Valvular diseases

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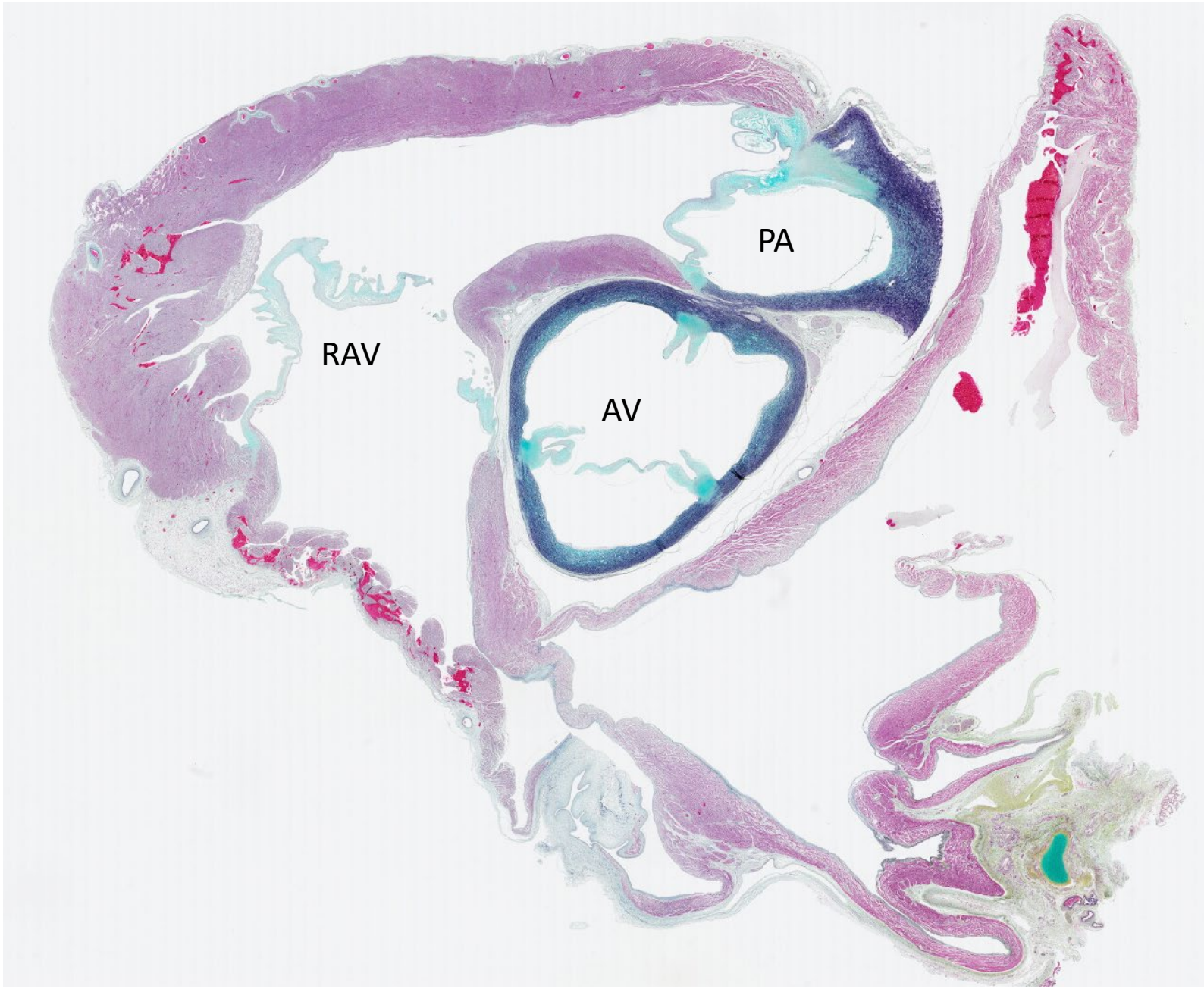
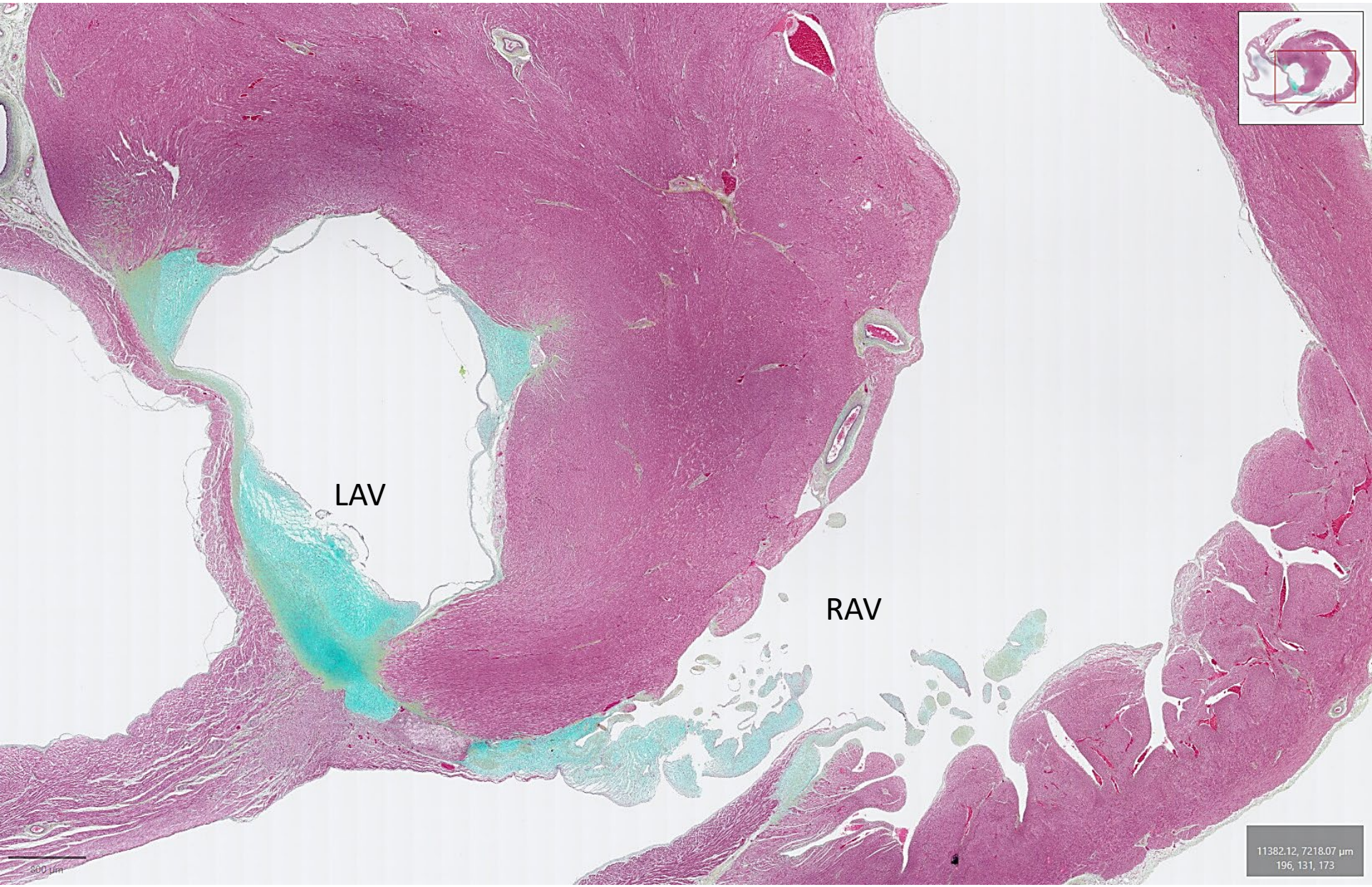
Acquired valvular diseases

- **Myxomatous atrioventricular valvular degeneration**
- **Infectious endocarditis**
- Fibrosis, calcification
- Immune-mediated
- Neoplastic
- Drug-induced

Transverse section/base of the heart

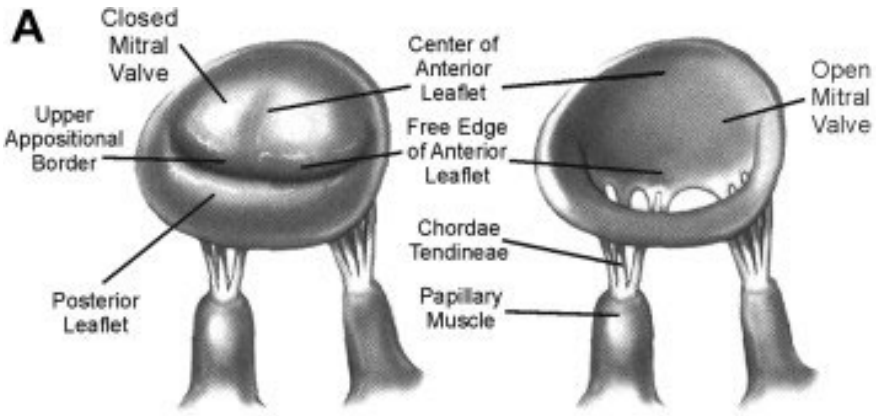



LAV
RAV
200 µm
11382.12, 7218.07 µm
196, 131, 173

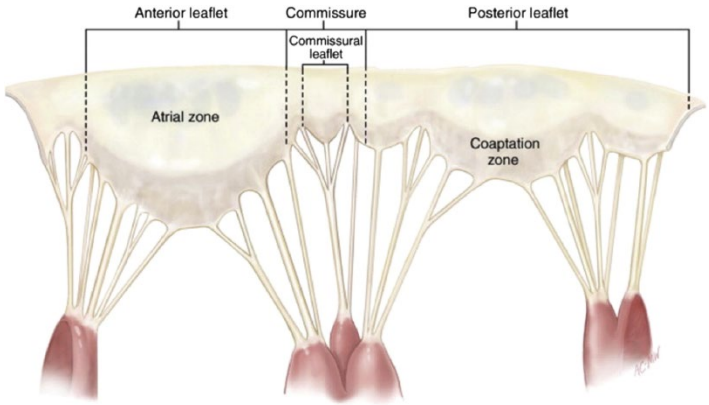
Normal left atrioventricular valve structure

Mitral valve apparatus:

- Posterior left atrial wall
- Mitral valve annulus
- Mitral valve leaflets
- Chordae tendinae
- Left ventricular papillary muscles
- Left ventricular wall



Patrick S. Connell, Richard I. Han, K. Jane Grande-Allen, Differentiating the aging of the mitral valve from human and canine myxomatous degeneration, Journal of Veterinary Cardiology, 2012



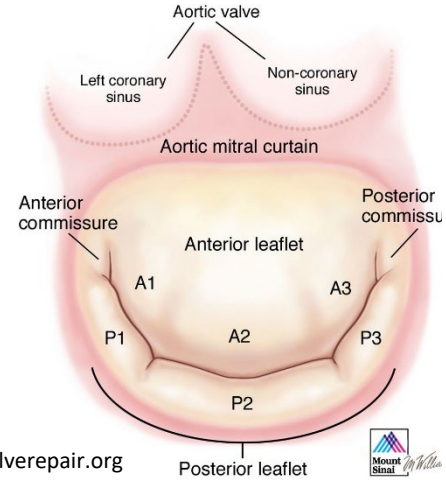
Dal-Bianco, Jacob P. et al. Anatomy of the Mitral Valve Apparatus. Cardiology Clinics, 2013

Normal left atrioventricular valve structure

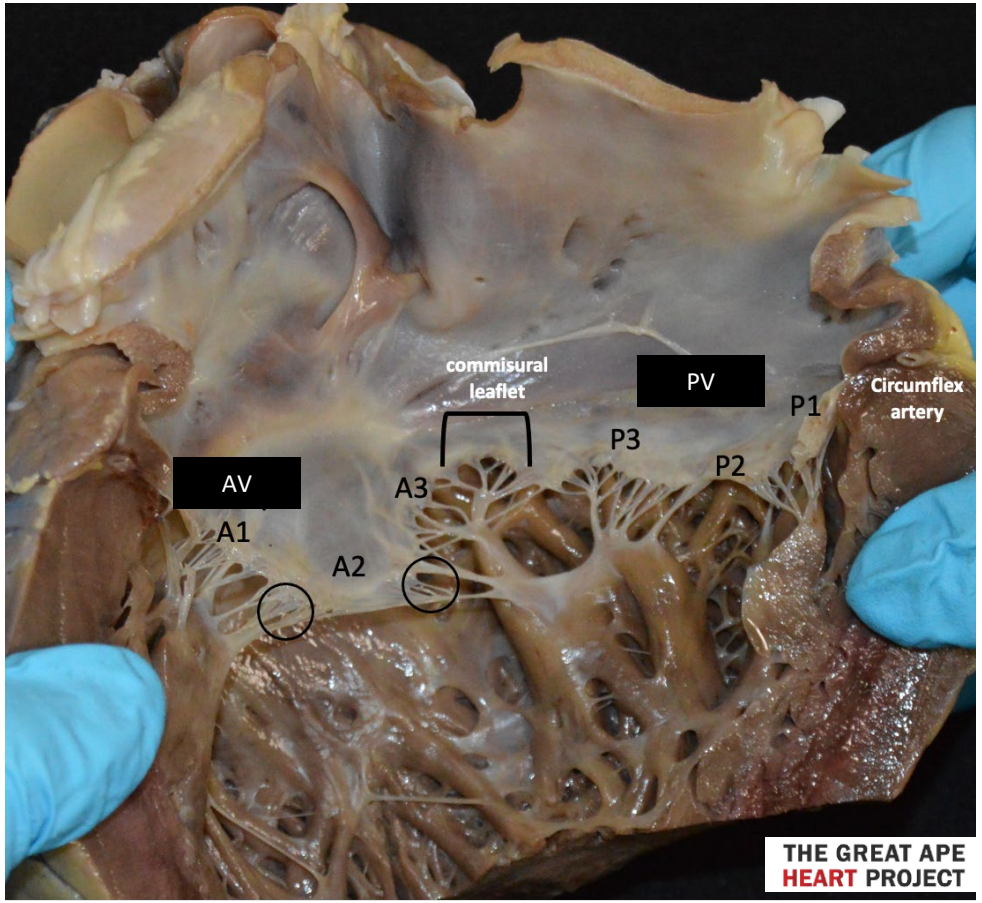
- Primary chordae: insert on the free margin of the valve leaflets
- Rupture causes valve insufficiency

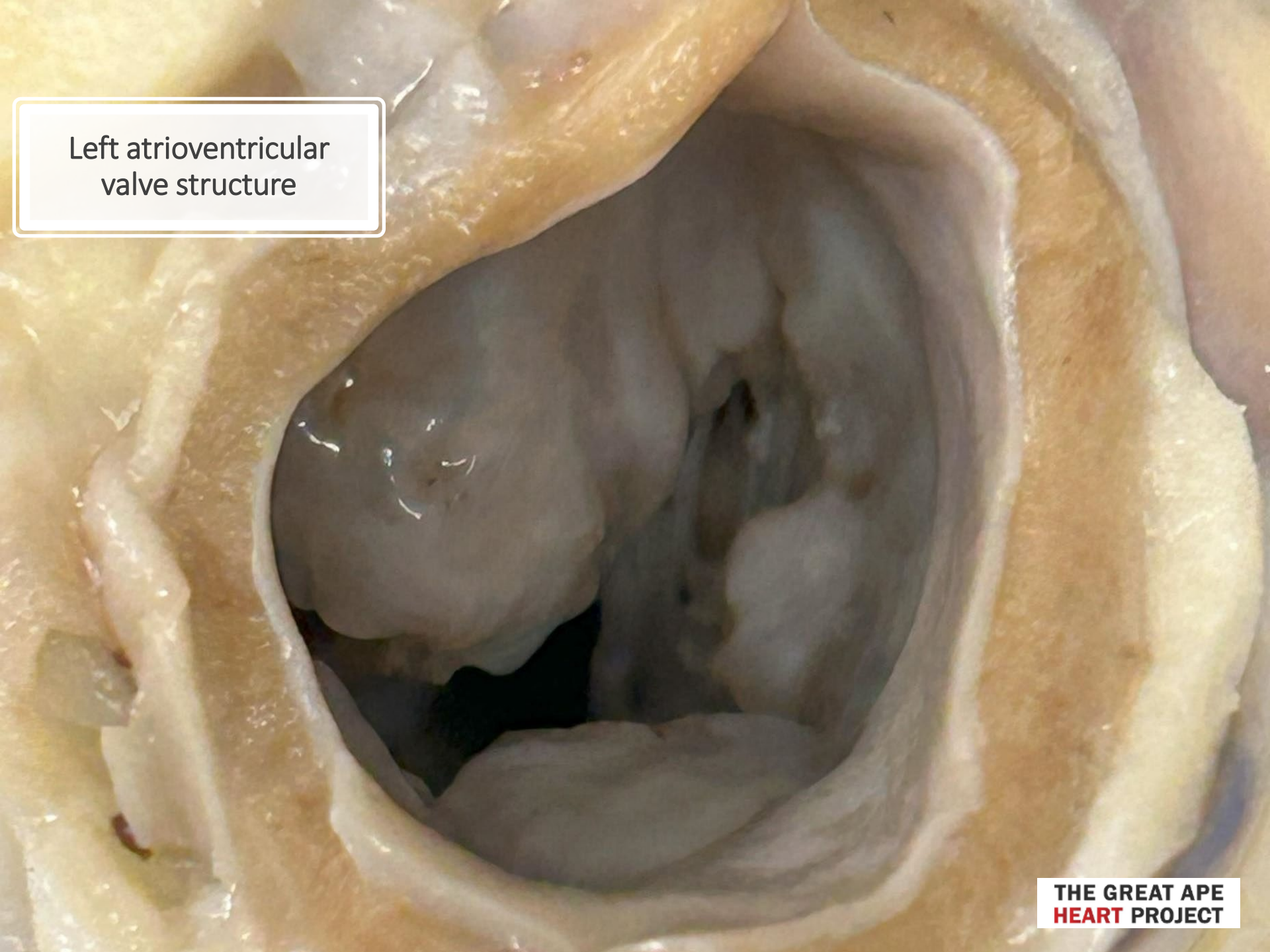
- Secondary chordae: insert on the rugged ventricular surface of the leaflets

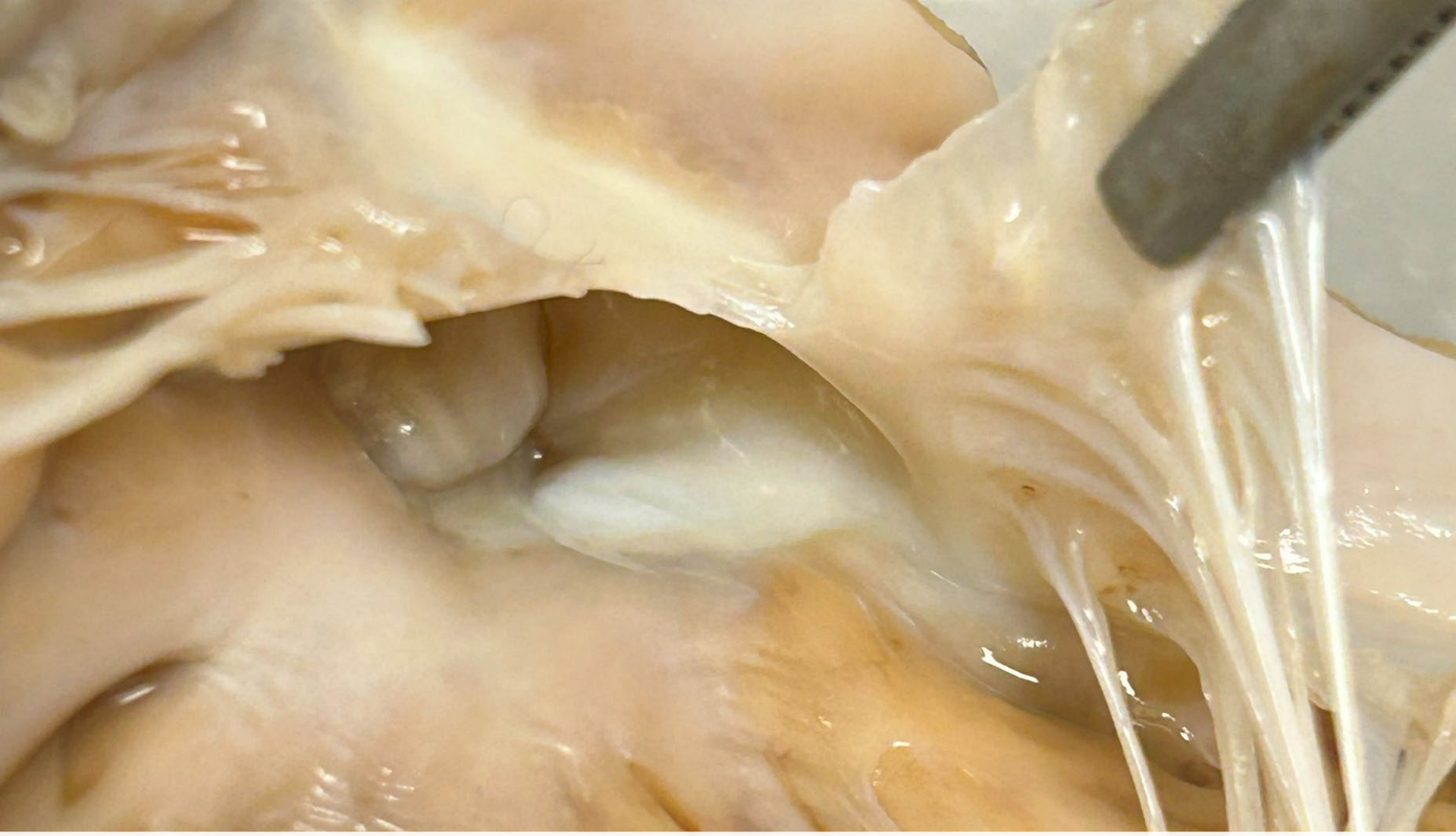
- Tertiary chordae: originate from the ventricular wall and insert only in the basal part of the posterior leaflet.



https://www.mitralvalverepair.org




Left atrioventricular valve structure
THE GREAT APE HEART PROJECT



Secondary chordae: insert on the rugged ventricular surface of the leaflets

Atrioventricular valves

- Core of connective tissue
  - Atrialis: elastic fibers, collagen
  - Spongiosa: proteoglycans, glycosaminoglycans
  - Fibrosa/ventricularis: dense collagen

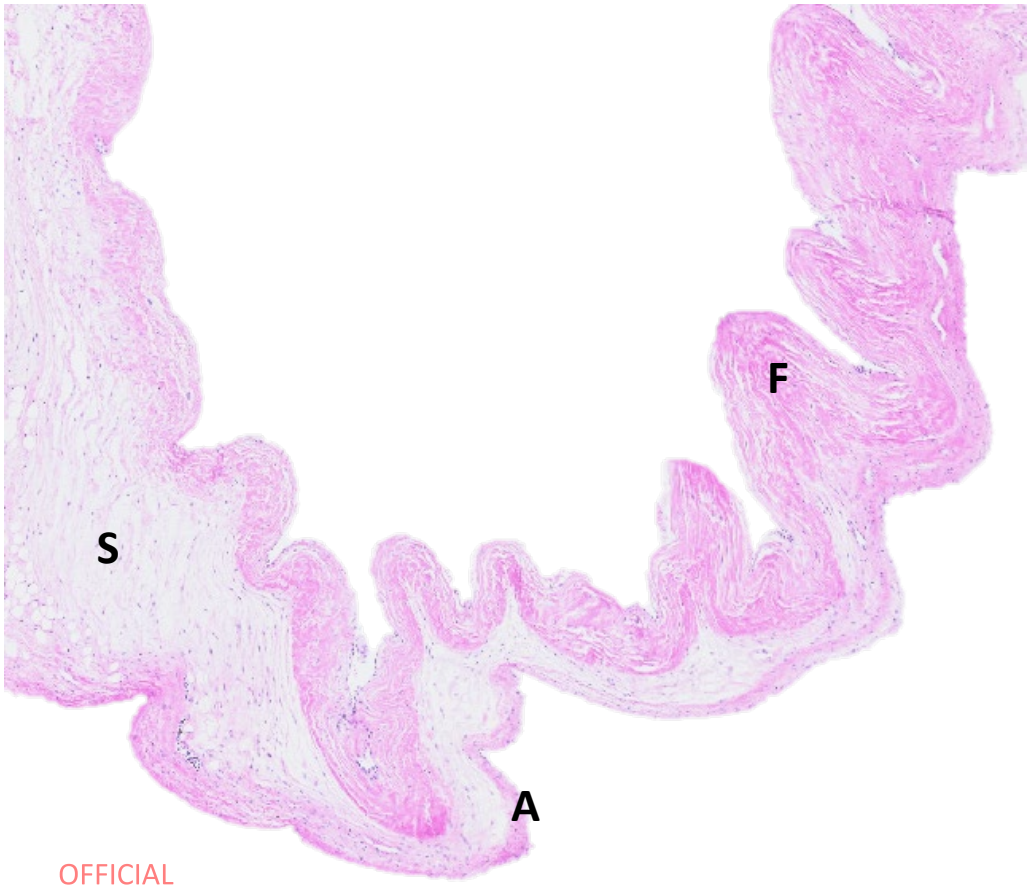
The core is covered by endothelium

Normally avascular: BV are found only on the base of the leaflet

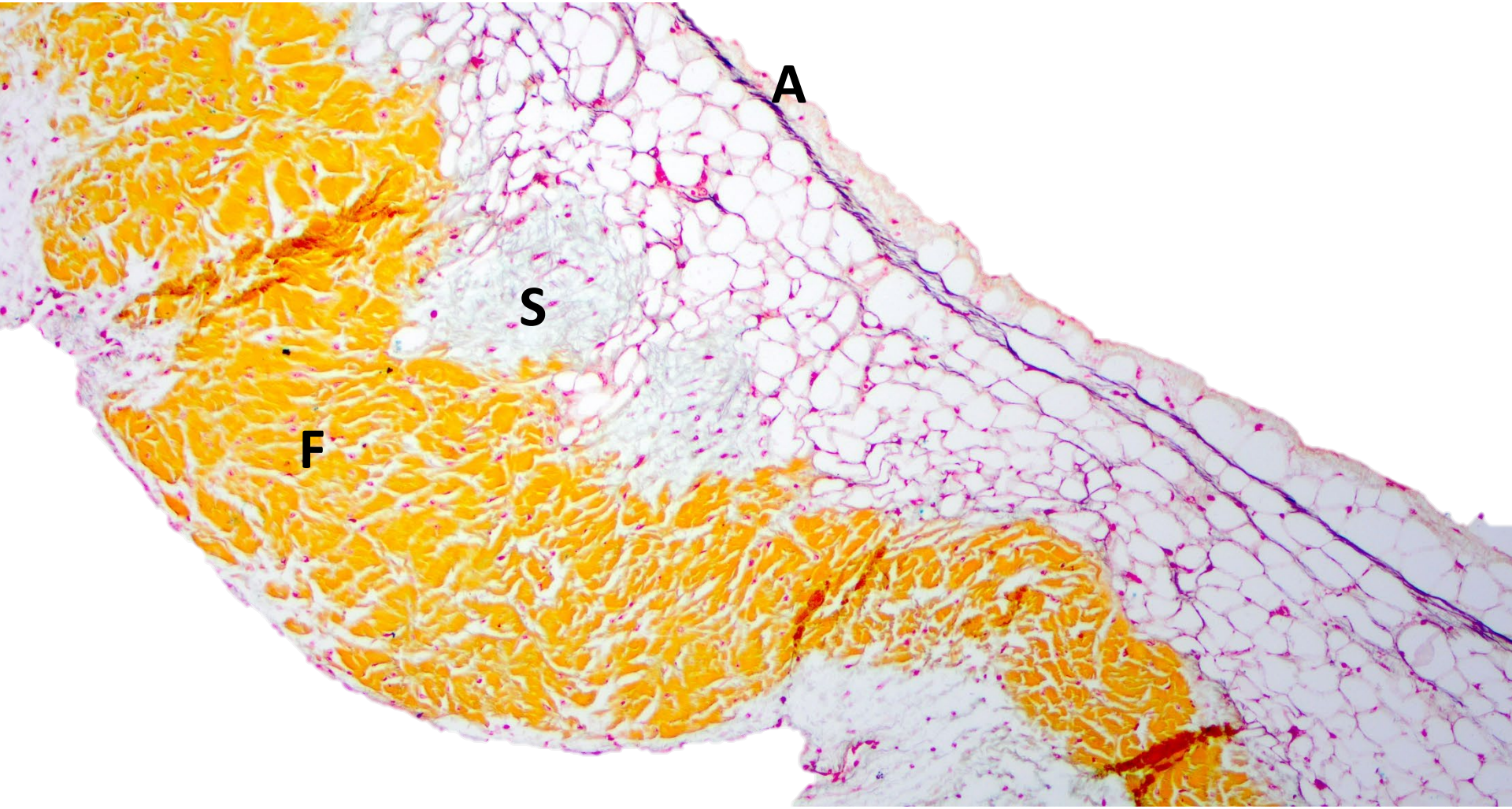
-Atrialis sustains high-frequency large tensile deformation in systole

-Spongiosa resists the compression between the layers, dampens the vibrations of the valve during the high-pressure closing motion, and gives flexibility to the valve

-Fibrosa fibers tensile strength and it connects to the mitral annulus, faces the high pressure in the left ventricle



Left atrioventricular valve

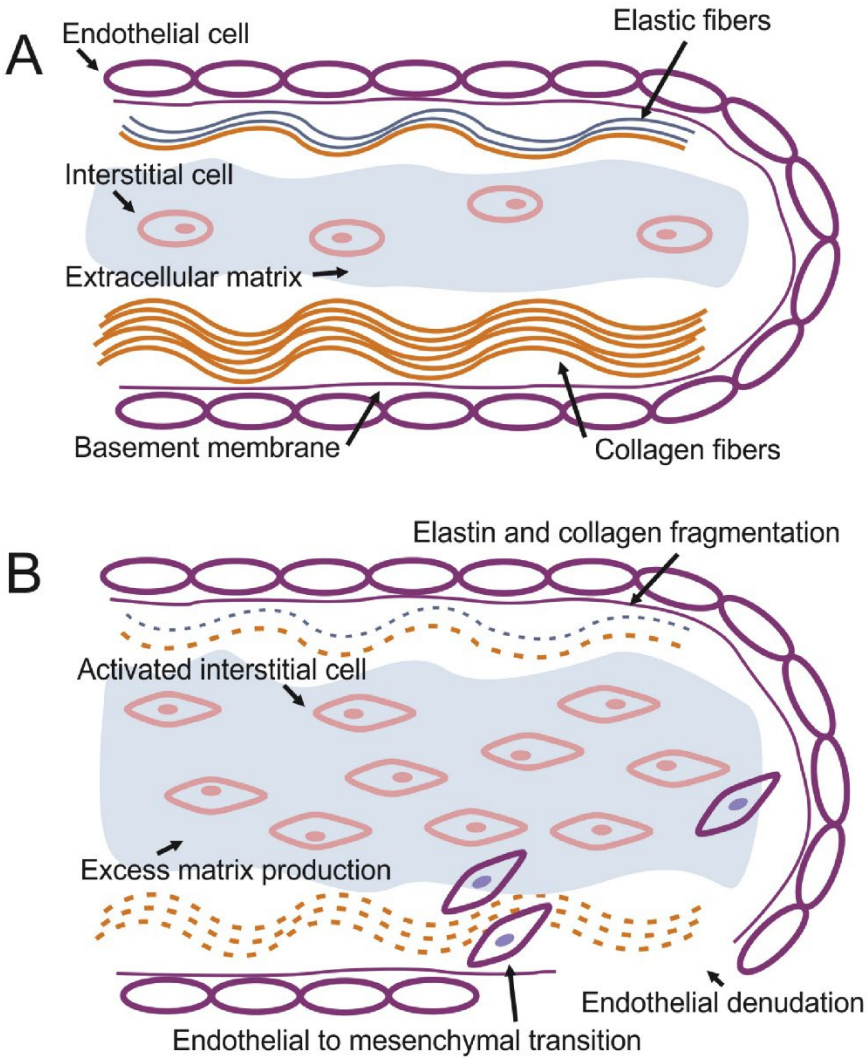


Myxomatous Mitral Valve Disease

- Most common canine heart disease - 75%-80% of all canine cardiac disease
- Uncertain etiology – Suspected polygenetic trait
- Mitral valve is most commonly affected
- Tricuspid involvement in ~30%
- Mostly small to medium-size breeds
  - Cavalier King Charles Spaniel, Poodle, Chihuahua, Maltese, Mini Schnauzer, Dachshund, Cocker, Norfolk terriers
- Inherited component identified in some breeds
  - Dachshund, CKCS

https://www.cavaliermatters.org/heart-disease-mvd-part-2/

Mechanism of myxomatous mitral valve disease (MVD)



NORMAL VALVE

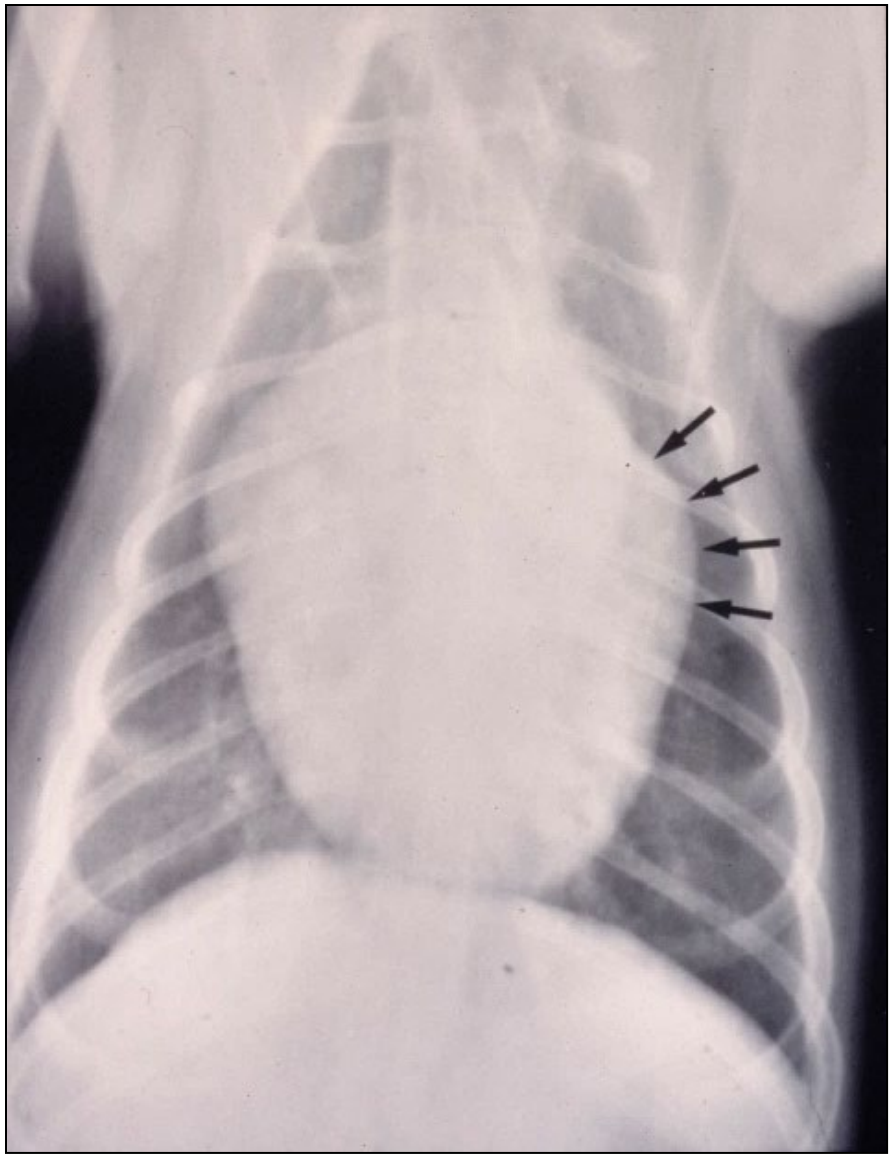
- Endothelial cells
- Atrialis (elastic, collagen fibers)
- Spongiosa (ECM-proteoglycans)
- Interstitial cells
- Fibrosa

MVD

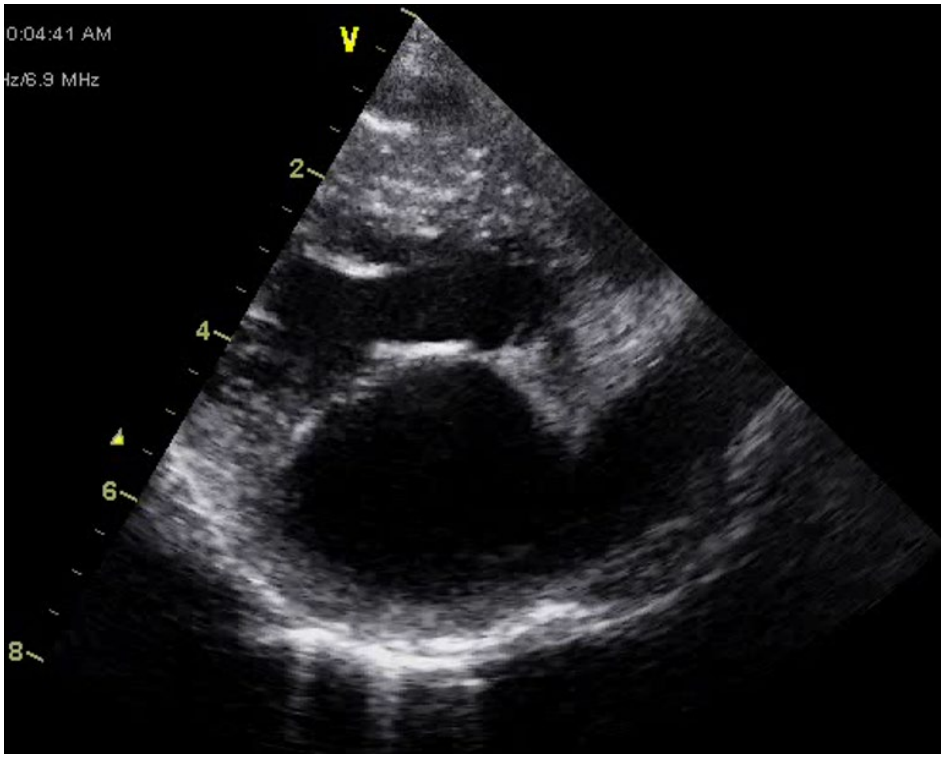
- IC activated into a myofibroblast-like phenotype
- Excessive deposition of ECM
- Dissolution and fragmentation of the elastic and collagen fibers of the atrialis and fibrosa
- Endothelial-to-mesenchymal cell transformation
- Migration of endothelial cells into the spongiosa
- Denudation of the endothelial cell lining and exposure of the subendothelial collagen

Mark A. Oyama, Chad Elliott, Kerry A. Loughran, Alexander P. Kossar, Estibaliz Castillero, Robert J. Levy, Giovanni Ferrari, Comparative pathology of human and canine myxomatous mitral valve degeneration: 5HT and TGF-β mechanisms, Cardiovascular Pathology 2020.

Mitral valve disease



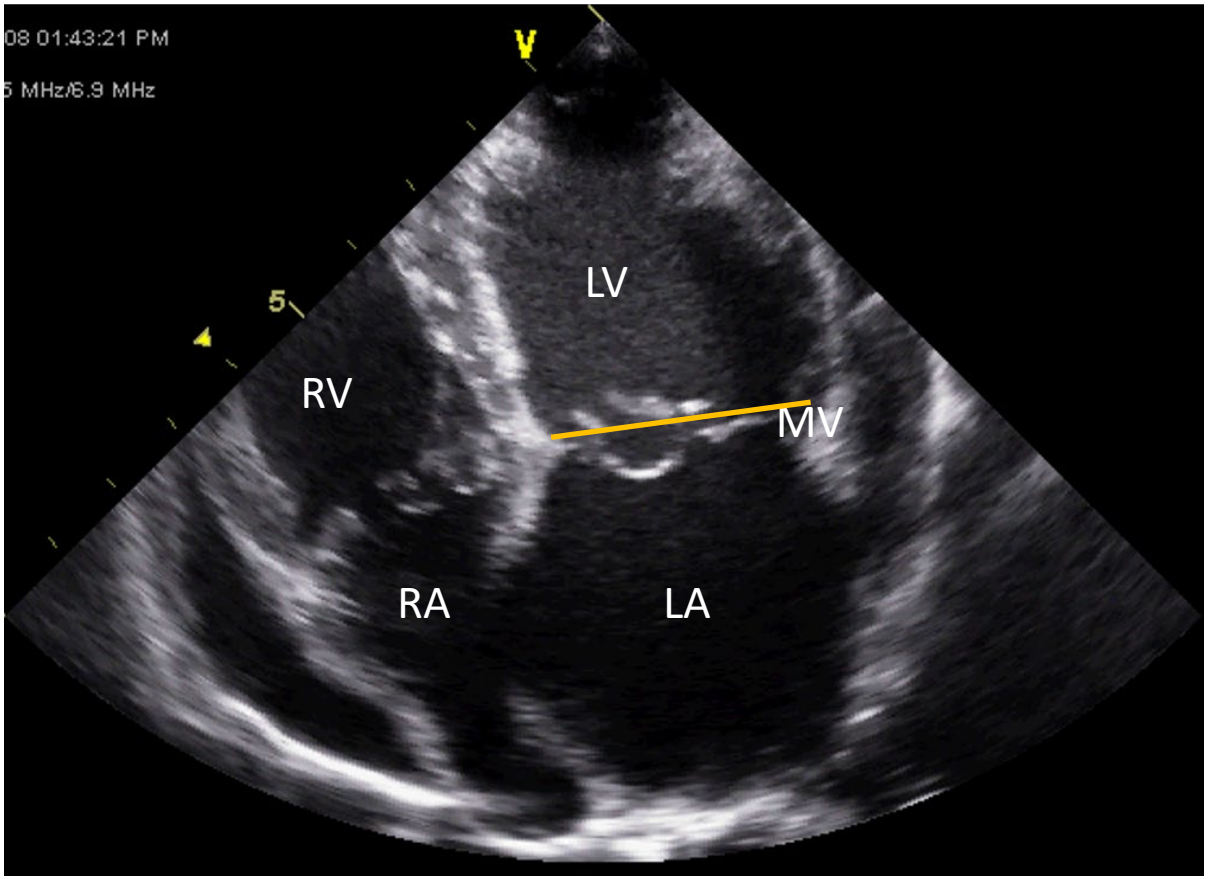
Left atrial enlargement (LA appendage)
Cardiomegaly

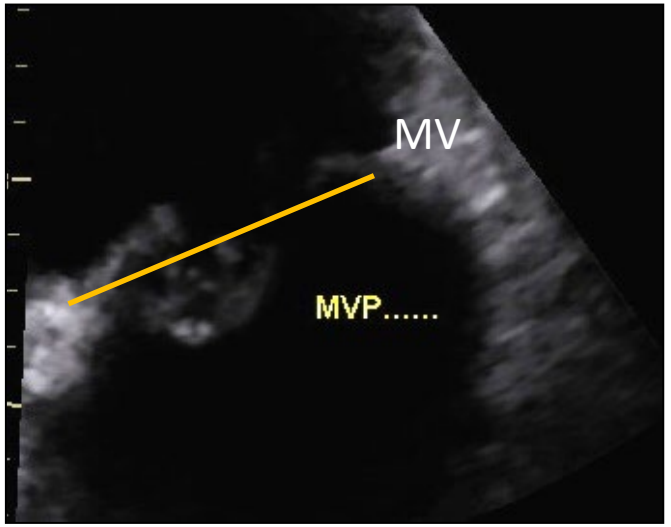


Left atrial enlargement

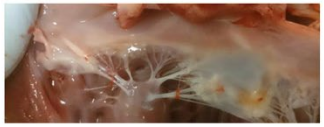
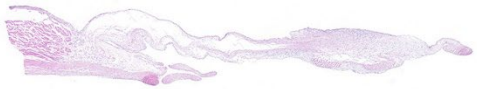
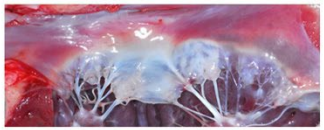
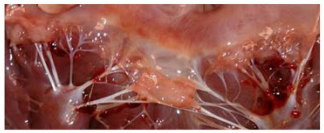
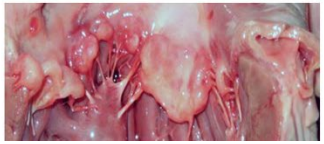
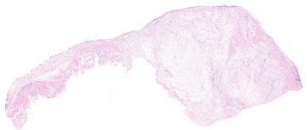
Mitral valve prolapse

Displacement of 1 or both mitral valve leaflets above the annulus within the LA in end-systole.



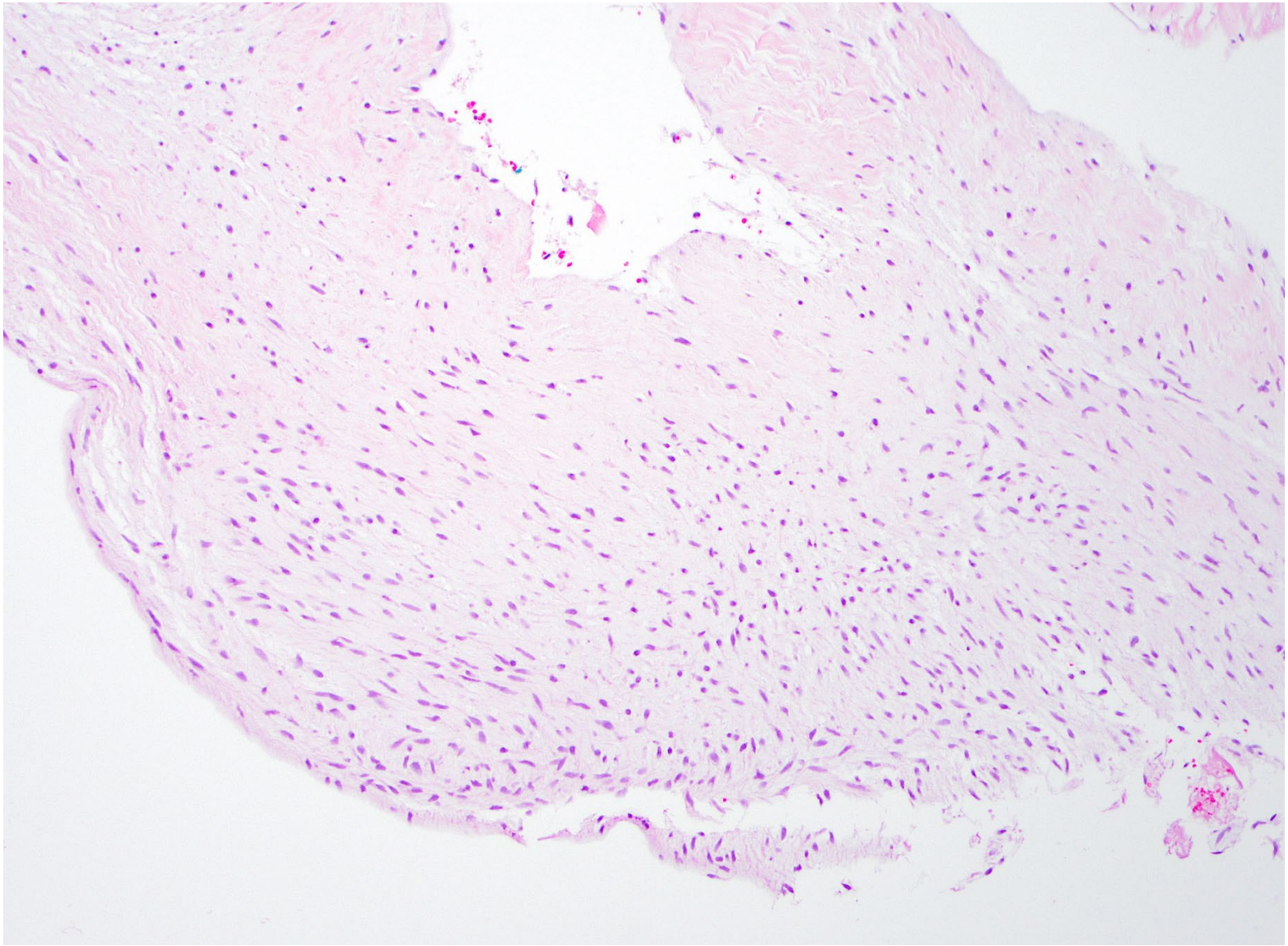


Whitney (1974) grading scheme for myxomatous valvular degeneration

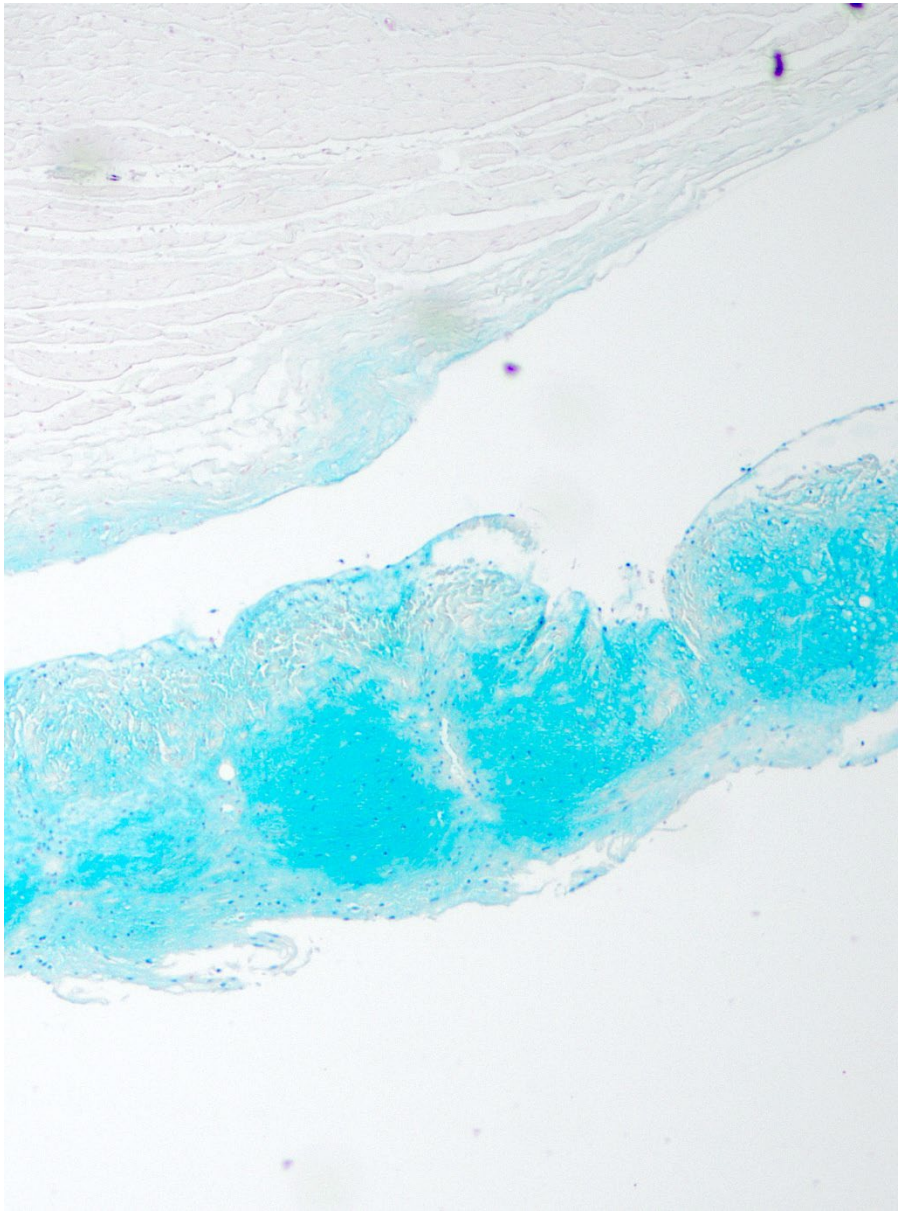
Grade	Gross	Histology	
0			
I			small numbers of discrete nodules on the free edge of the leaflet
II			larger nodules
III			coalescence of the nodules
IV			involvement of the chordae and gross distortion and ballooning of the leaflets with marked chordal thickening and eventual chordal rupture

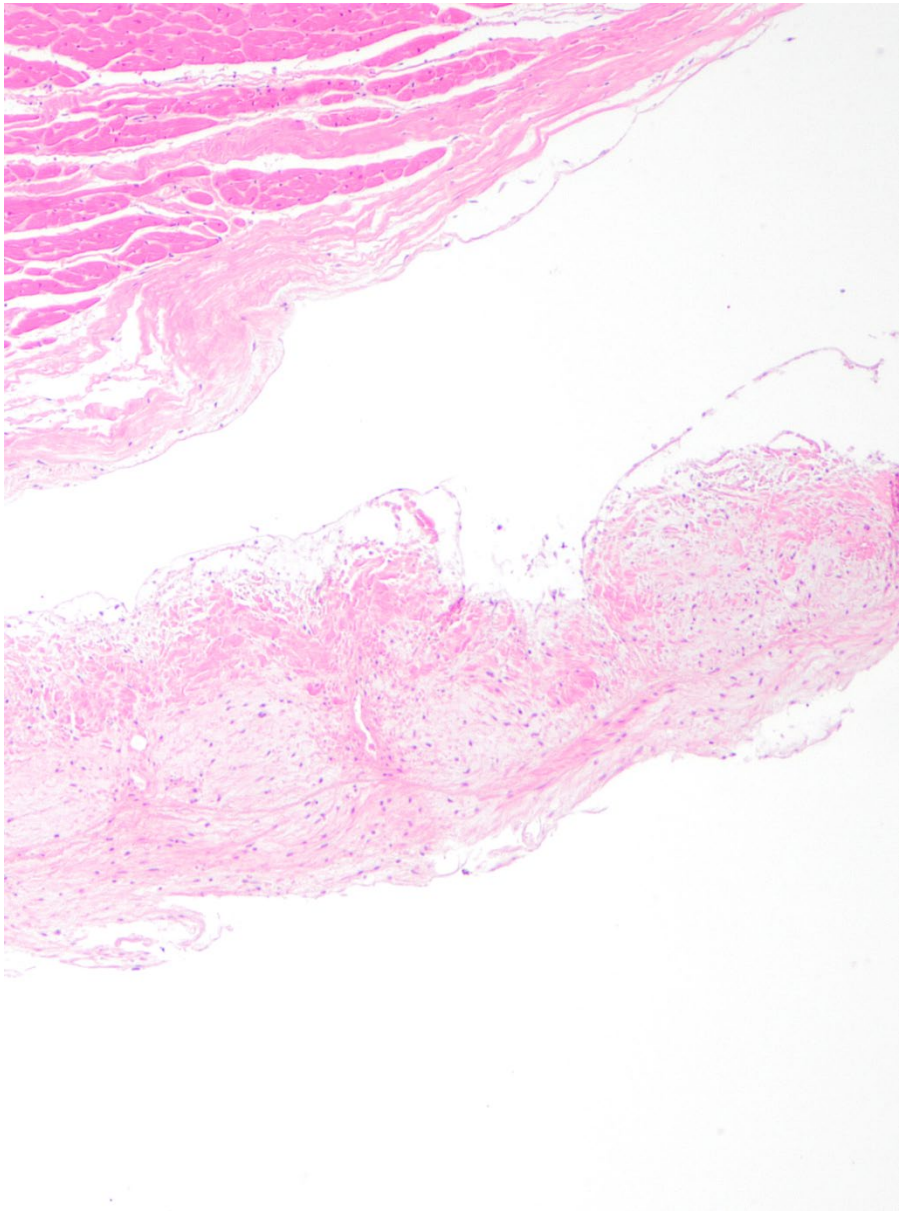
G. Markby, K.M. Summers, V.E. MacRae, J. Del-Pozo, B.M. Corcoran, Myxomatous Degeneration of the Canine Mitral Valve: From Gross Changes to Molecular Events, Journal of Comparative Pathology, 2017.

Myxomatous valvular degeneration grade II

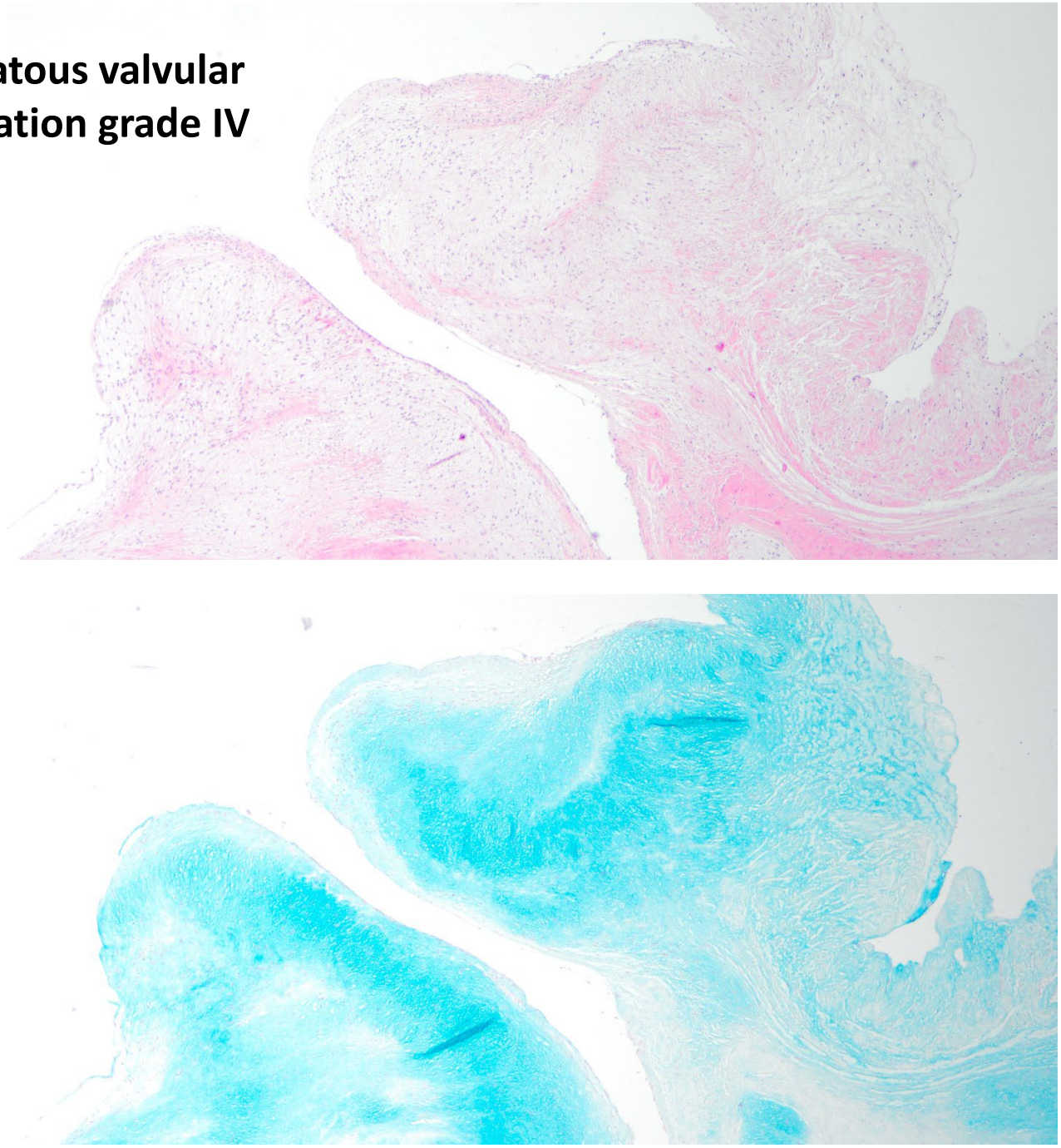


Myxomatous valvular degeneration grade III

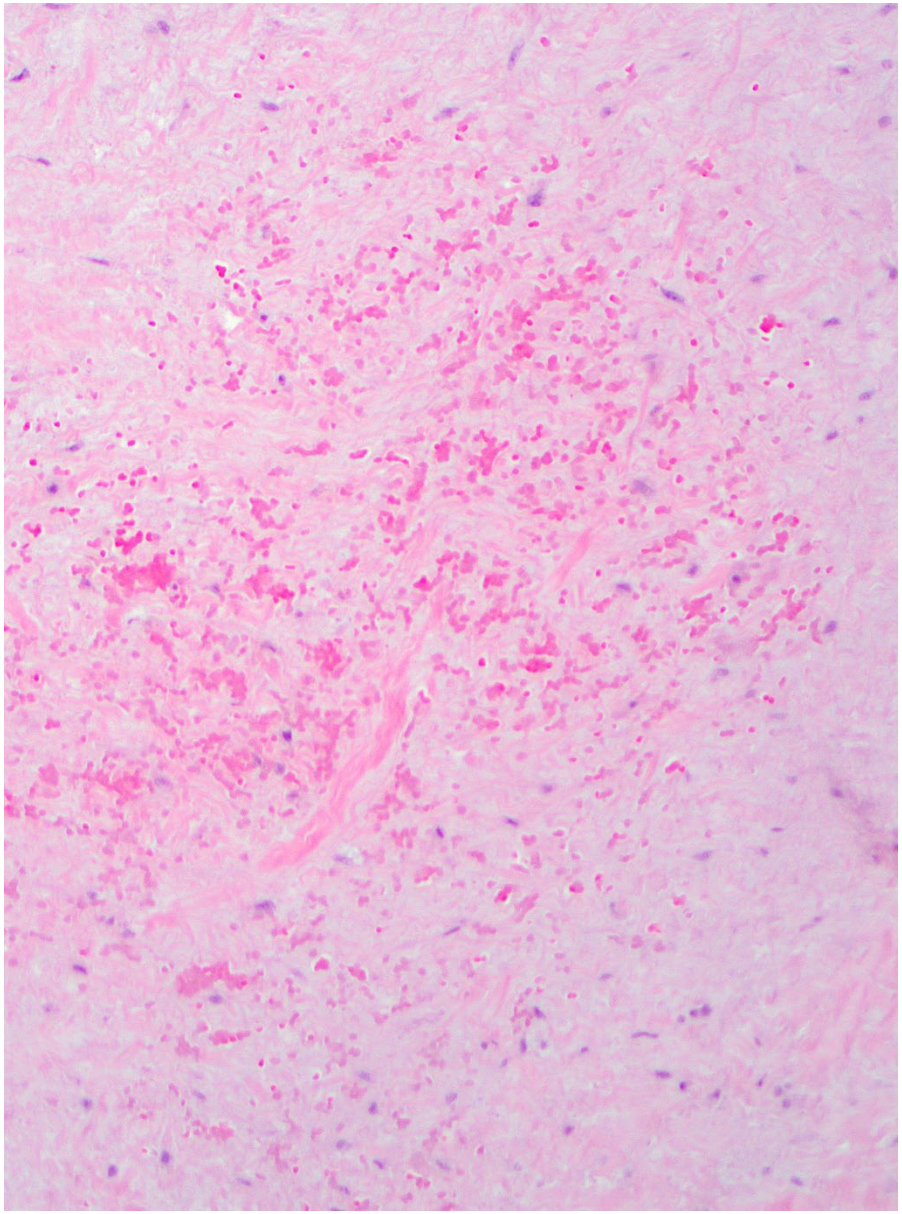




Myxomatous valvular degeneration grade IV



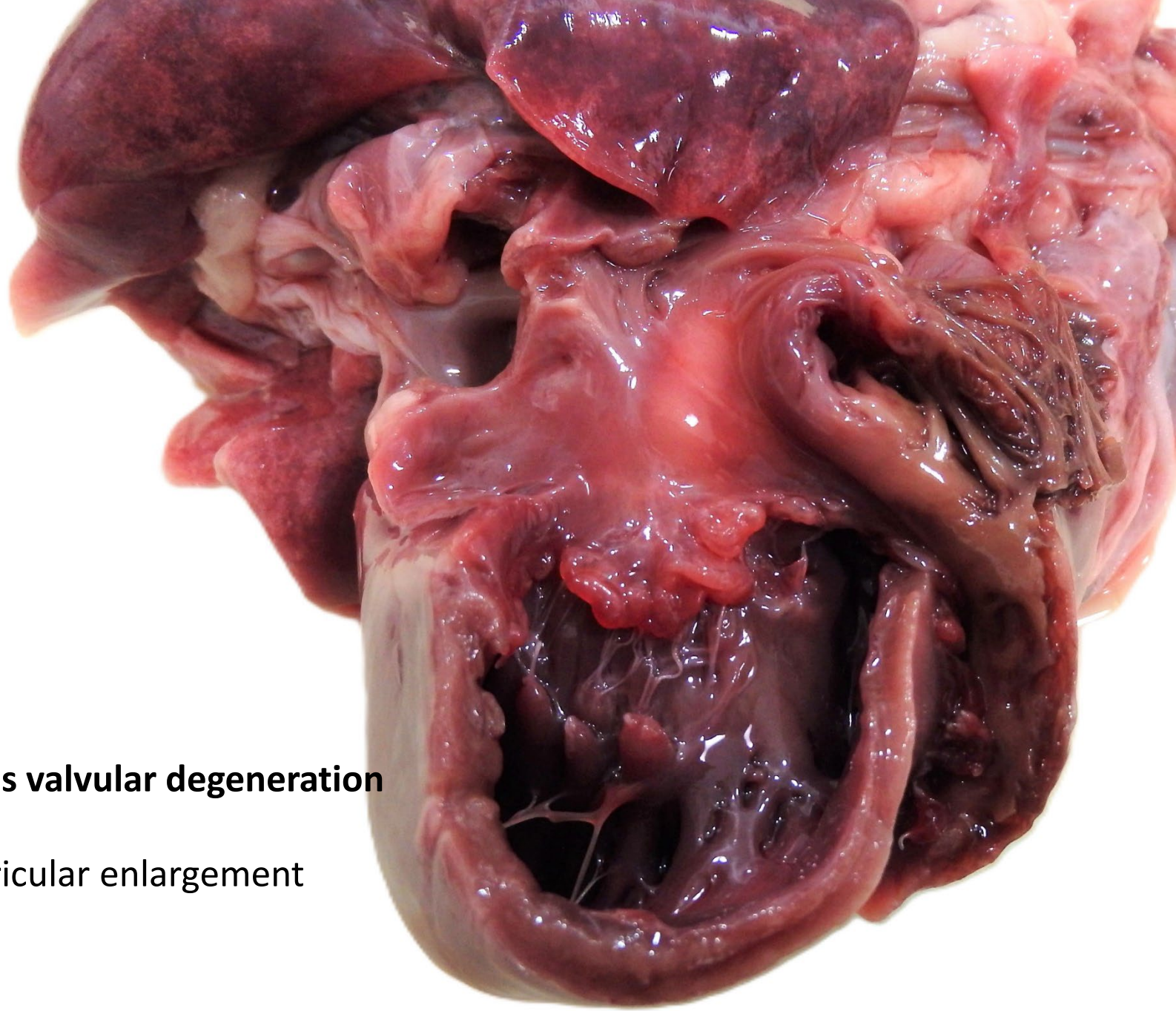
Myxomatous valvular degeneration grade IV



Myxomatous mitral valve disease

Gross findings

- Mitral and tricuspid leaflets
- Thickened, curled, nodules at the edges
- Hemorrhage
- Chordae tendinae thickened or ruptured
- Atrial jet lesions (fibrosis)
- Left atrial and left ventricular enlargement

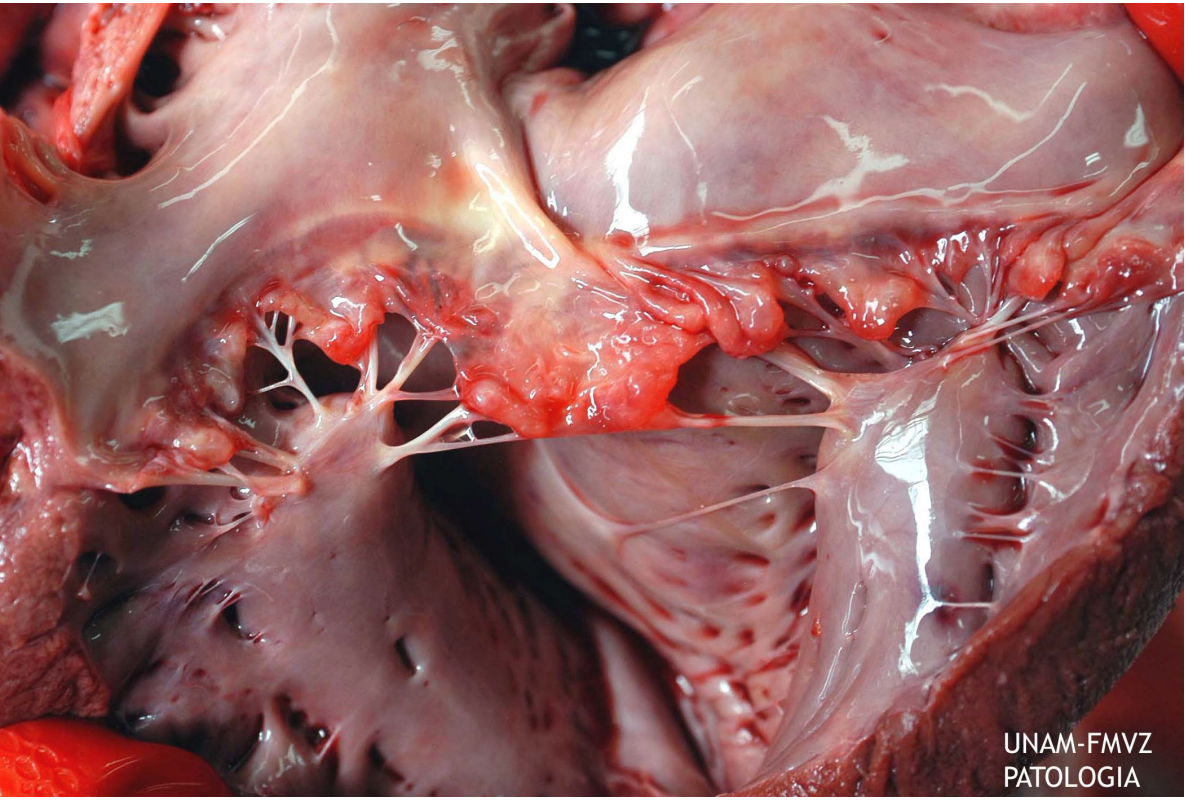


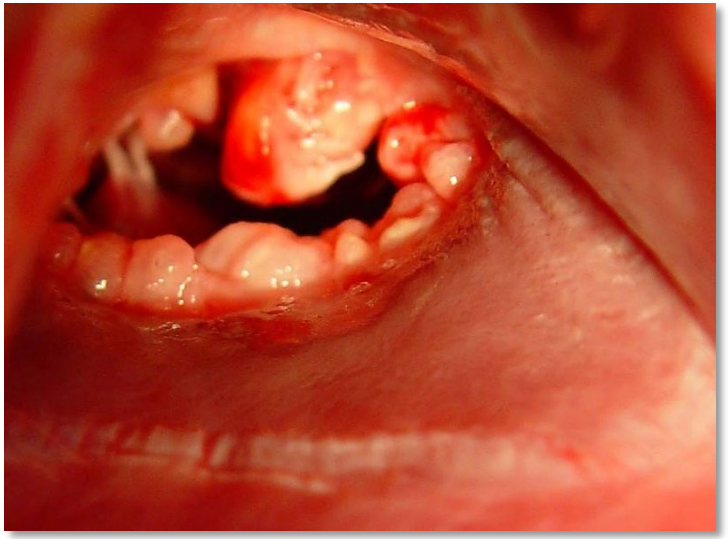
Myxomatous valvular degeneration grade III

- Left ventricular enlargement

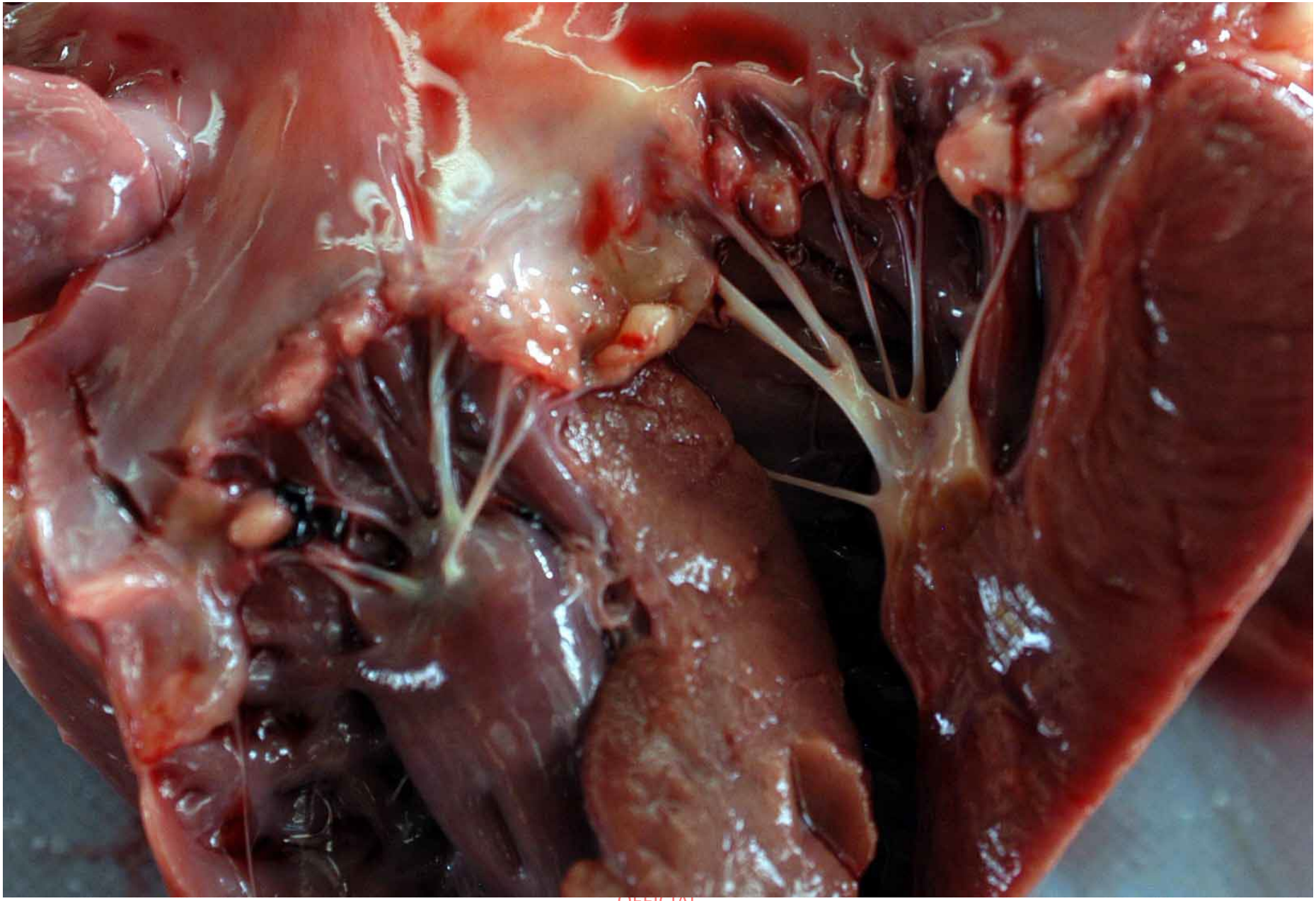
Myxomatous valvular degeneration grade III

Endocardial splitting (may precede full thickness tear)
Advanced atrial enlargement

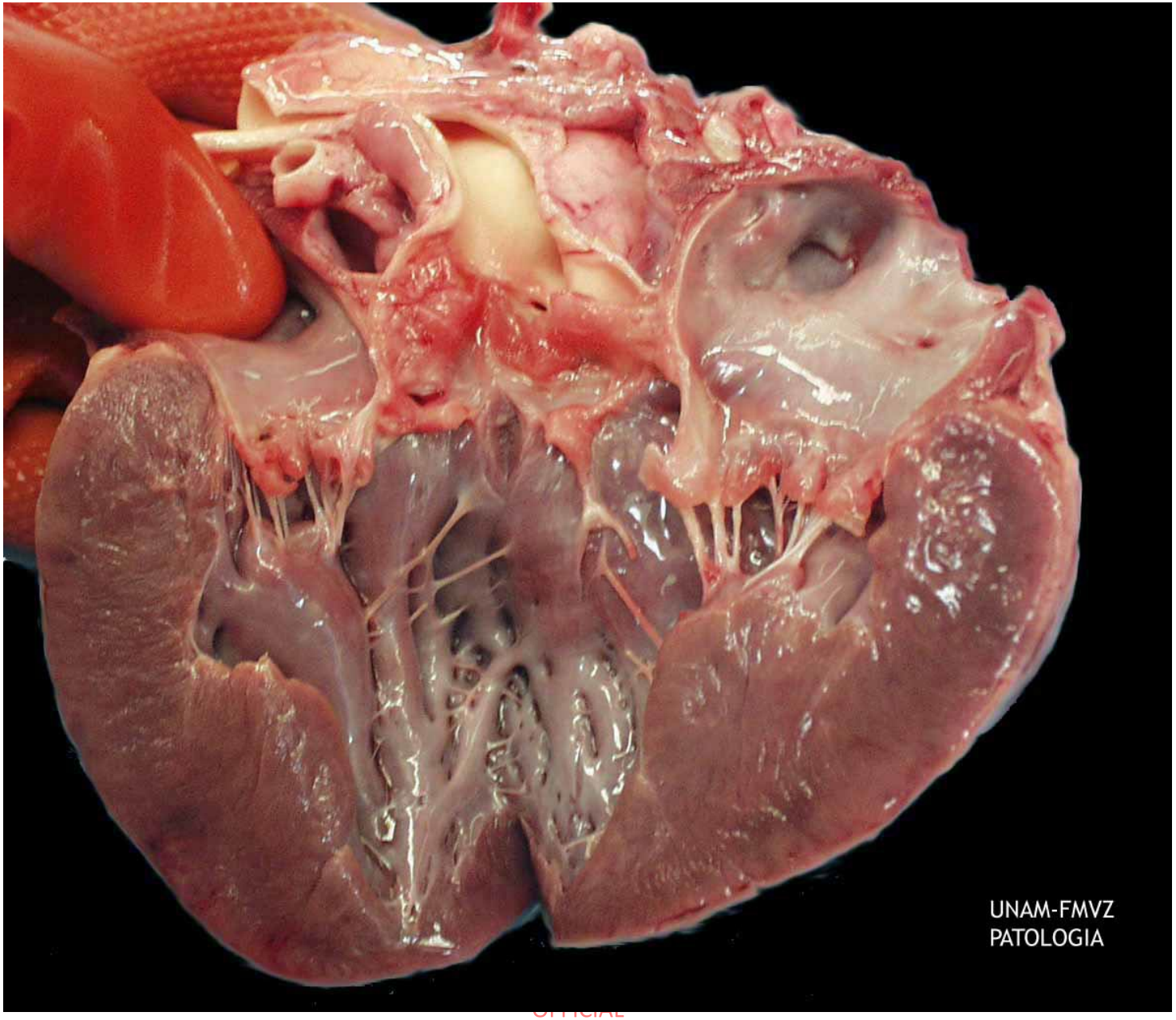




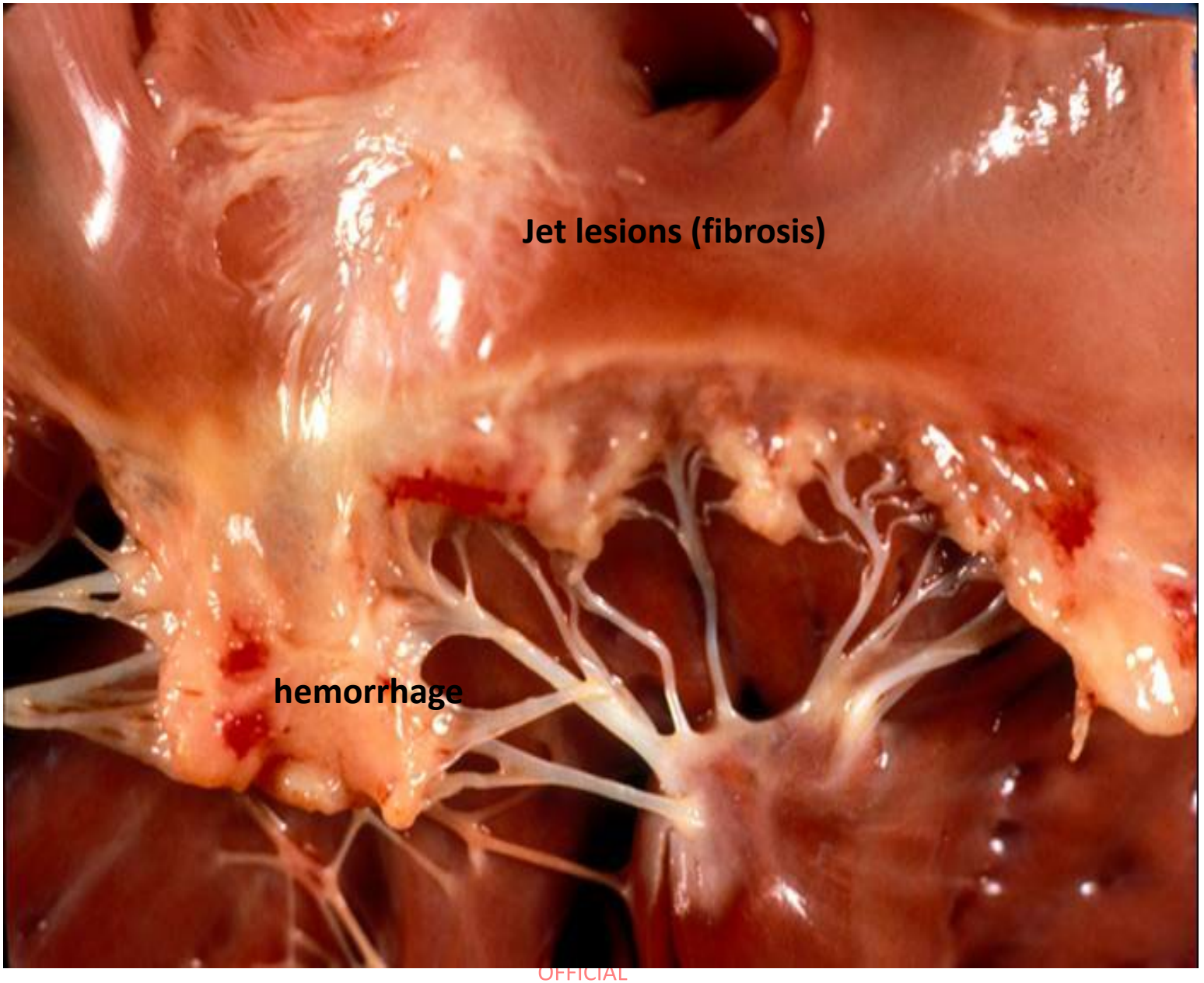
Myxomatous valvular degeneration grade III



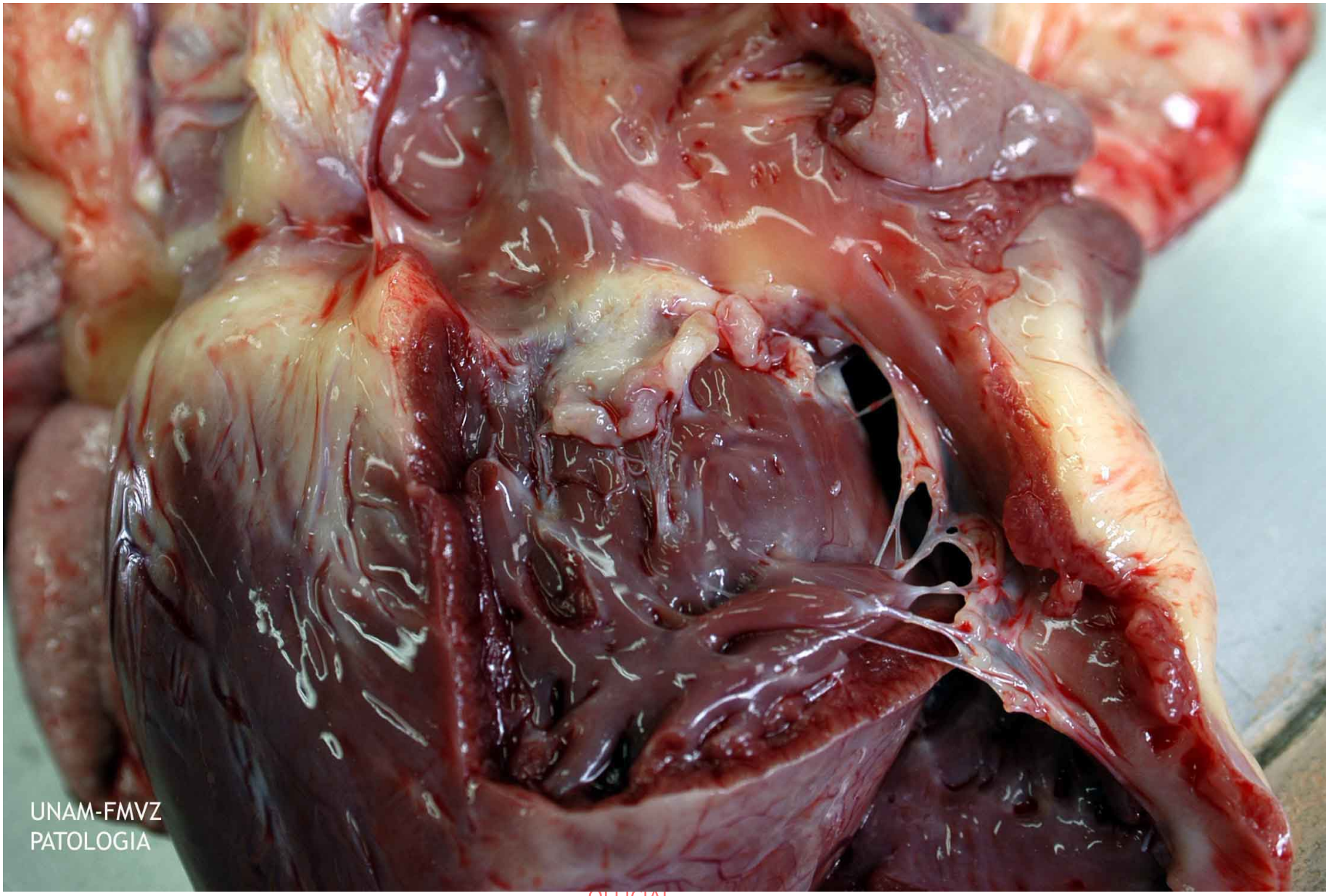
Myxomatous valvular degeneration grade III



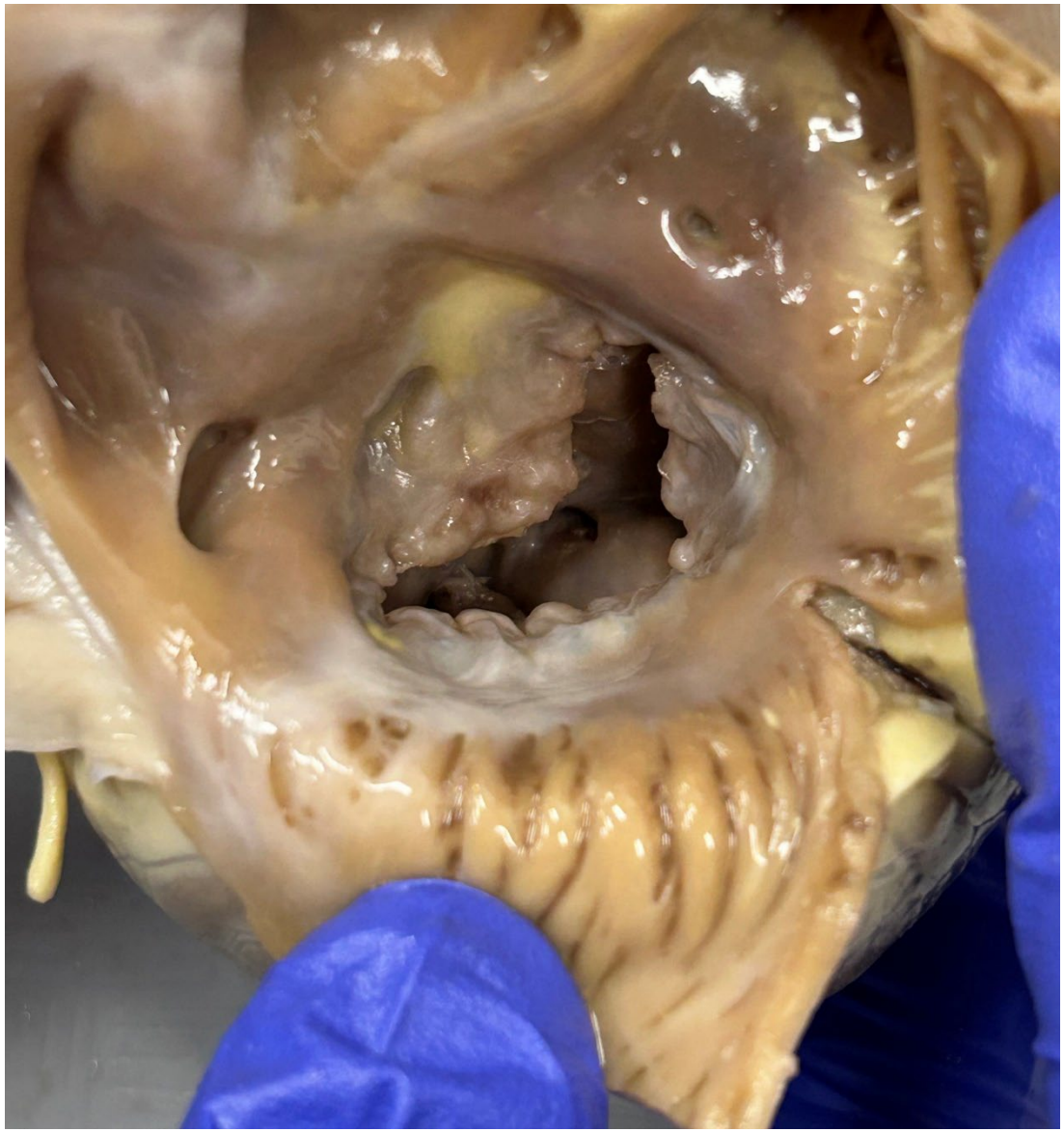
Left AV myxomatous valvular degeneration

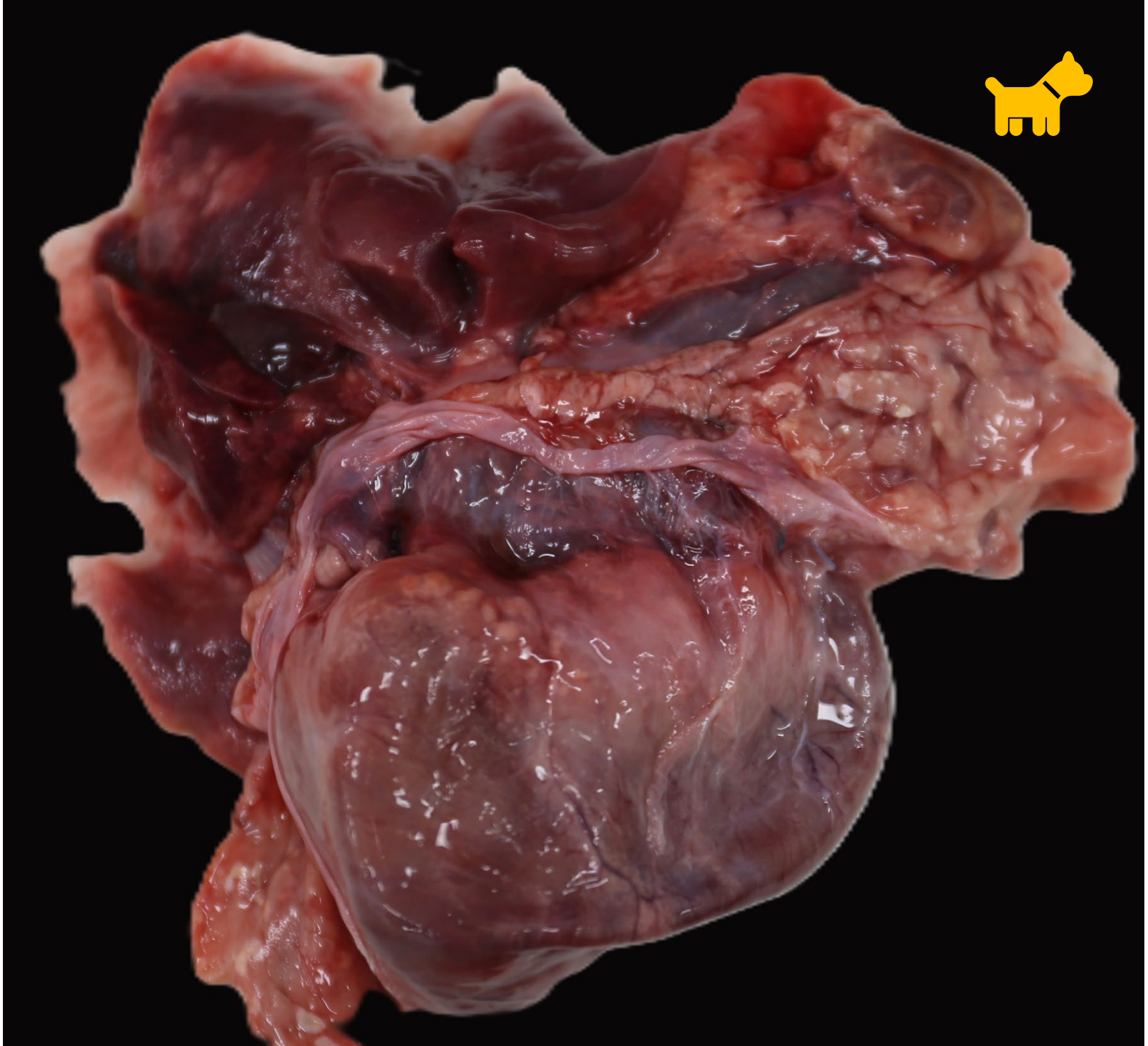


Right myxomatous valvular degeneration



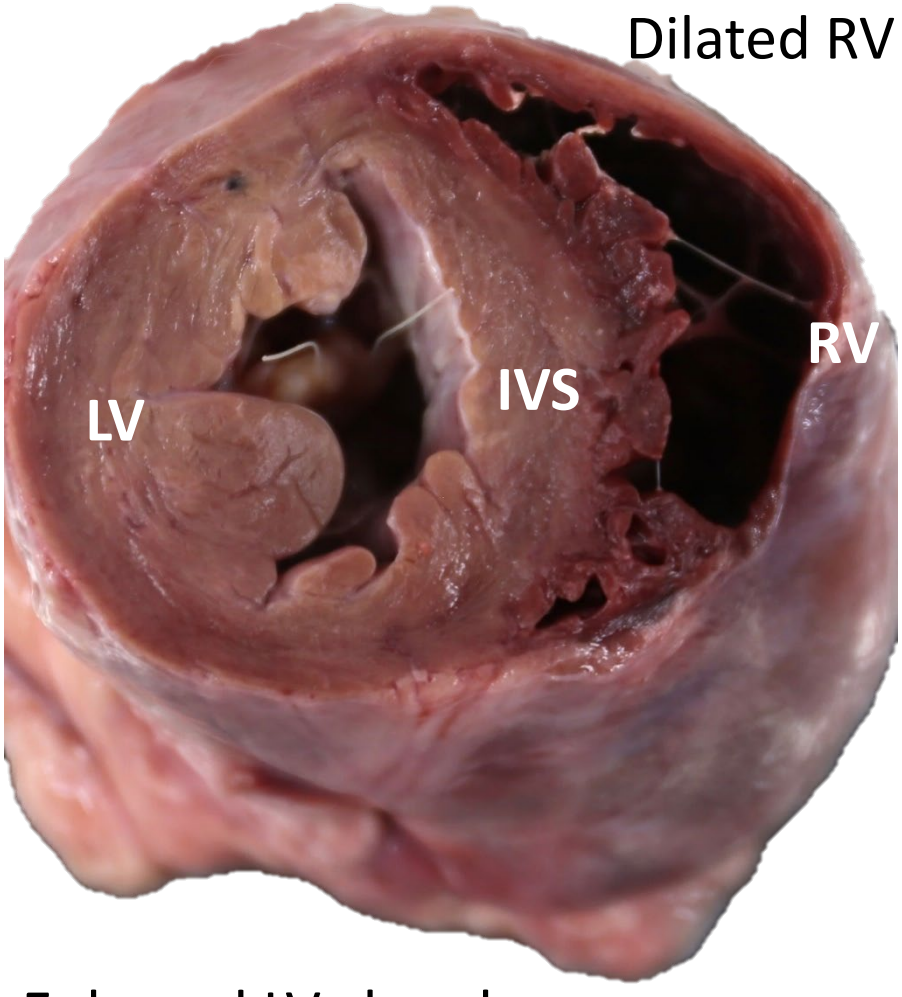
Right AV valve with myxomatous degeneration



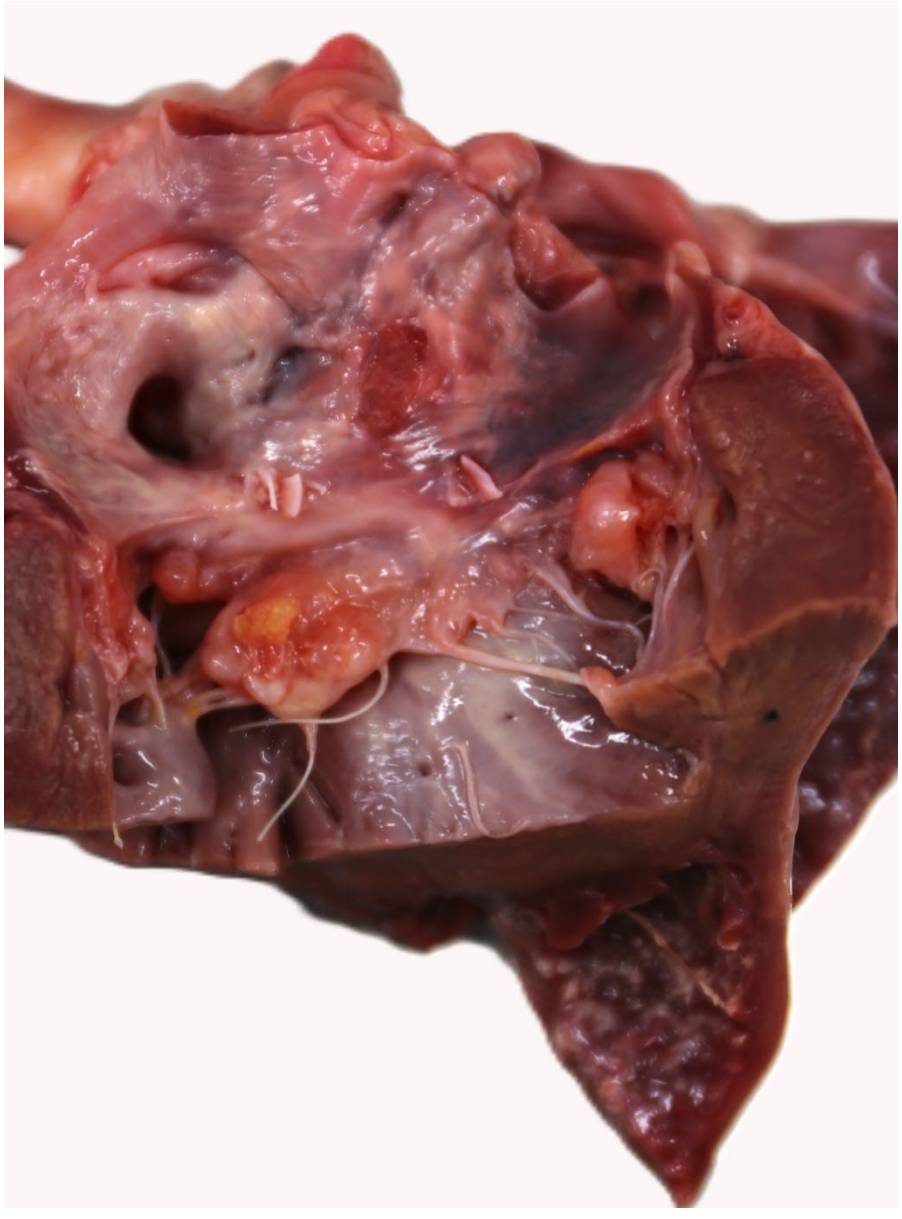


Severe MVD

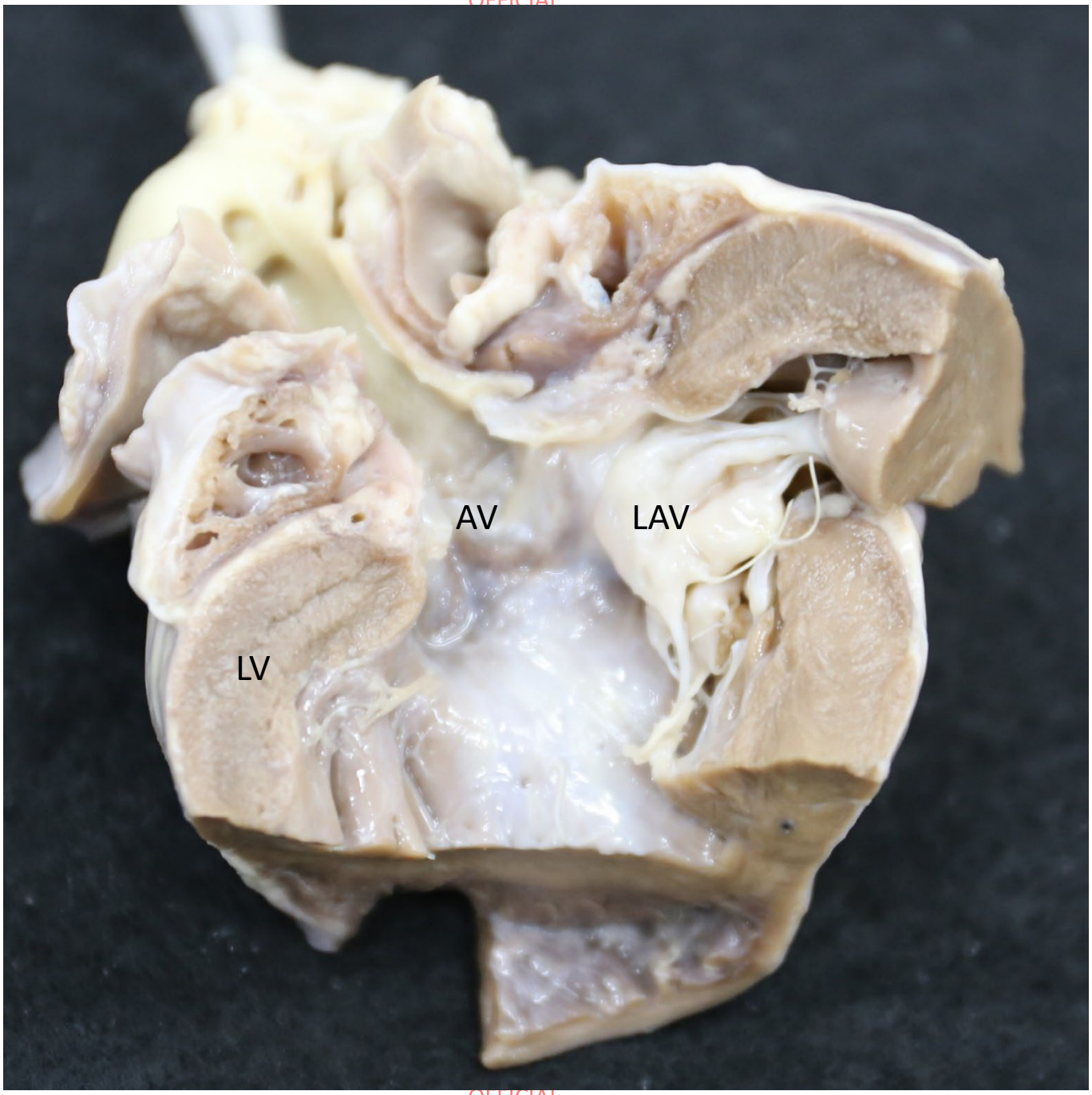
Annuloplasty and artificial neochordae



Enlarged LV chamber

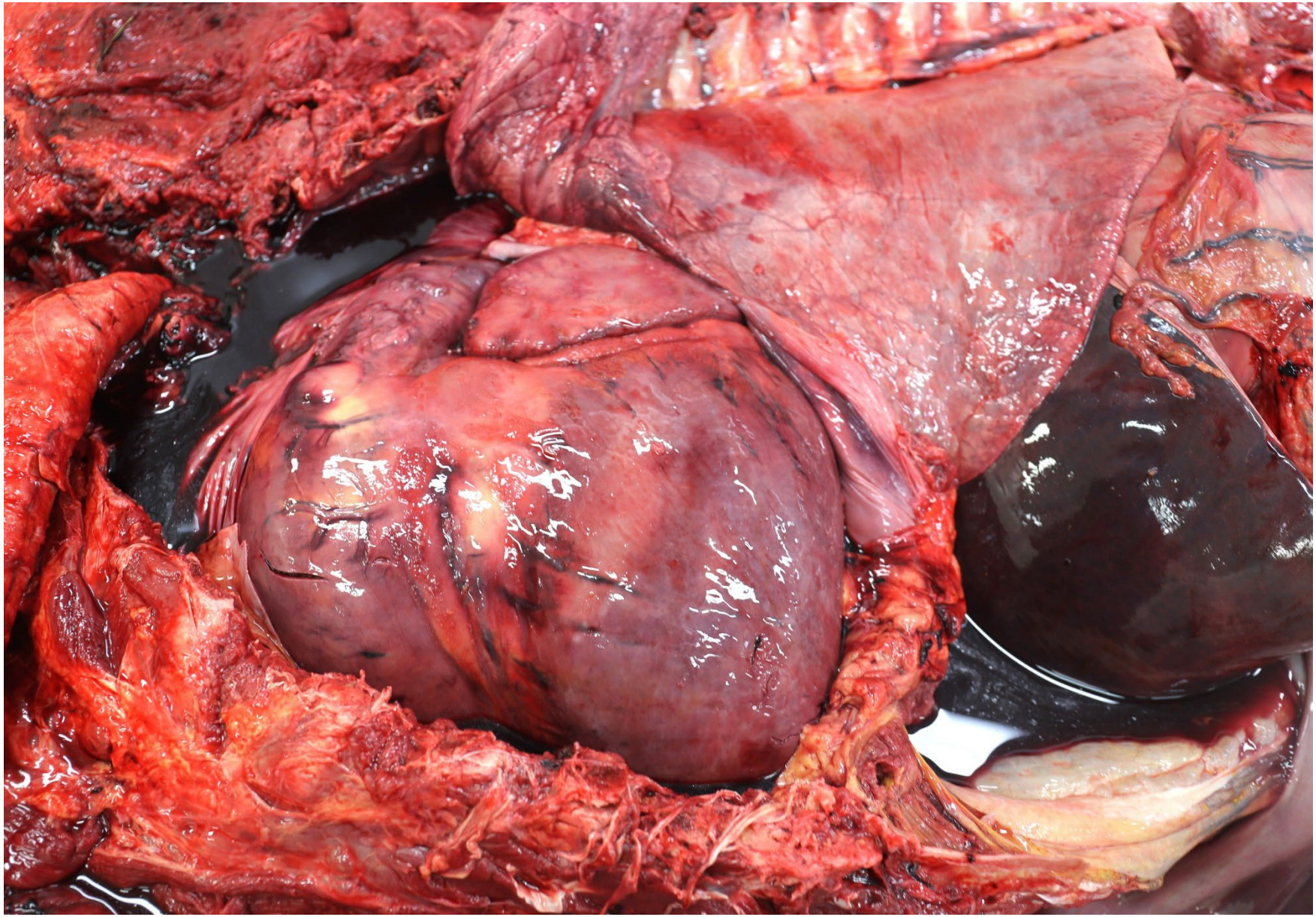


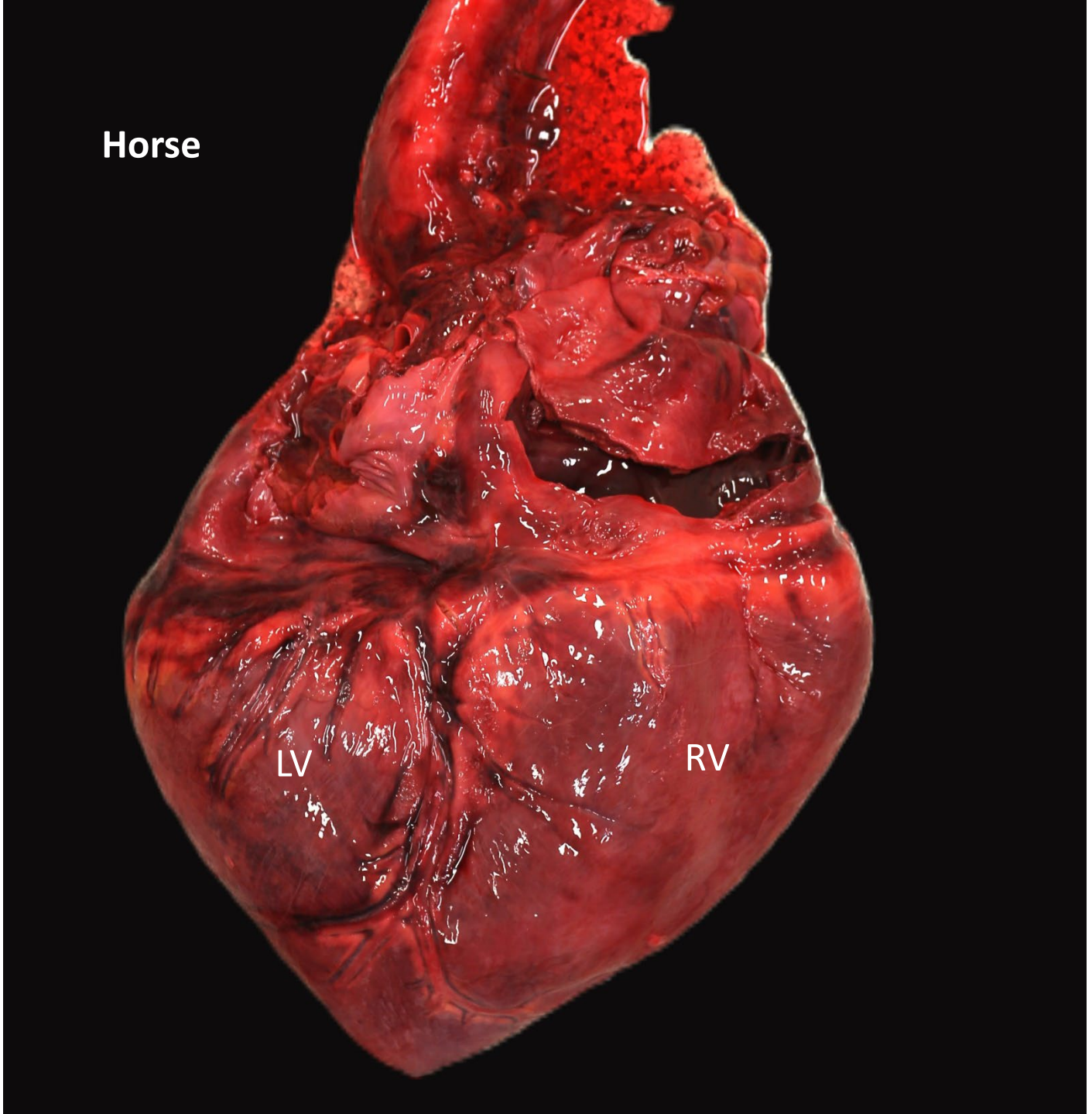

Two artificial chordae tendinae are
connected to the anterior valve



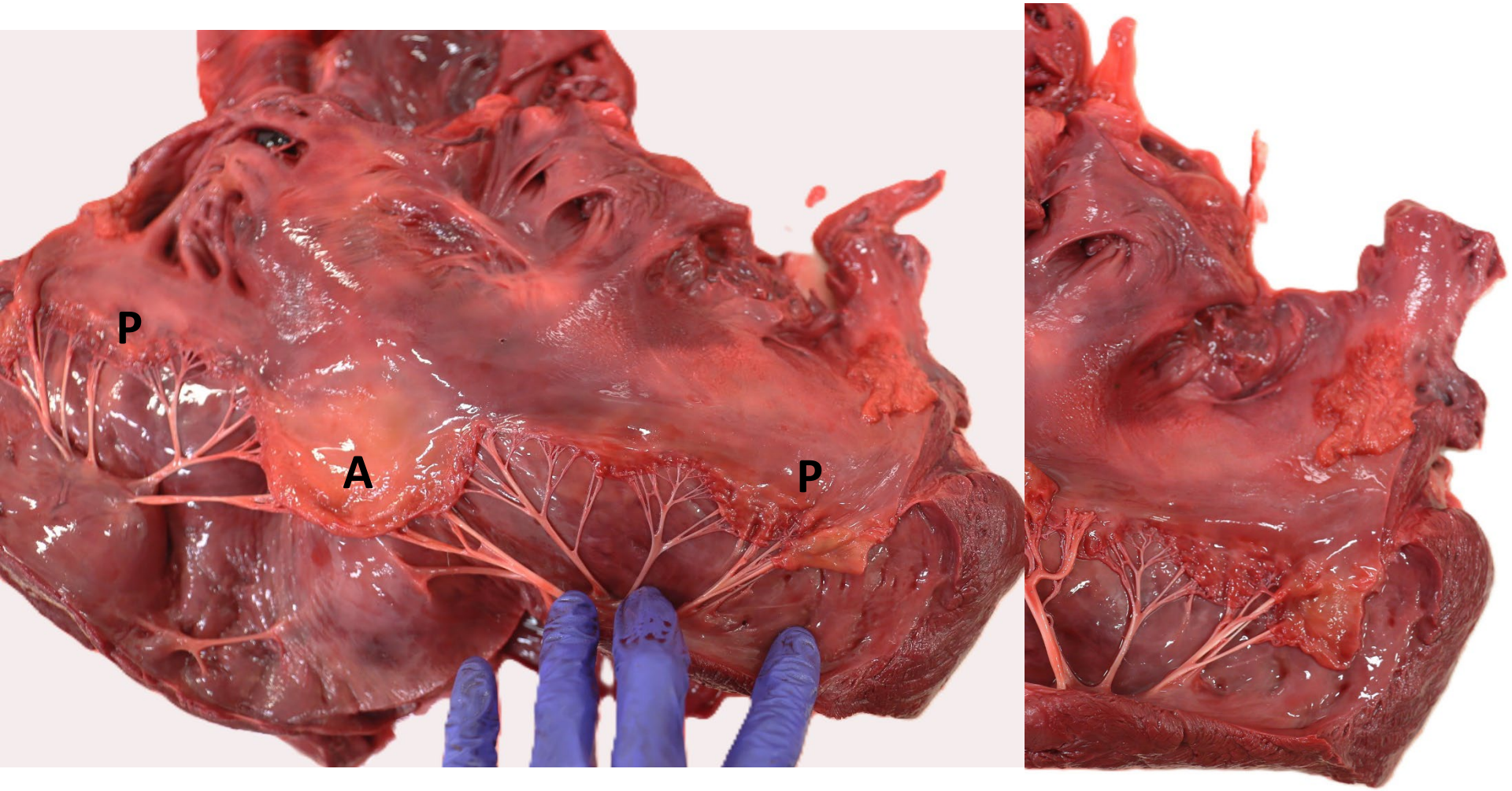
Righ AV valve with severe myxomatous valvular degeneration

Horse with cardiomegaly

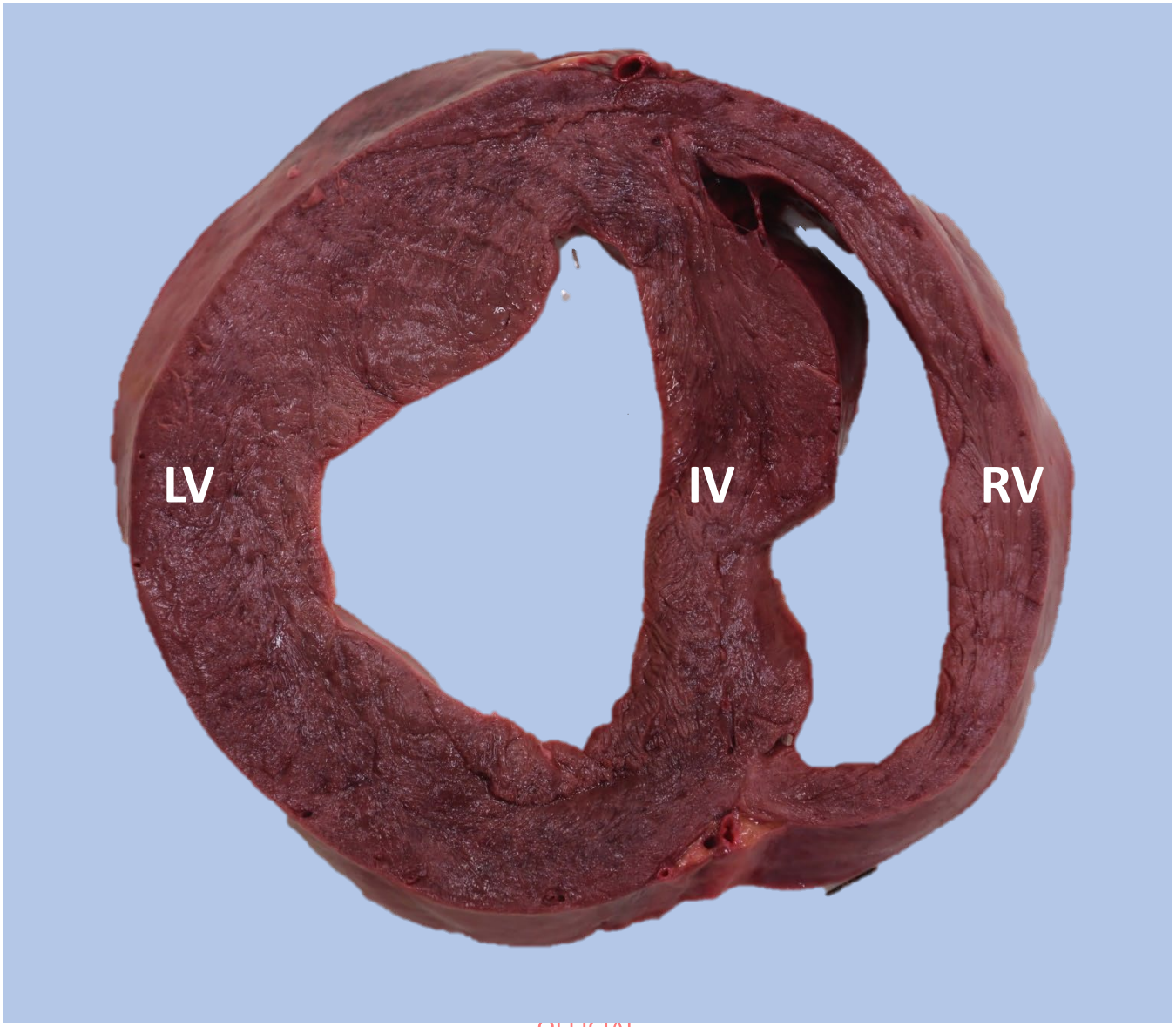


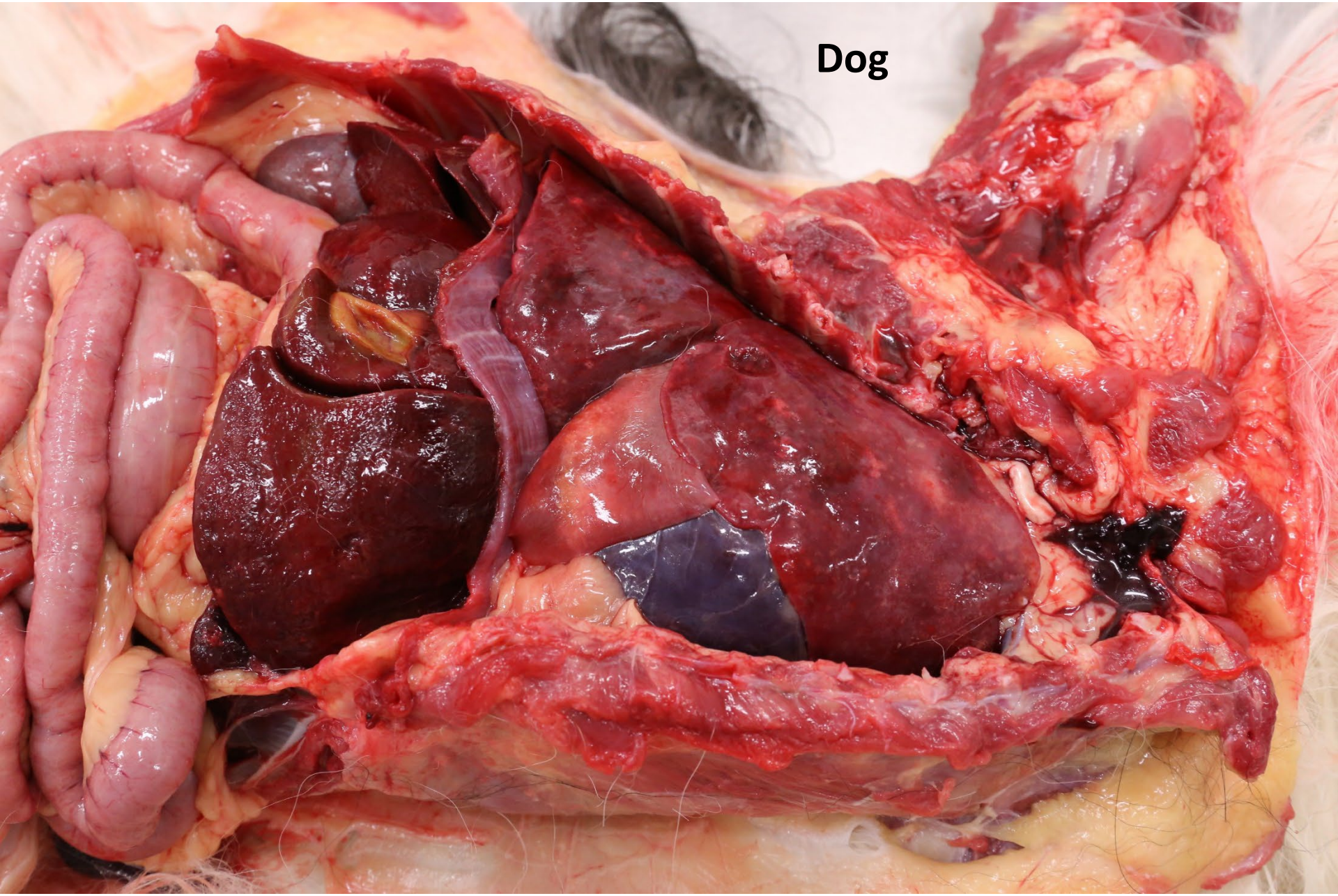

Horse
LV
RV

Left AV valve with myomatous valvular degeneration and jet lesions (fibrosis)
Horse

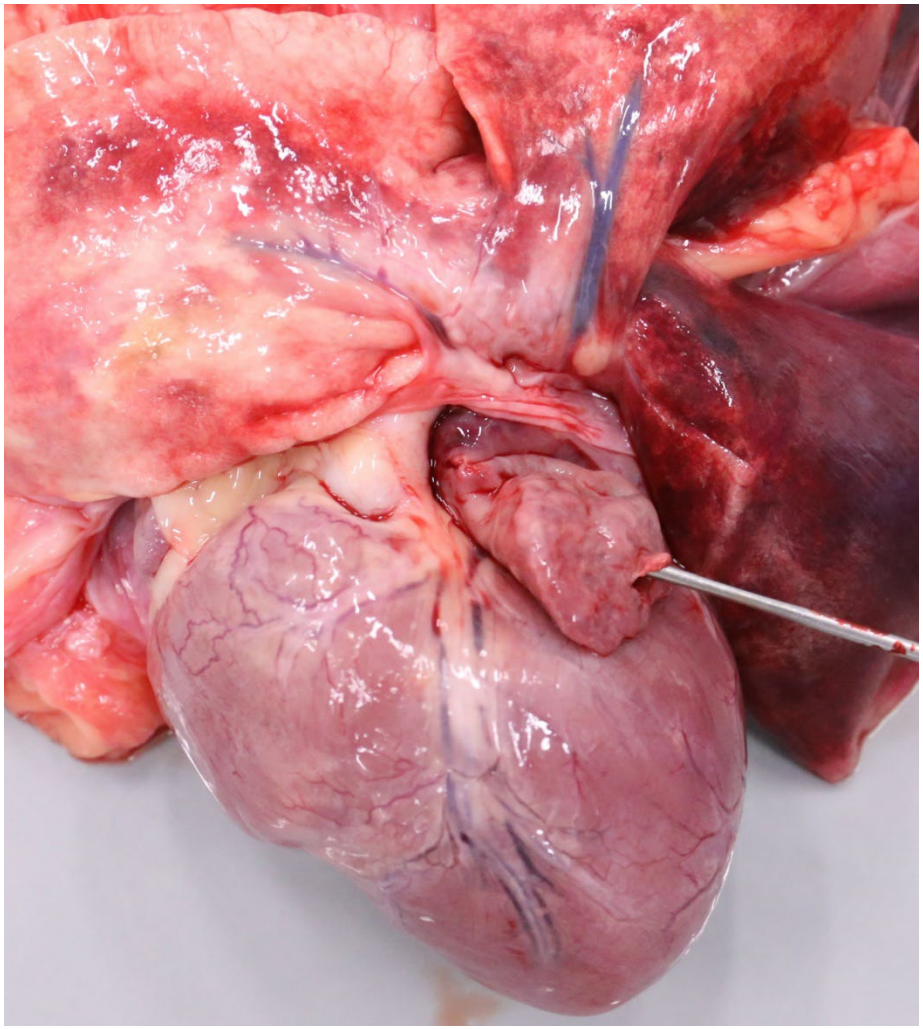


Enlarged left ventricular chamber and thin ventricular wall
Horse

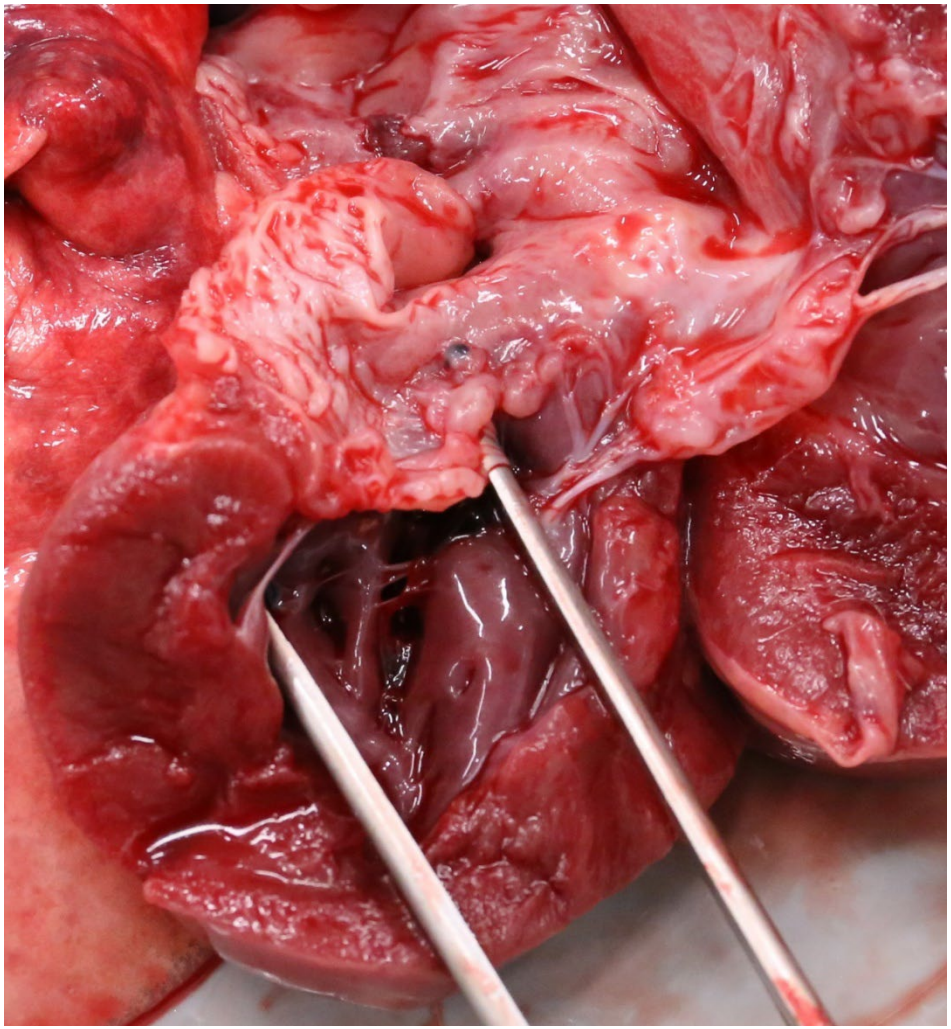


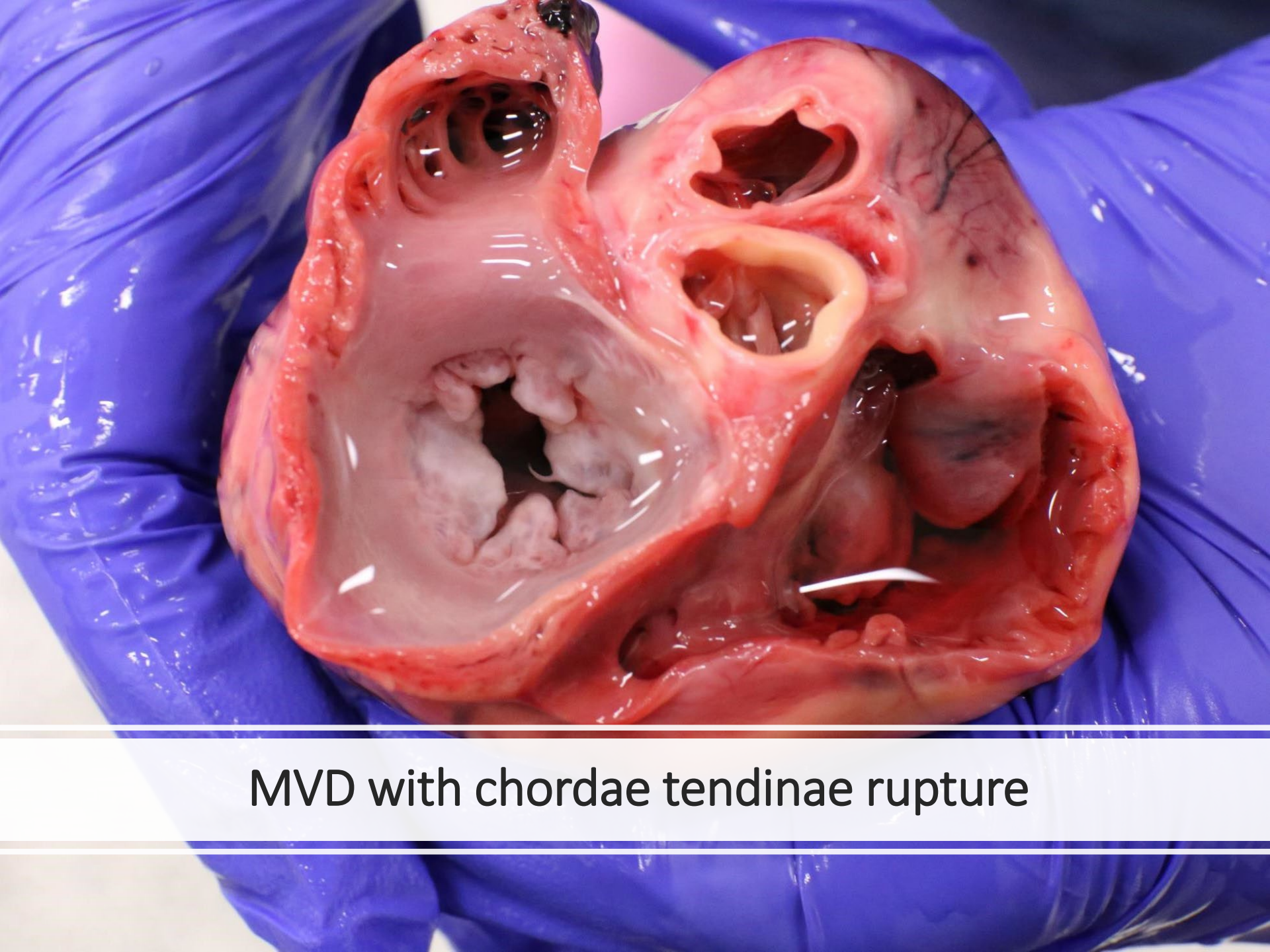

Dog

Left atrial rupture



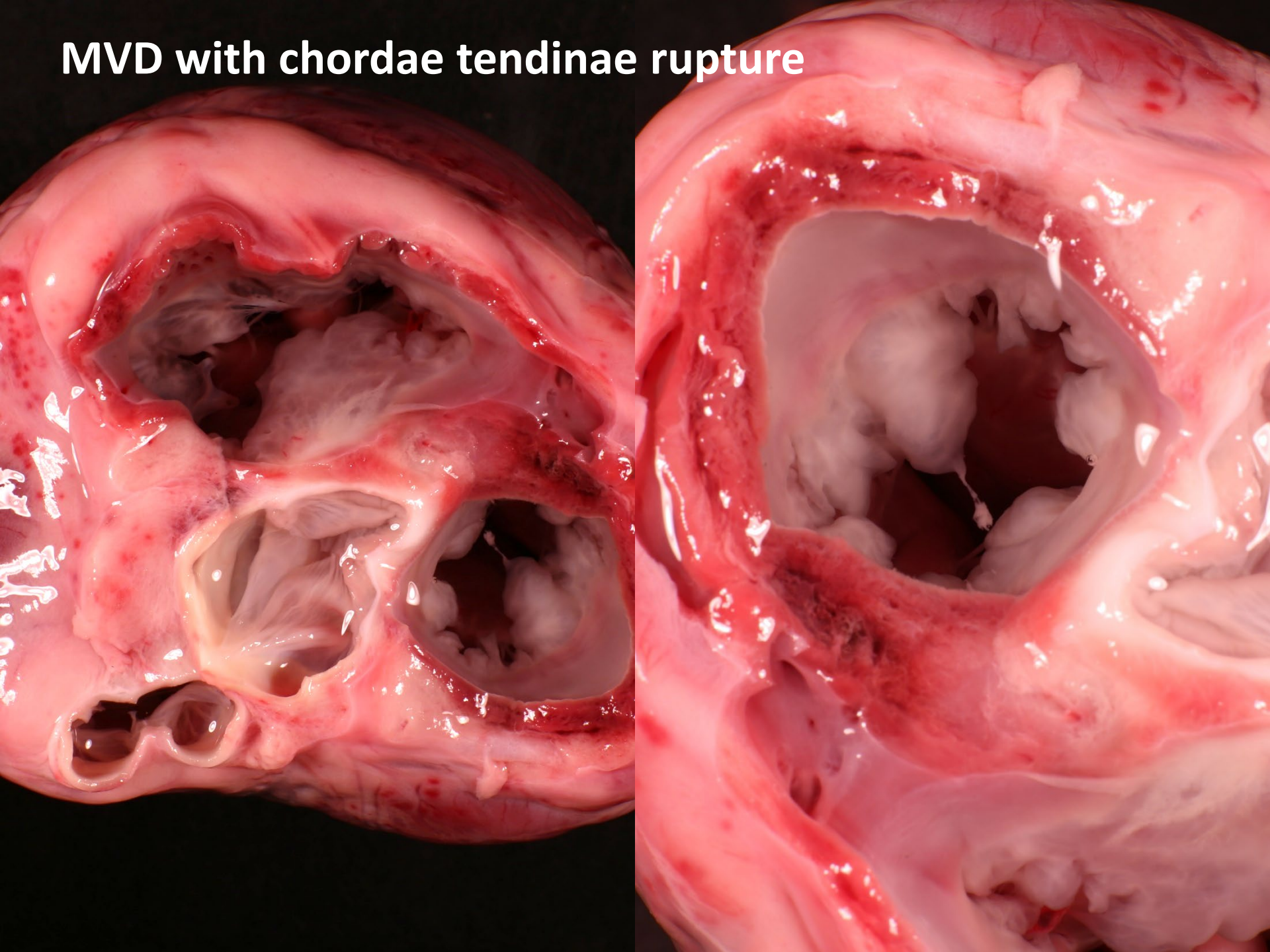
Severe MVD



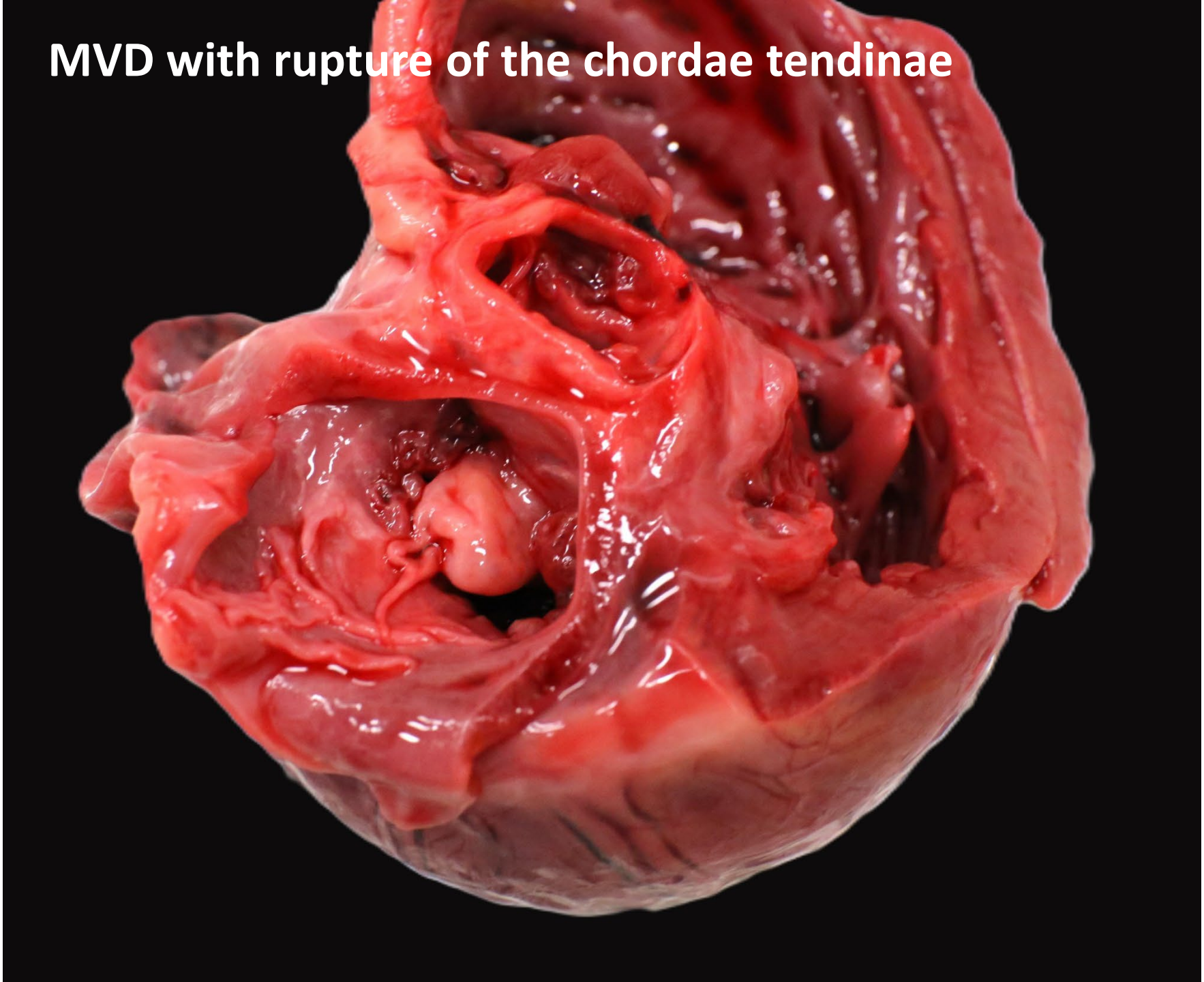


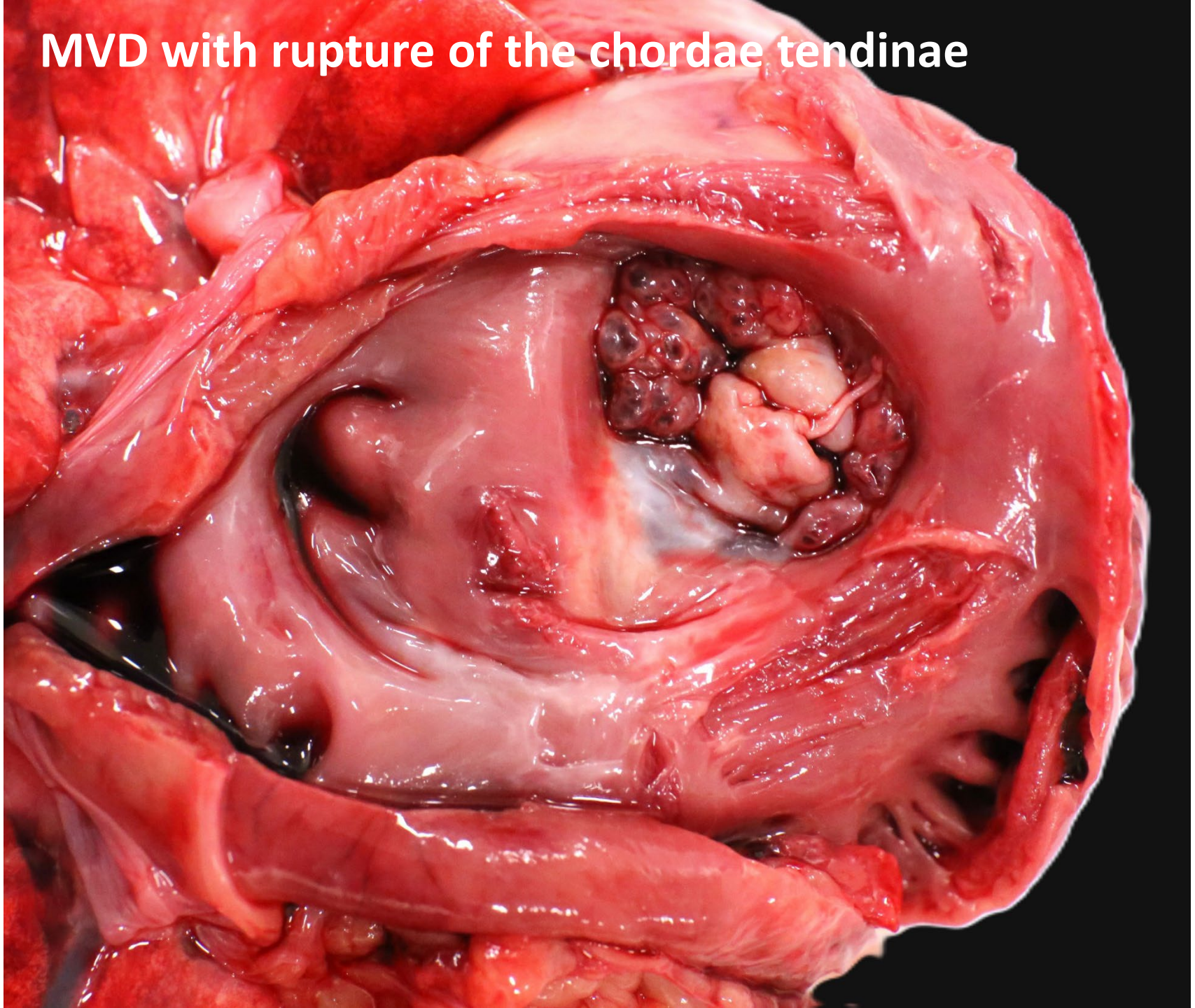
MVD with chordae tendinae rupture

MVD with chordae tendinae rupture

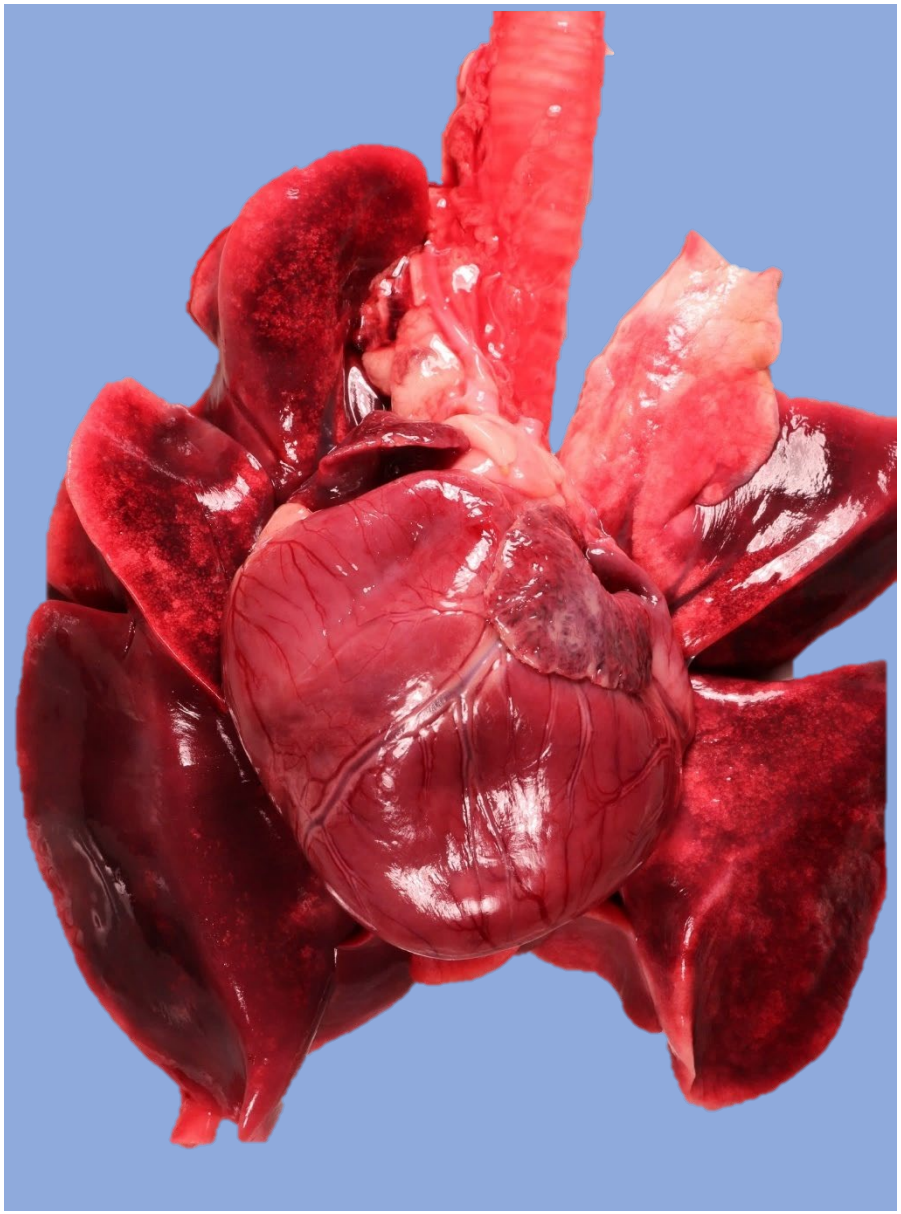


MVD with rupture of the chordae tendinae

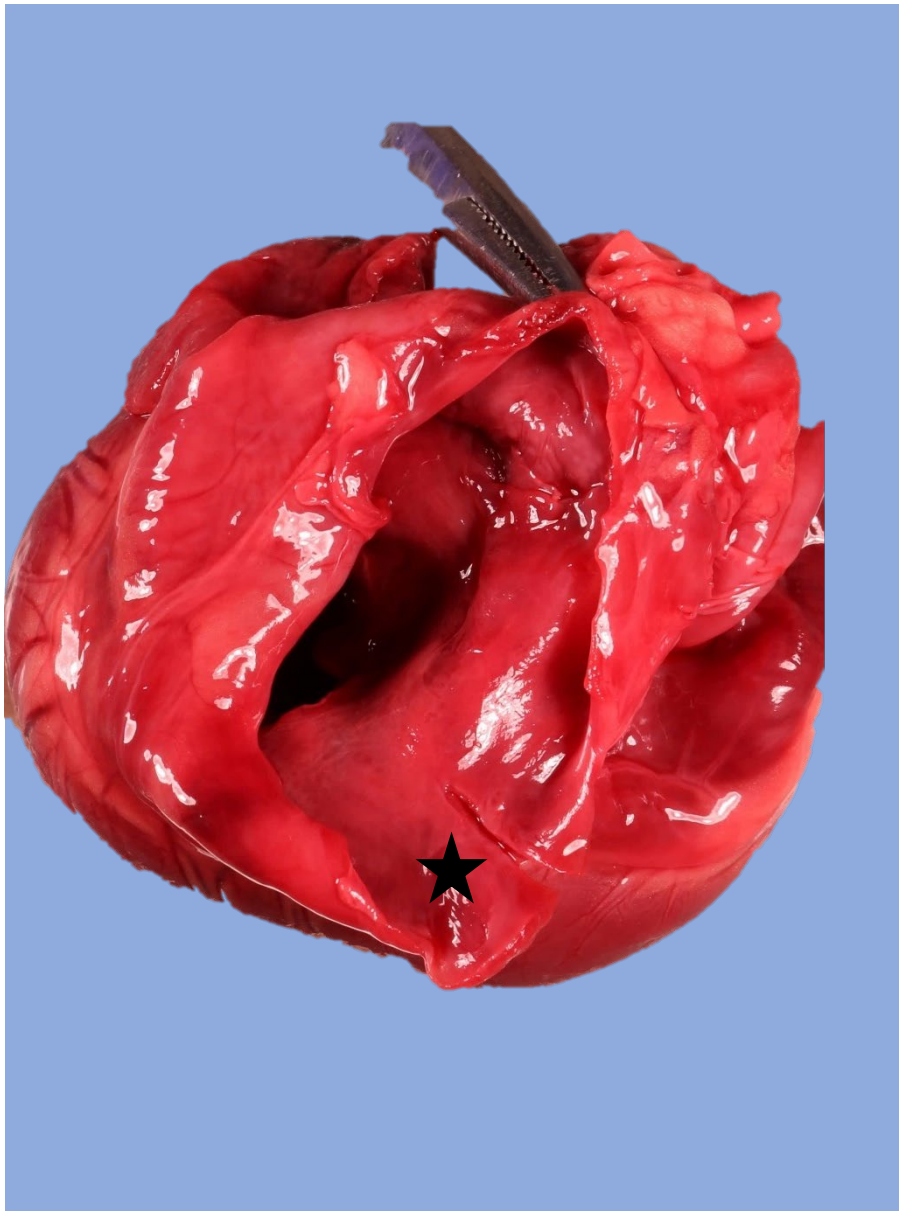


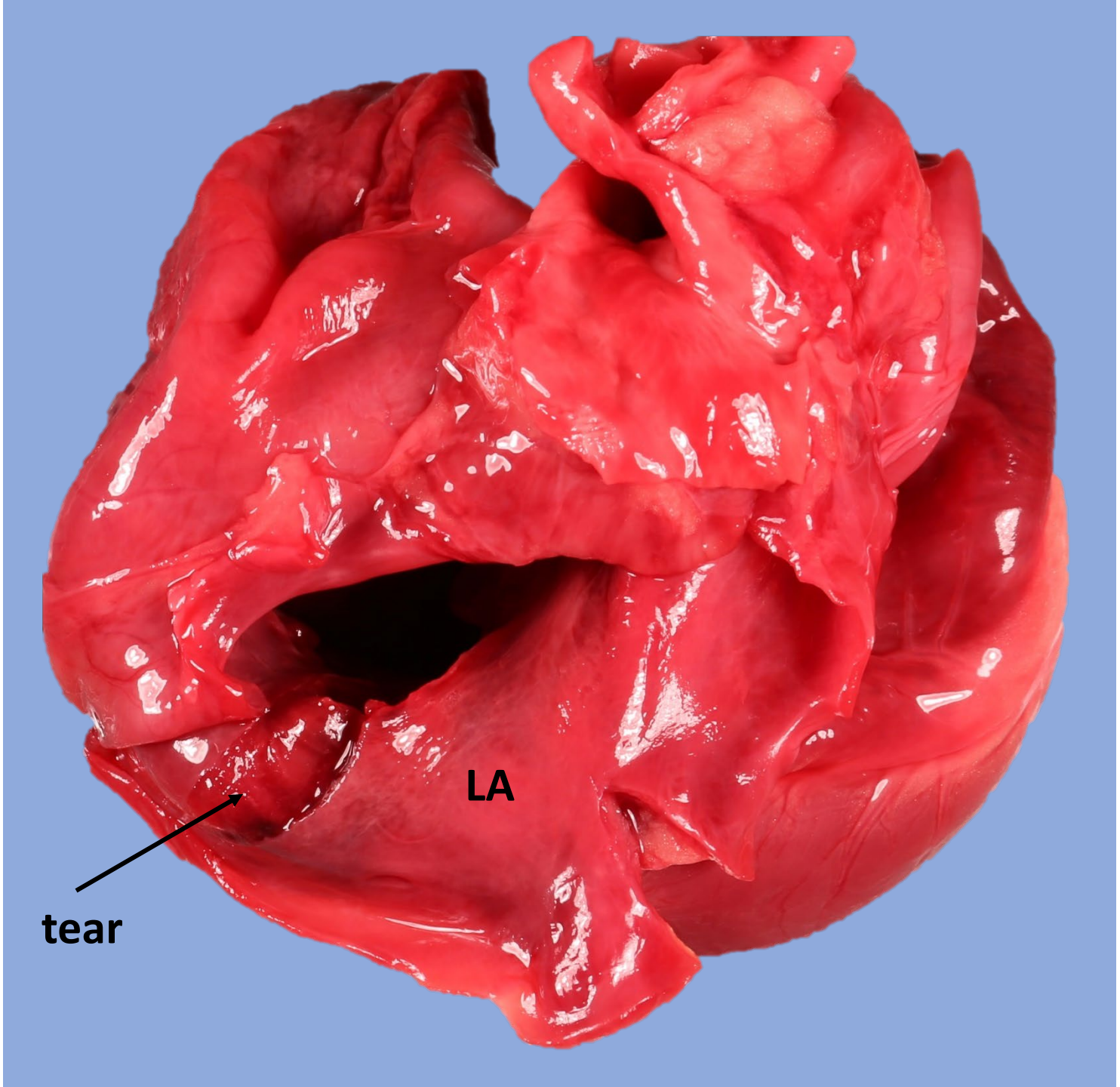

MVD with rupture of the chordae tendinae

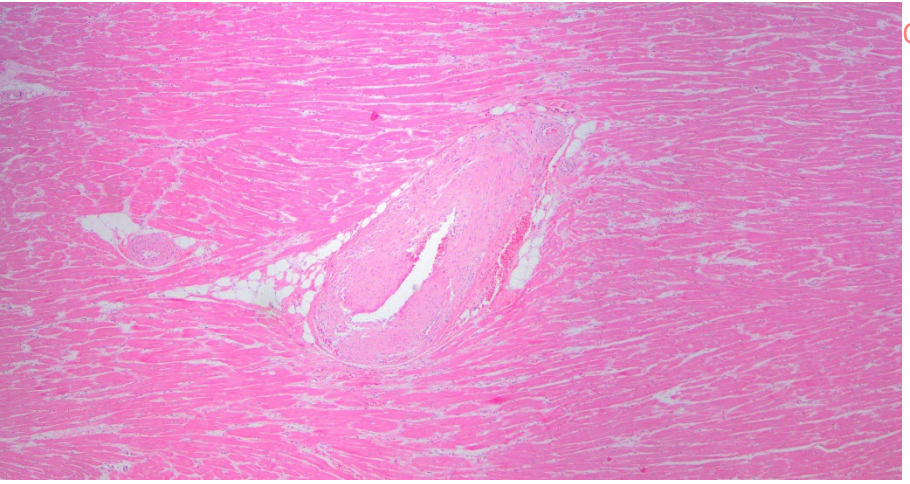
Biventricular congestive HF
Mitral valve disease



Left atrial with full-thickness tear
Dog



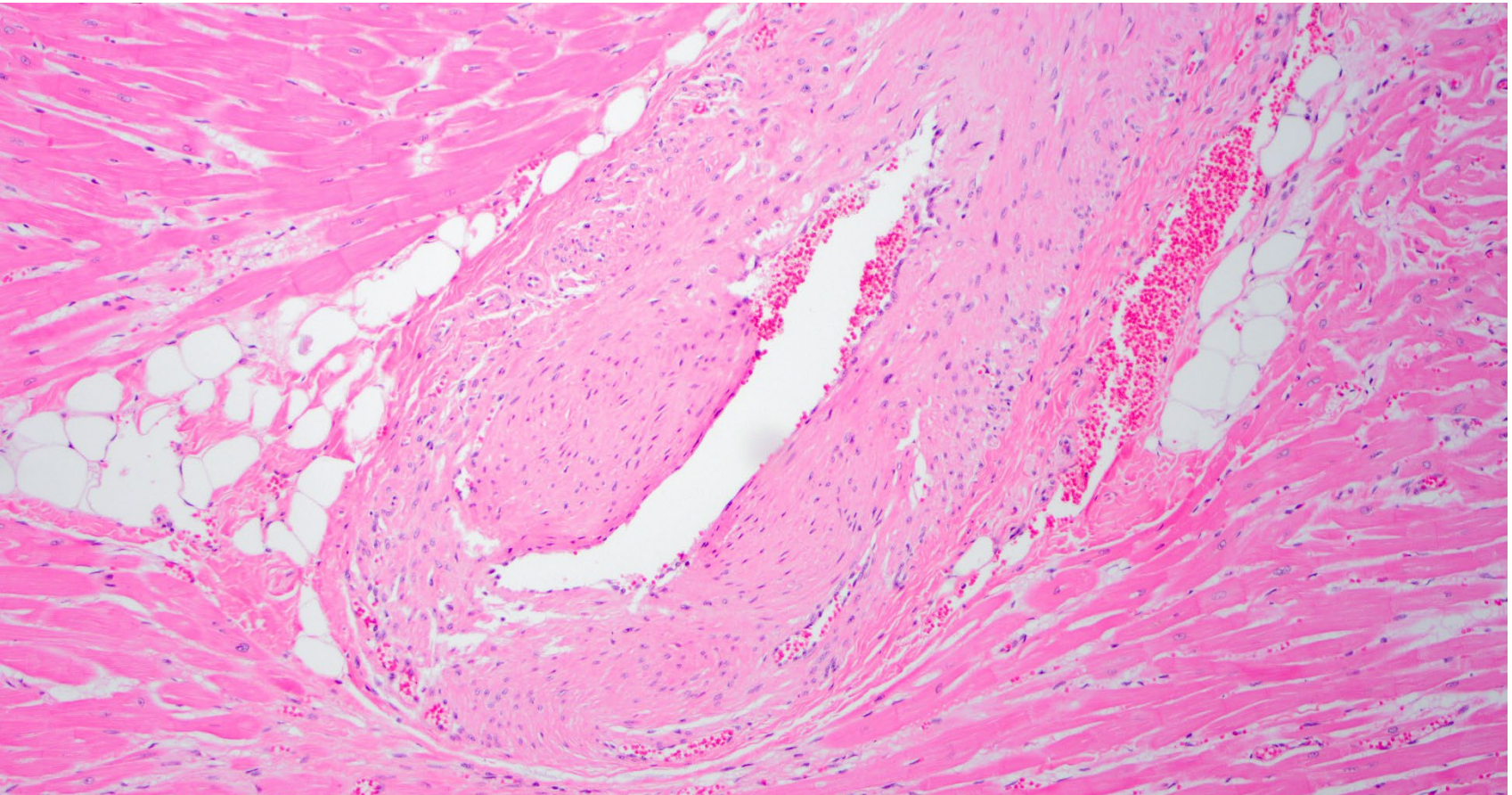

LA
tear



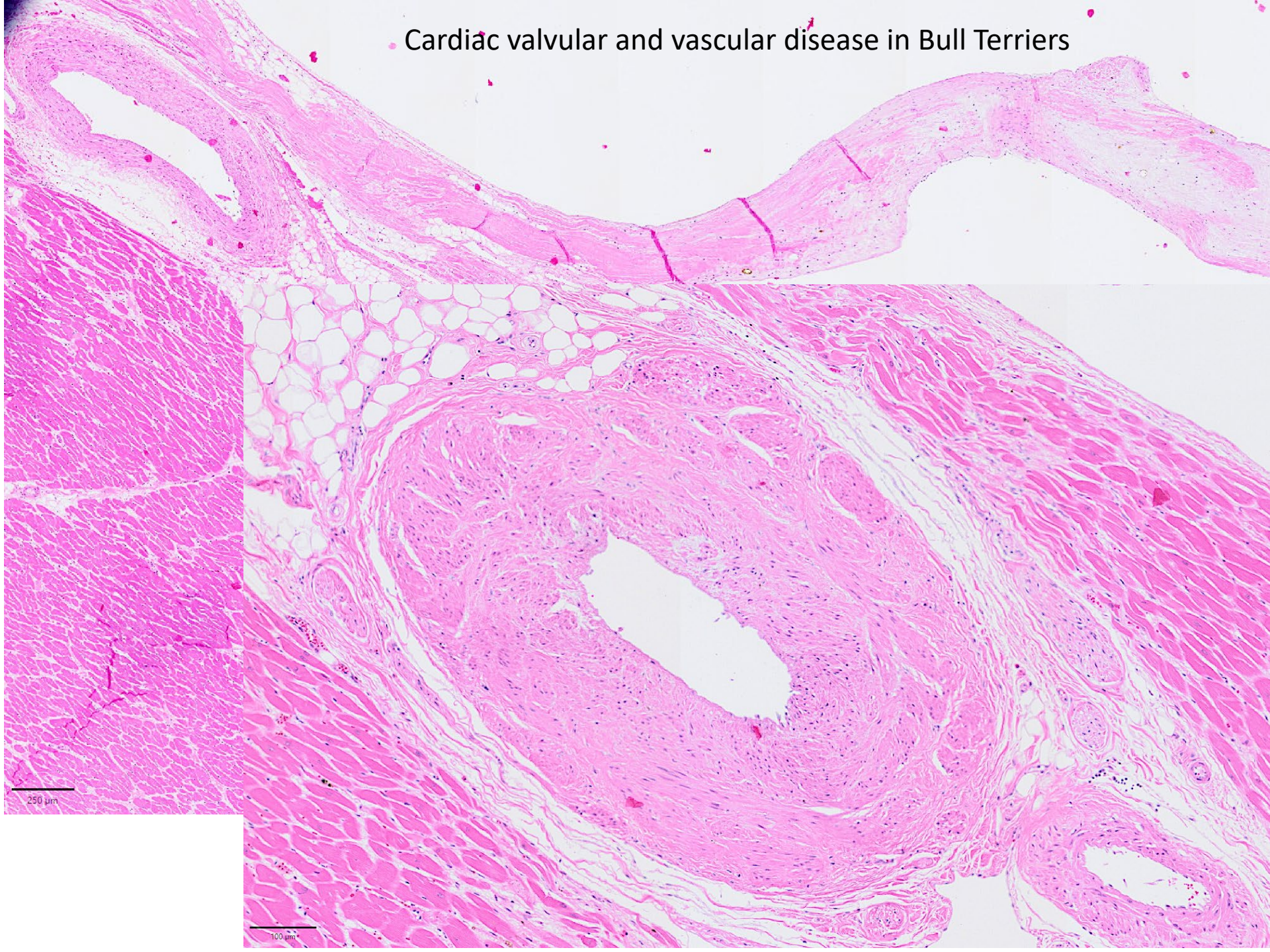
Cardiac valvular and vascular disease in Bull Terriers (young dogs)

- MVD
- Myxomatous aortic valve degeneration
- Intimal and medial fibromuscular hyperplasia; medial hypertrophy in IVS, LVFW, PMs
- Fibrosis of the conduction system

O'Leary CA, Wilkie I. Cardiac Valvular and Vascular Disease in Bull Terriers. *Veterinary Pathology*. 2009;46(6):1149-115



Cardiac valvular and vascular disease in Bull Terriers

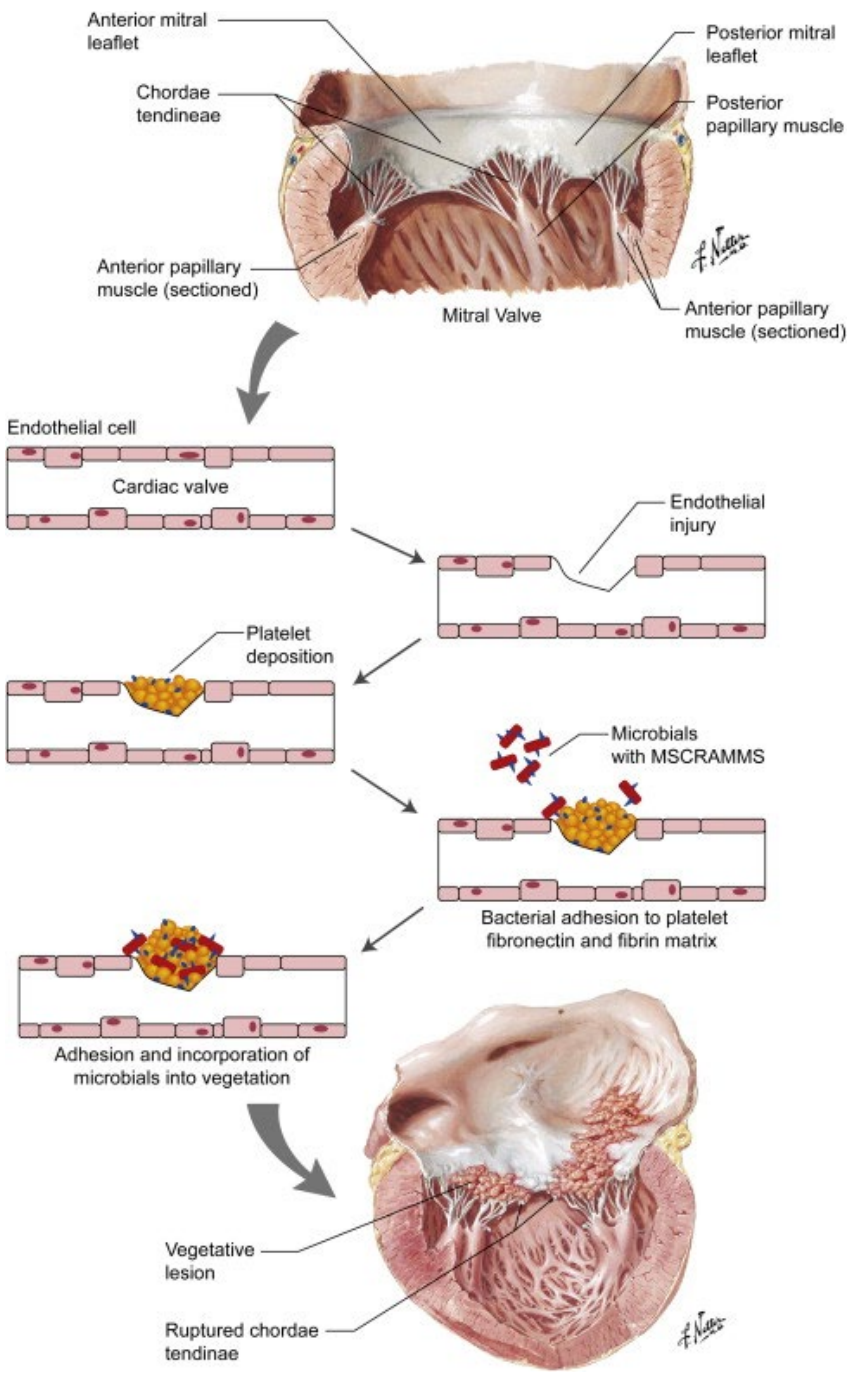


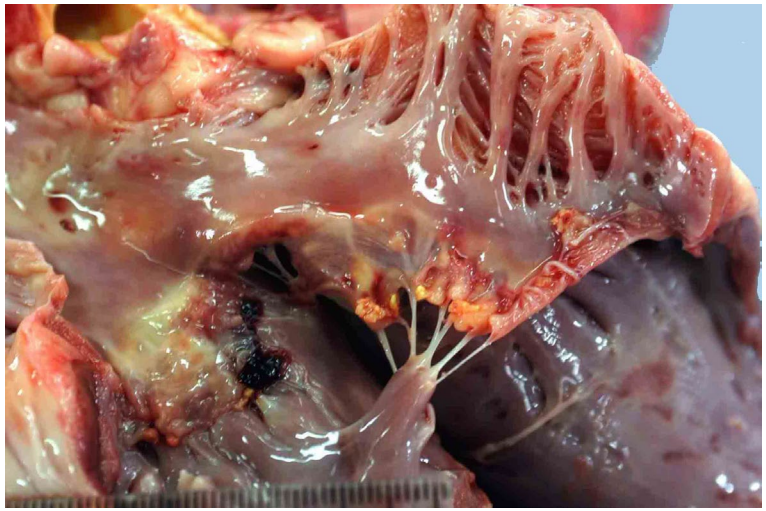
Endocarditis

Infective endocarditis is a severe infection that affects the endocardium and cardiac valves due to the invasion of infectious agents.

Dog	Cat	Horse	Cattle	Swine
Mitral > Aortic > Tricuspid > Pulmonic *Streptococcus* spp (*canis*), *Staphylococcus* spp (*aureus, intermedius*), *E-coli, Bartonella* species, *Klebsiella, Pseudomonas aeruginosa, Mycobacterium, Erysipelothrix rhusiopathiae*, other gram negatives	Aortic = Mitral > Tricuspid > Pulmonic *Streptococcus, Staphylococcus, Bartonella,* enteric gram negatives	Mitral and Aortic >> Tricuspid and Pulmonic *Strep equi* and *Strep zooepidemicus*, *Actinobacillus equi*, *Menningococcus*	Tricuspid > Pulmonic > Mitral > Aortic Alpha hemolytic Streptococcus, *T. pyogenes, Mycoplasma*	Mitral and Aortic > Tricuspid and Pulmonic *Erysipelothrix, Streptococcus*

Pathogenesis of infectious endocarditis





MacDonald. Infective Endocarditis in Dogs: Diagnosis and Therapy
Veterinary Clinics: Small Animal Practice, Volume 40, Issue 4, 665 - 684

Complications

SYSTEMIC

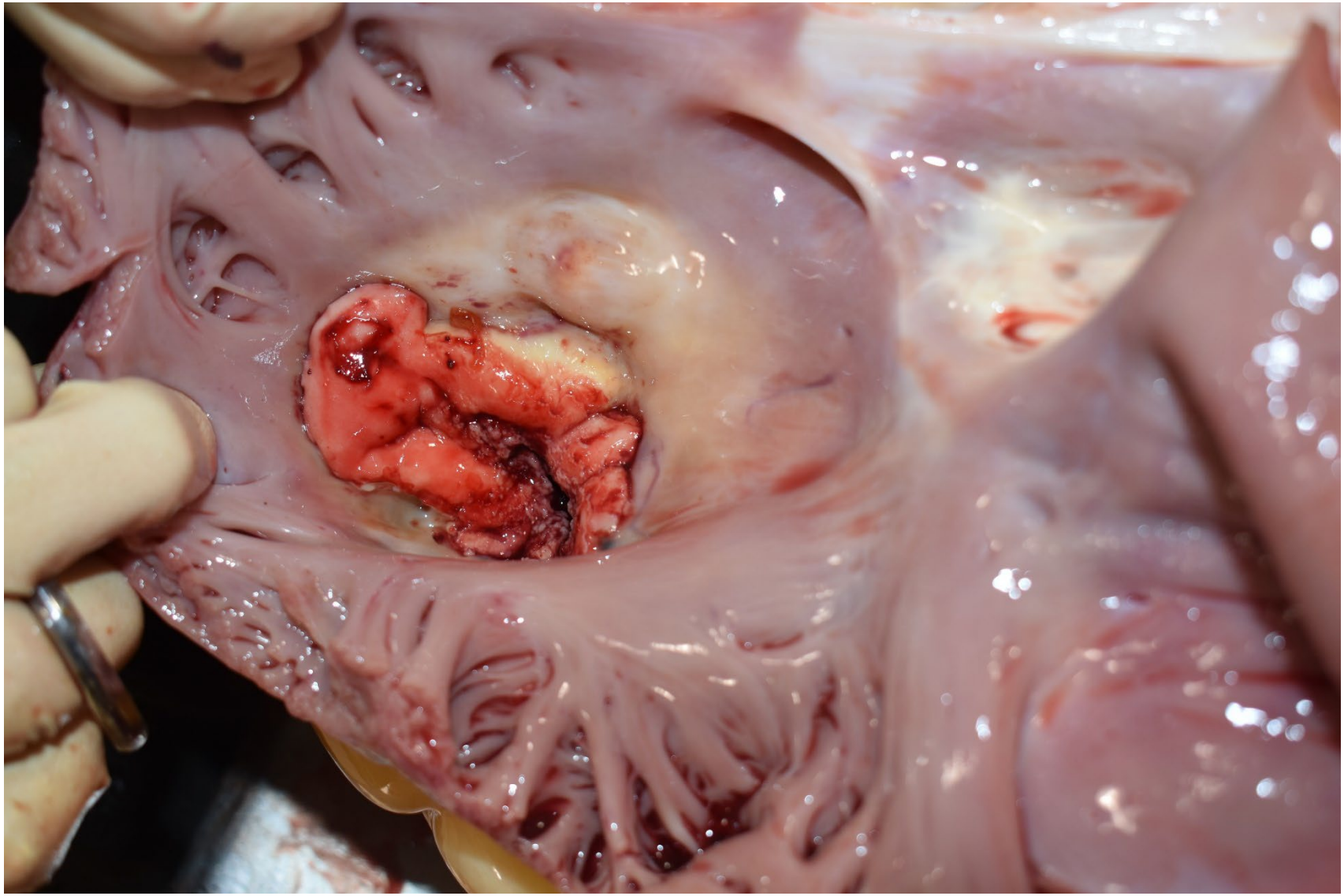
- Bacteria shed from the valves can result in:
  - Pyelonephritis and UTI
  - Meningitis
  - Septic arthropathy
  - Myocarditis and pneumonia
- Infarcts:
  - Spleen, kidney, heart, lungs, brain, GI tract, heart, lungs
- Immunologic reaction to chronic infection can lead to:
  - Formation of immune complexes
  - Immune-mediated polyarthropathy
  - Glomerulonephritis

CARDIAC

- Valve stenosis or regurgitation
- Ventricular hypertrophy
- Congestive heart failure
- Arrhythmias – sudden cardiac death
- Pulmonary thromboembolism

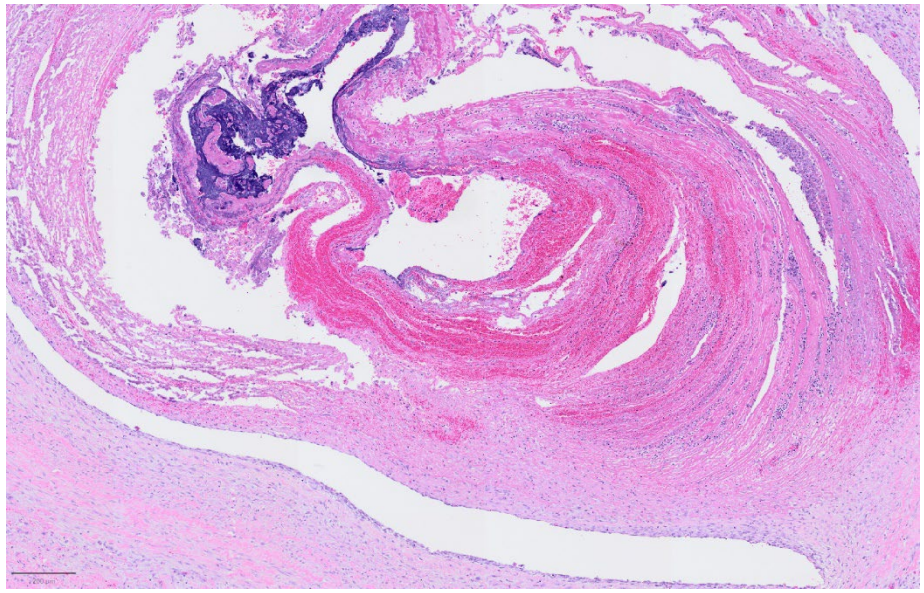
Bovine
Trueperella pyogenes

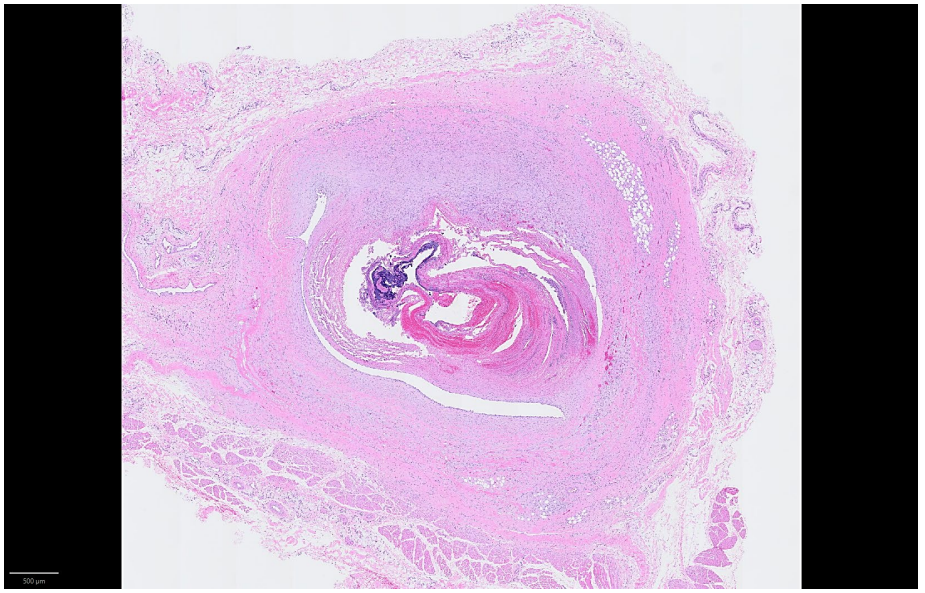
Large vegetations obstruct blood flow, leading to stenosis

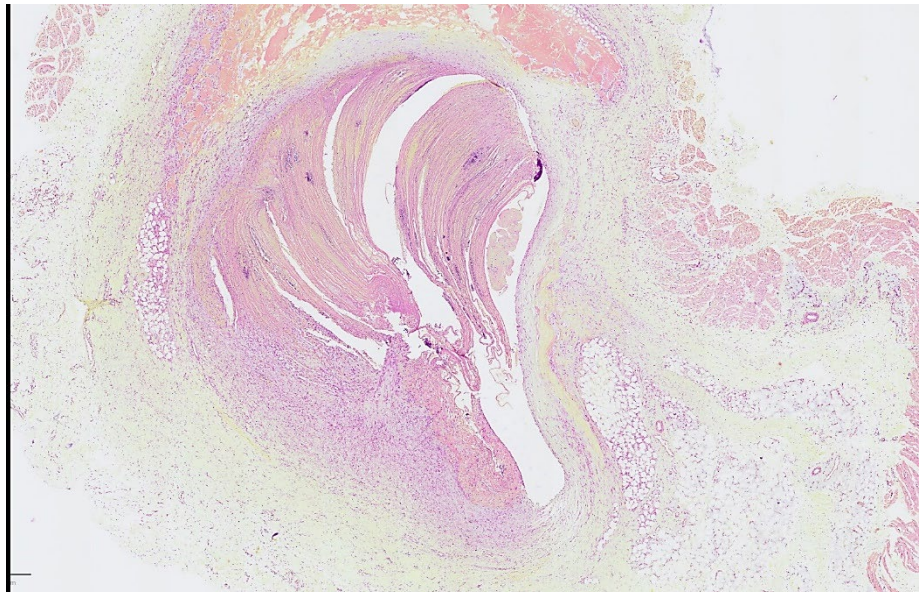


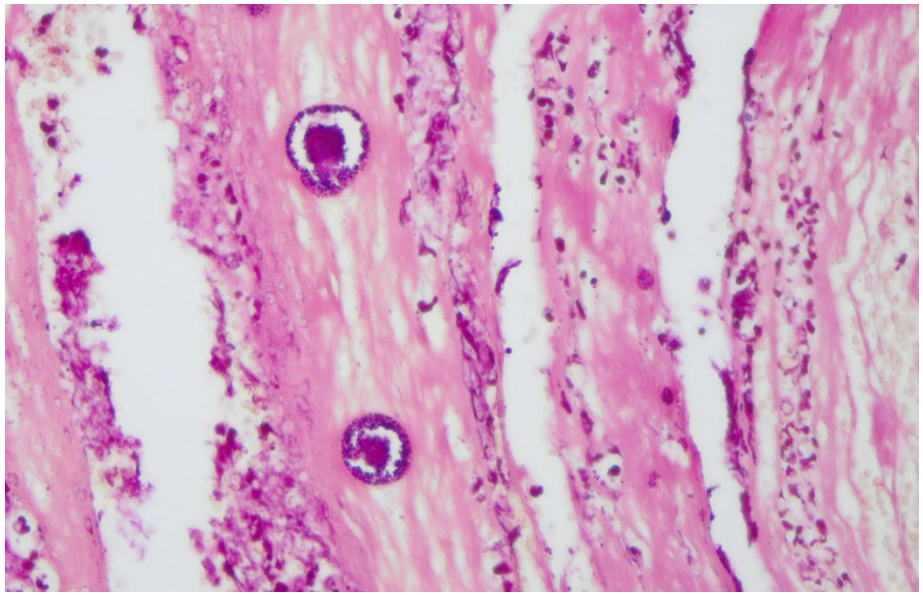
Goat

Jugular vein with thrombosis containing Gram-positive cocci (*Enterococcus*)

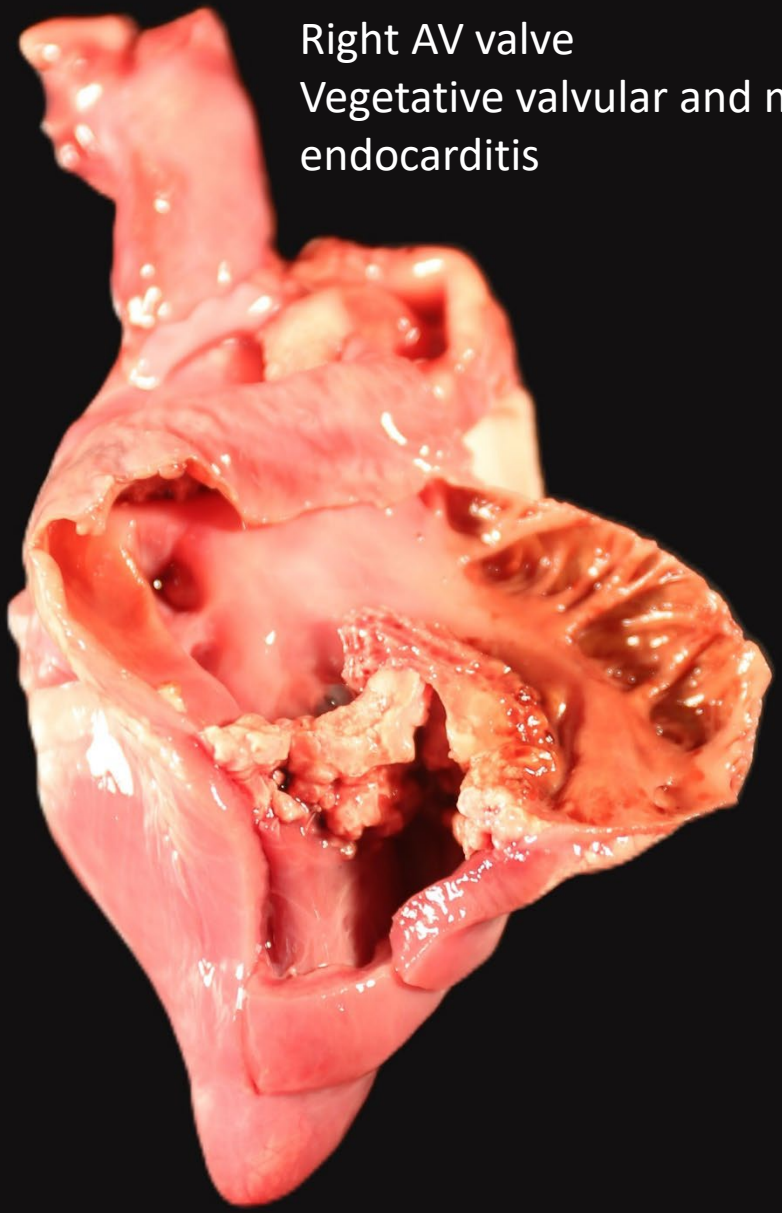








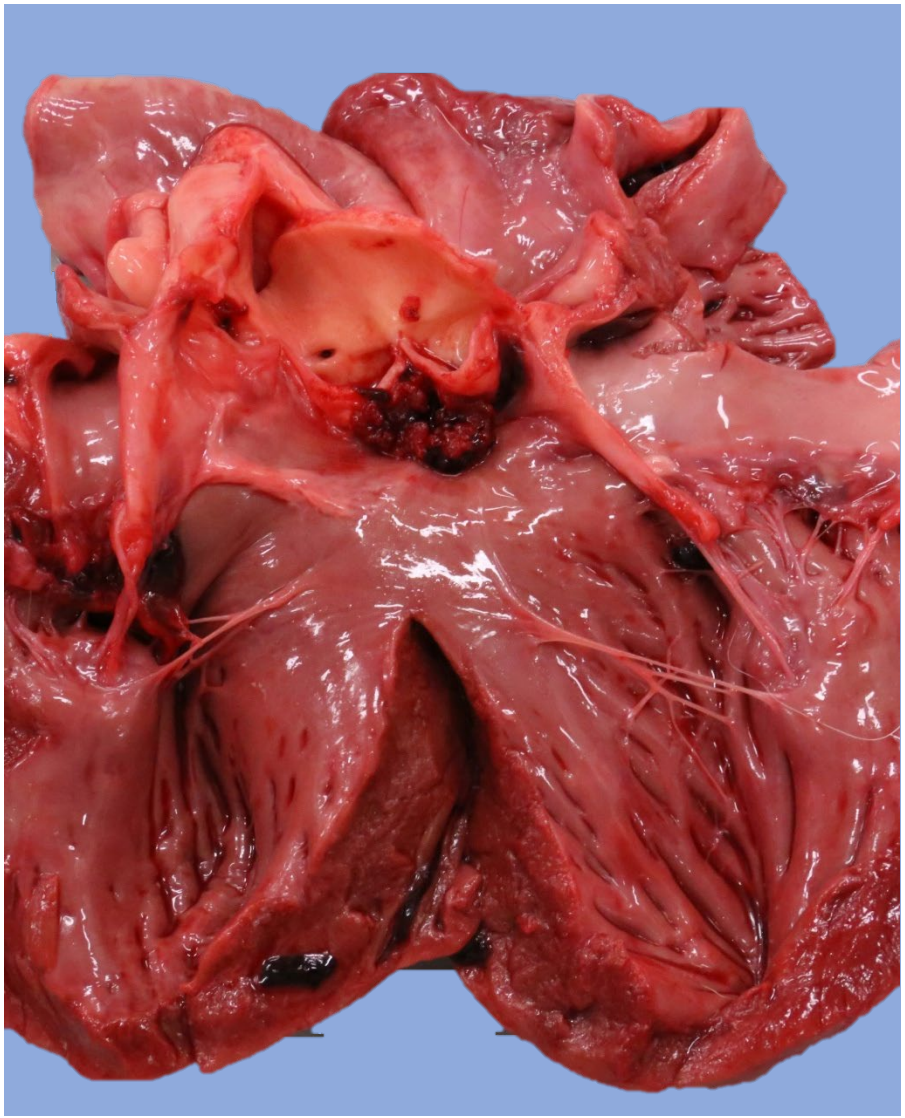
Goat

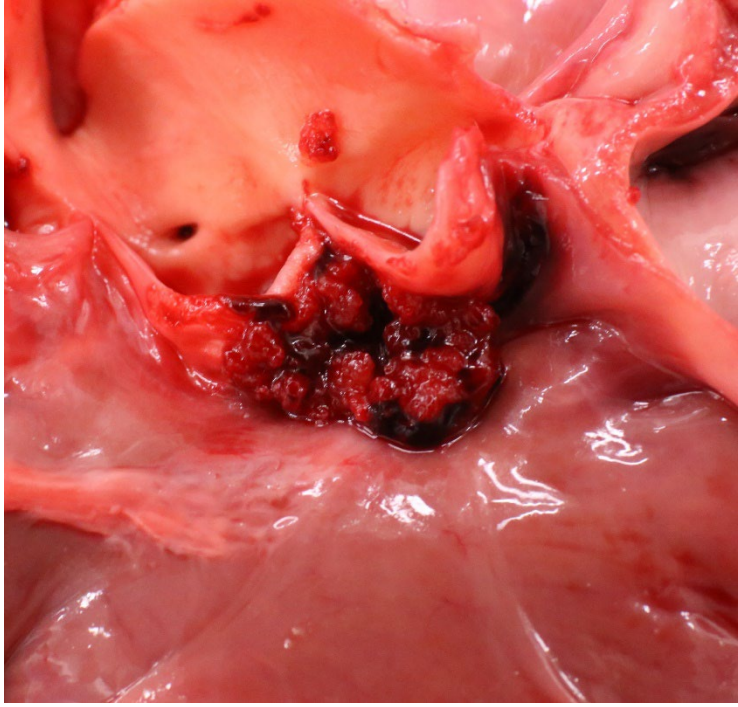


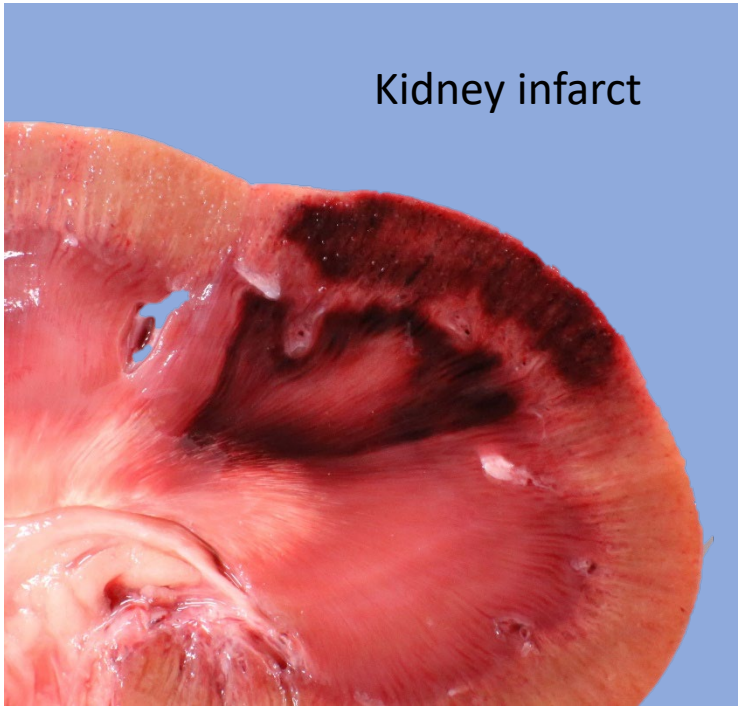
Right AV valve
Vegetative valvular and mural endocarditis

Goat

Dog
Subaortic stenosis
Aortic valvular endocarditis
Turbulent flow----endotelial damage---bacterial colonization

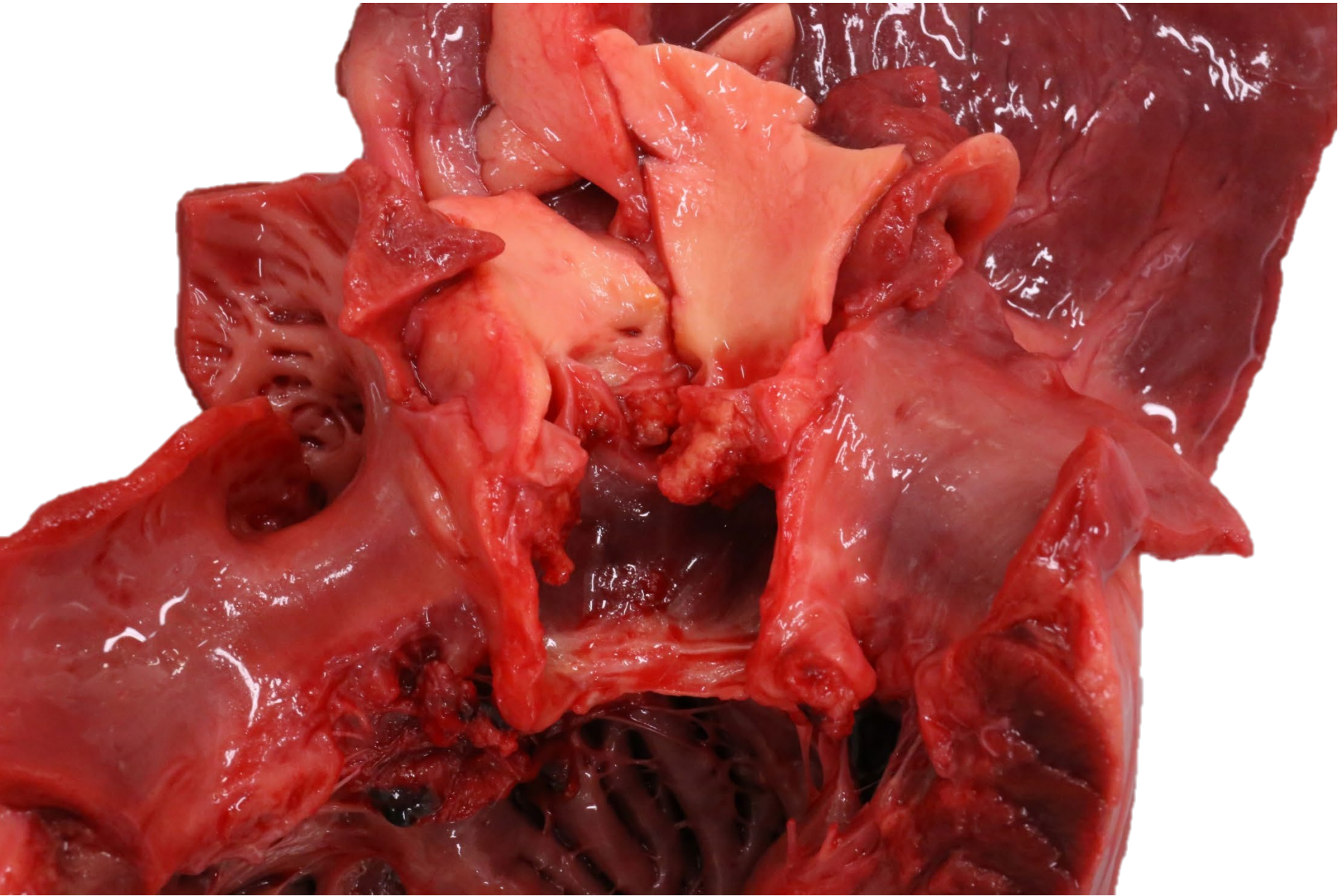






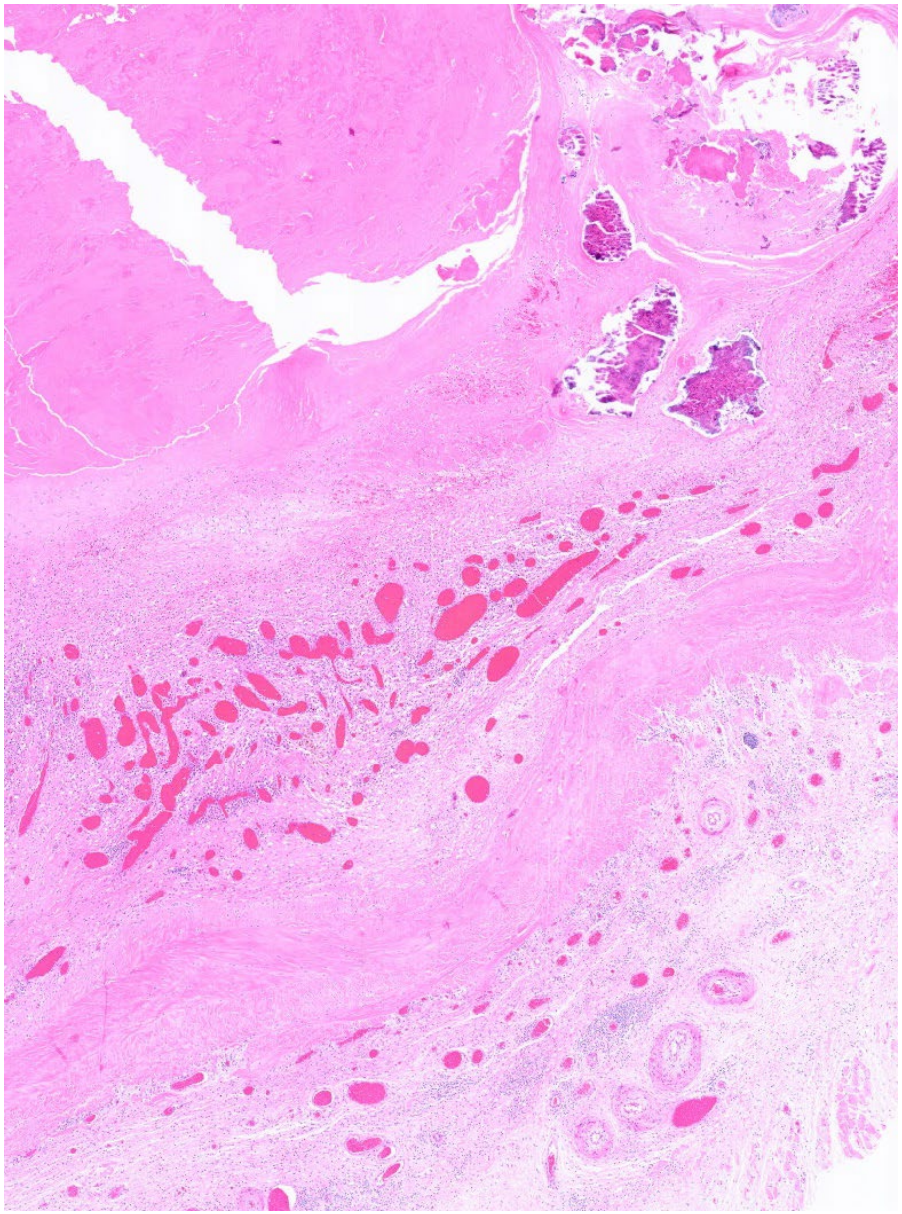
Pulmonary
and
splenic infarcts

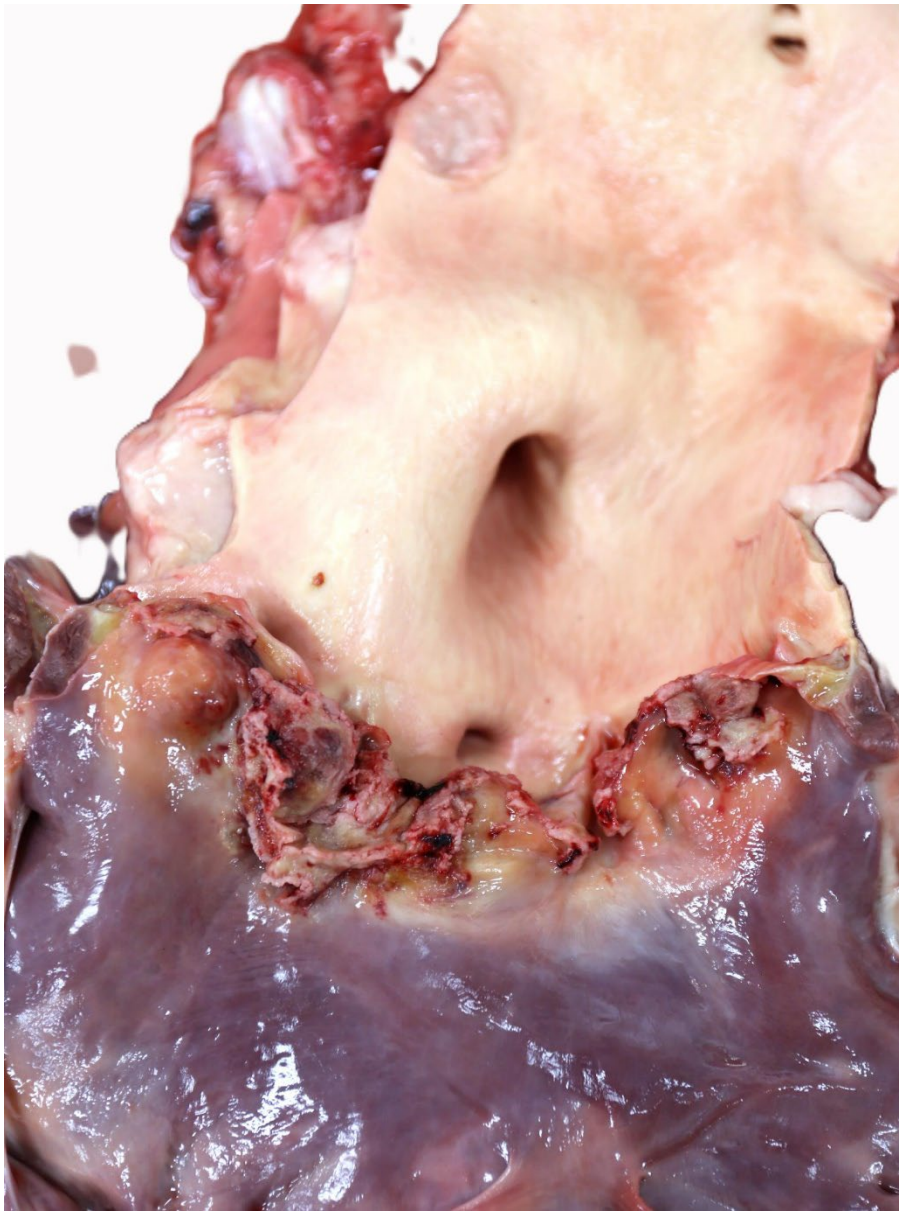
Mitral and aortic valvular endocarditis/congenital subaortic stenosis



Horse

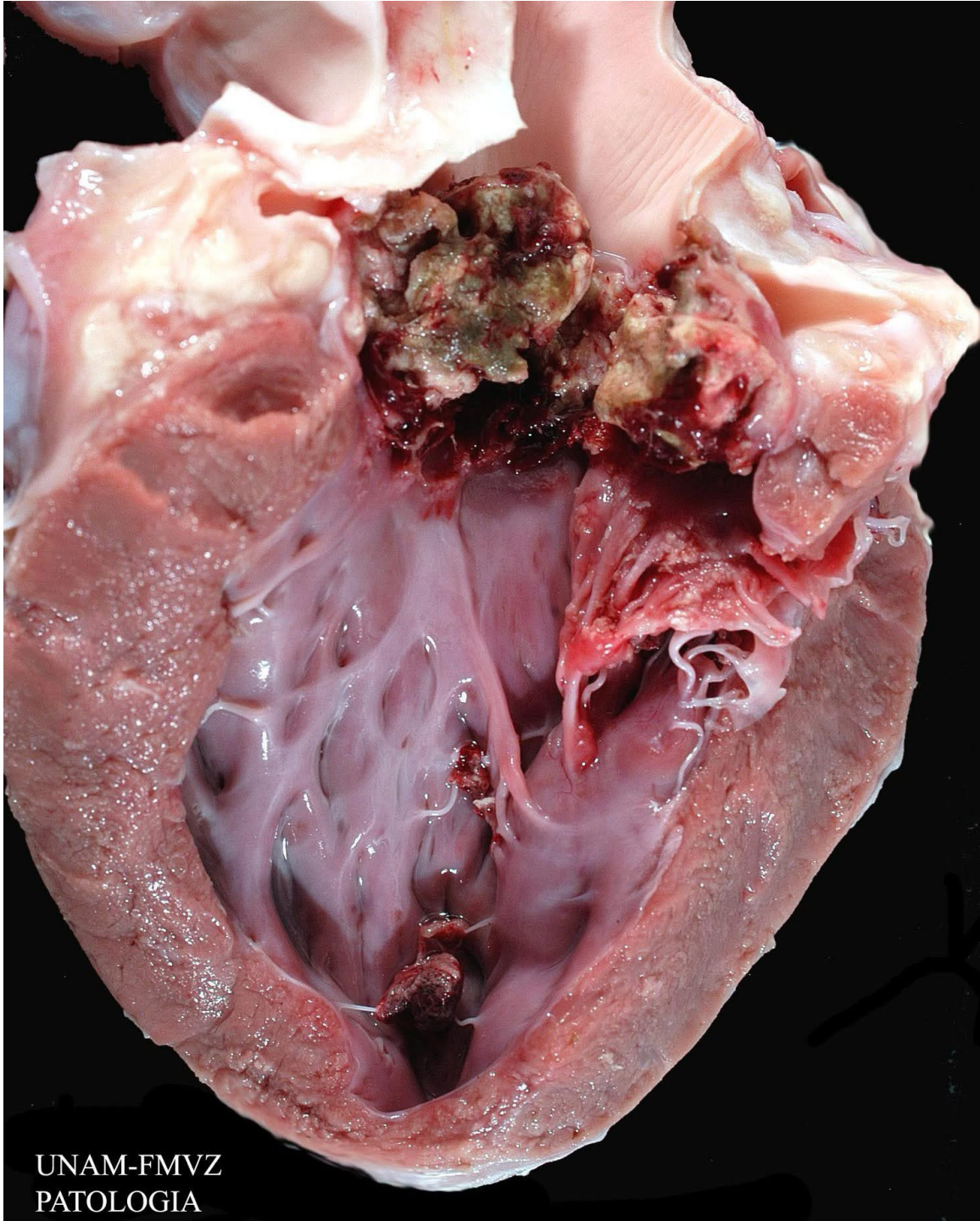
Vegetative valvular endocarditis due to *Streptococcus* sp.





Vegetative valvular endocarditis

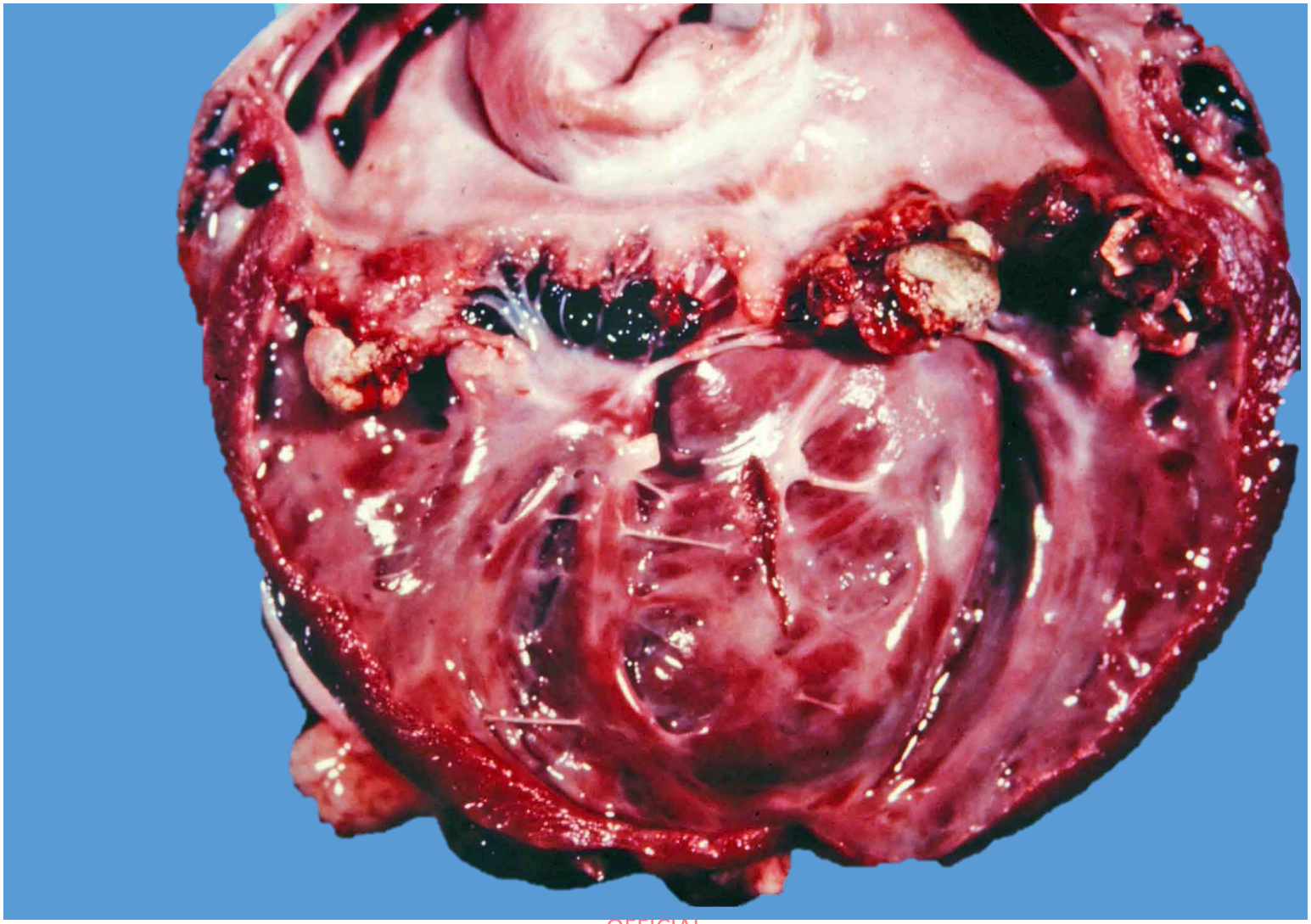
Aortic and left AV valve



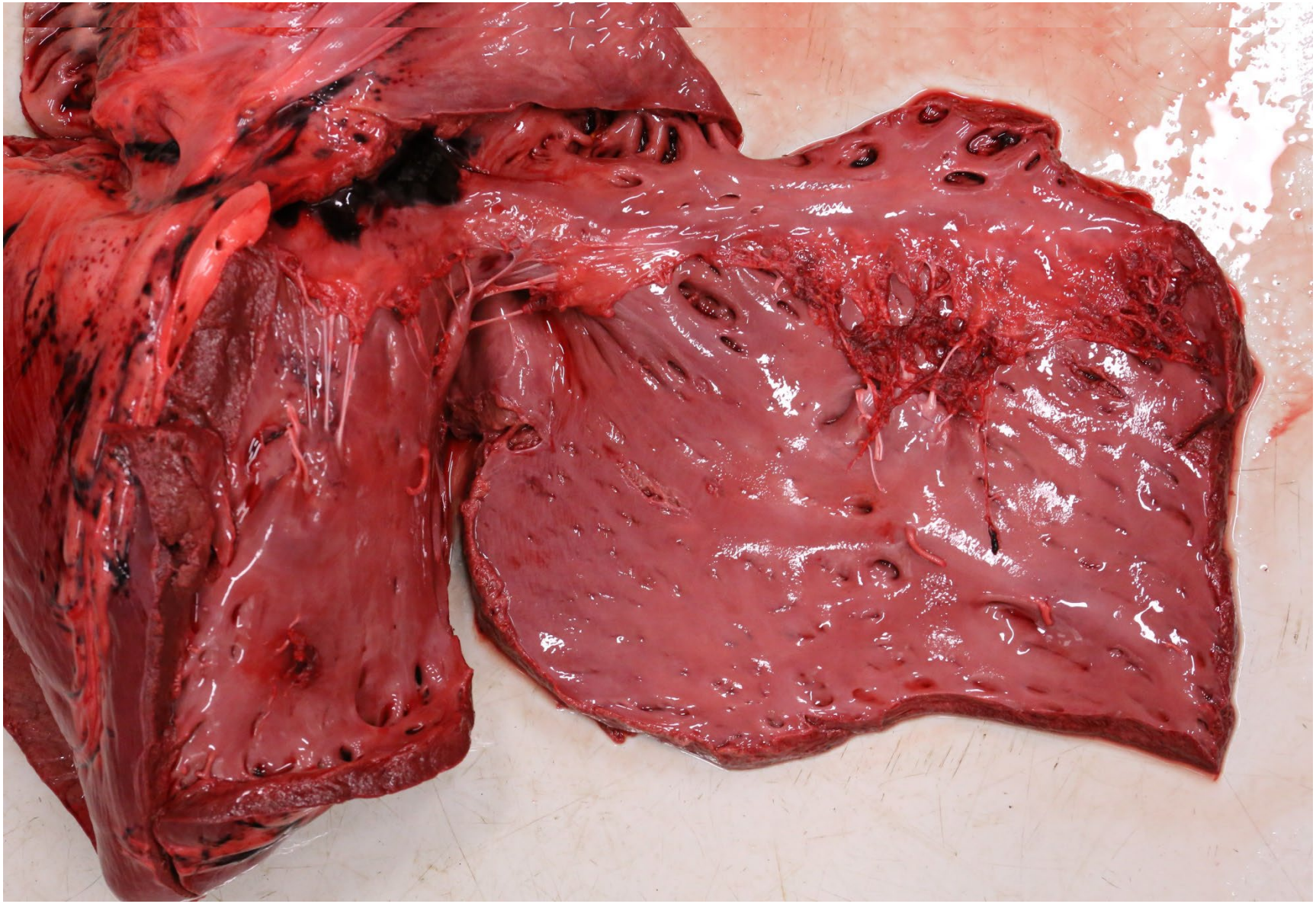
Pig

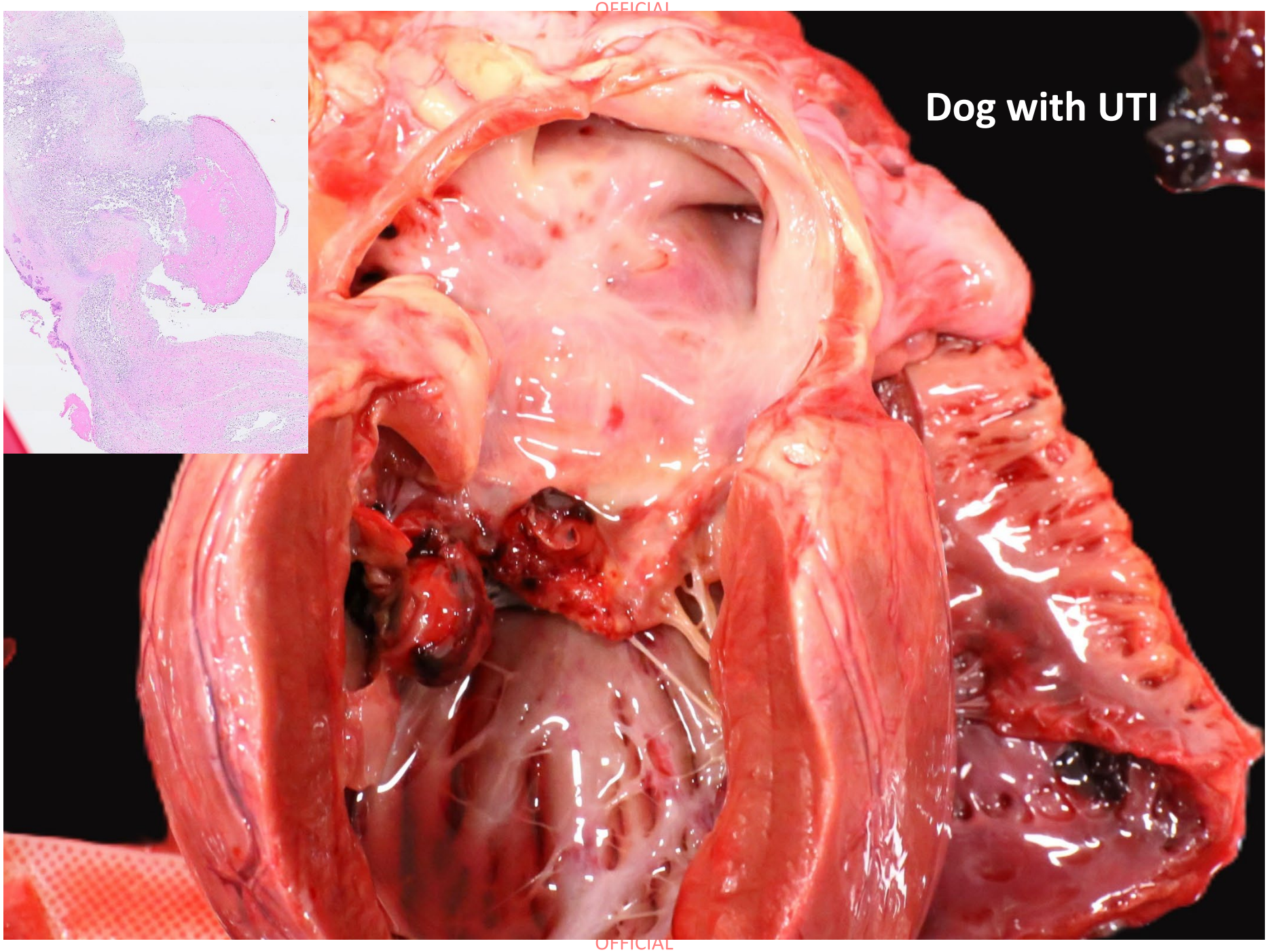
Vegetative valvular endocarditis

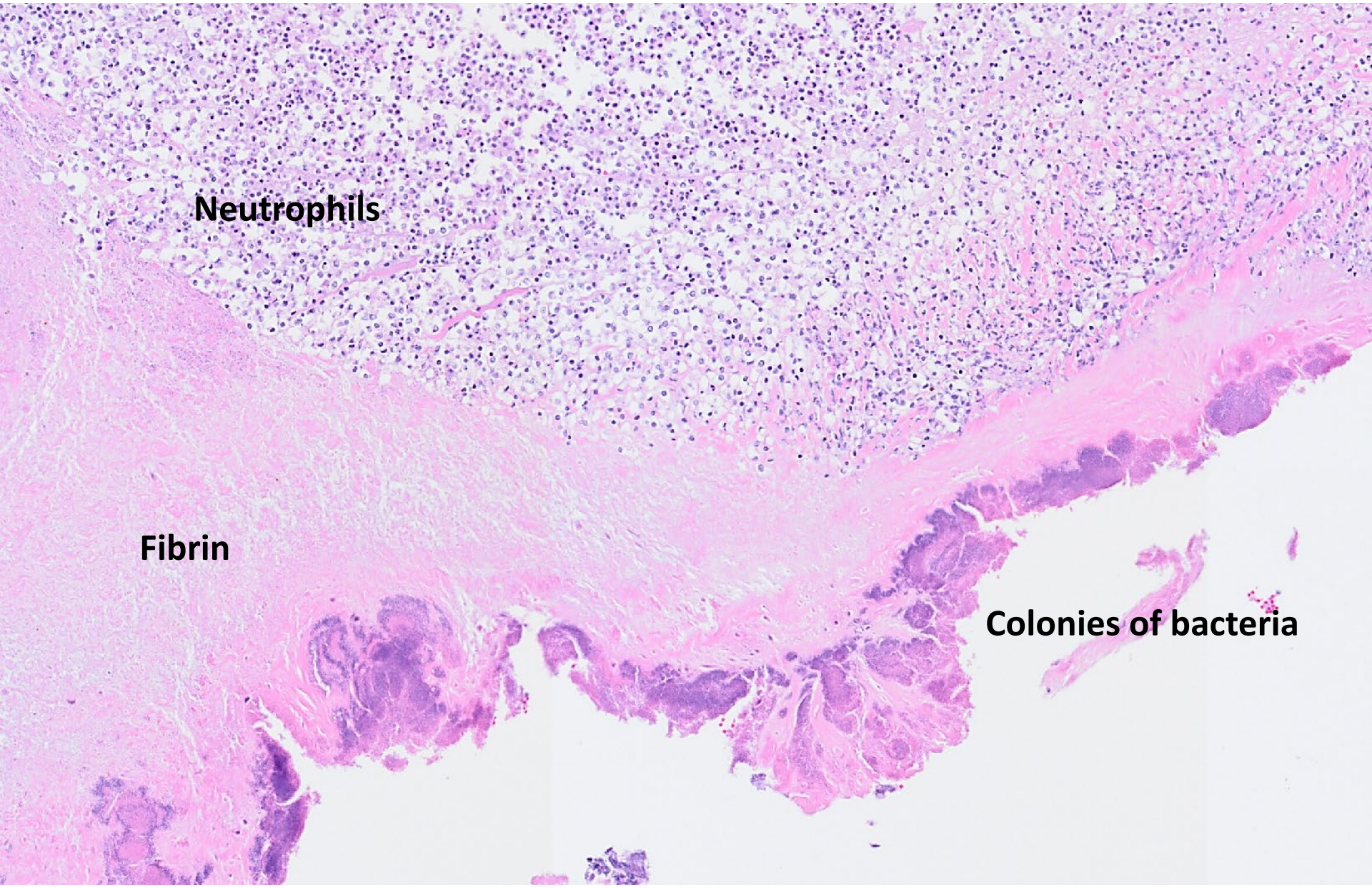
Streptococcus sp.



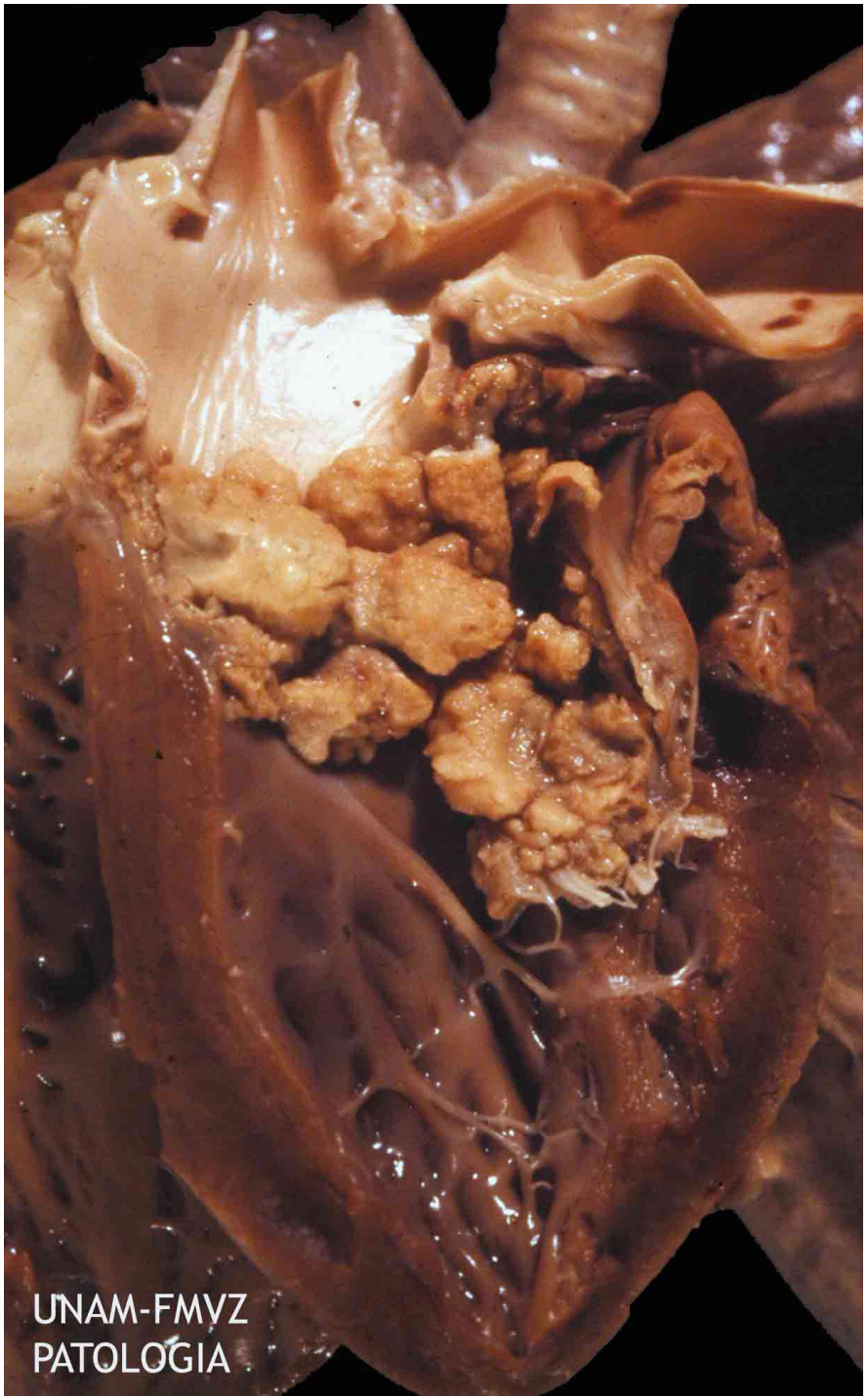
Horse
Bacterial valvular endocarditis







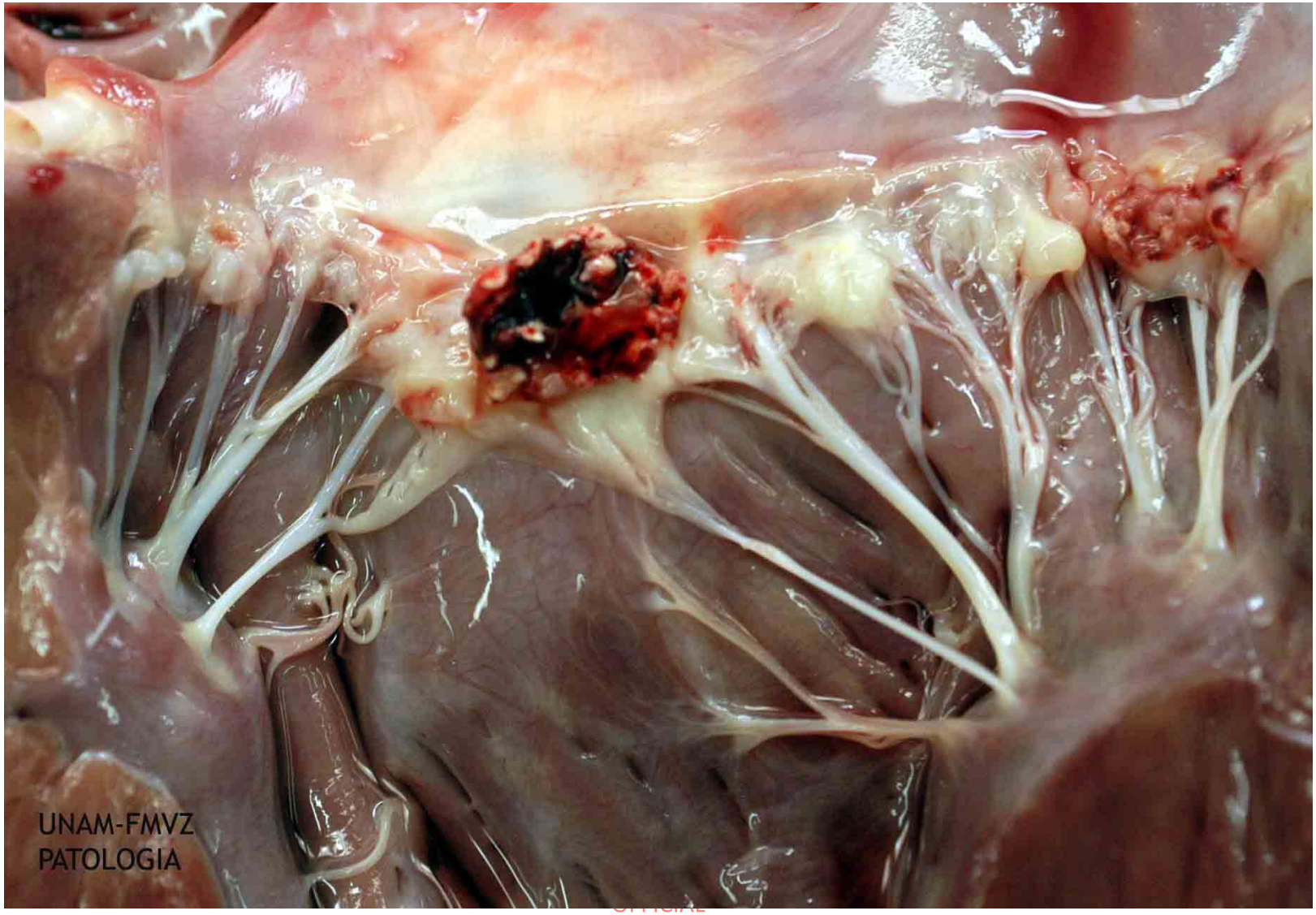
Pig
Vegetative mural endocarditis
Erysipelothrix rhusiopathiae



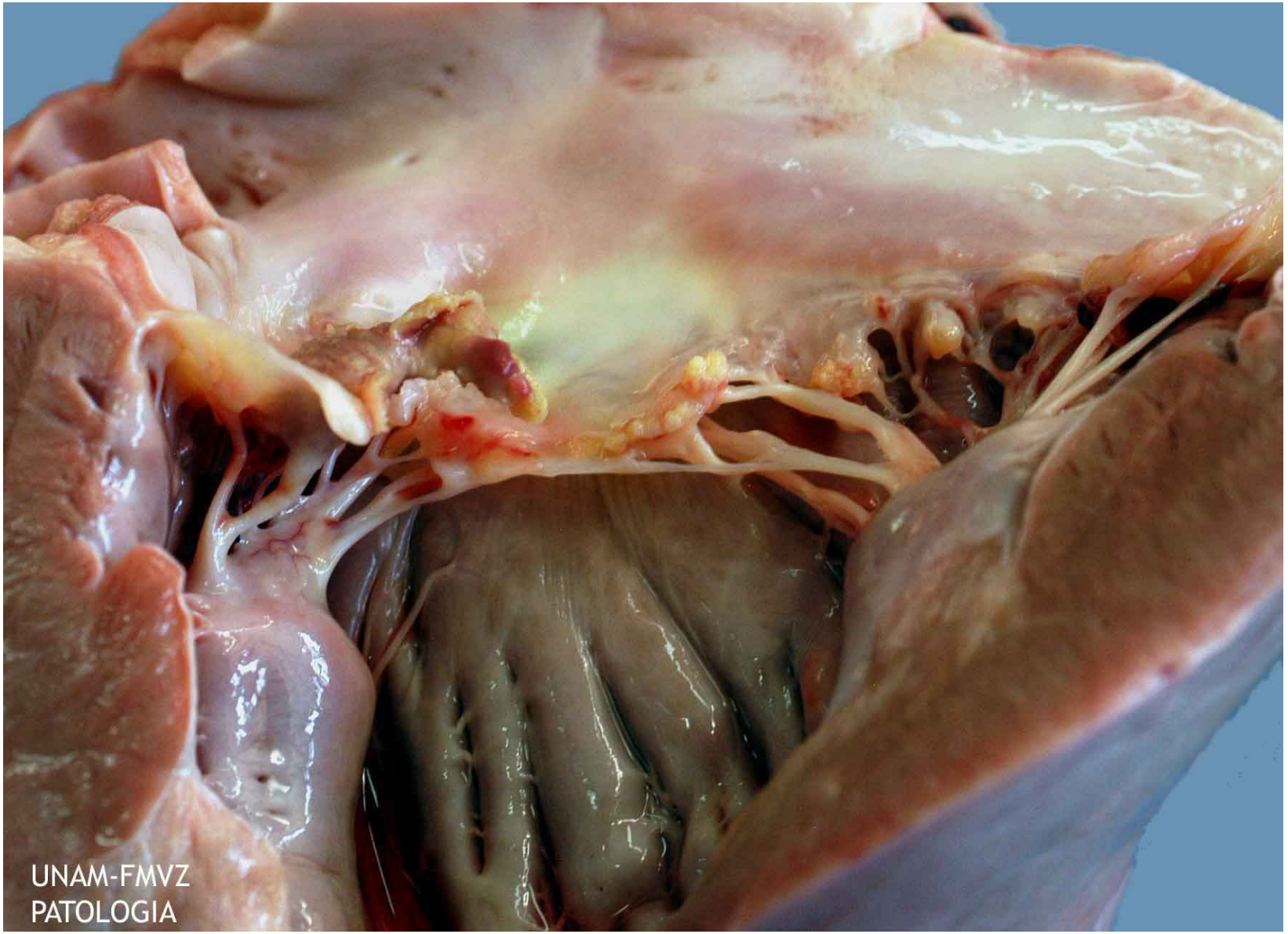
Dog

Myxomatous valvular degeneration

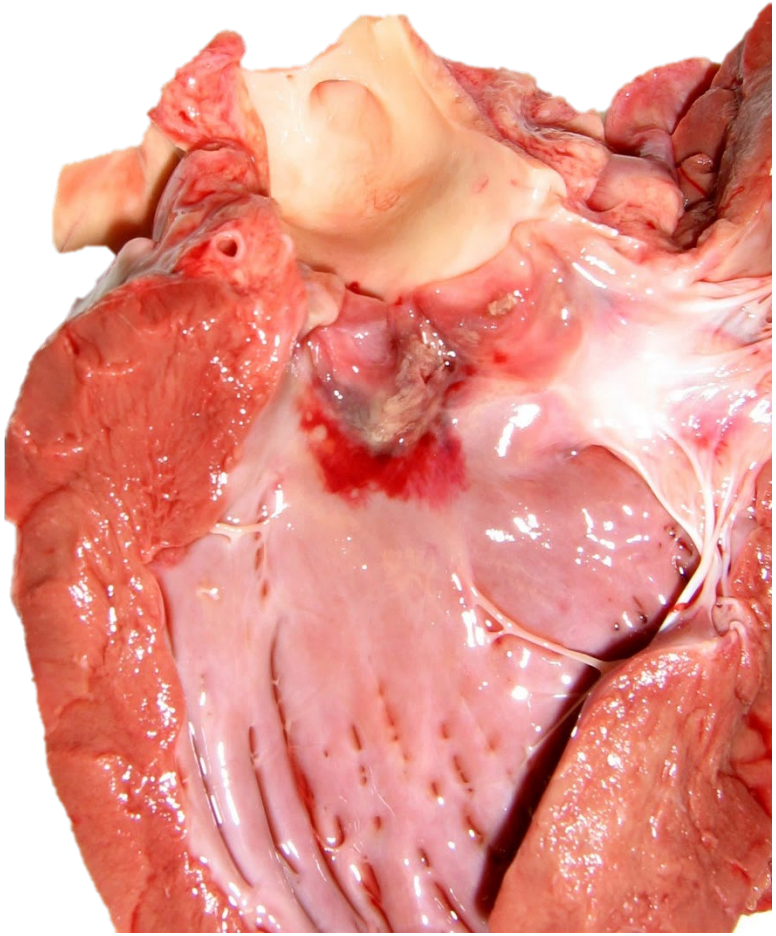
Vegetative valvular endocarditis

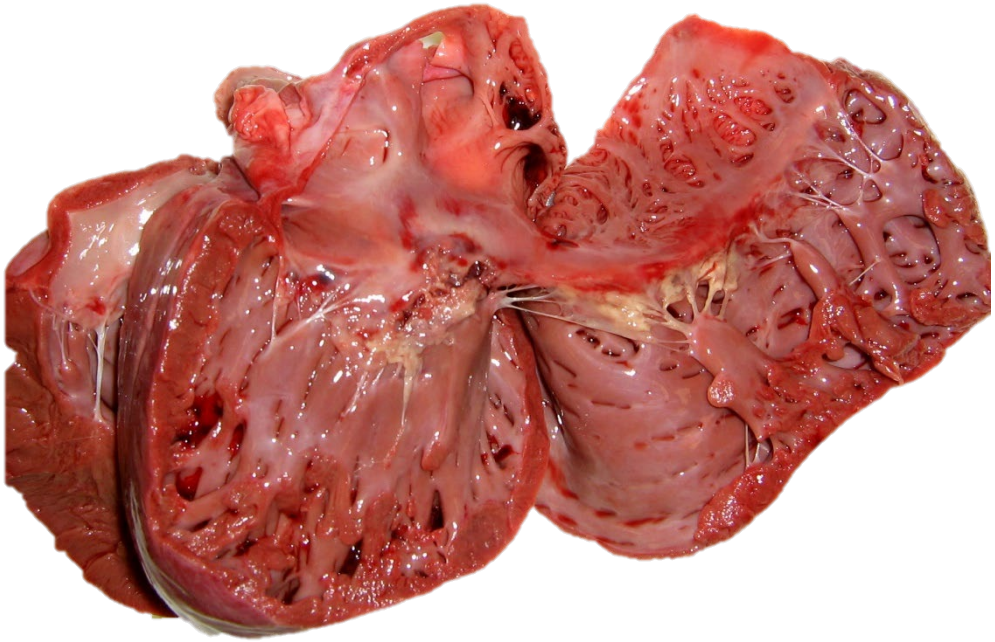


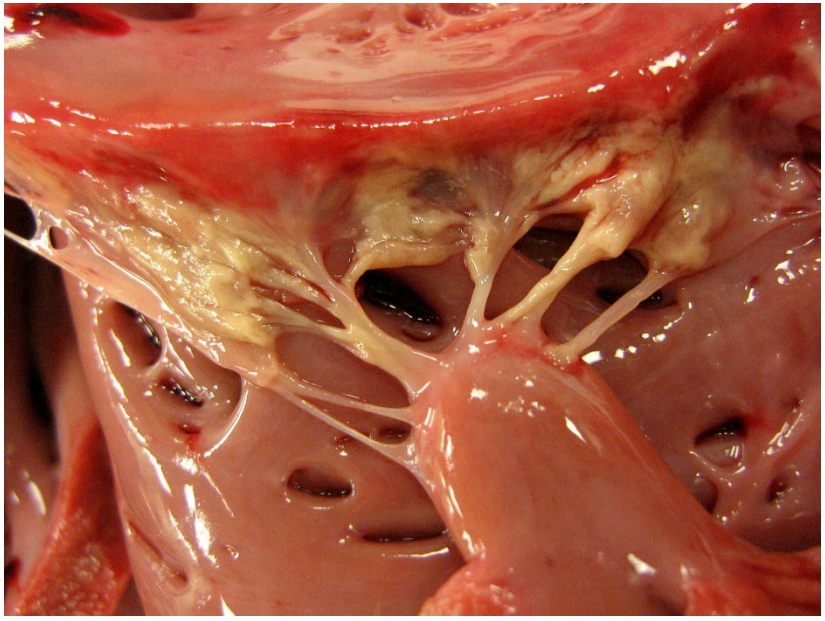
Myxomatous valvular degeneration
Vegetative valvular endocarditis



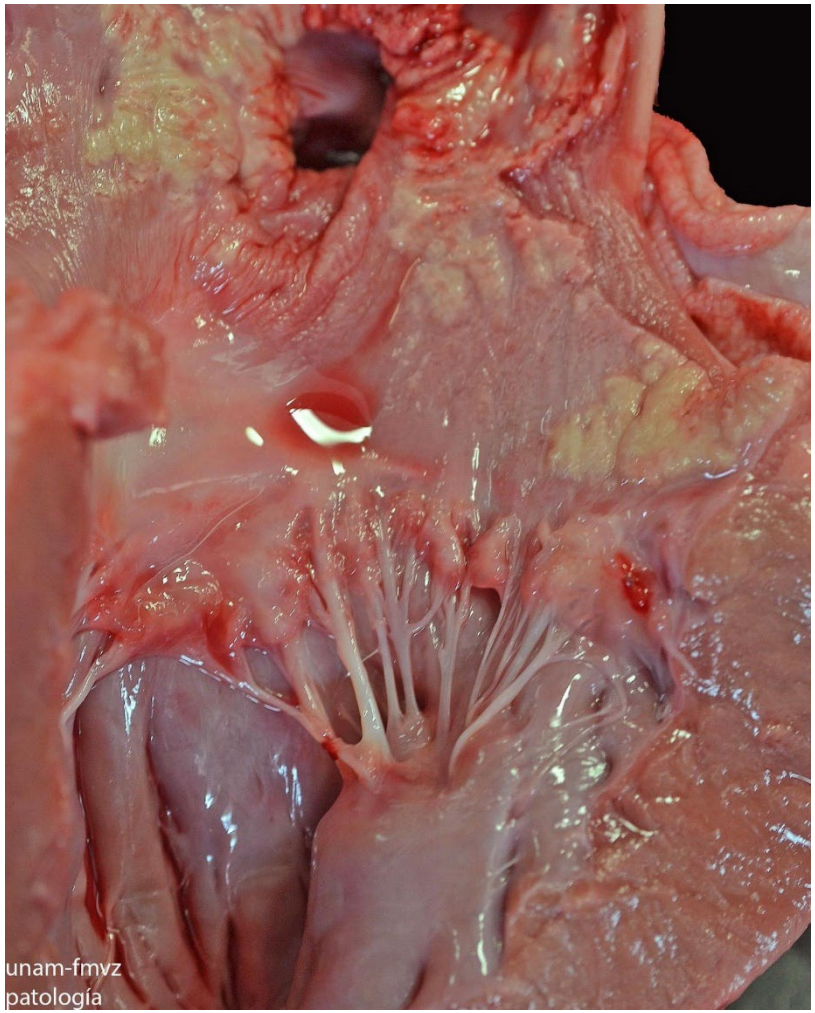
Dog Aortic and LAV with endocarditis





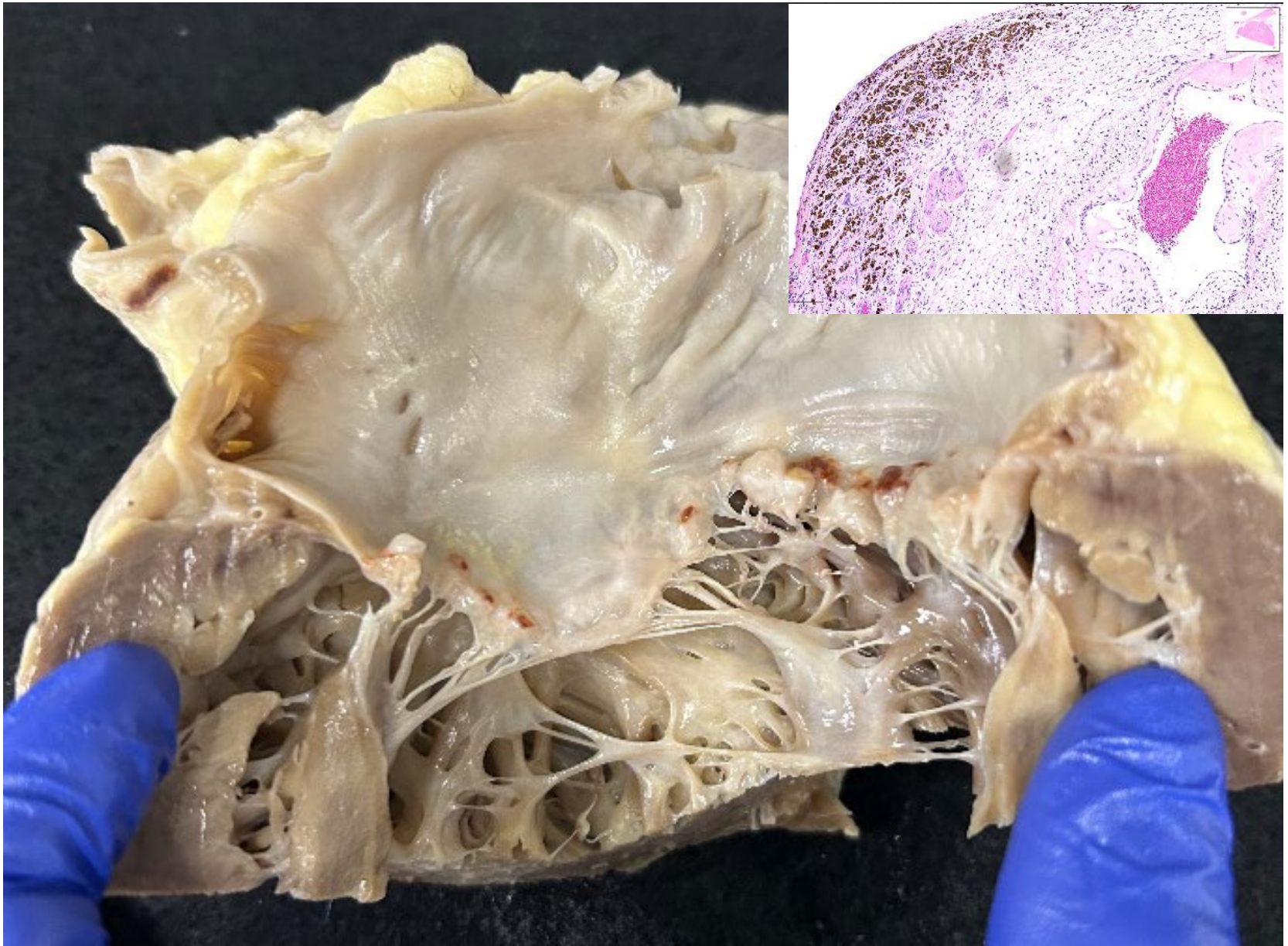


More valvular/endocardial diseases



Ulcerative atrial endocarditis
Uremia: damage to endothelial cells

Valvular hemosiderosis/hemorrhage
Myxomatous valvular degeneration
Great ape

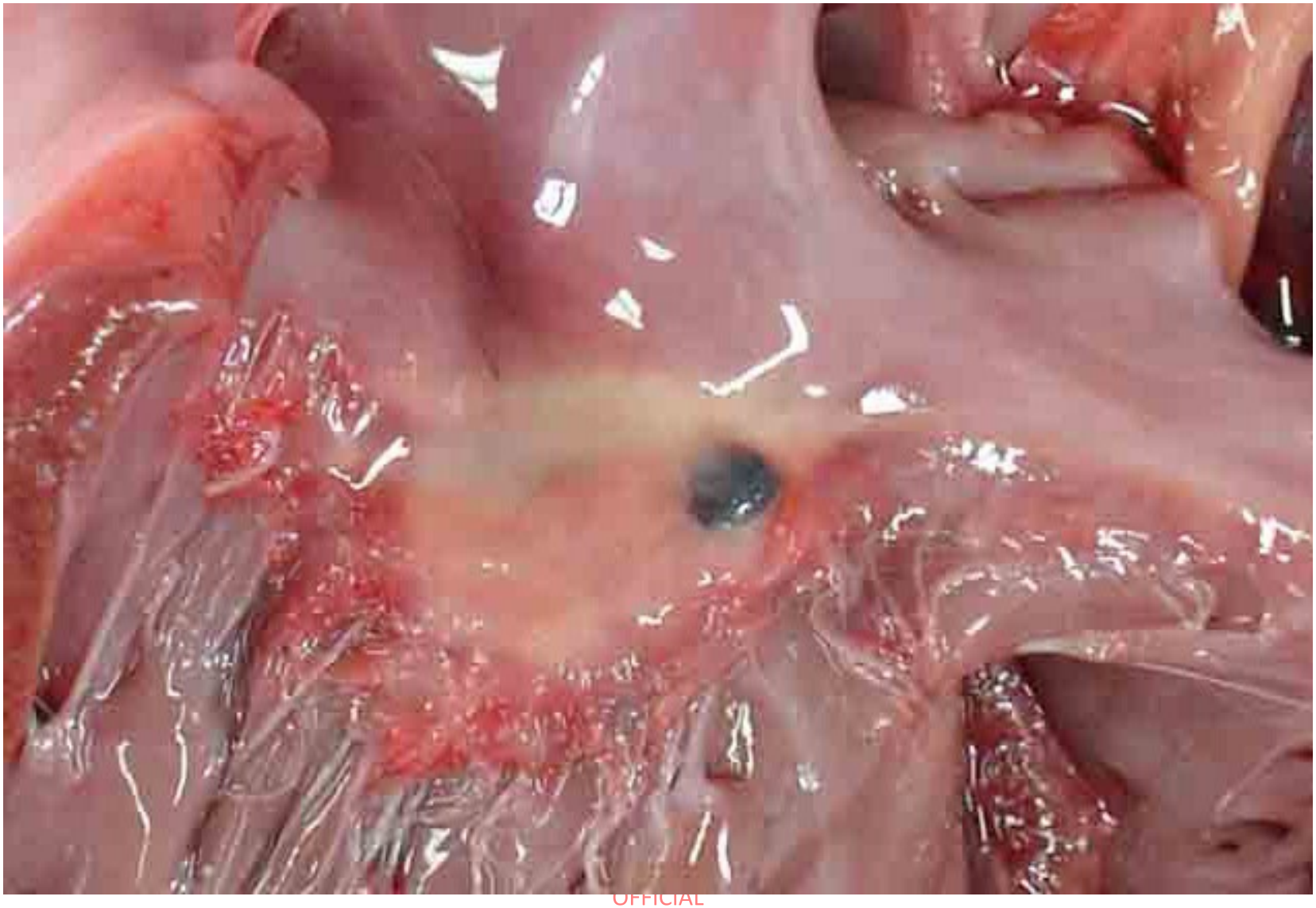


Valvular cysts

Bovine Adults > Young animals

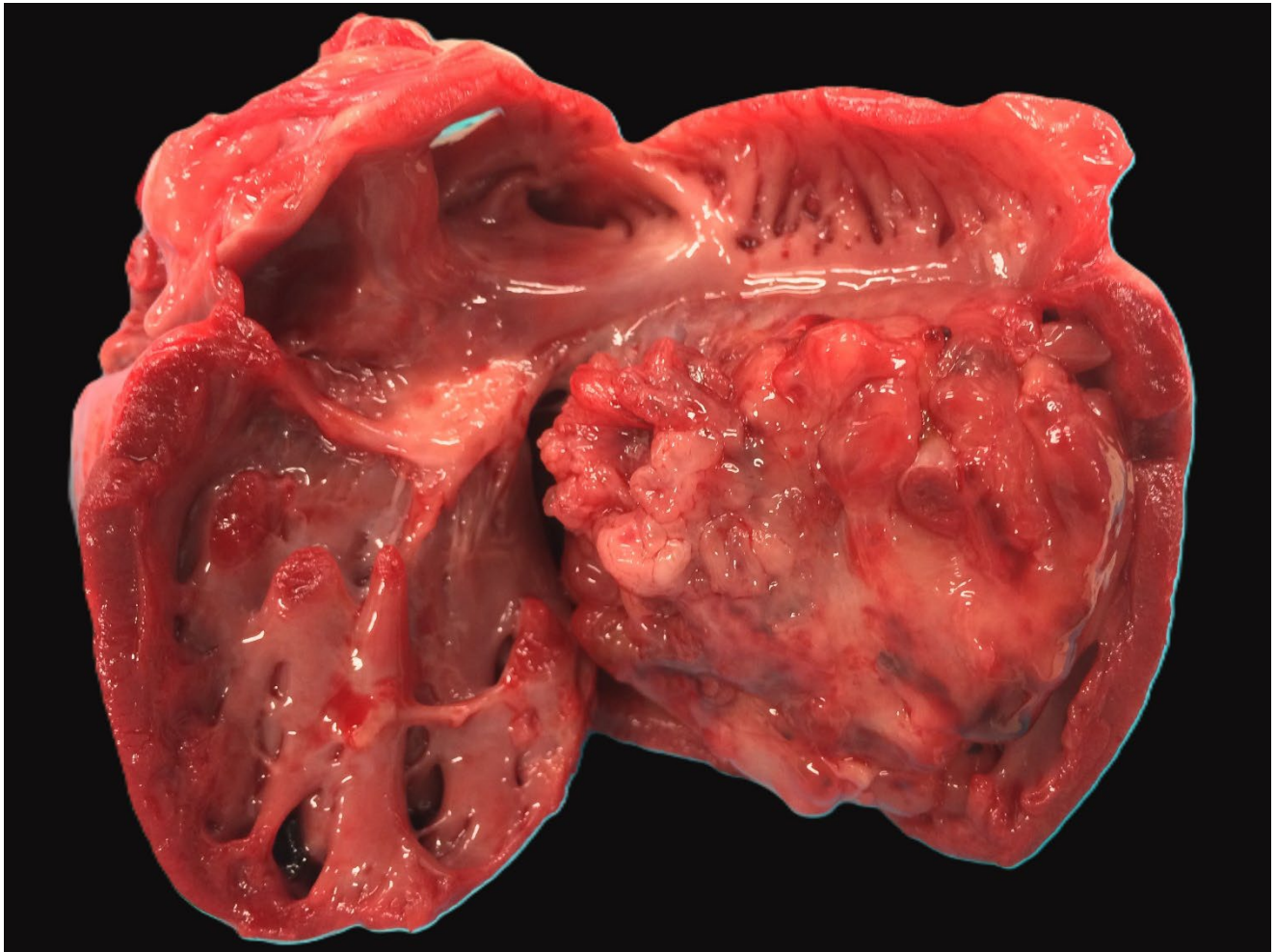
Serous and blood cysts lined by endothelium

Derive from the dilation of blood and lymphatic valvular vessels

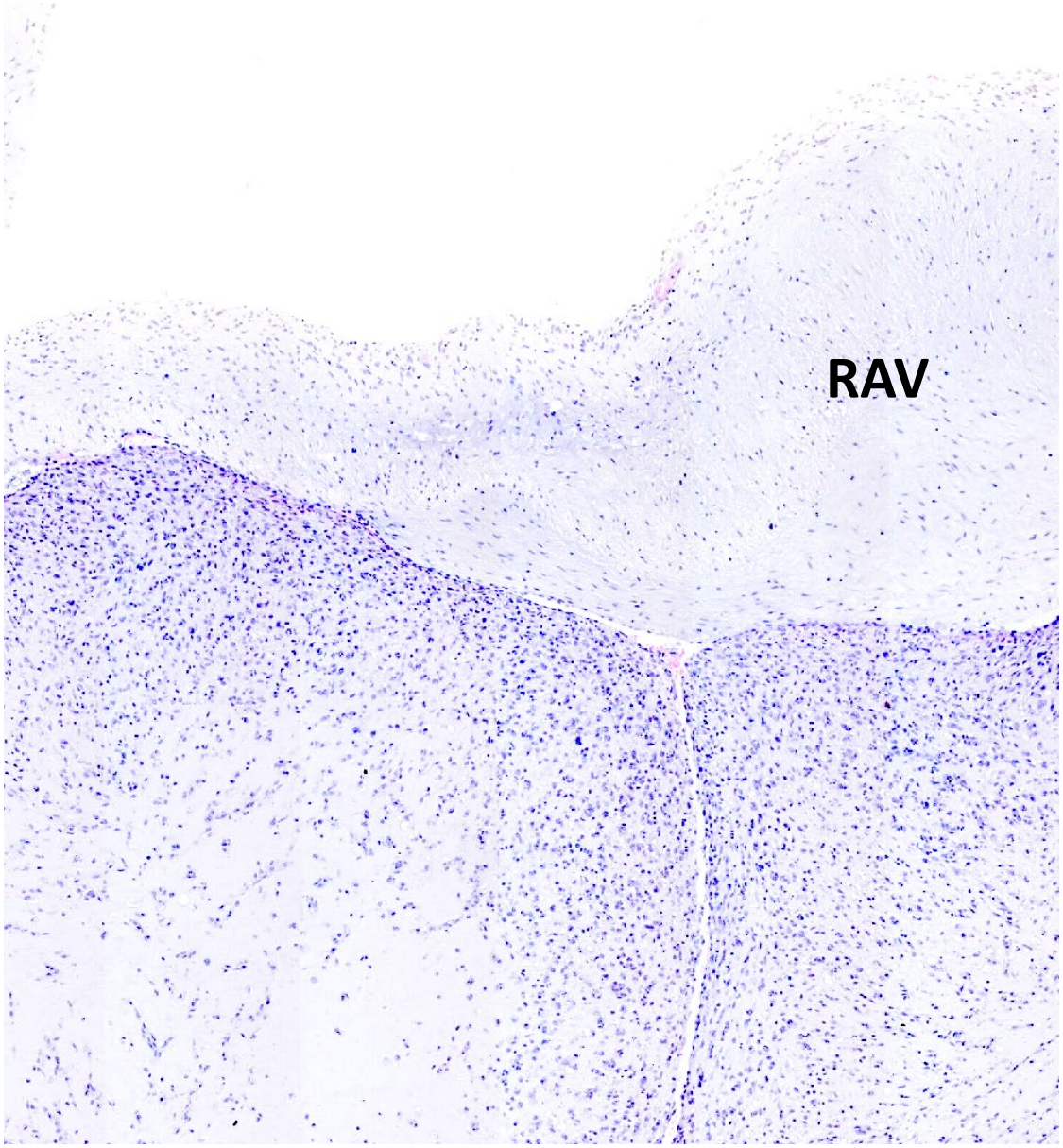


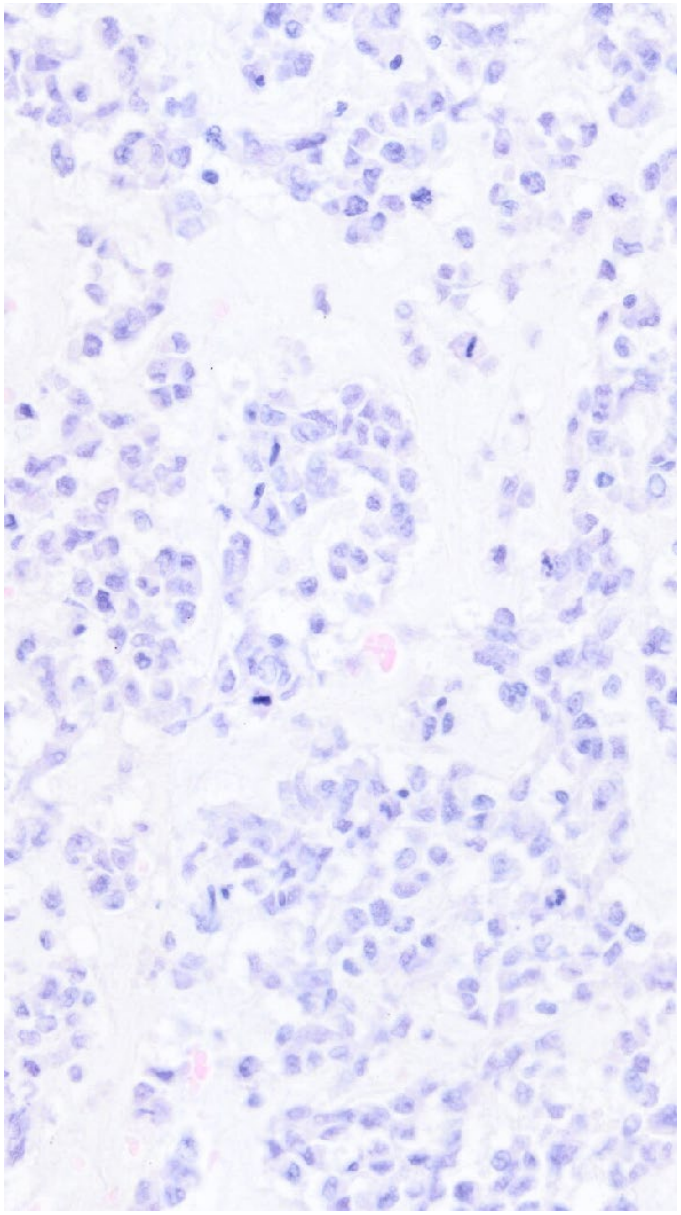
Valvular neoplasms

Myxoma/myxosarcoma
Originates from multipotential mesenchymal cells in the subendocardial layer
Right AV valve
Myxoid matrix is alcian blue positive
IHC: vimentin, apha-SMA



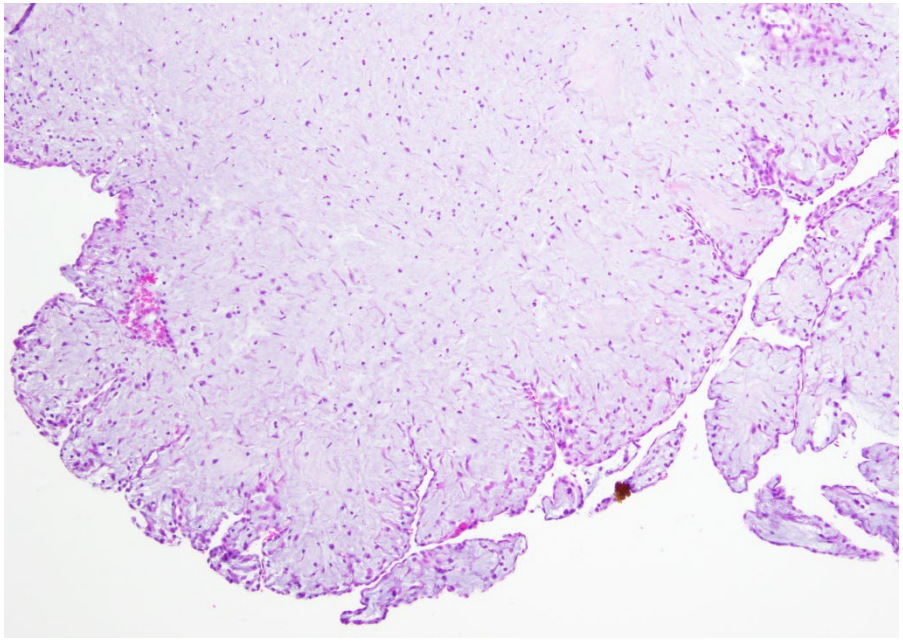
Myxosarcoma

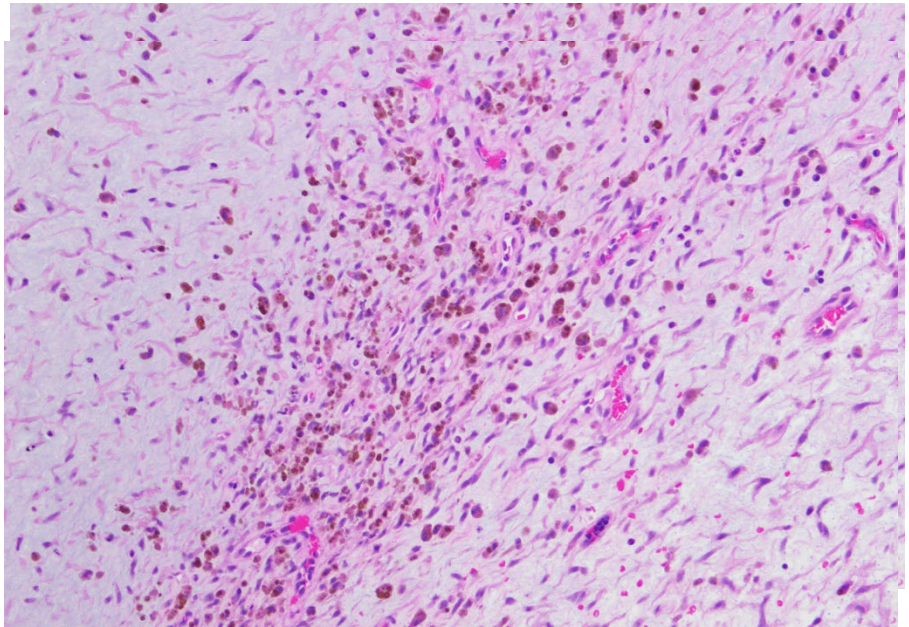


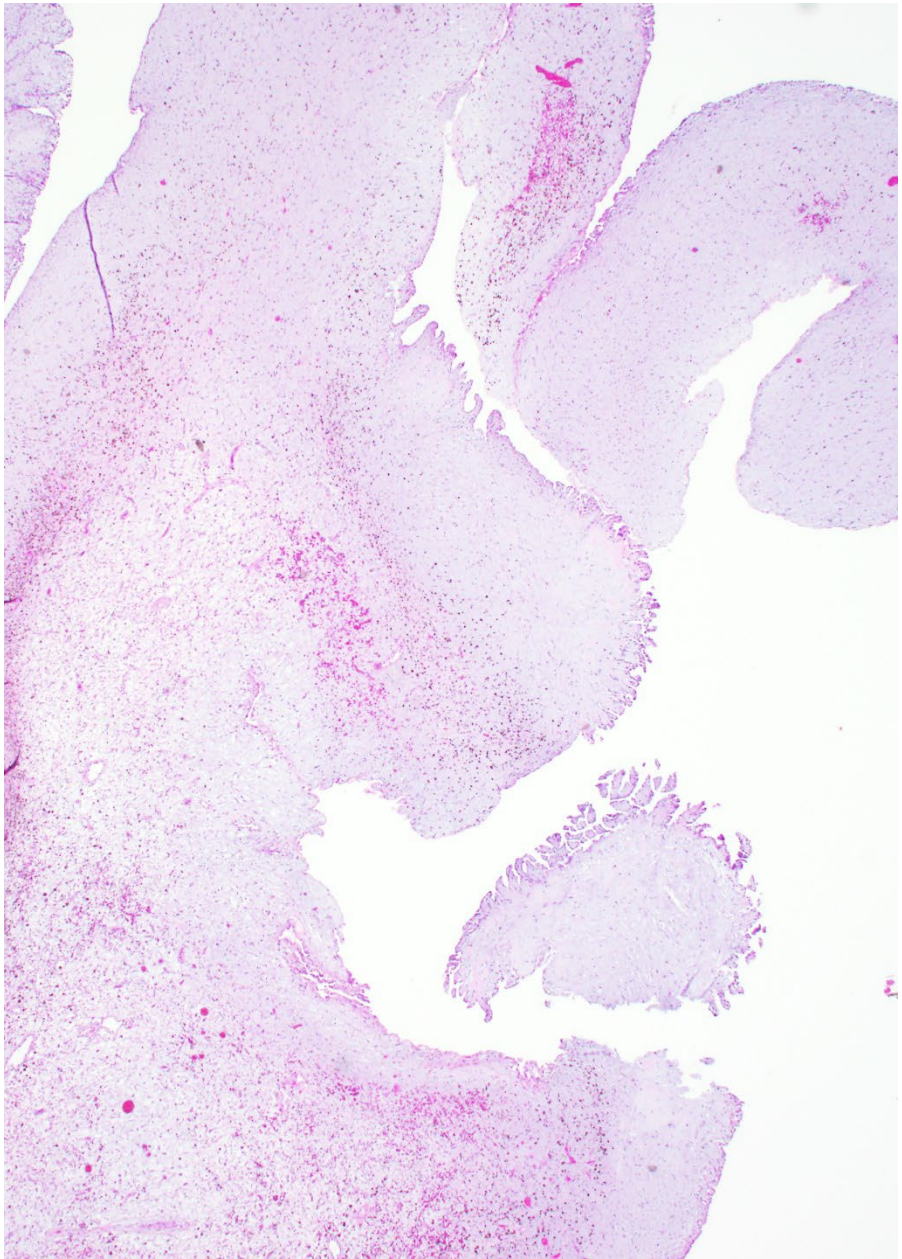


Biopsy from the right atrioventriucular valve

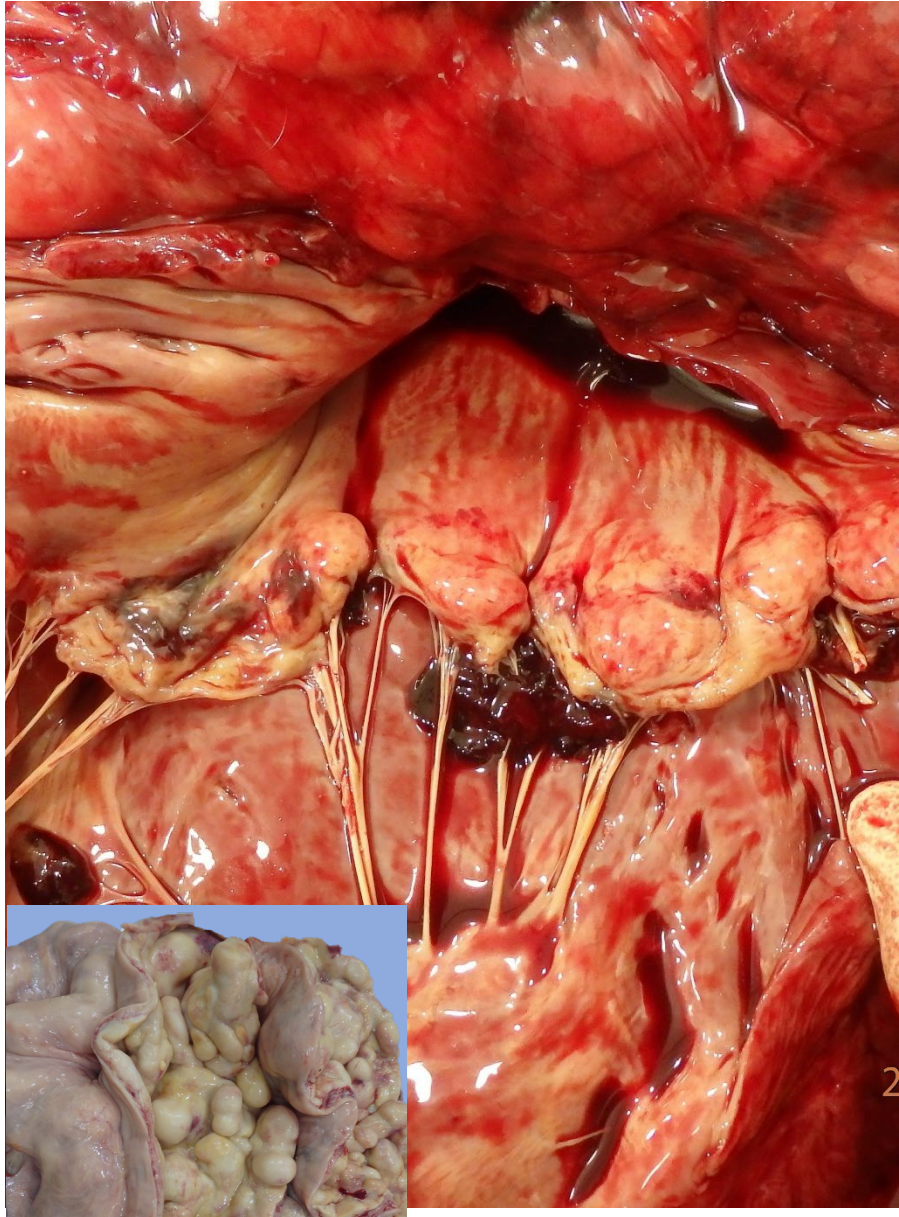
Myxoma







Bovine Lymphoma



Mexico city

Axolotl (*Ambystoma mexicanum*)

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Dr. Lisa Freeman- Department of Clinical Sciences

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