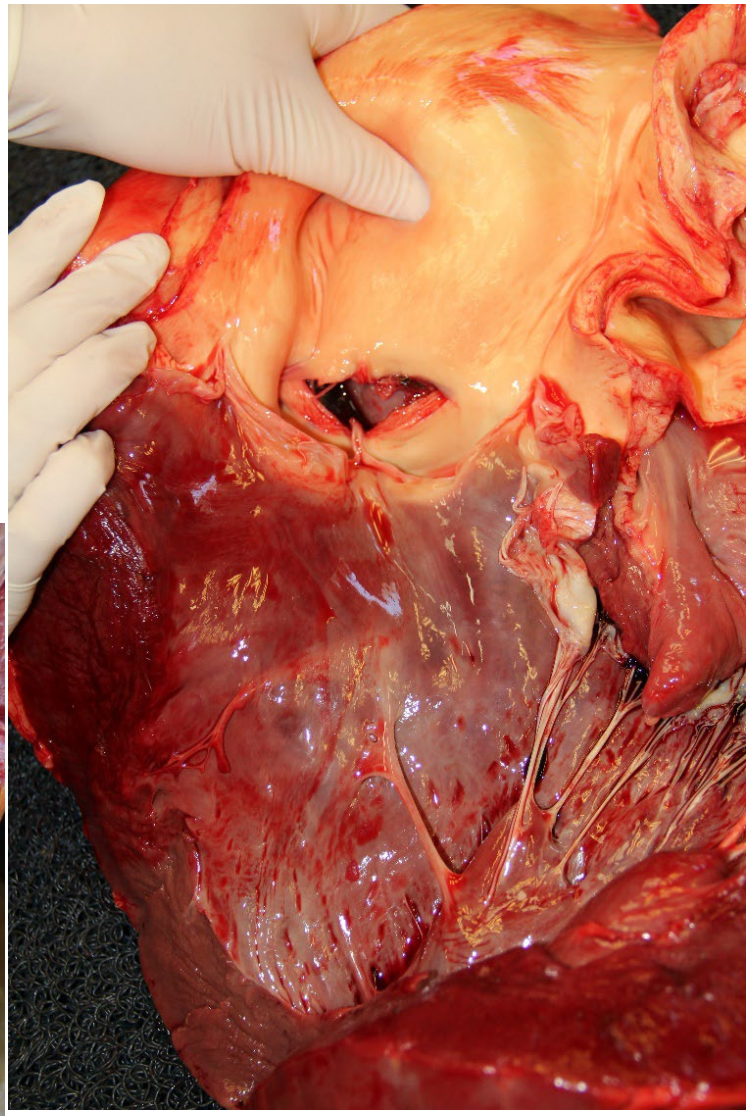
Aortic rupture

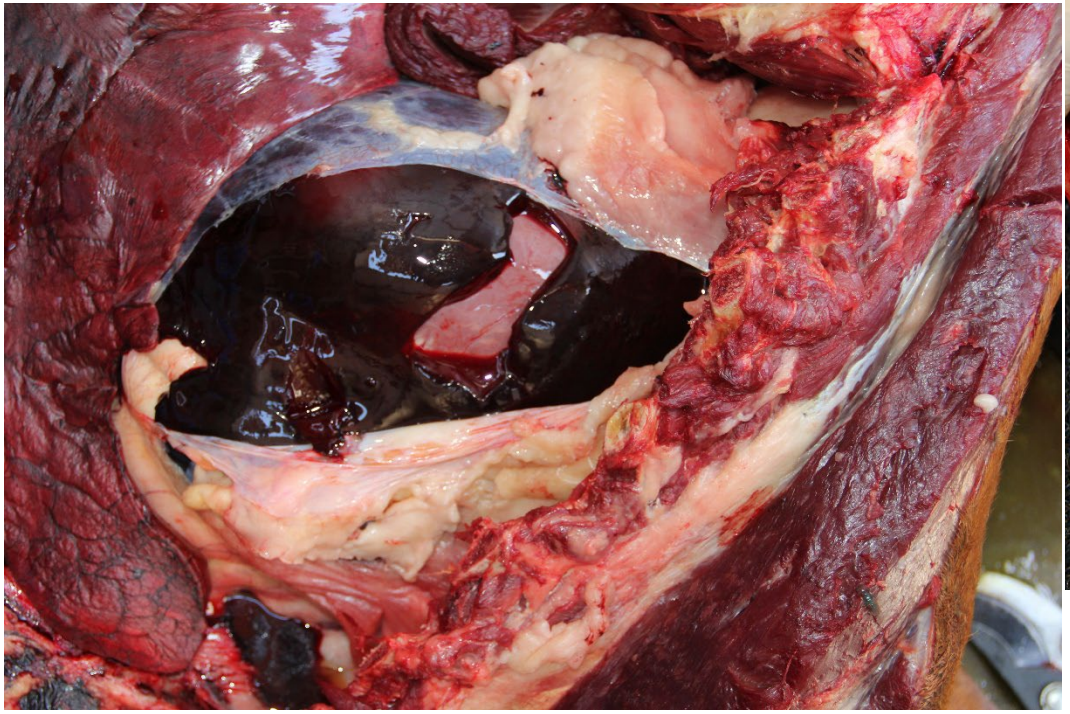


Aortic rupture

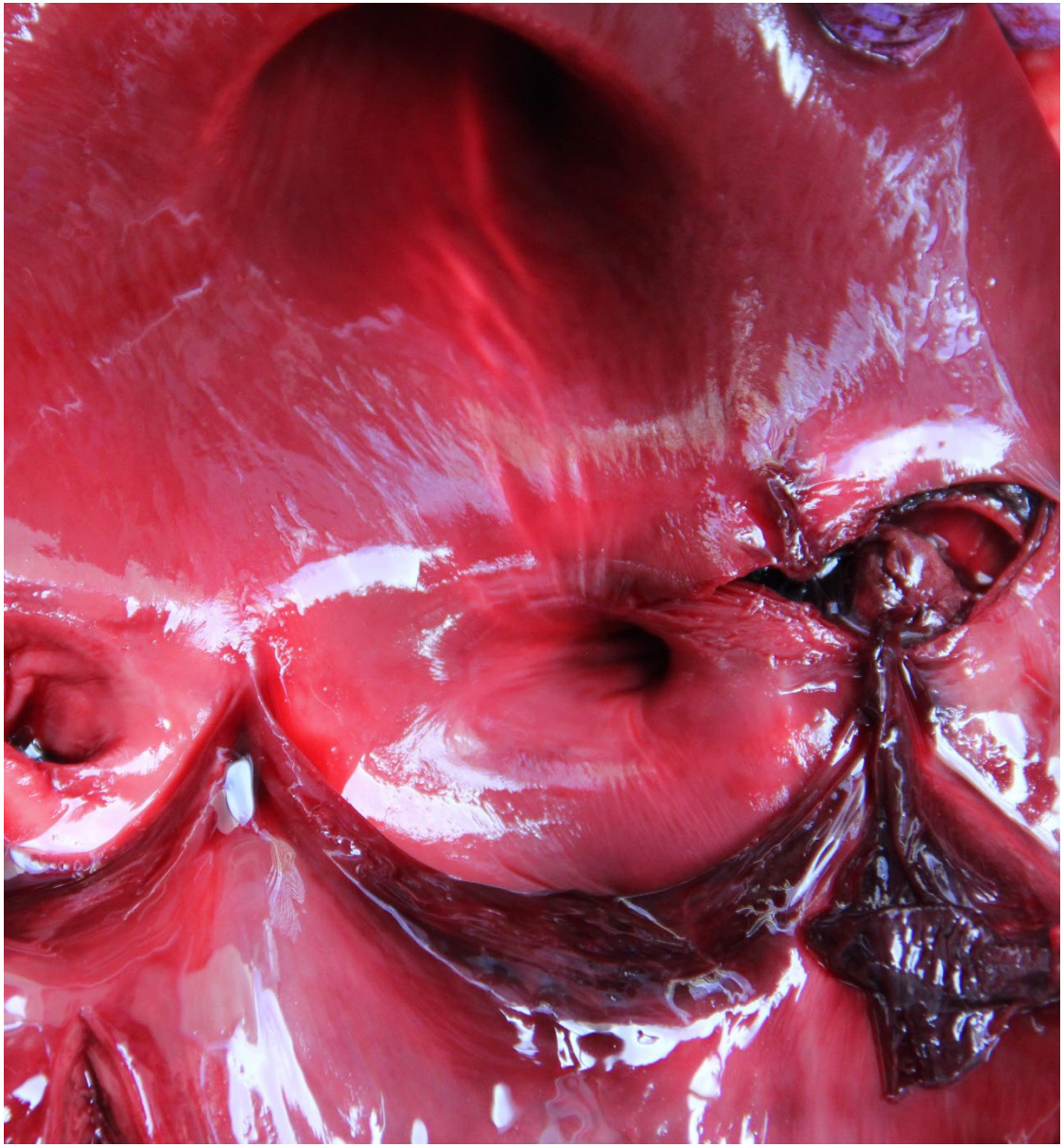
Horse

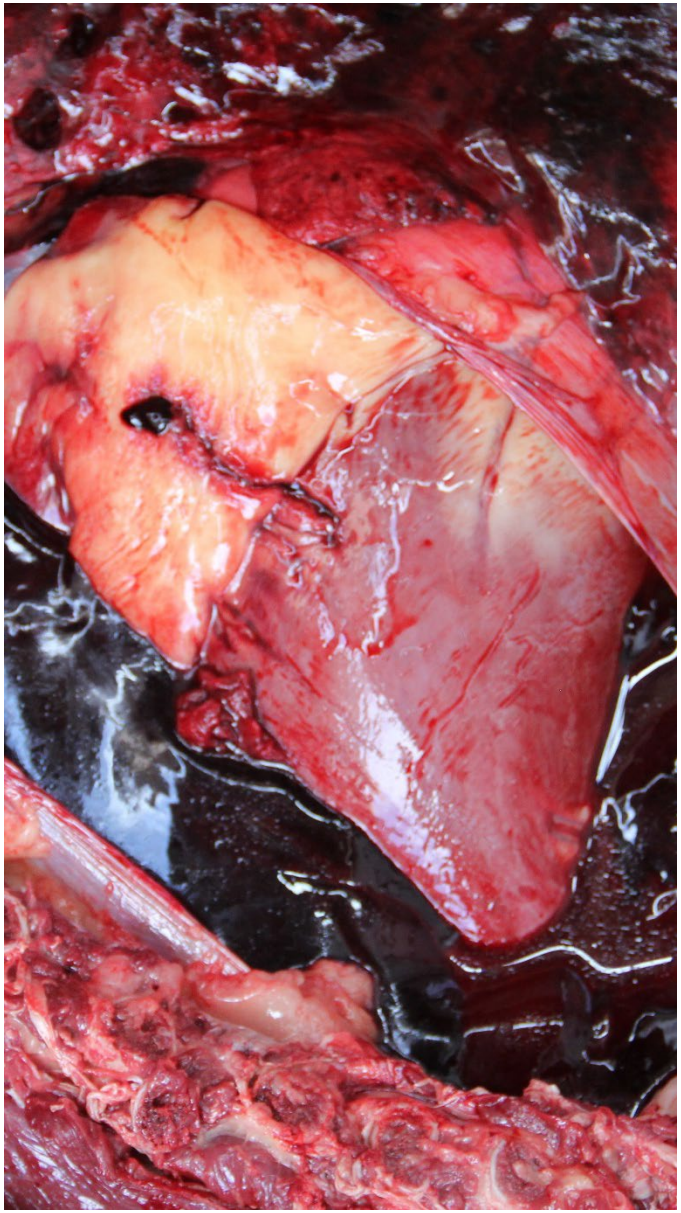
- High prevalence of aortic rupture in young Friesian horses
- Aortic rupture: root or aortic arch
- Aortic arch near the ligamentum arteriosum can lead to aortopulmonary fistulation
- Acute-chronic



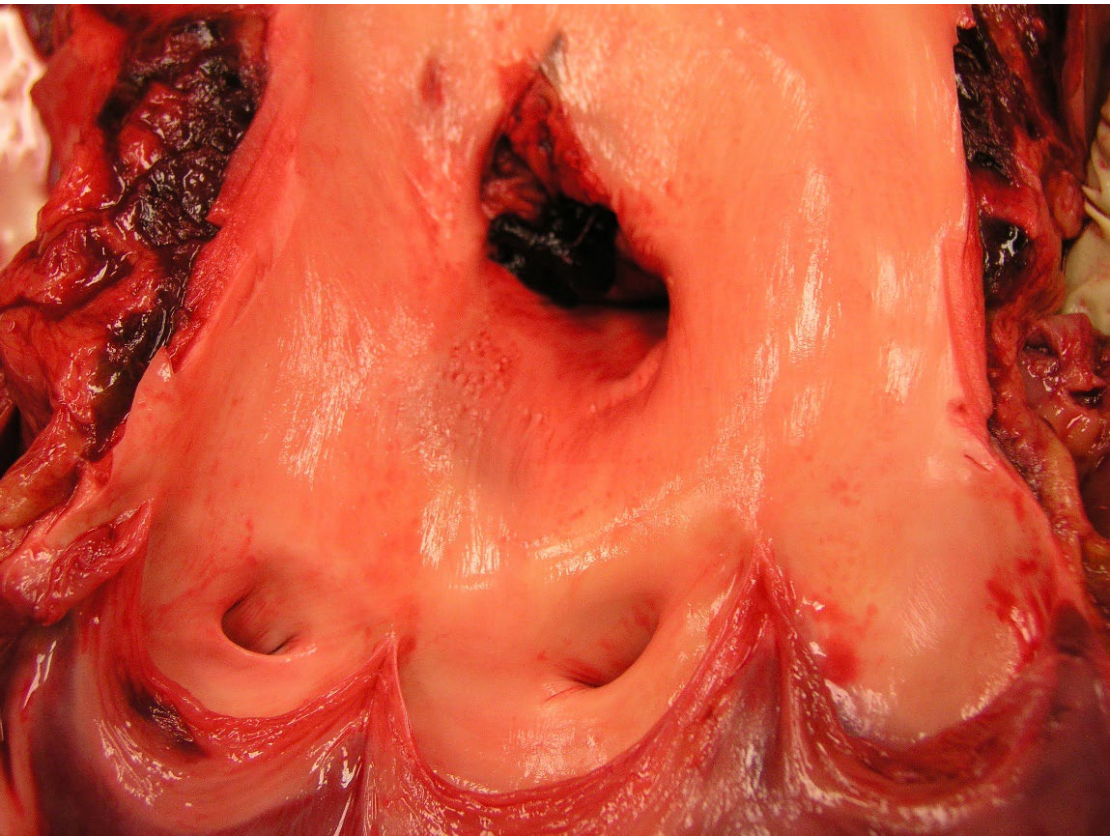


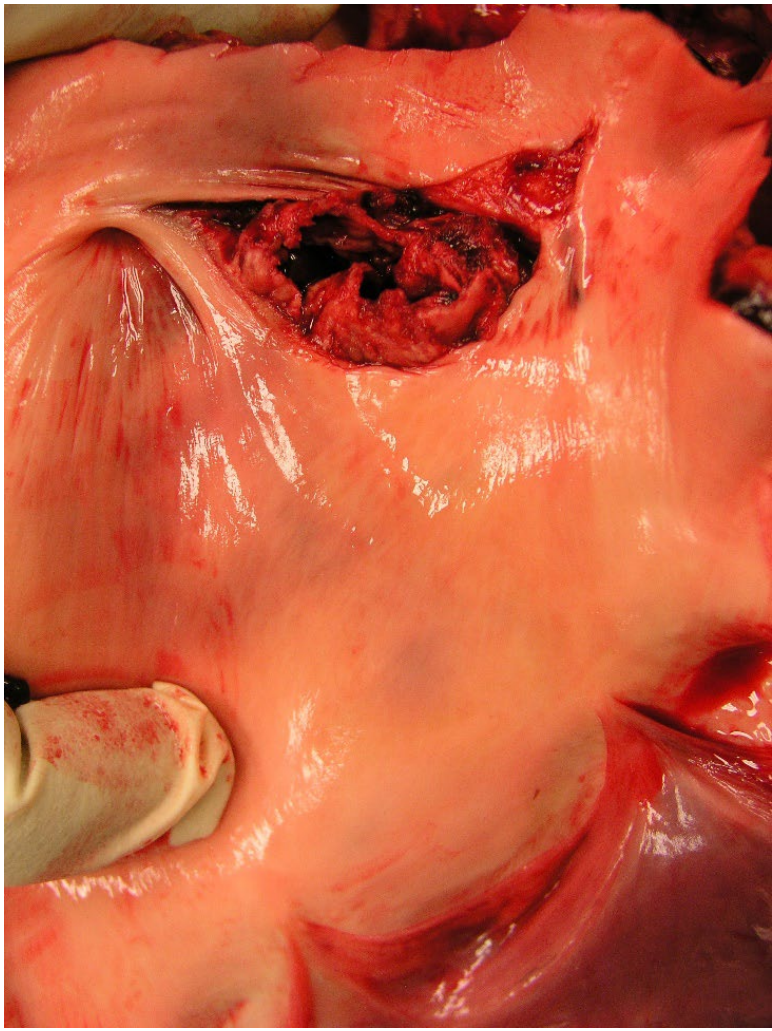
Aortic rupture



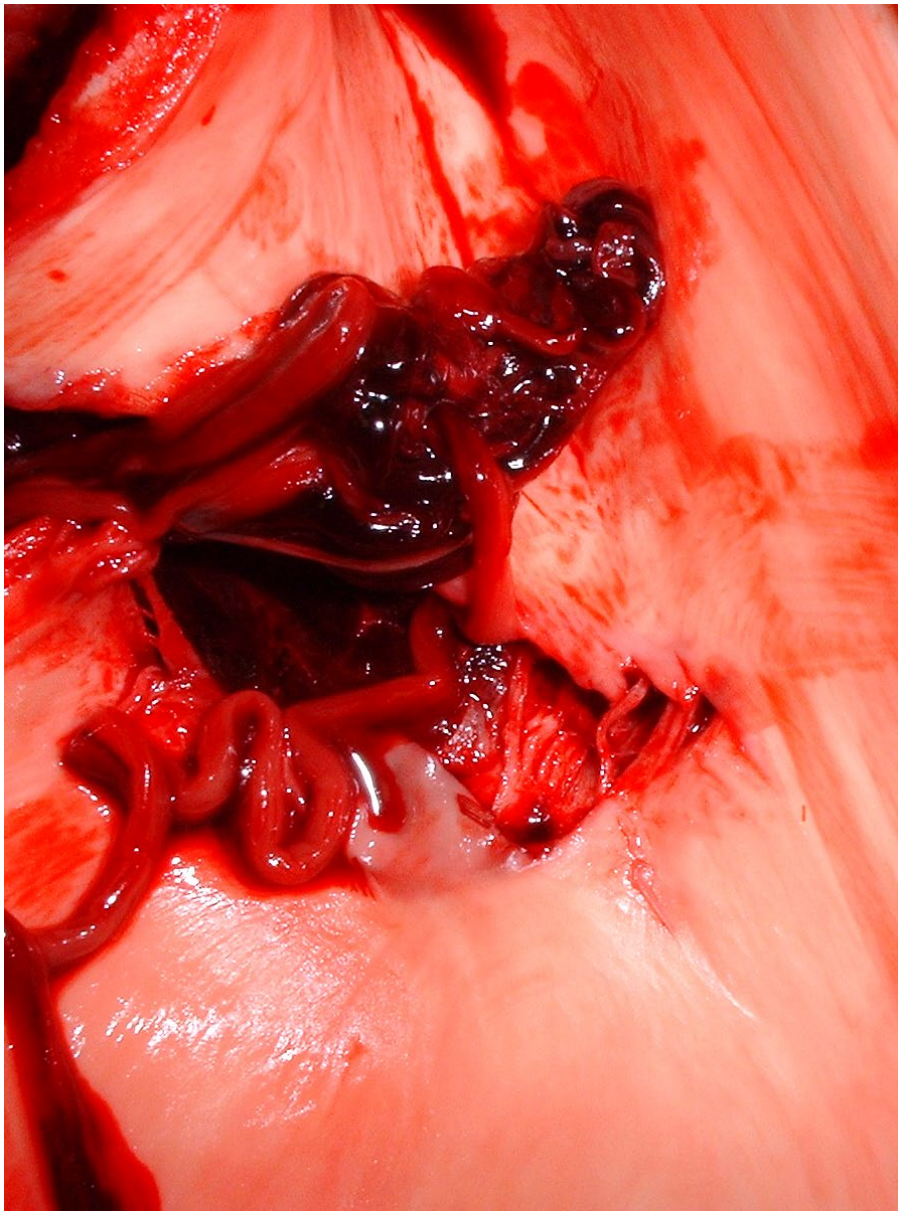


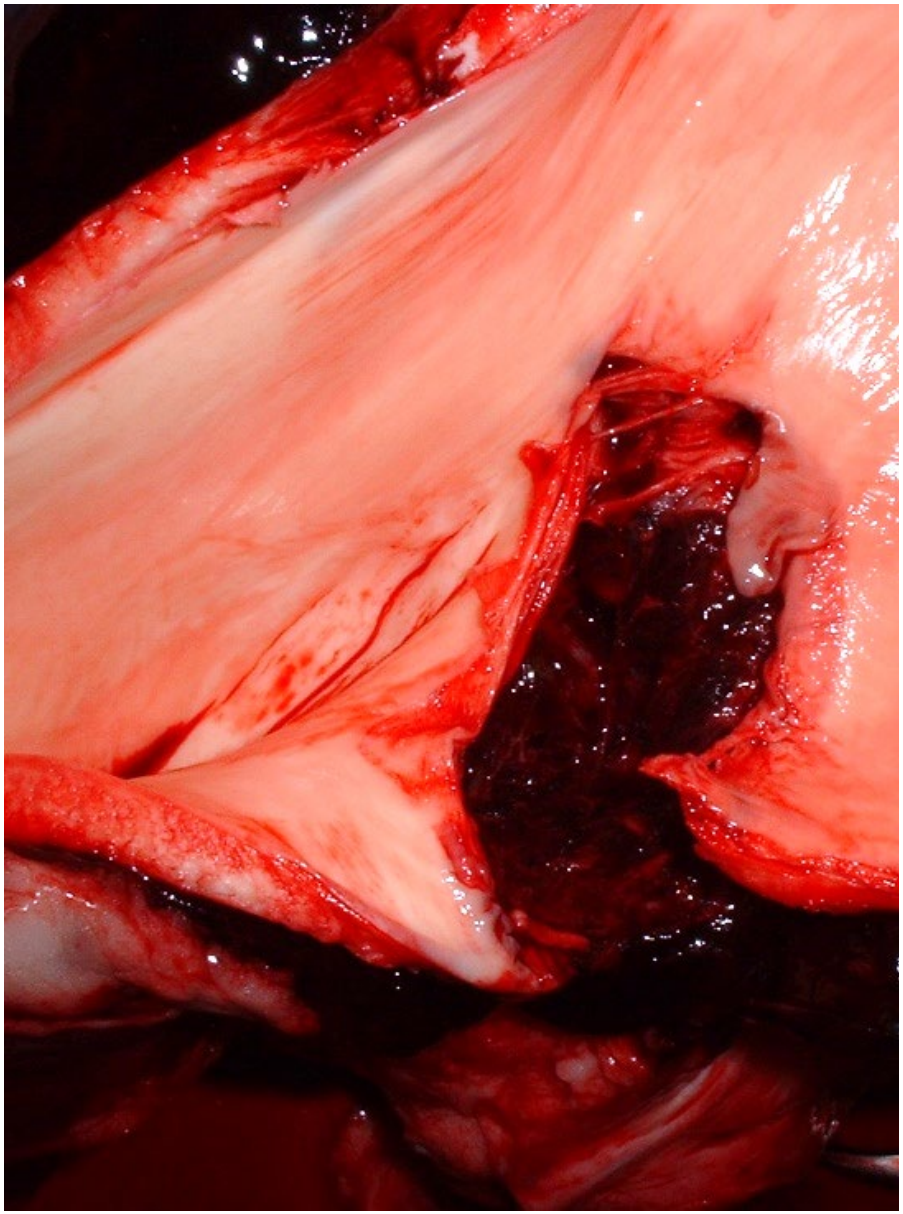
Aortic rupture



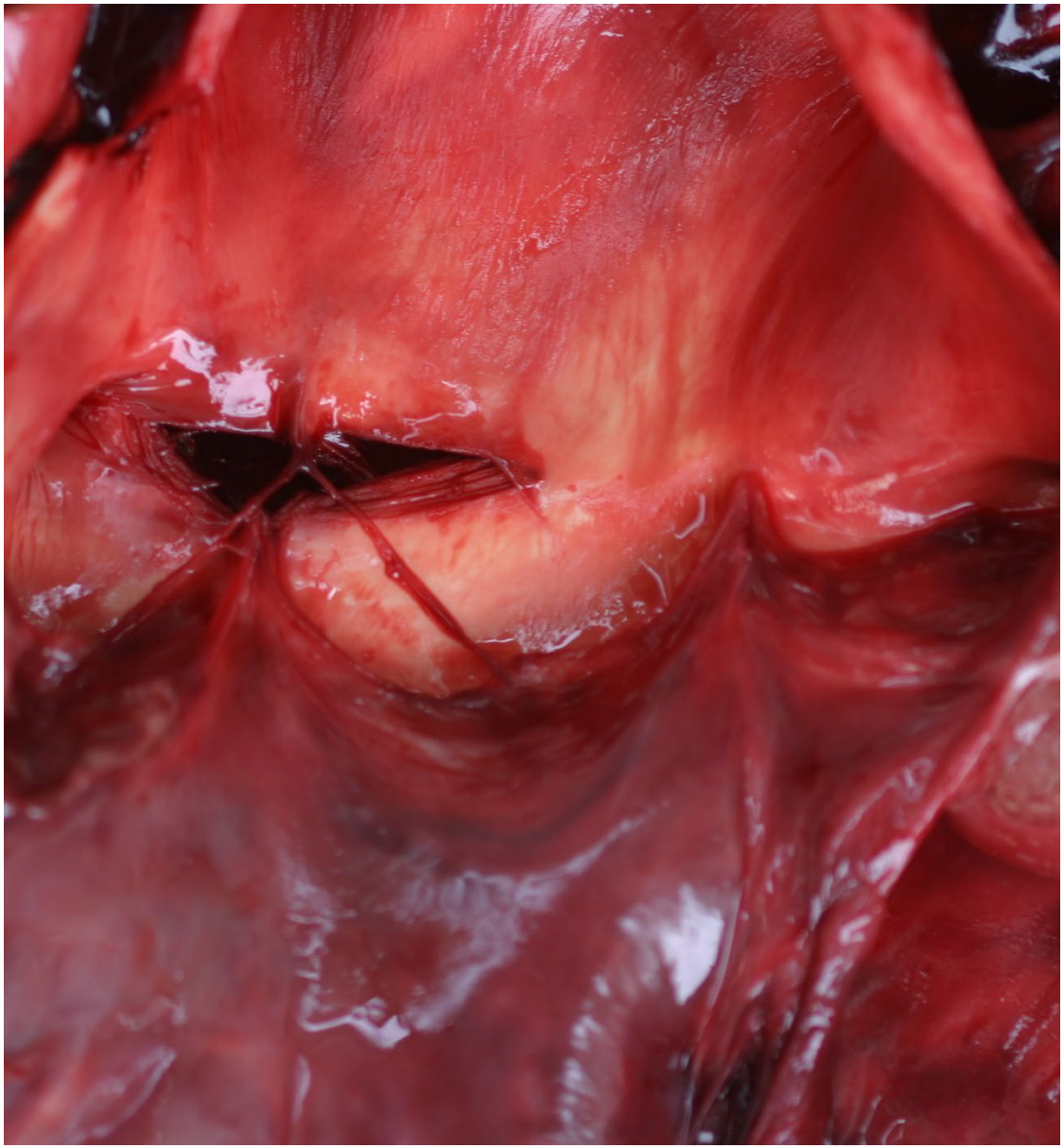


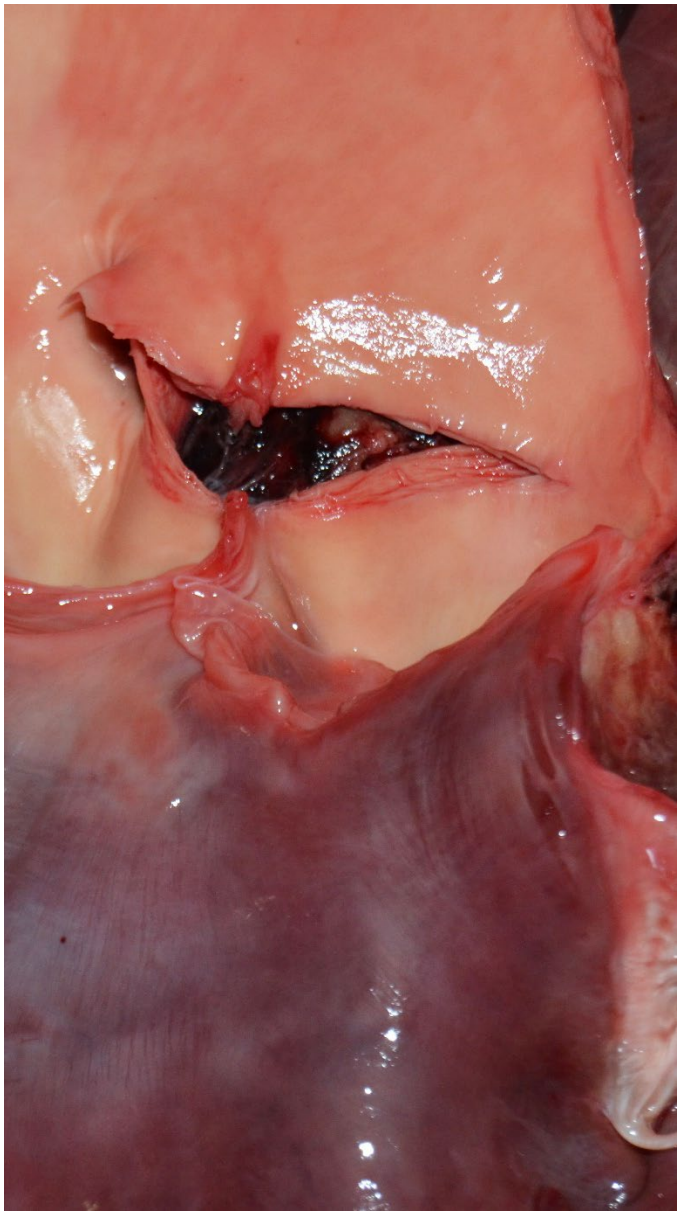
Aortic rupture

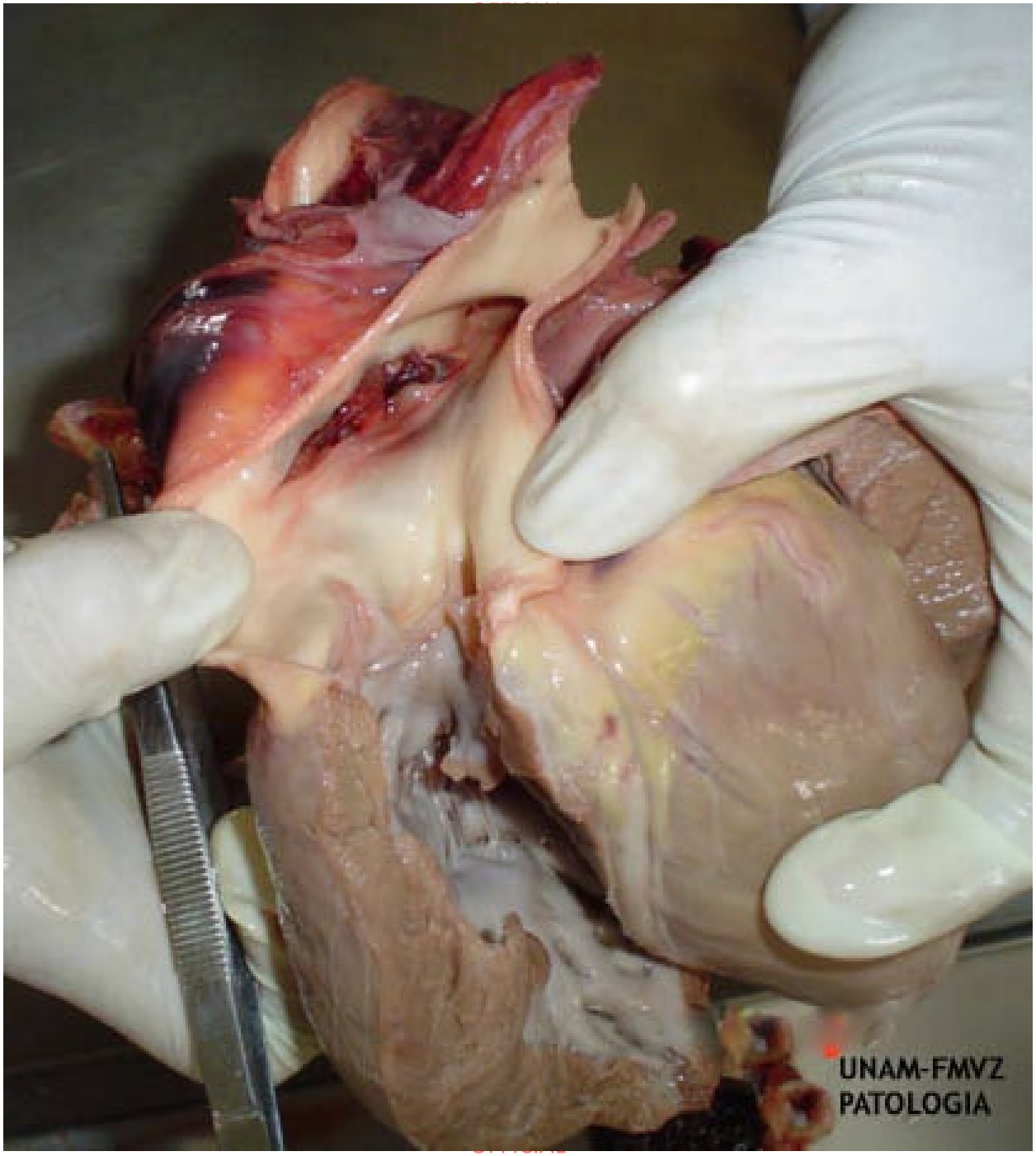




Aortic rupture



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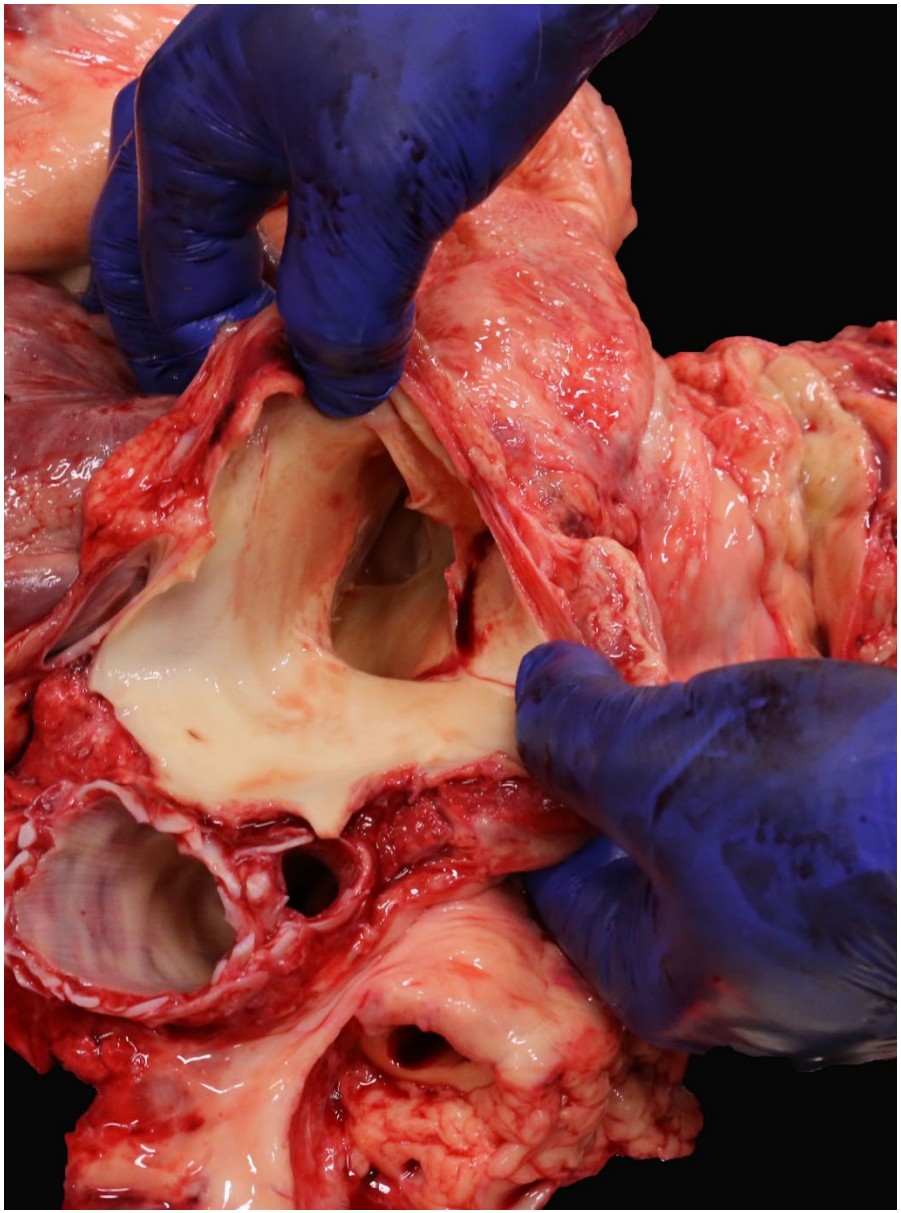
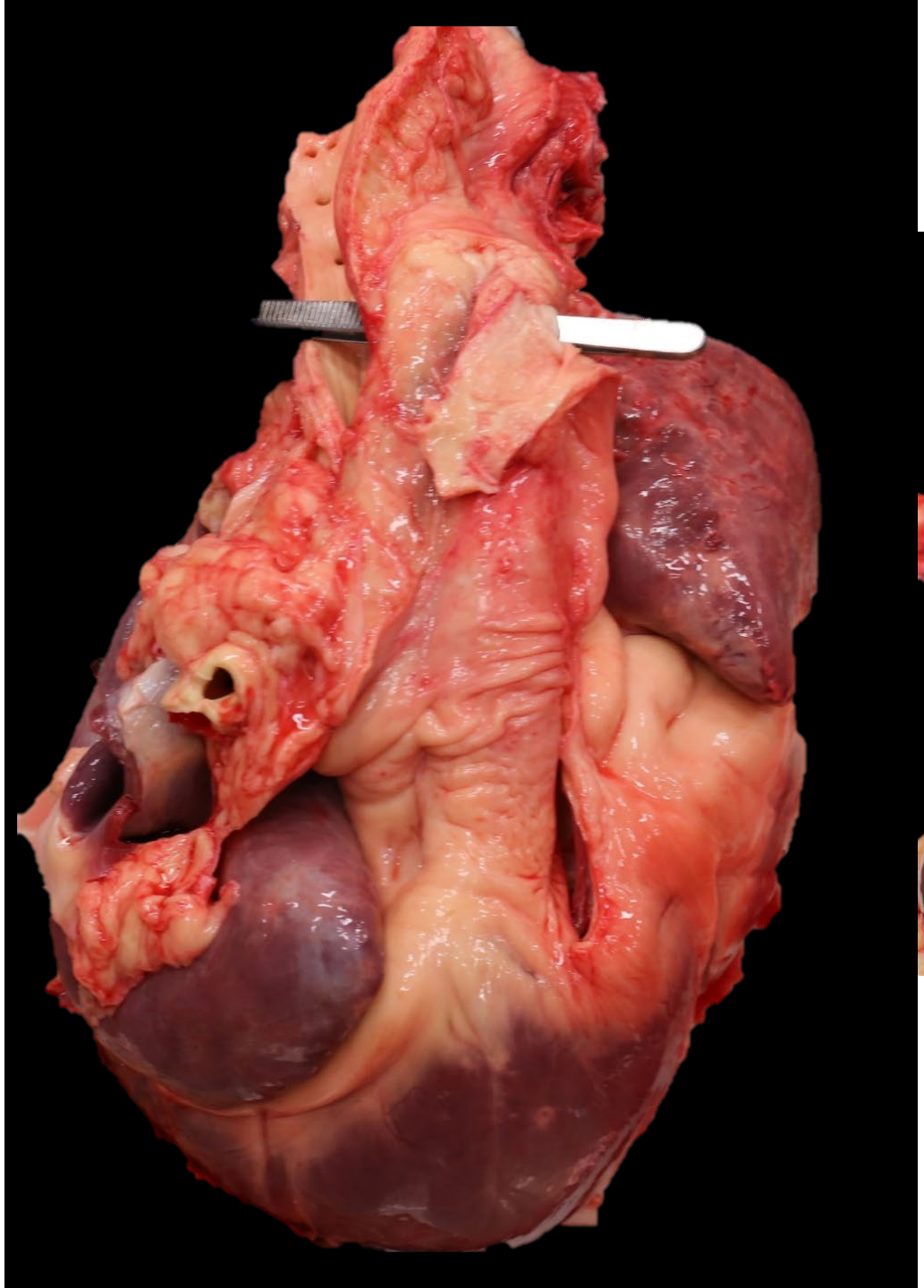
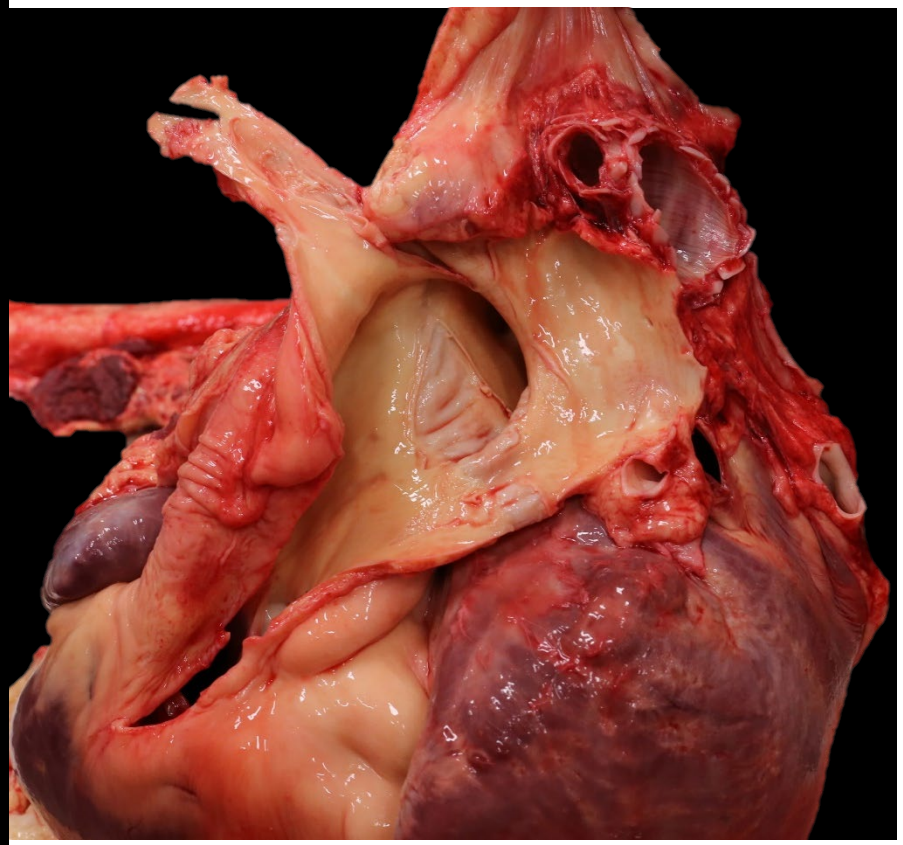
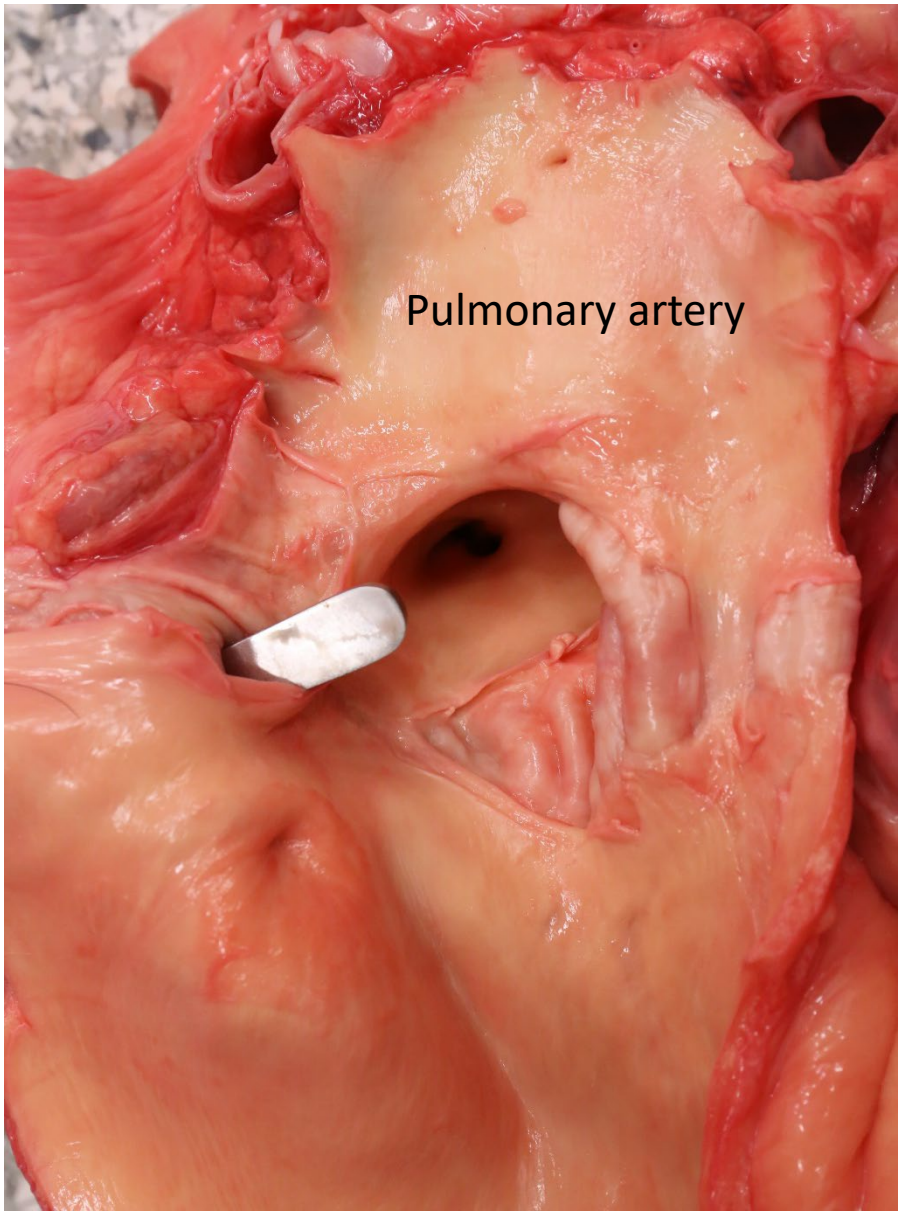
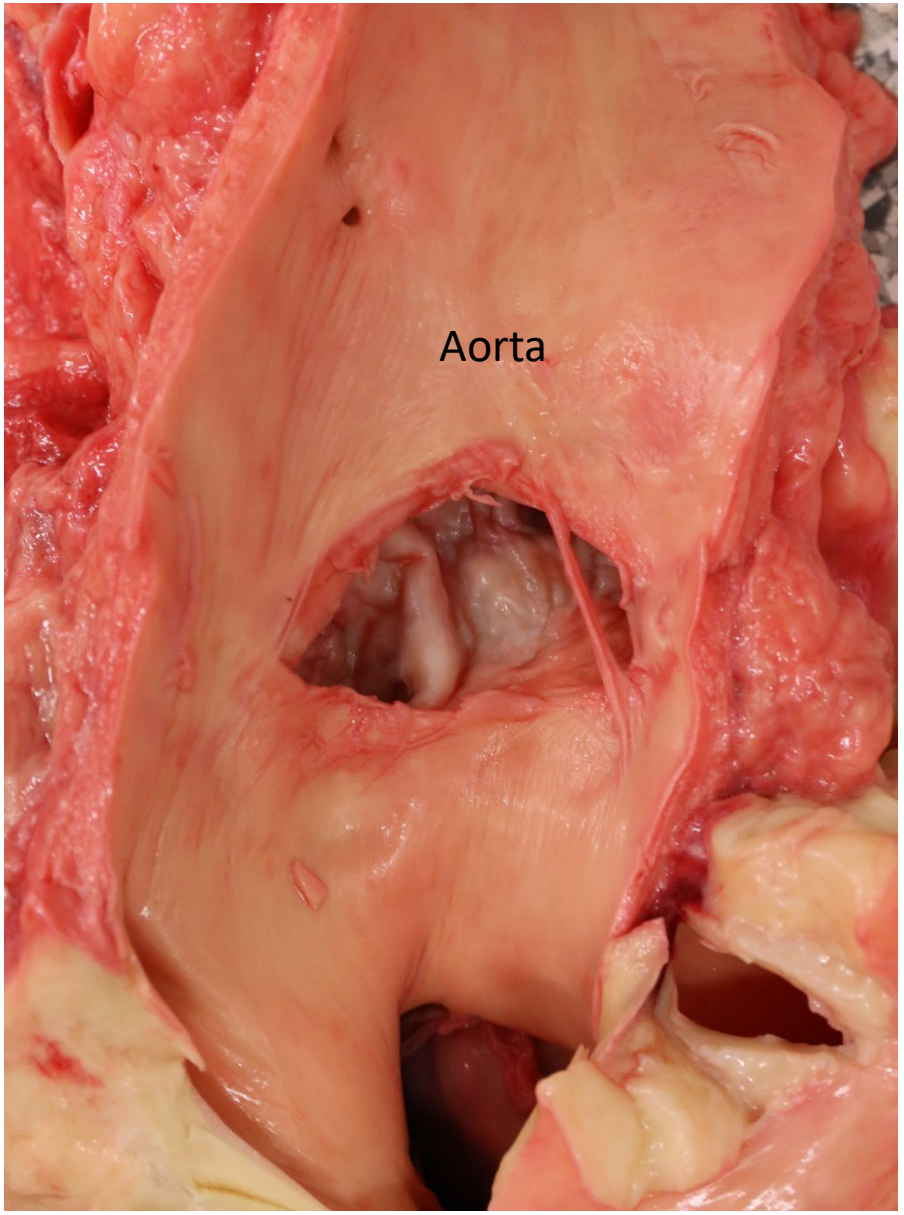
Aortopulmonary fistulation








Pulmonary artery


Aorta

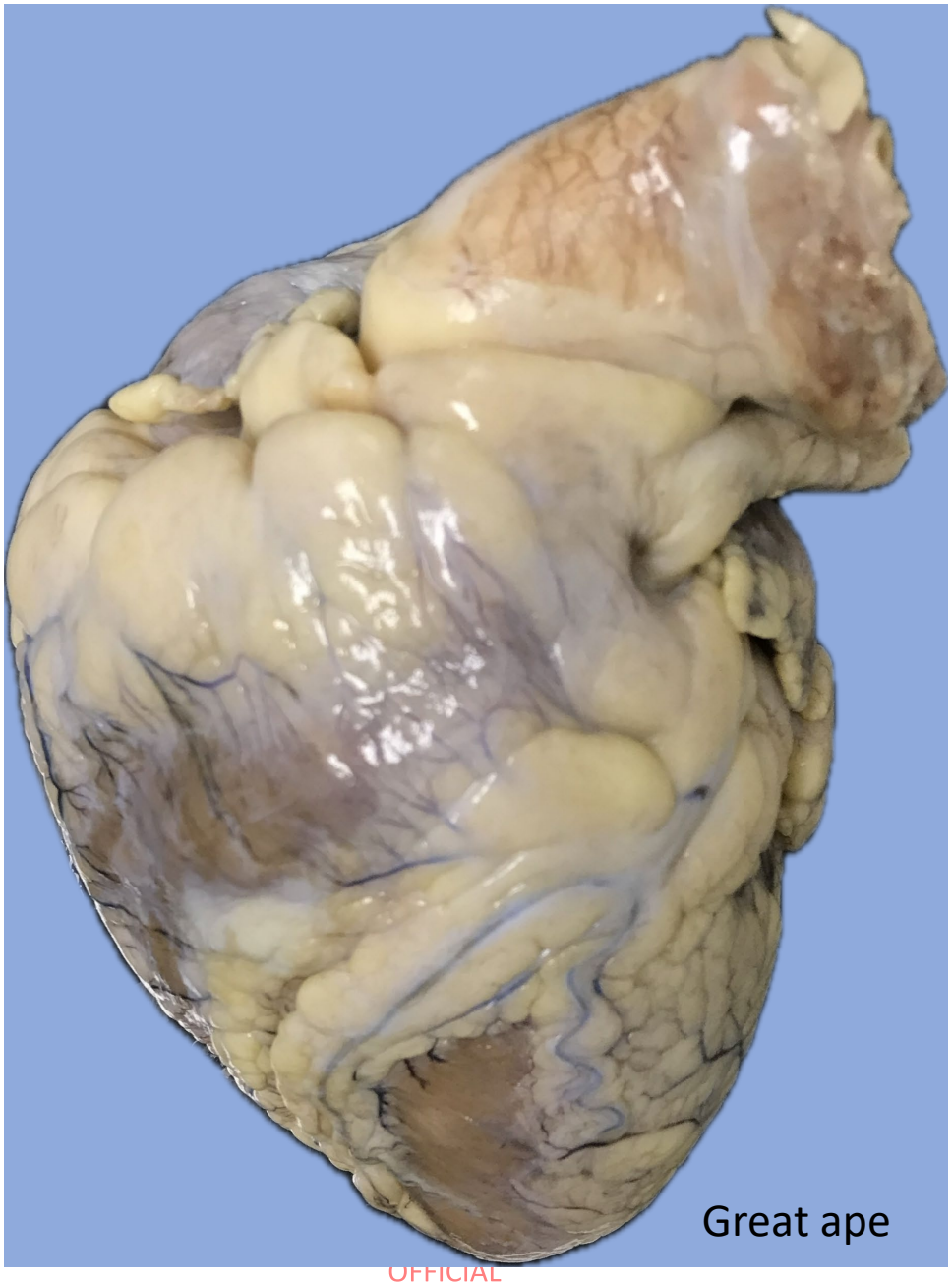
Dilation of the ascending aorta

Causes:

- Hypertension
- Age-related

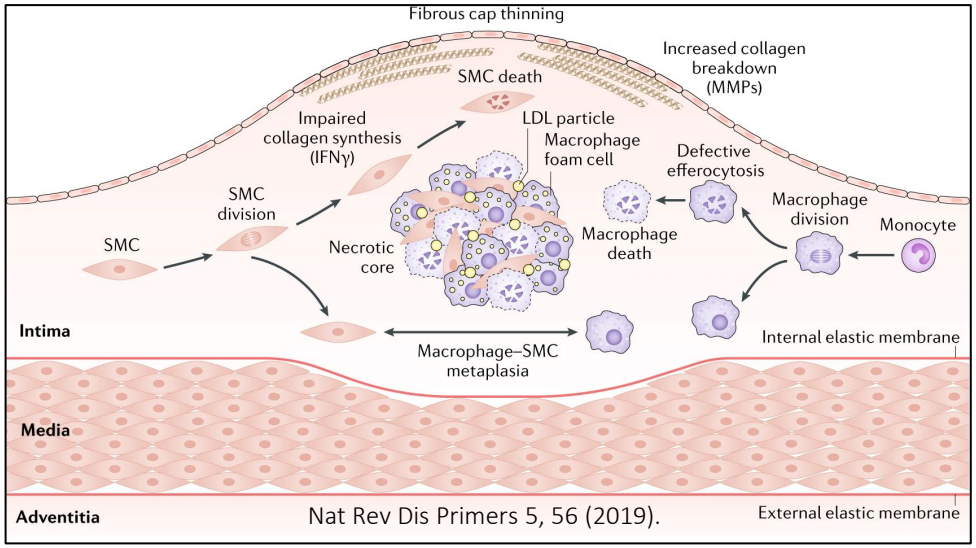
High risk for:

- Aneurysm
- Rupture



Atherosclerosis

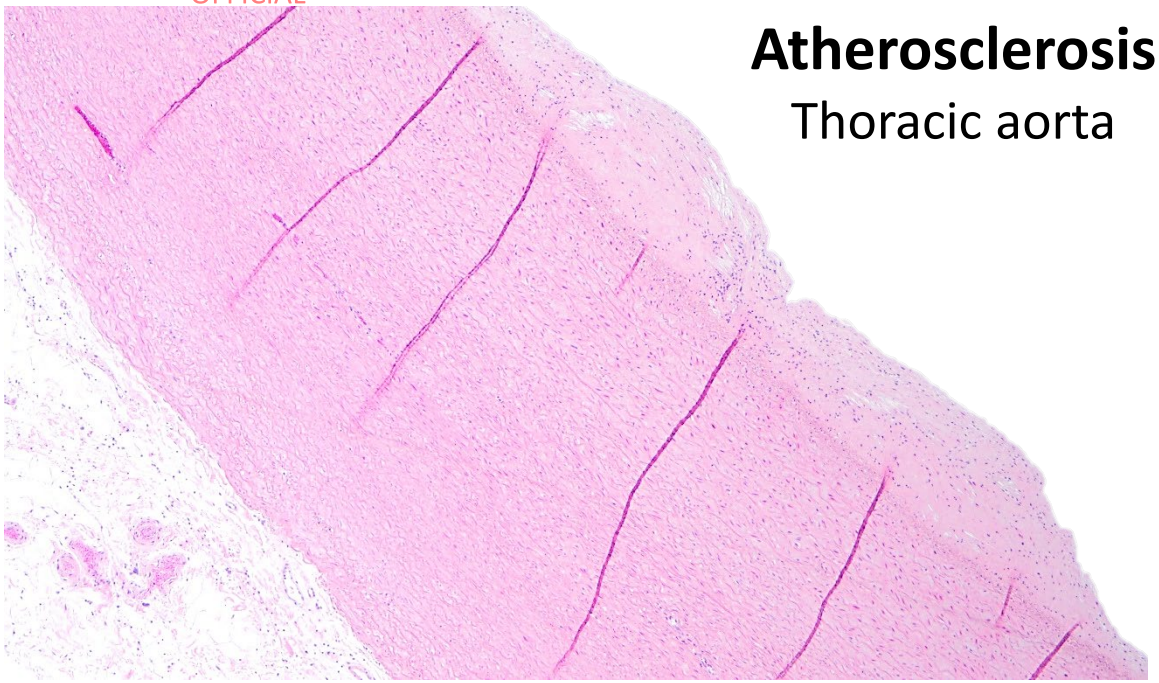
Thickening and loss of elasticity of the walls of arteries that is associated with the formation of fibrofatty lesions within the arterial intima.

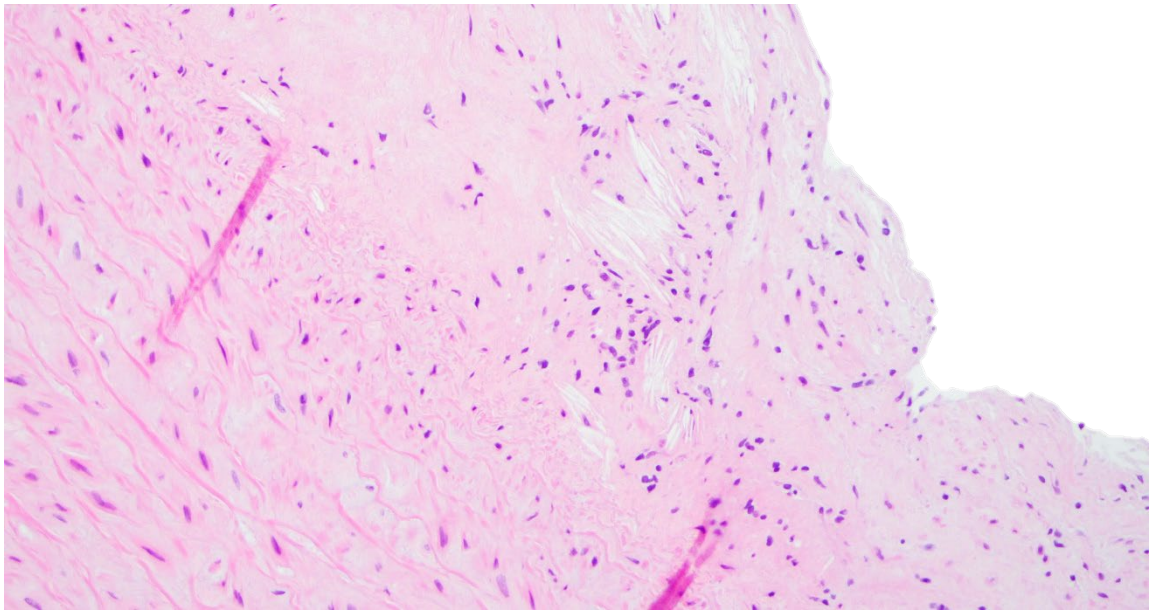


Nat Rev Dis Primers 5, 56 (2019).

Atherosclerosis

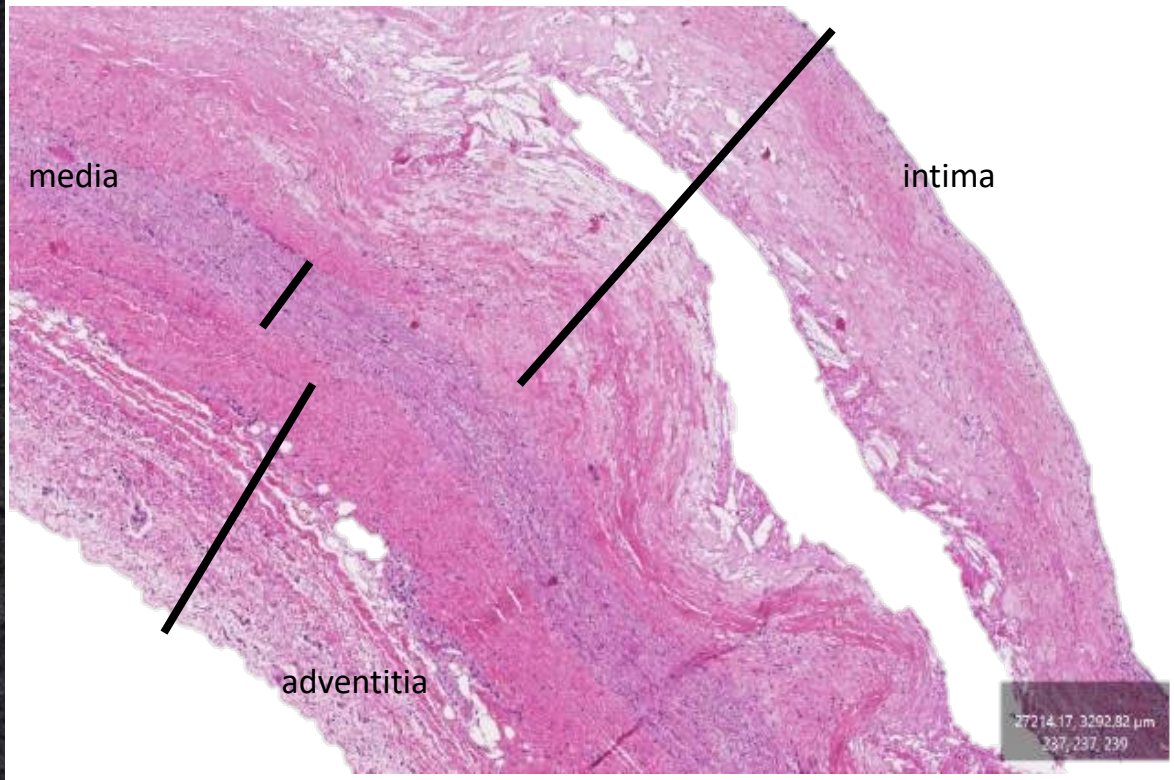
Thoracic aorta





ATHEROSCLEROSIS

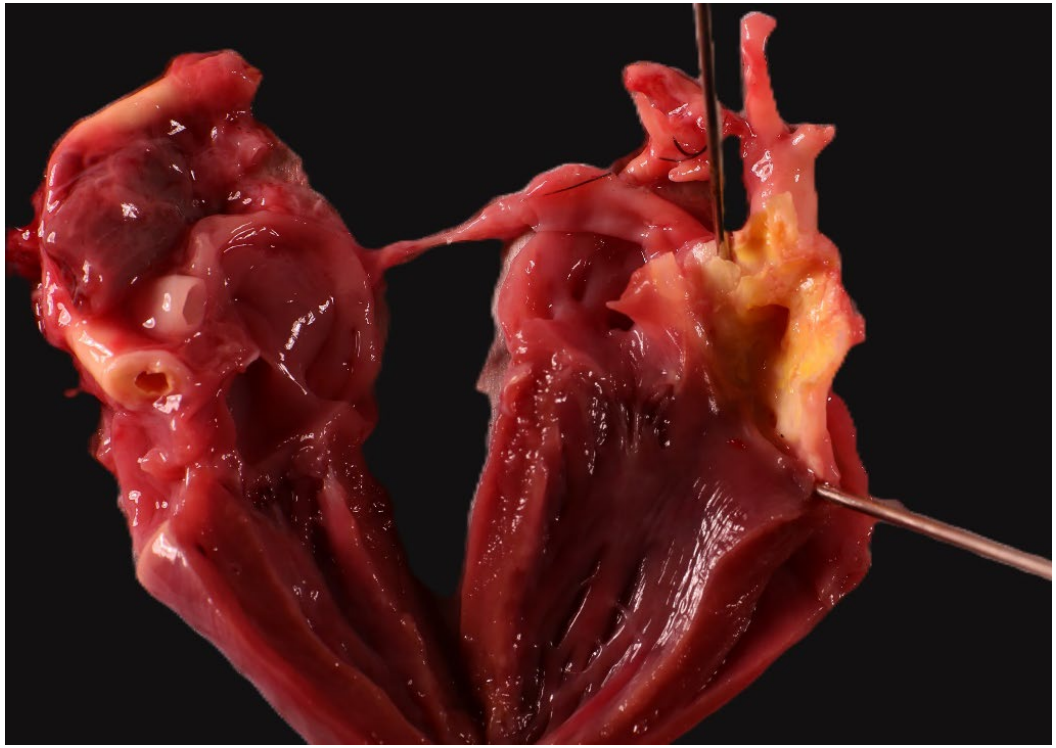
Abdominal aorta

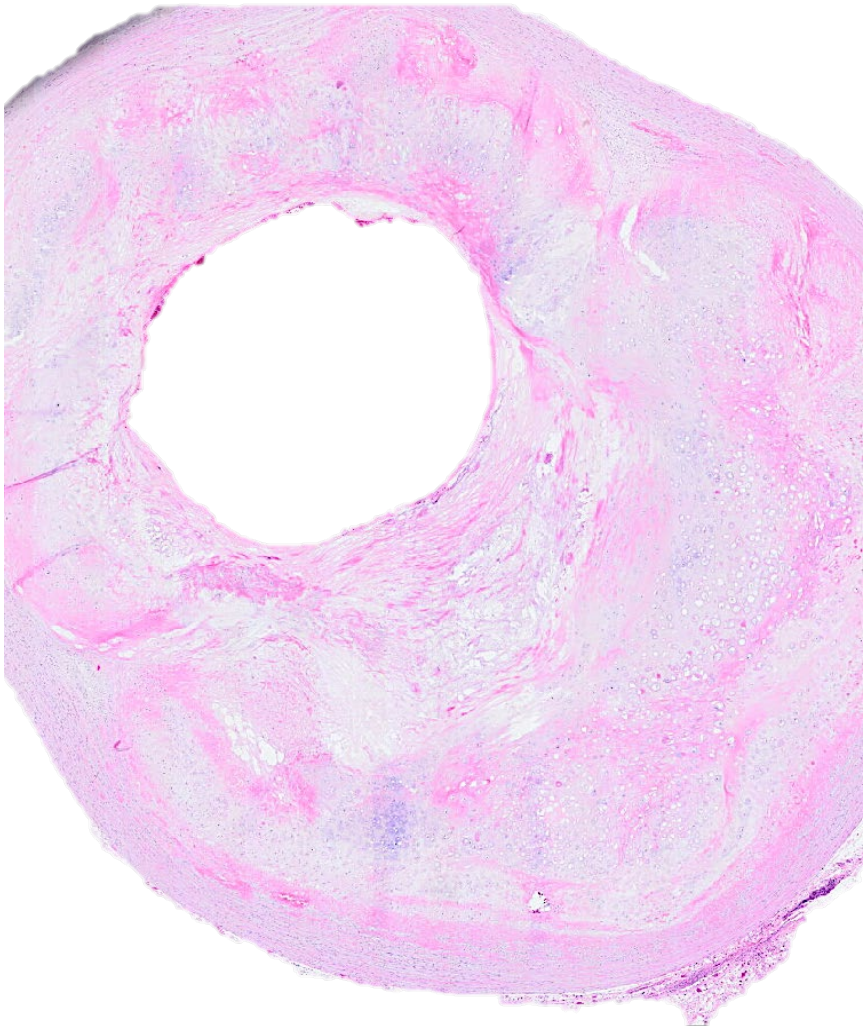


Great ape

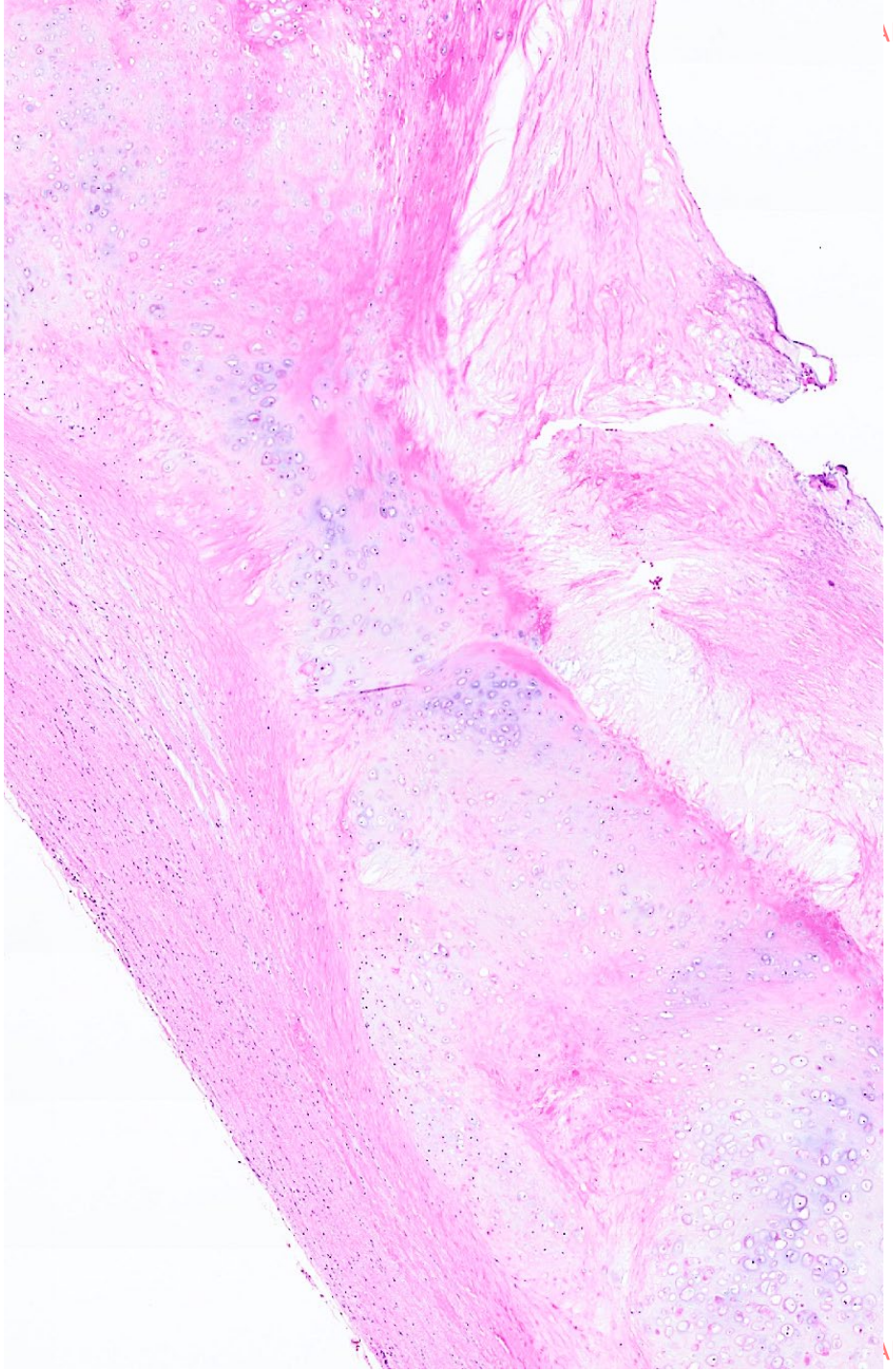
Atherosclerosis

Aorta





- Described in almost all orders of birds.
- Most lesions occurred in the major arteries, but also in the carotid and coronary arteries.
- Risk factors: elevated plasma cholesterol level, diet composition, social stress and inactivity



Atherosensitive species: rabbits, guinea pigs, birds, and pigs

Atheroresistant species: dogs, cats, cattle, goats

Metabolism of HDL and LDL

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

Facultad de Medicina Veterinaria y Zootencia-UNAM Mexico
Dr. Feliz Sanchez Godoy- Departamento de Aves
Dr. Elizabeth Morales Salinas- Departamento de Patologia
Dr. Gerardo Salas Garrido- Departamento de Patologia