Cardiomyopathies

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Contemporary definition of the cardiomyopathies

A heterogeneous group of myocardial diseases associated with:

- Mechanical dysfunction
- and/or Electrical dysfunction
- Usually resulting in ventricular hypertrophy or dilatation
- Due to a variety of causes, frequently genetic

Often lead to weakness, exercise limitation, syncope, progressive heart failure, or cardiovascular death

Maron BJ et.al. Circulation, 2006

Contemporary classification of the cardiomyopathies

Maron BJ et.al. Circulation, 2006

Primary cardiomyopathies

- Myocardial disease primarily affecting heart
  - Genetic mutation is the cause for many
  - Nongenitic, acquired

Secondary cardiomyopathies

- Myocardial disease secondary to another identifiable systemic disease
  - Infiltrative
  - Storage
  - Toxicity
  - Endomyocardial
  - Inflammatory
  - Endocrine
  - Neuromuscular/neurological
  - Nutritional deficiencies
  - Autoimmune
  - Electrolyte imbalance
  - Consequence of cancer therapy

Anatomic and hemodynamic classification of cardiomyopathies

Dilated cardiomyopathy

- Chamber dilation, thinned walls
- Systolic (+/- diastolic) dysfunction

Hypertrophic cardiomyopathy

- Concentric hypertrophy, small cavity, +/- left ventricular outflow tract obstruction
- Diastolic (+/- systolic) dysfunction

Restrictive cardiomyopathy

- Endomyocardial fibrosis, LA enlargement
- Typically diastolic dysfunction

Arrhythmogenic right ventricular cardiomyopathy

Nonspecific cardiomyopathy

Common cardiomyopathies in animals

- **HYPERTROPHIC CARDIOMYOPATHY**
- **DILATED CARDIOMYOPATHY**
- **RESTRICTIVE CARDIOMYOPATHY**
- **ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY**

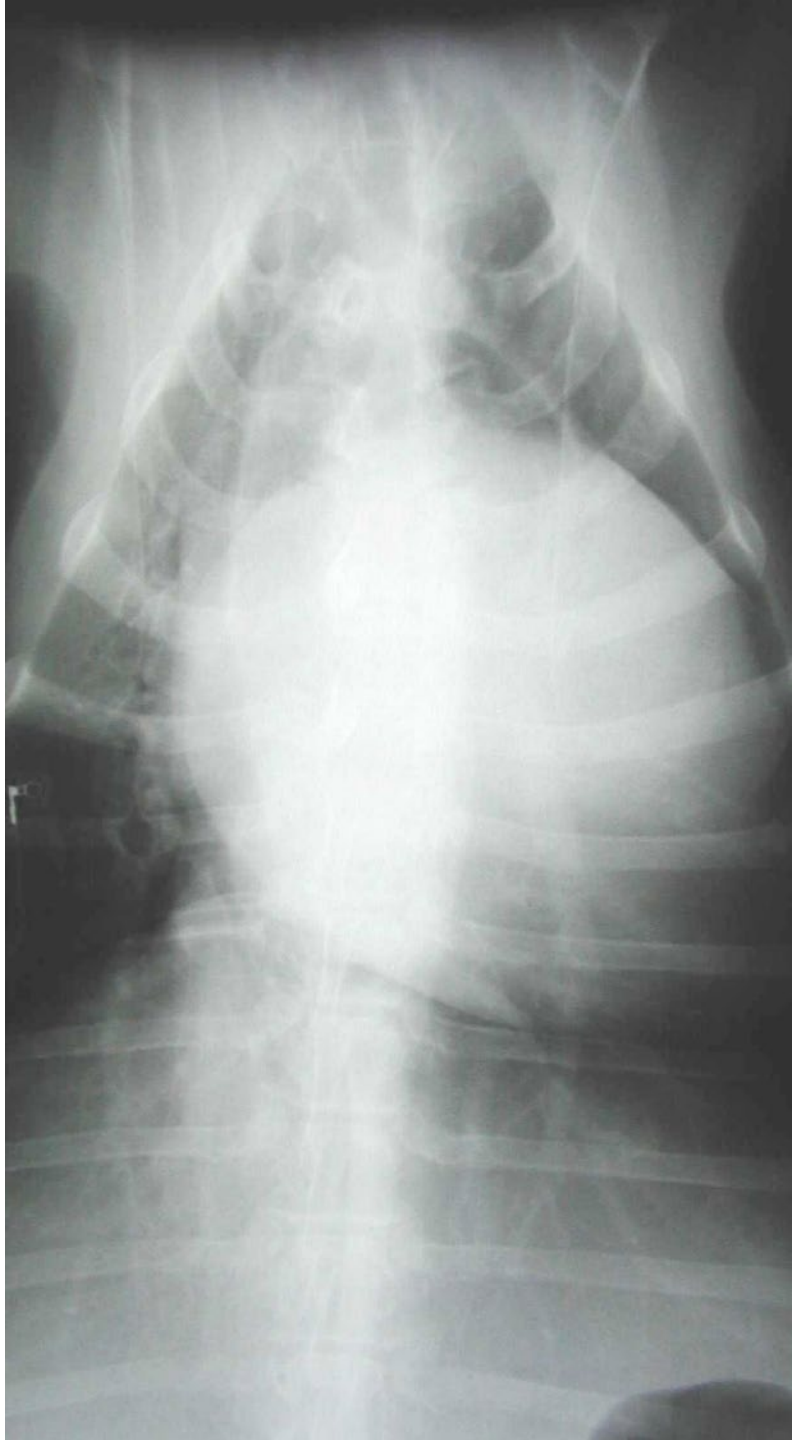
- **MYOCARDITIS**
- **TACHYCARDIA-INDUCED CARDIOMYOPATHY:** caused by supraventricular or ventricular tachyarrhythmia (ventricular systolic dysfunction and dilation; clinically HF that is reversible with normalization of heart rate).

- Cat – Most common cause of heart disease (70-90% of all feline heart disease)
- Dog – 2nd most common heart disease (12-20% of canine heart disease)
- Ferret – common heart disease
- Horses, primates, hamsters, mice, rats, turkeys, cattle, sheep, goats, zoo ruminant species

Canine dilated cardiomyopathy

- Heterogenous condition
- End-stage of myocyte damage/dysfunction
- DCM genetics
  - Doberman pinschers: Pyruvate dehydrogenase kinase 4 and Titin gene
    - Schnauzers – Giant and Standard – RBM20 variant
    - Welsh Springer Spaniel- Phospholamban

- Systolic dysfunction
  - Hallmark finding
- Diastolic dysfunction
  - In cases with CHF

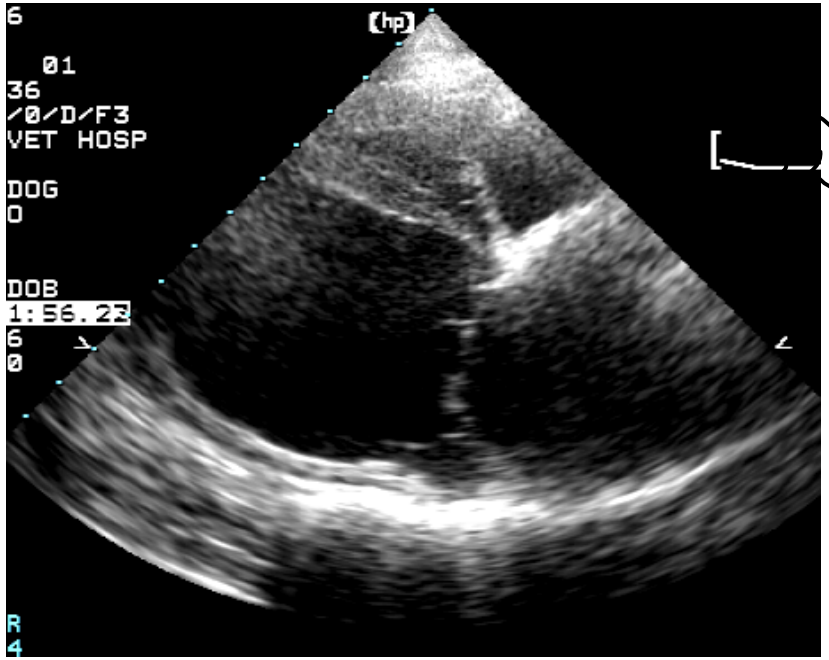


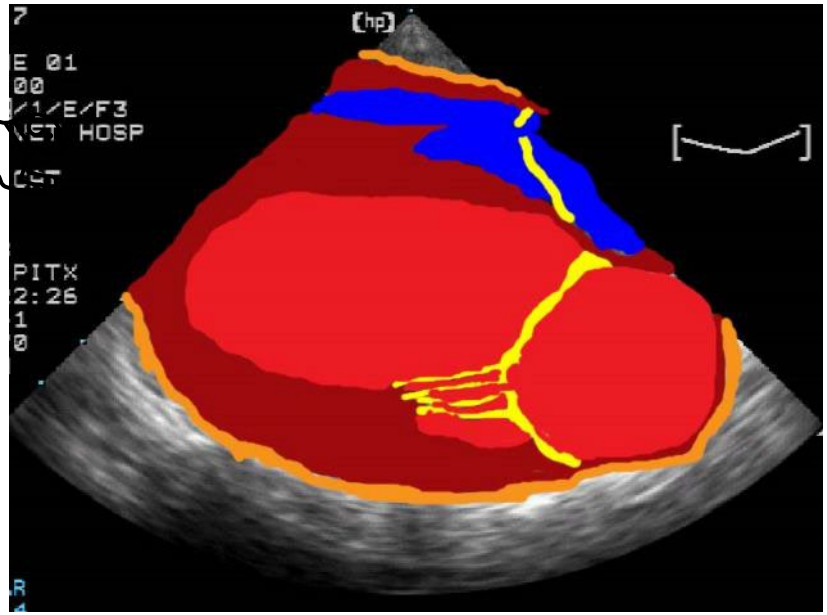
Generalized cardiomegaly

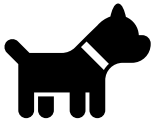
Canine dilated cardiomyopathy

Echocardiography

- Dilation of all cardiac chambers (LV)
- Reduced ejection fraction (<45%)
- LV walls are thinned
- Papillary muscles atrophied
- Left atrial enlargement if CHF
- Mitral and tricuspid regurgitation





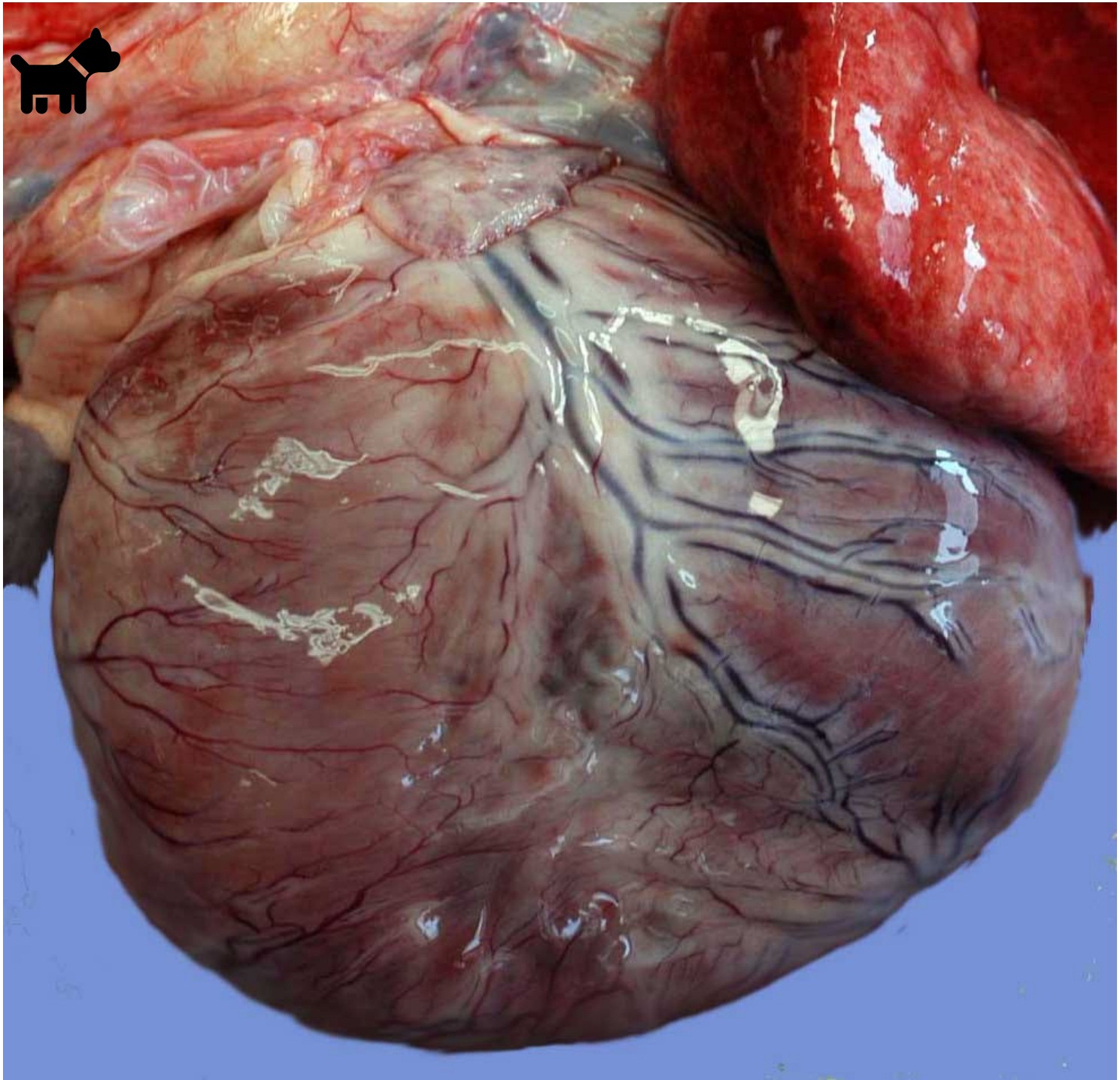


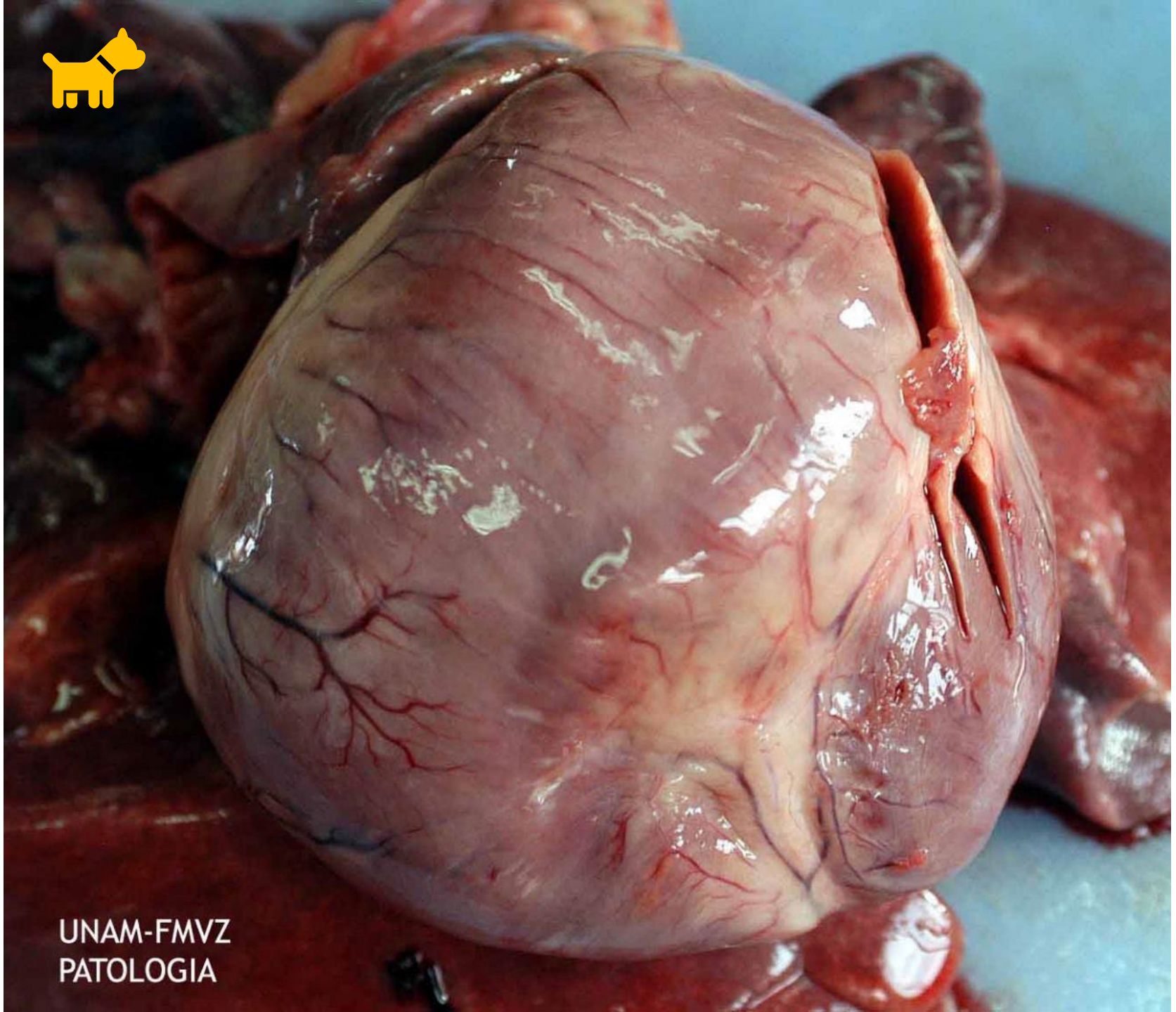
Canine dilated cardiomyopathy

Most common gross and histologic findings

- Dilation of all 4 cardiac chambers
- Thinning of the IVS, LV and RV walls
- Atrophy of the papillary muscles
- Ascites, pleural or pericardial effusion
- Pulmonary edema
- Hepatomegaly

- Fatty infiltration pattern
  - Doberman, Great Danes, Boxer
  - Myodegeneration, atrophy
- Wavy fiber pattern
  - Giant-breed dogs
  - Right atrium and ventricle

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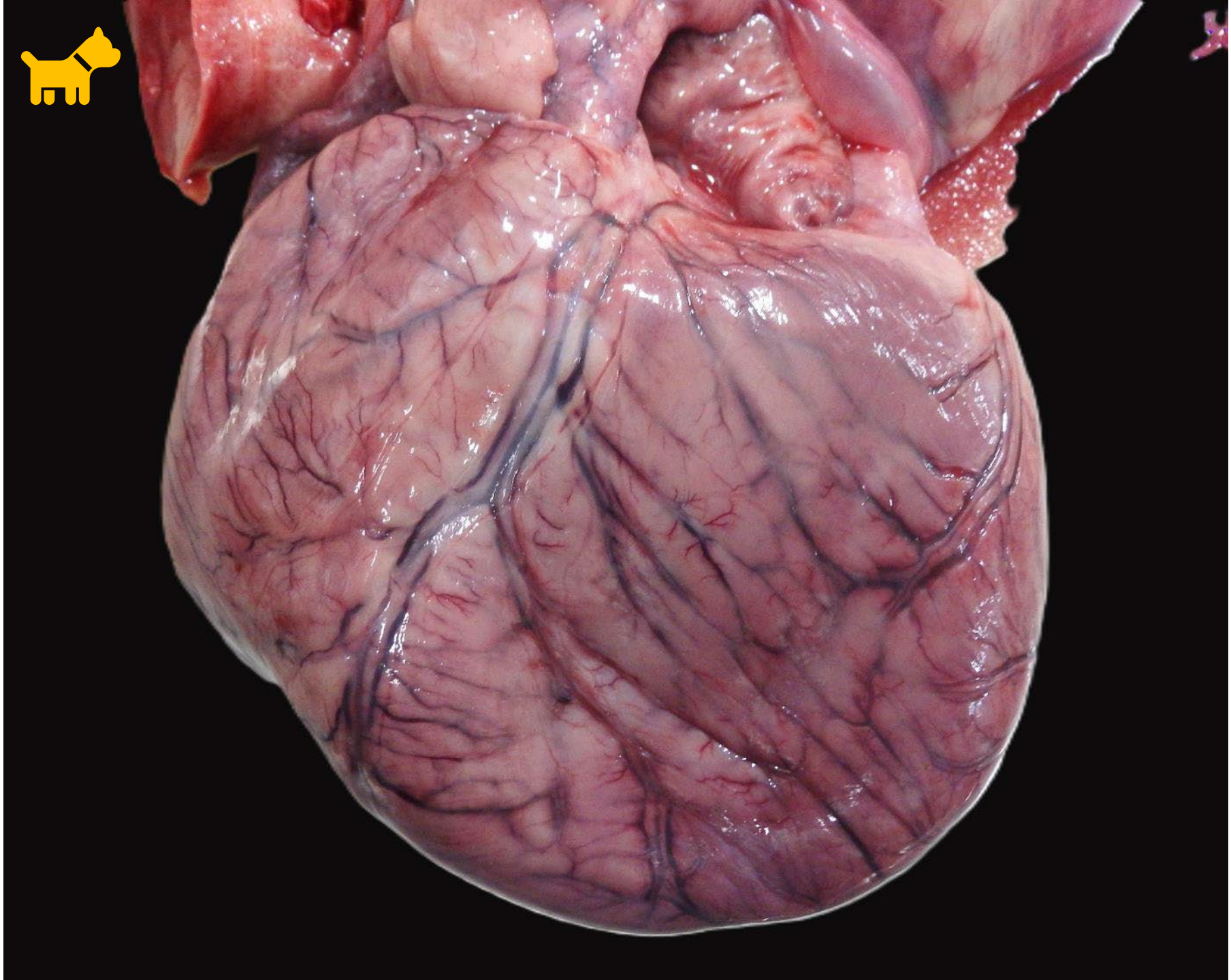

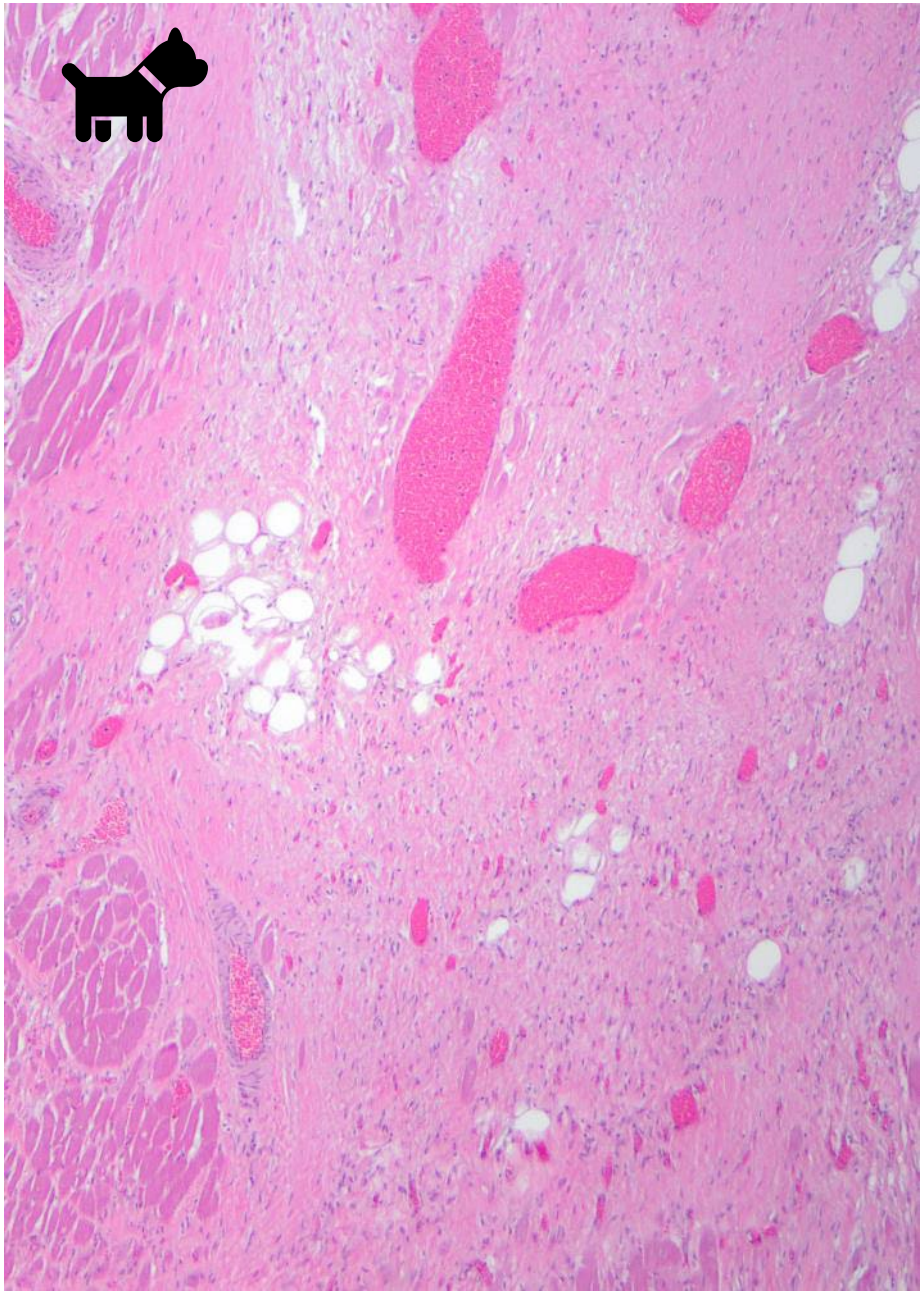

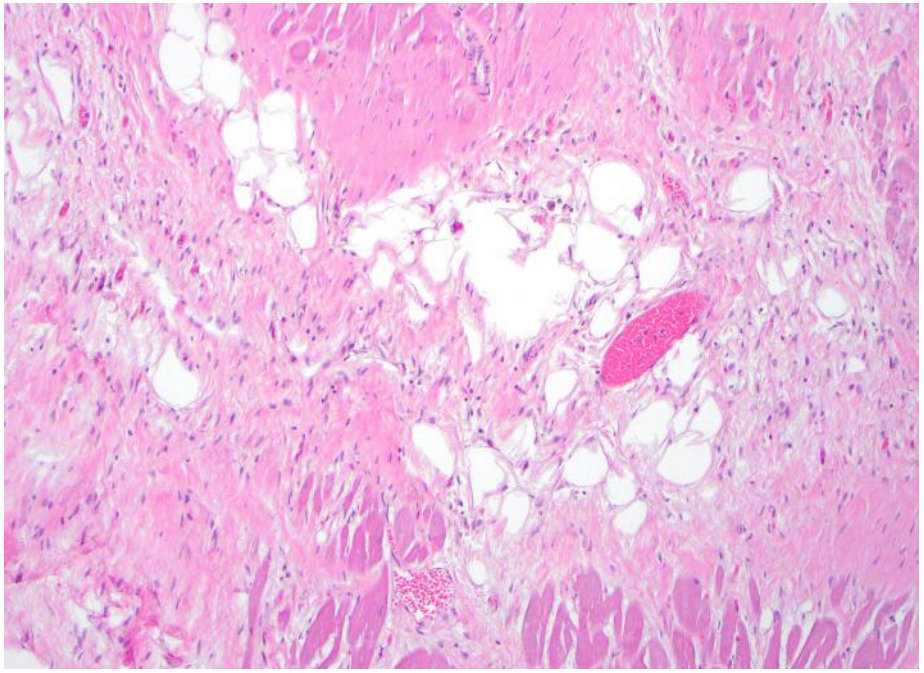

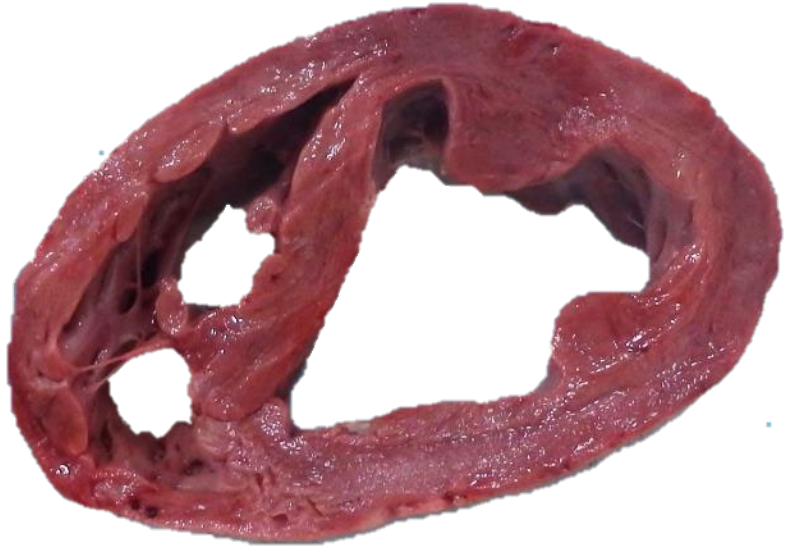

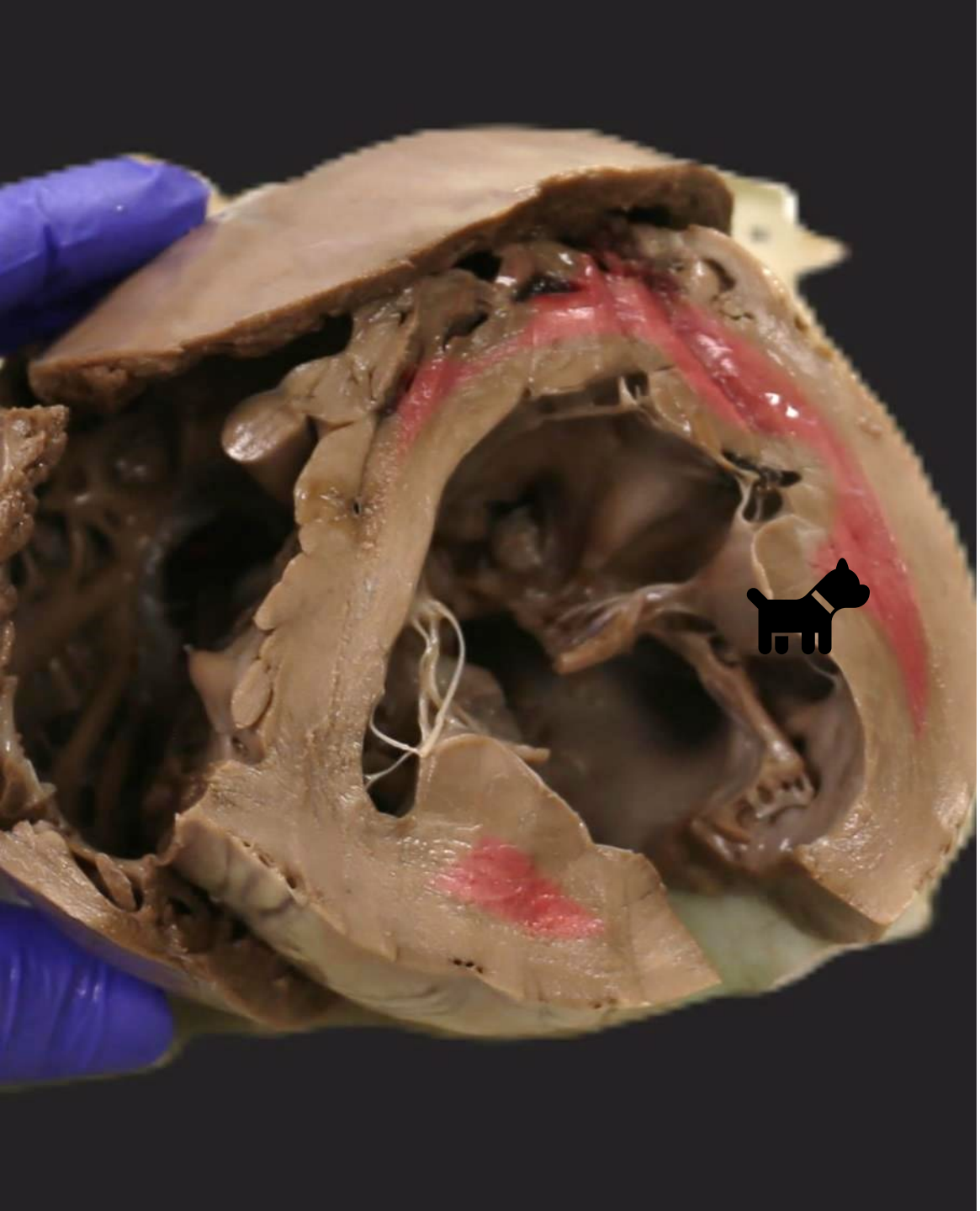

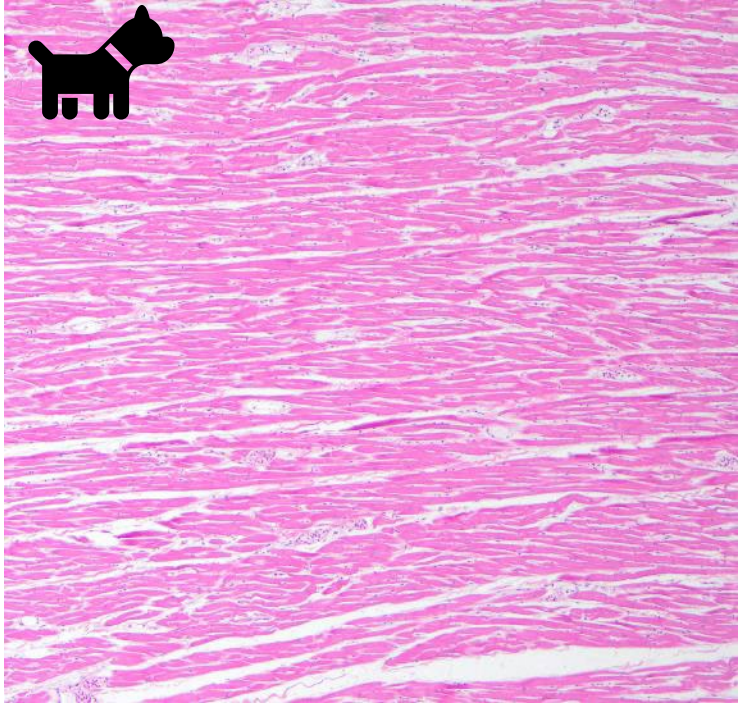

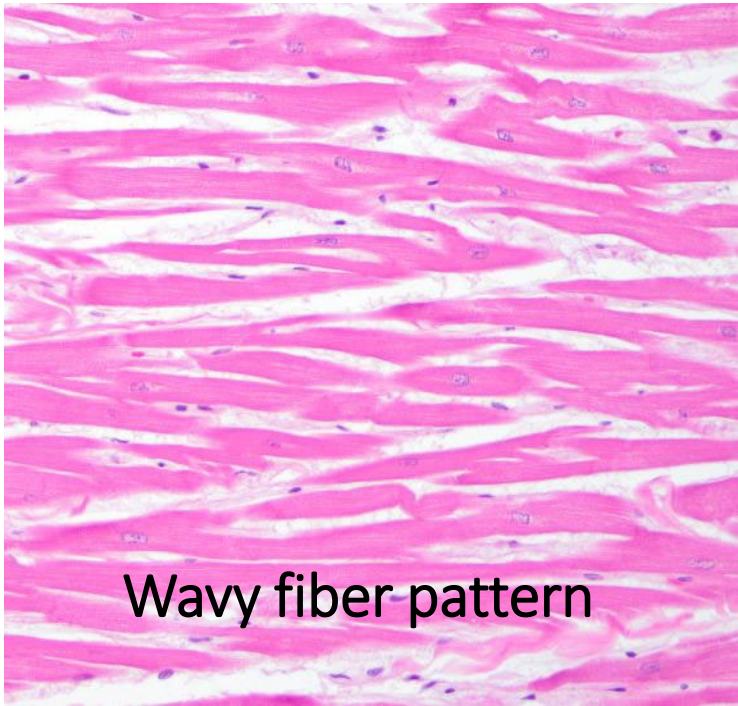

Wavy fiber pattern

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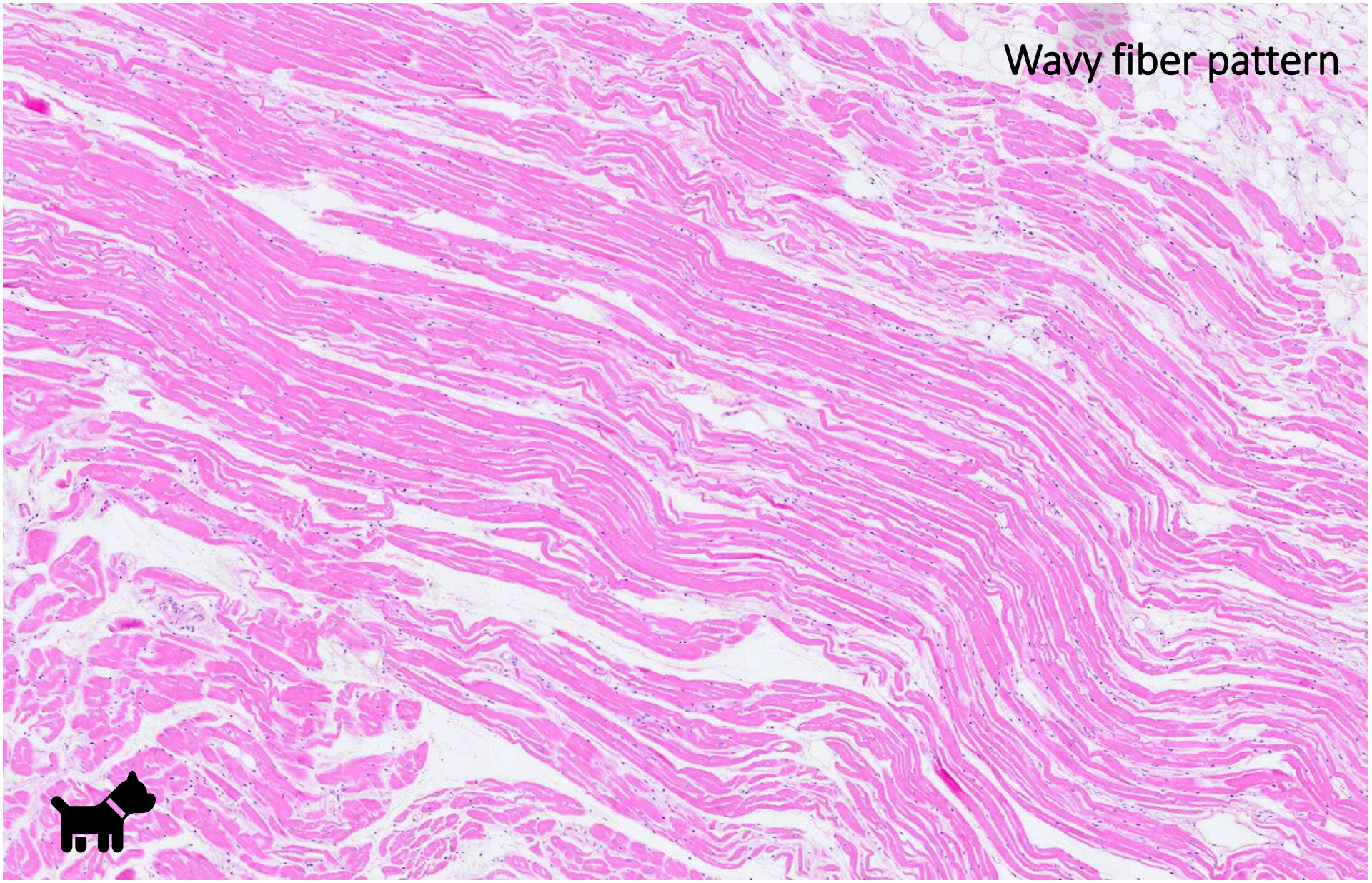
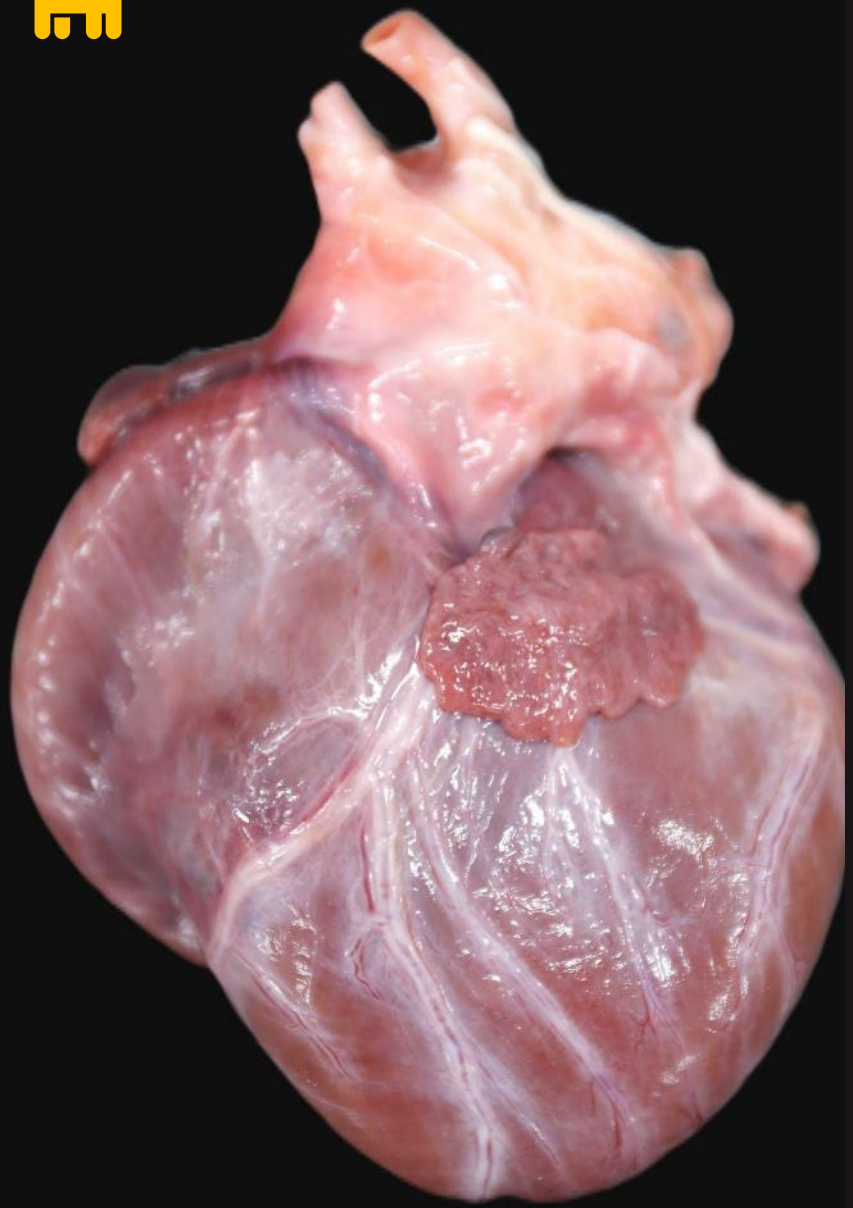
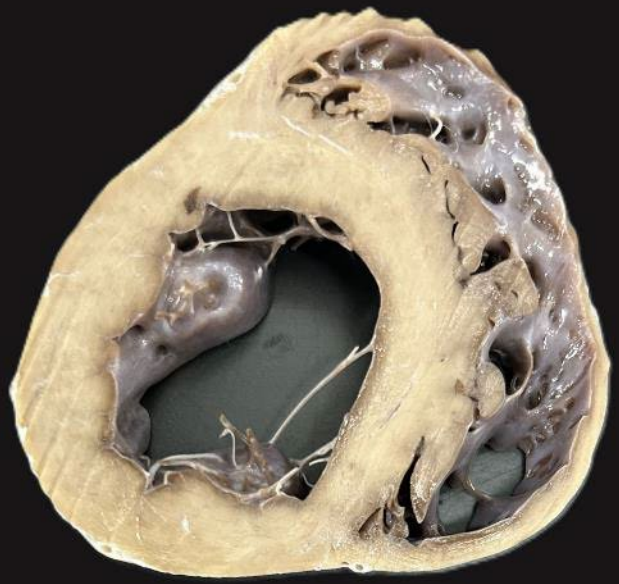
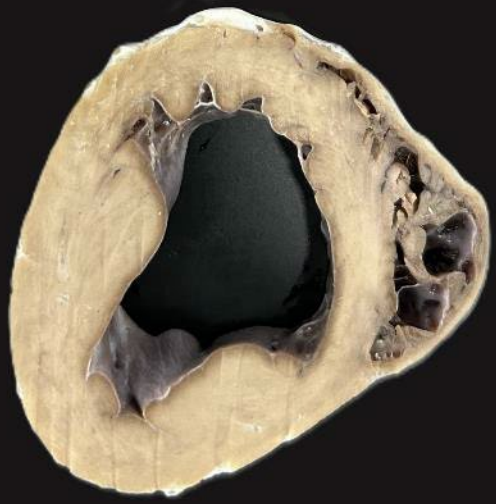
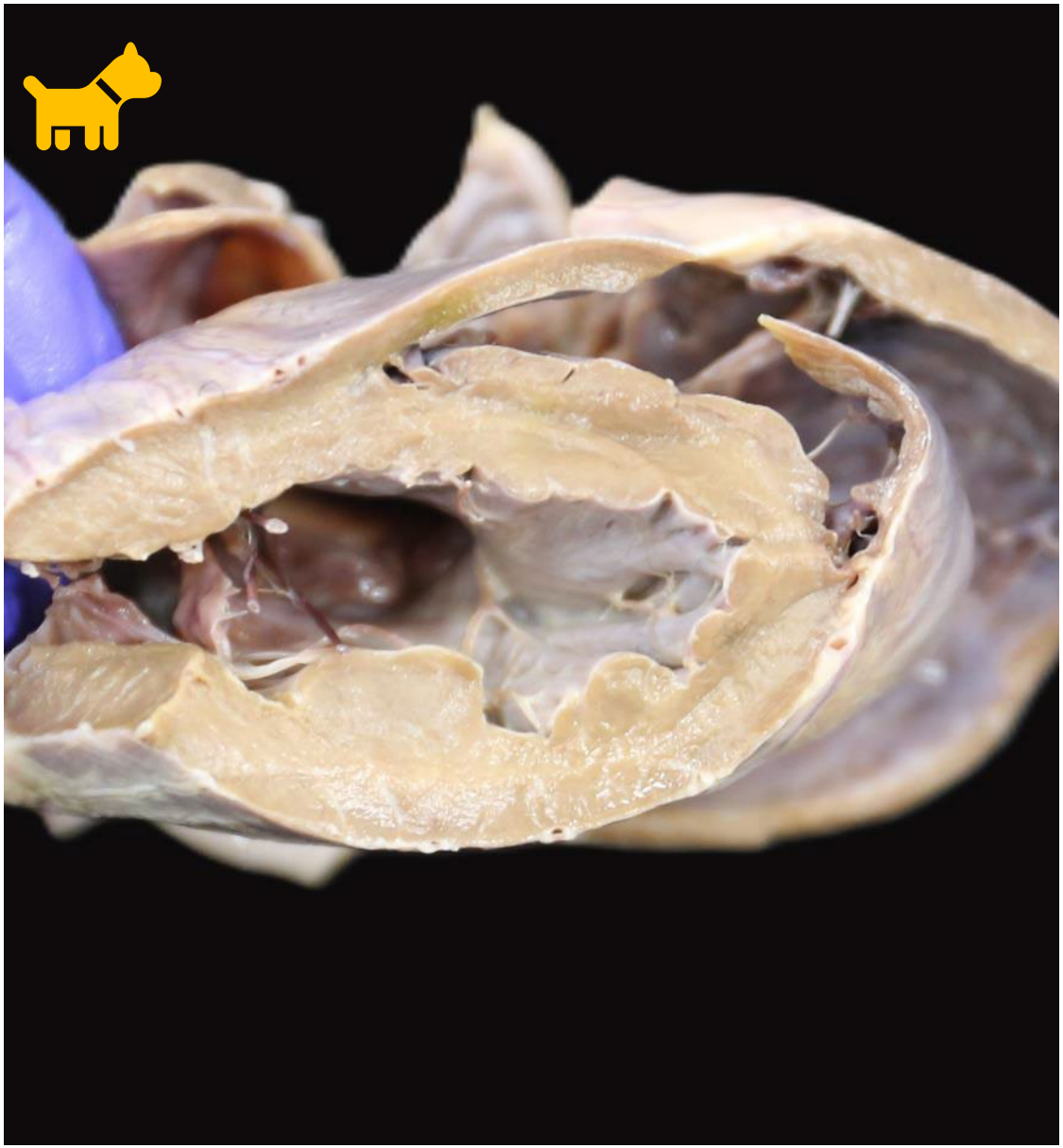
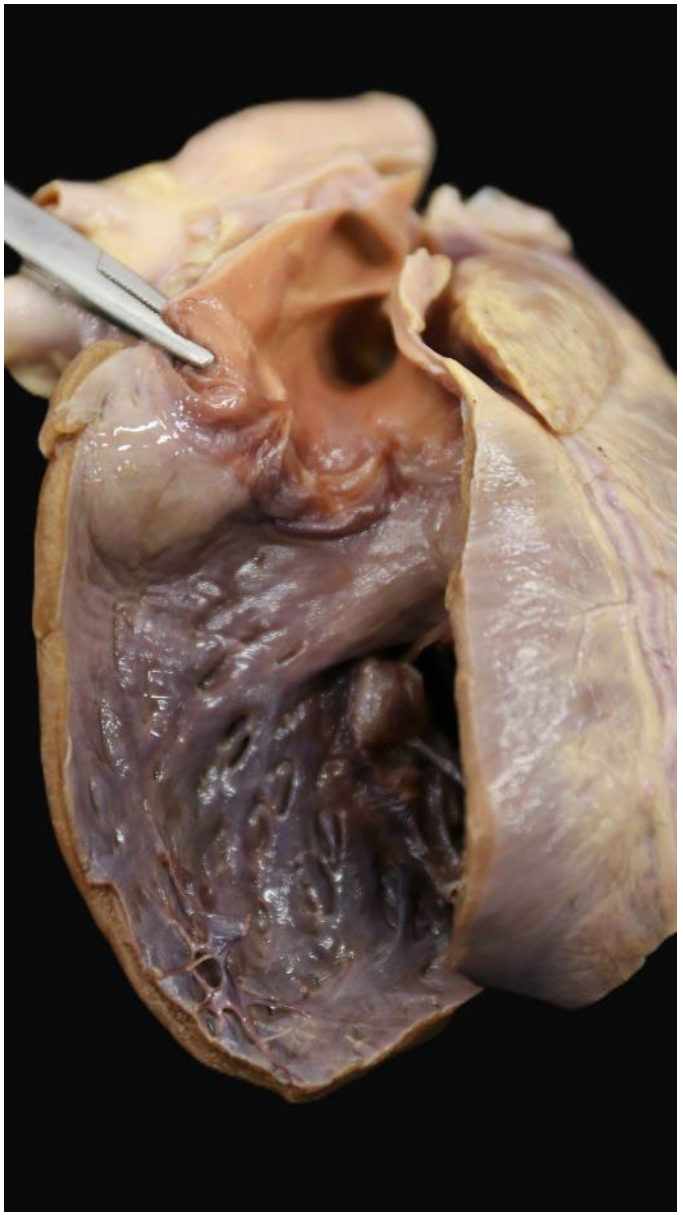


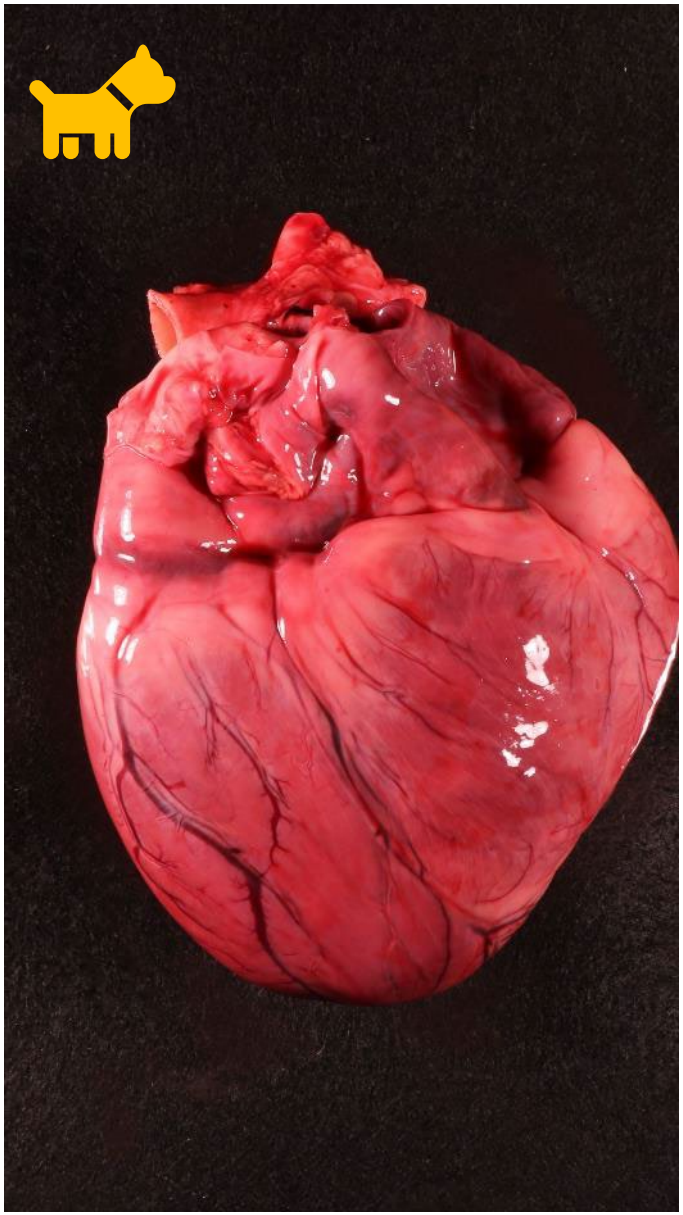


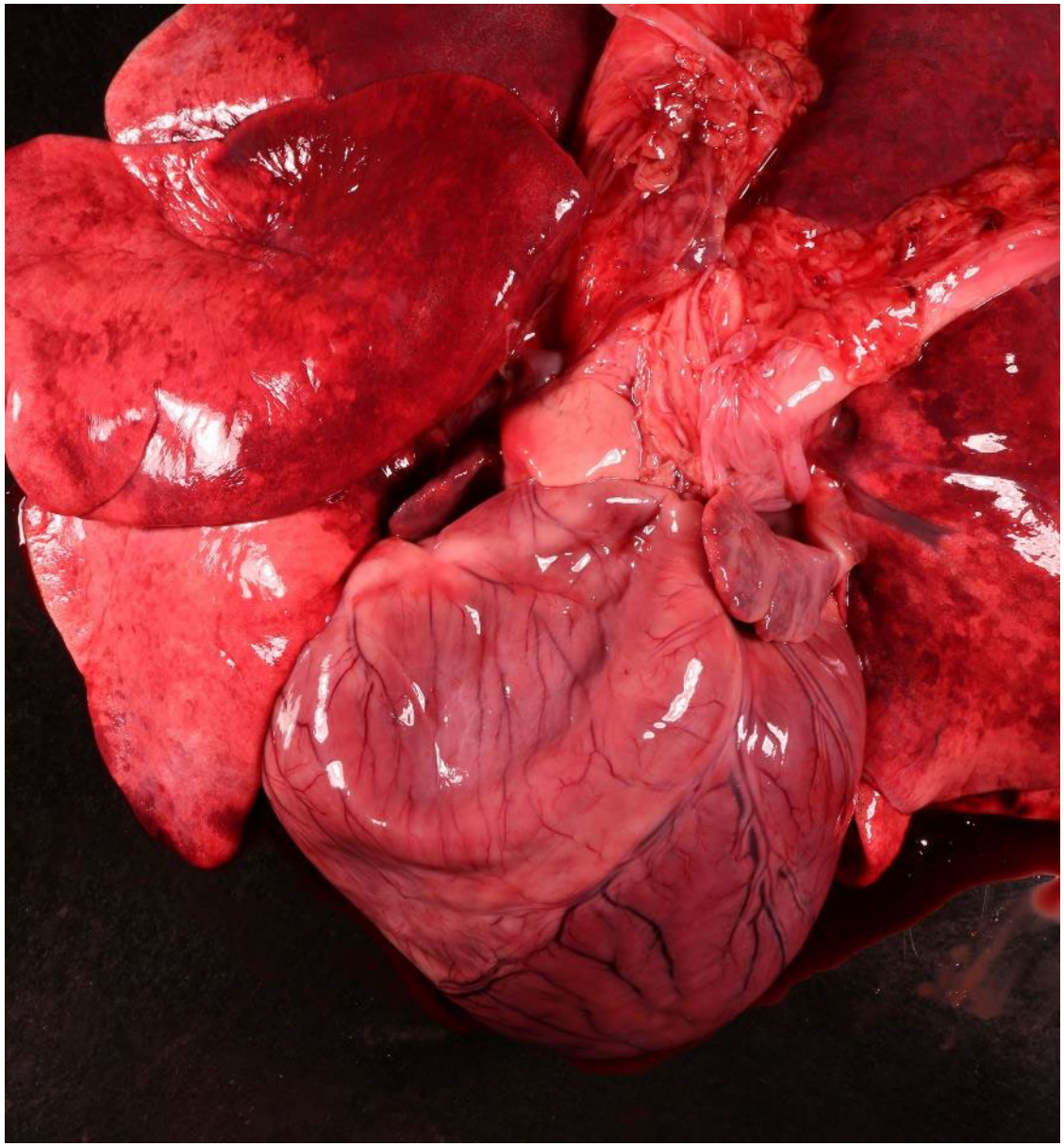


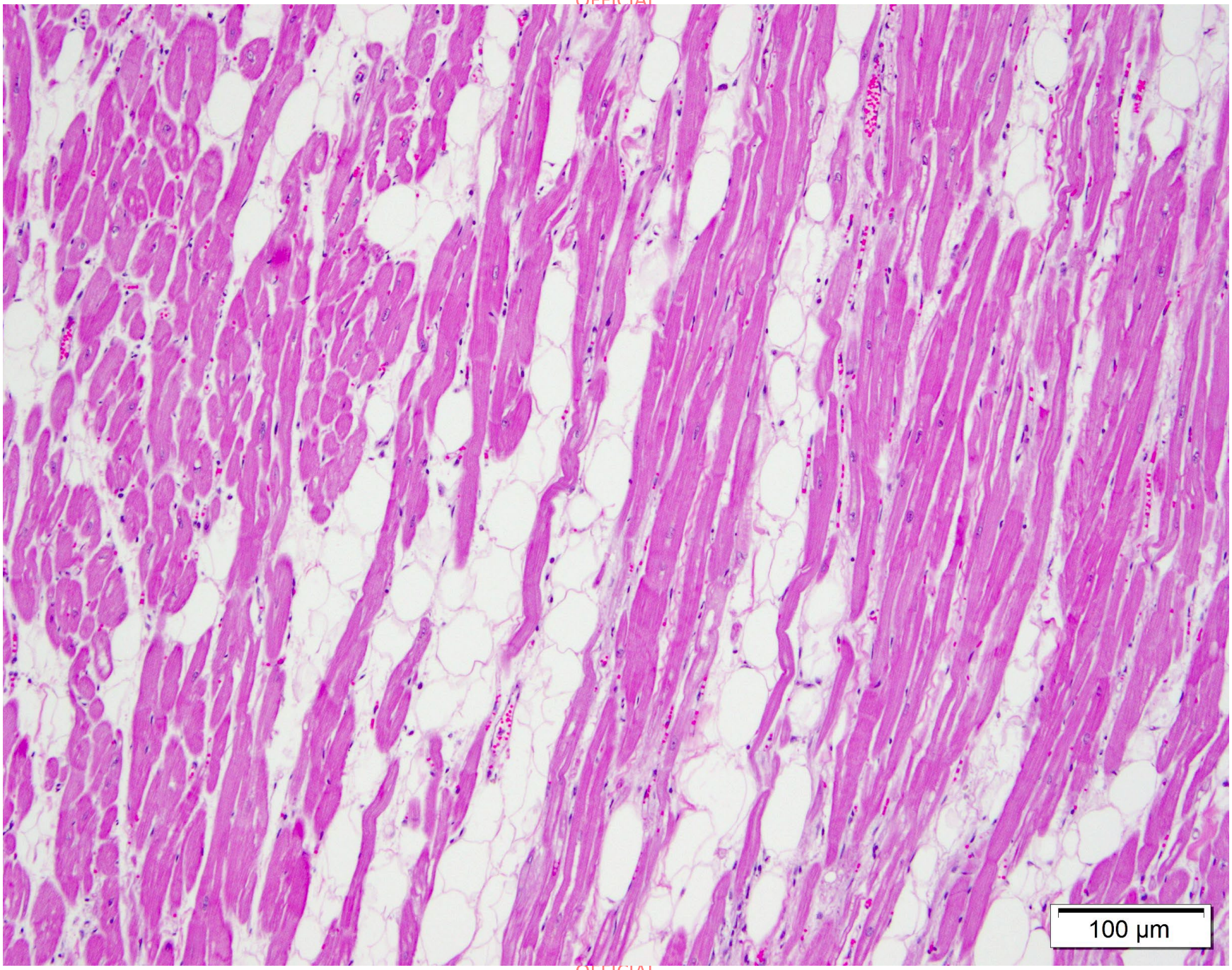


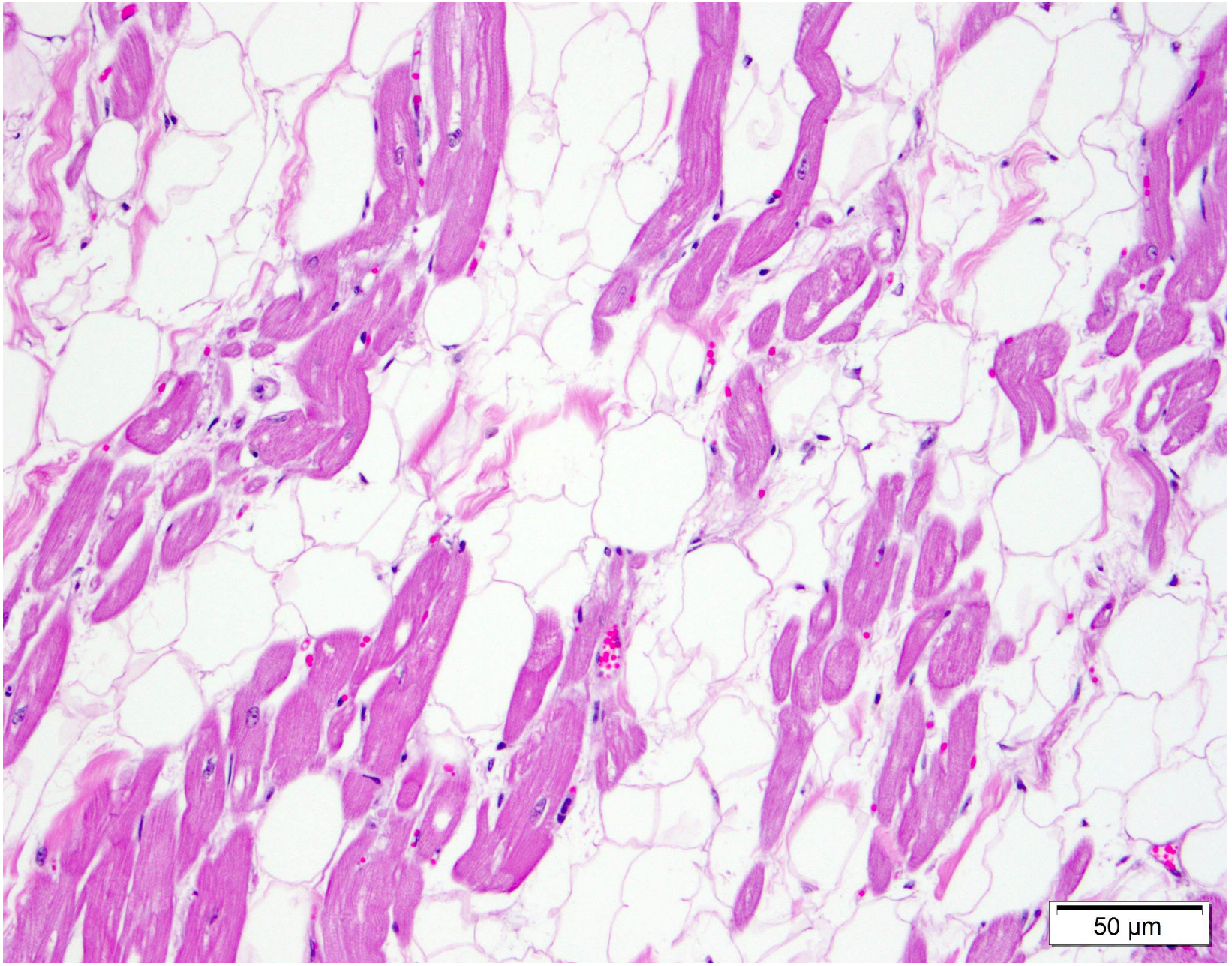


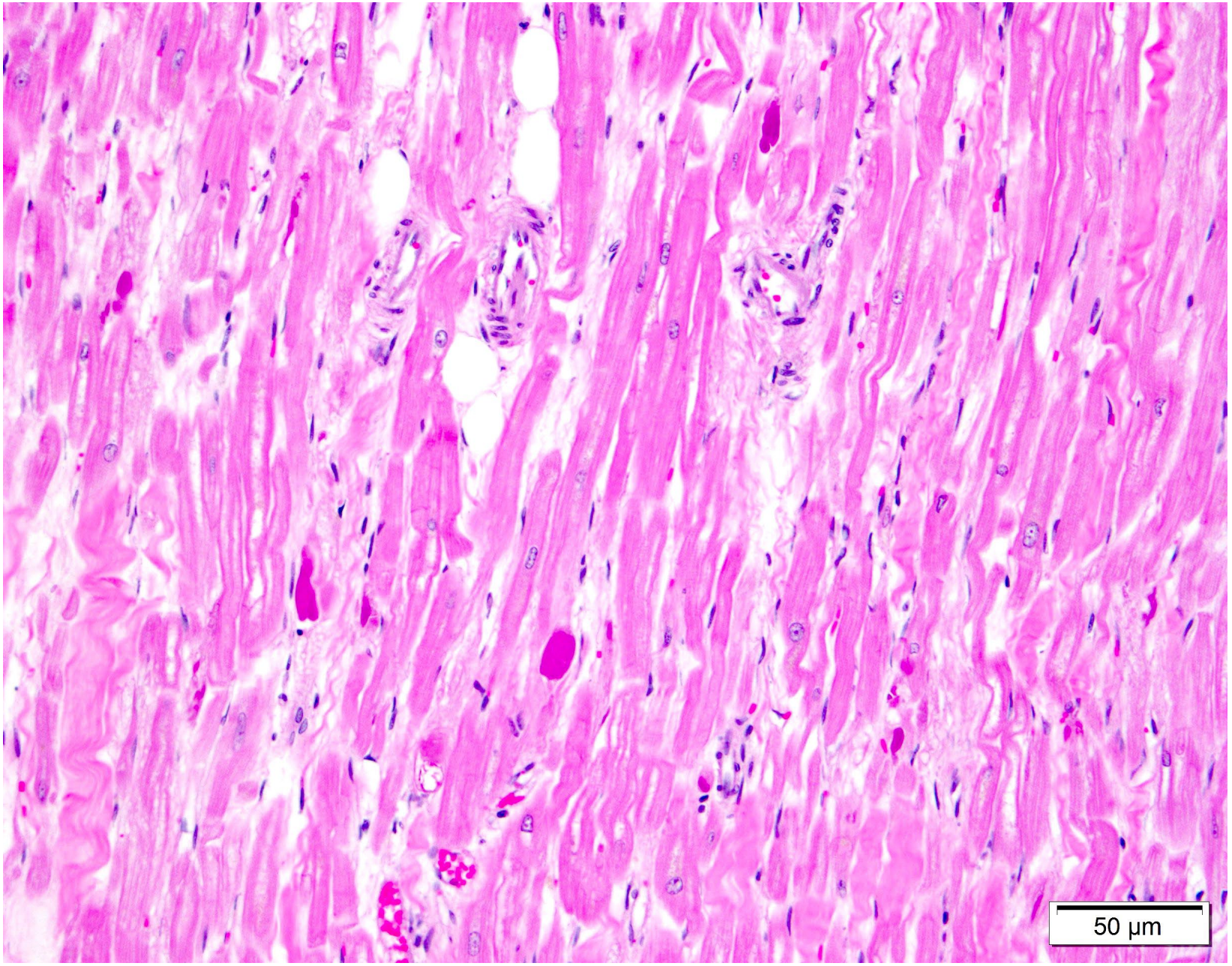






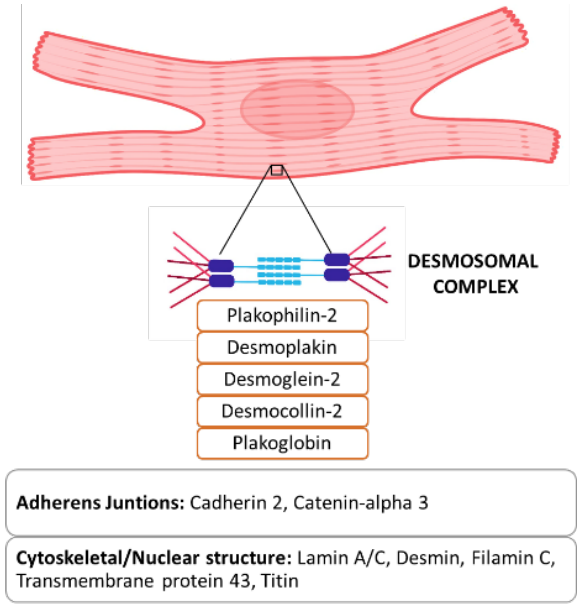






Arrhythmogenic right ventricular cardiomyopathy

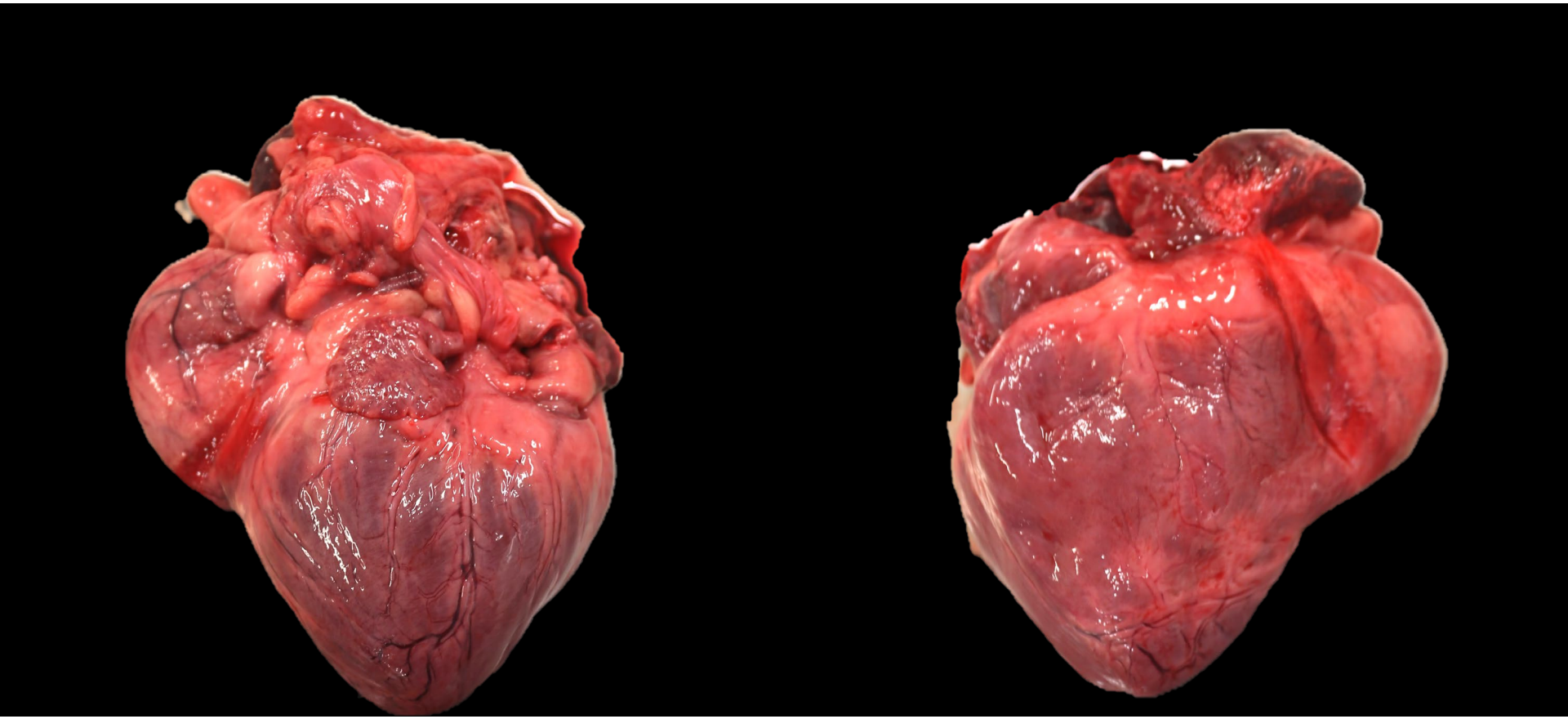
- Boxer; English Bull dog, Labrador Retriever, Dachshund, Siberian Husky, Dalmatian
- Horse and chimpanzees (case reports)
- Right dominant, biventricular, left dominant phenotypes
- Fibrofatty and fatty variants, inflammation, myocyte degeneration/necrosis
- Ventricular arrhythmias (RV)
- Disease of the cardiac desmosome (genetic mutations)

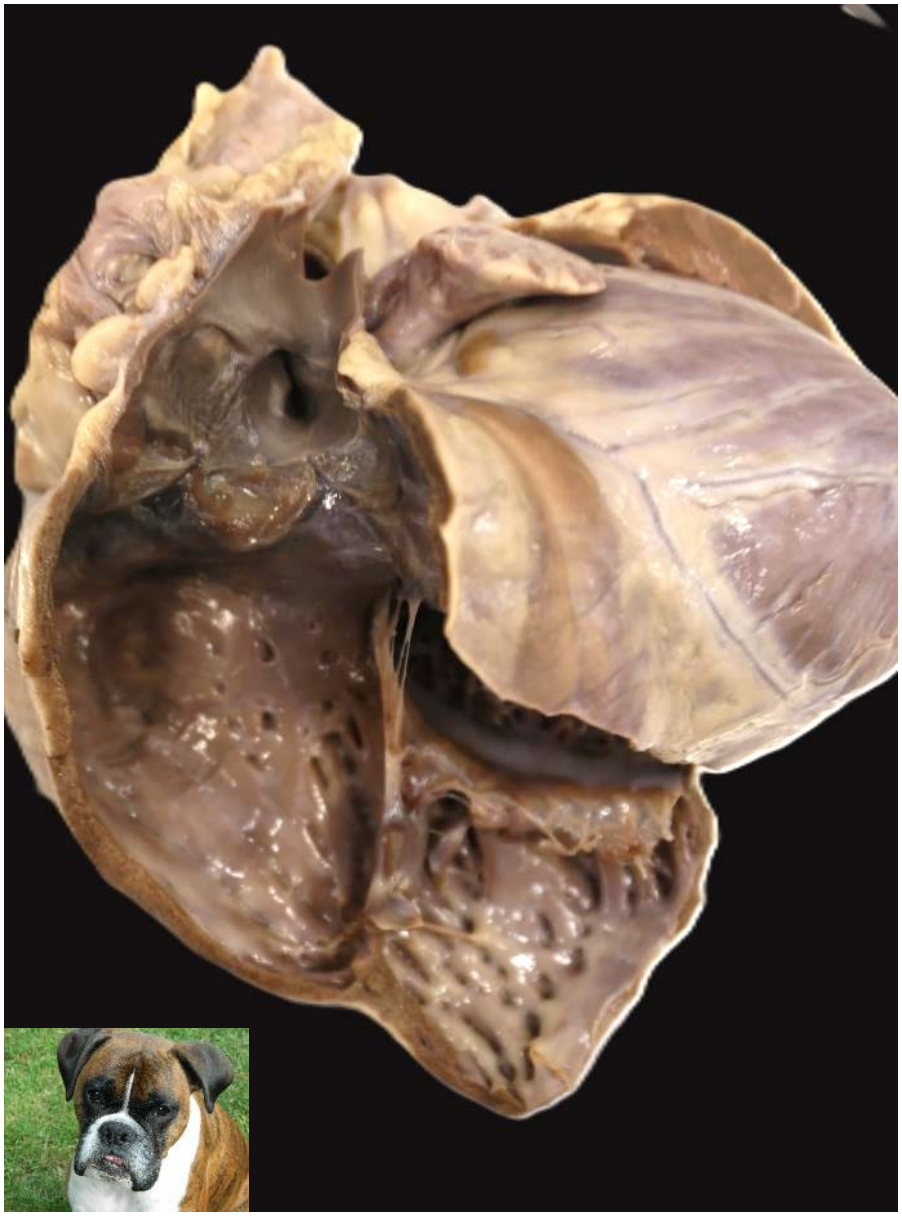


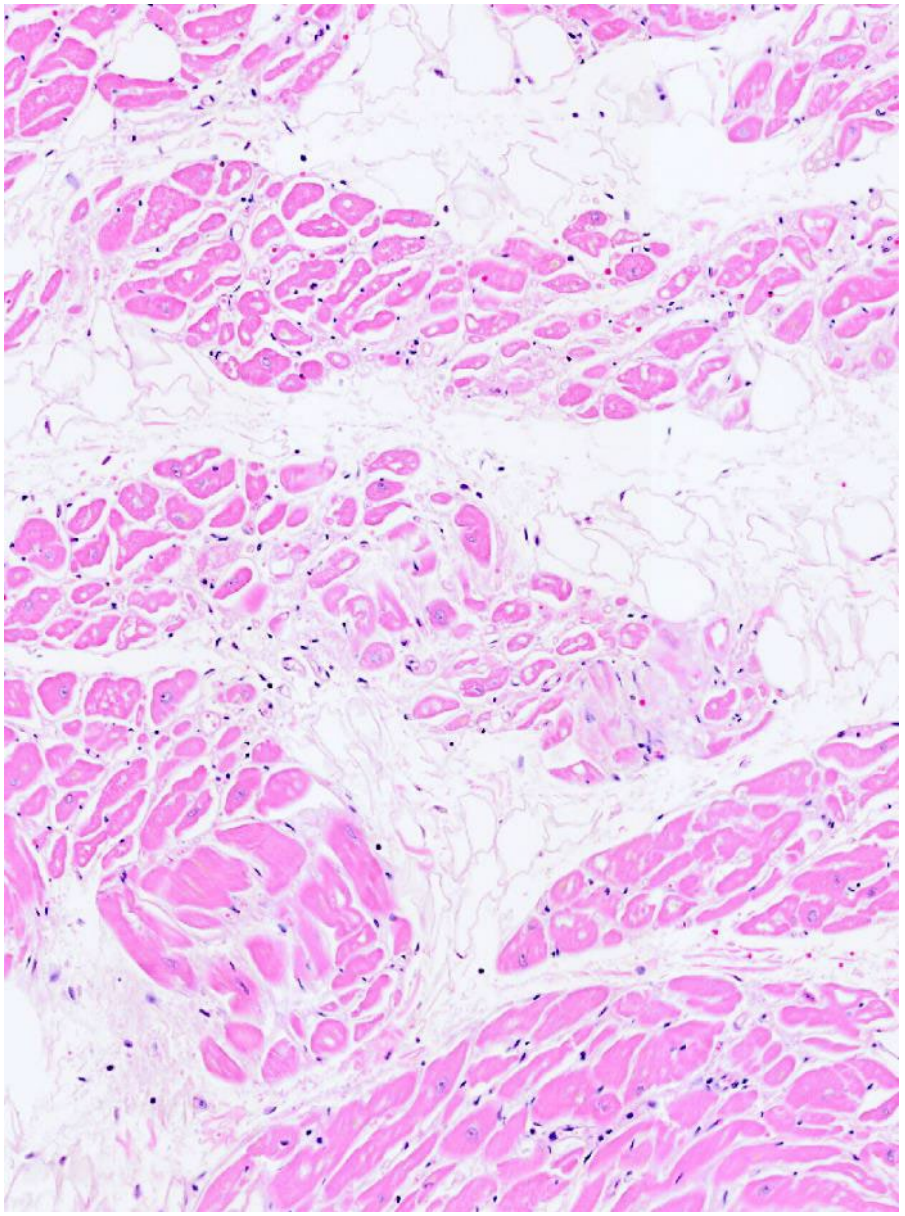
- ARVC1- deletion mutation in the striatin gene (scaffolding protein localized to intermediate filaments and the intercalated disk)
- ARVC2- single-nucleotide polymorphism in a regulatory gene involved in cardiac proteins

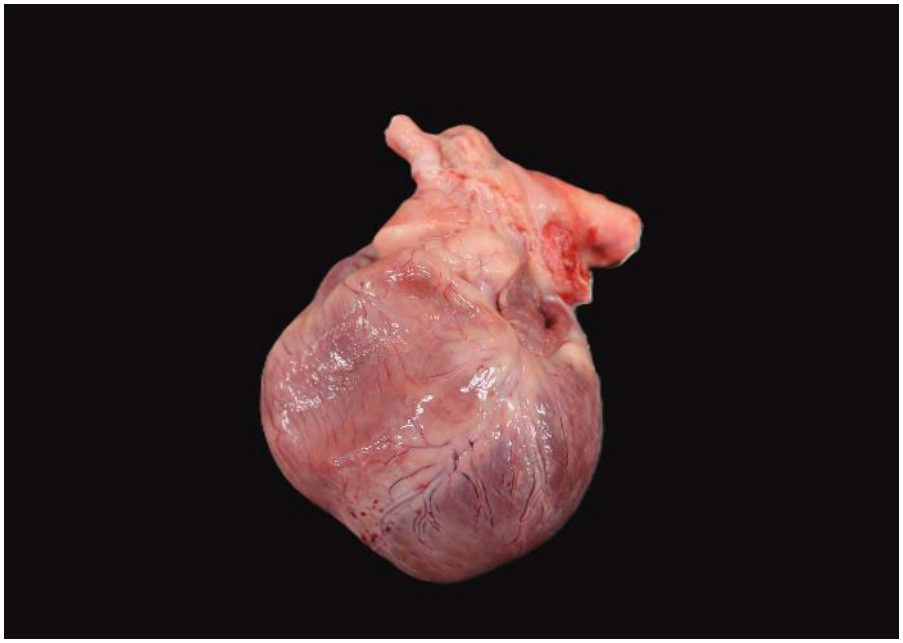
Decreased Wnt signaling in the myocardium of genetically engineered mouse models of ARVC appears to be responsible for increased myocardial adipo- and fibrogenesis.

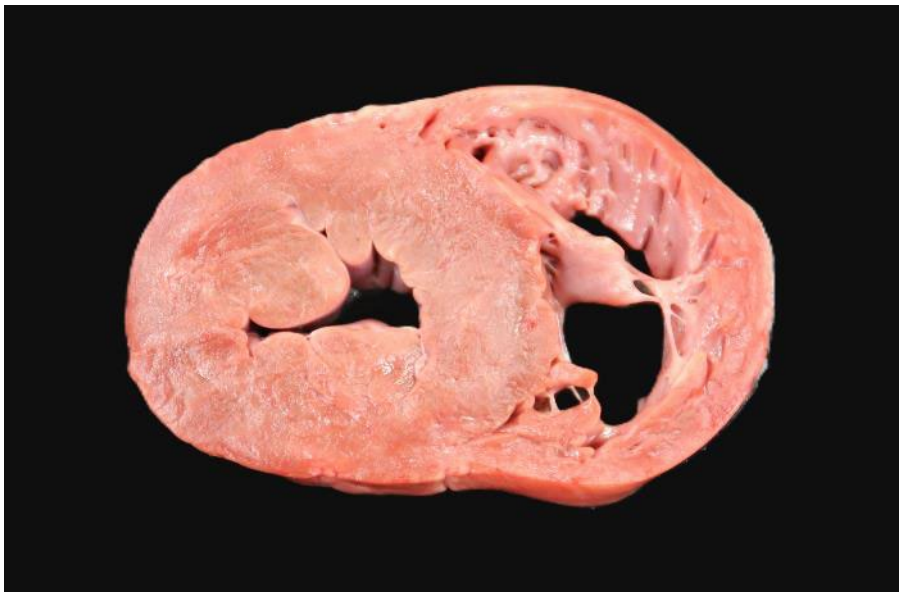
Arrhythmogenic right ventricular cardiomyopathy

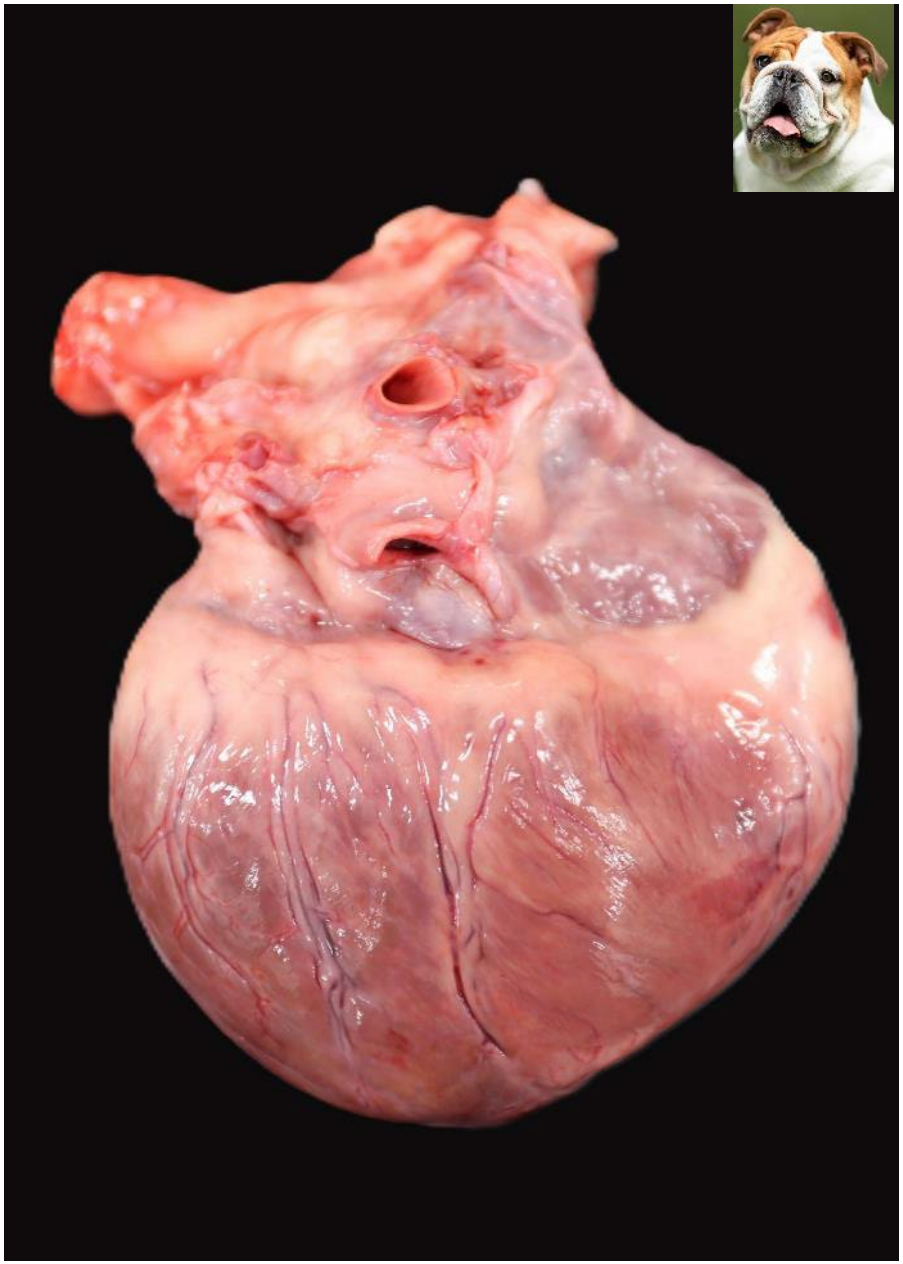


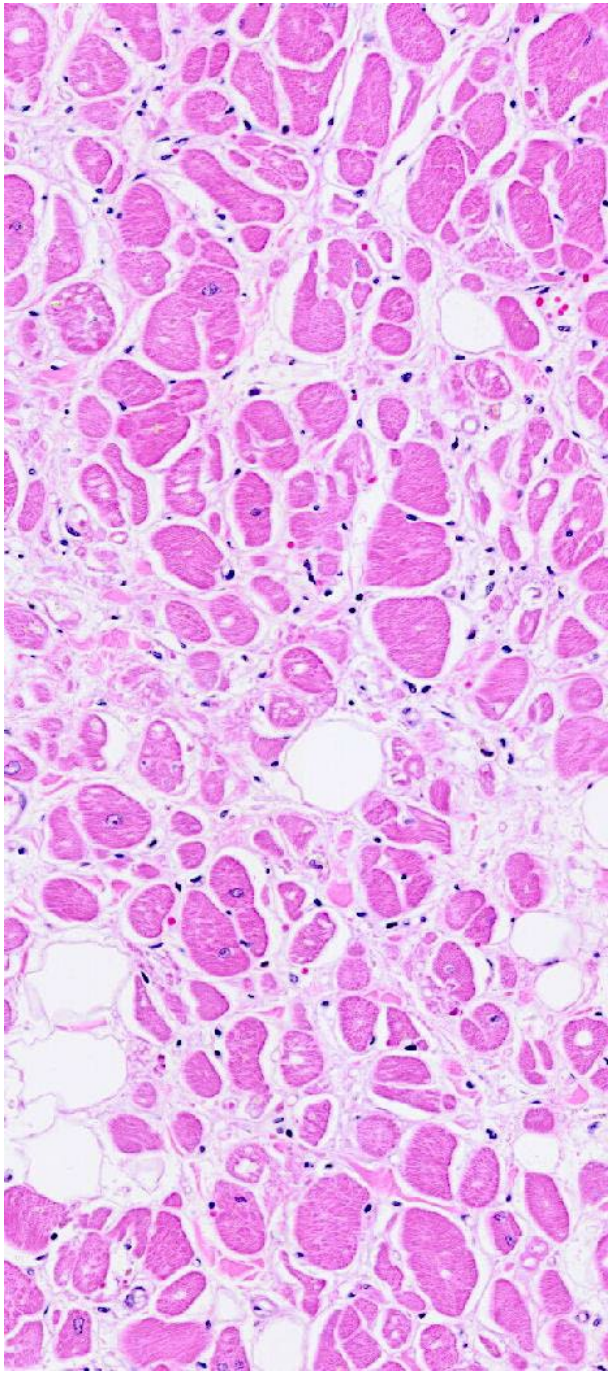


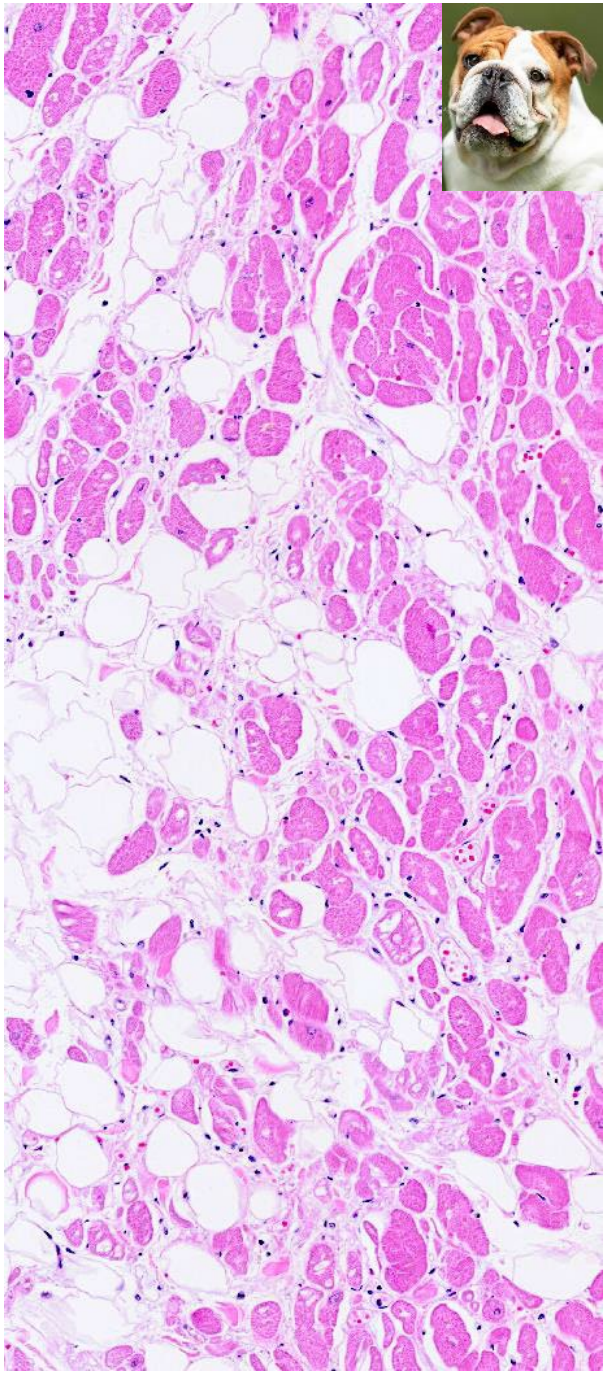


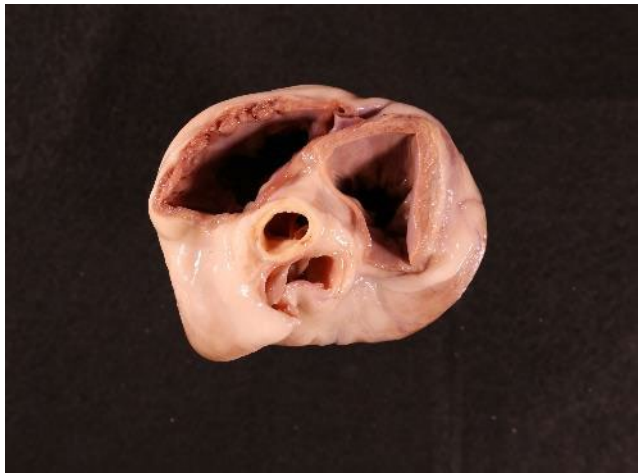


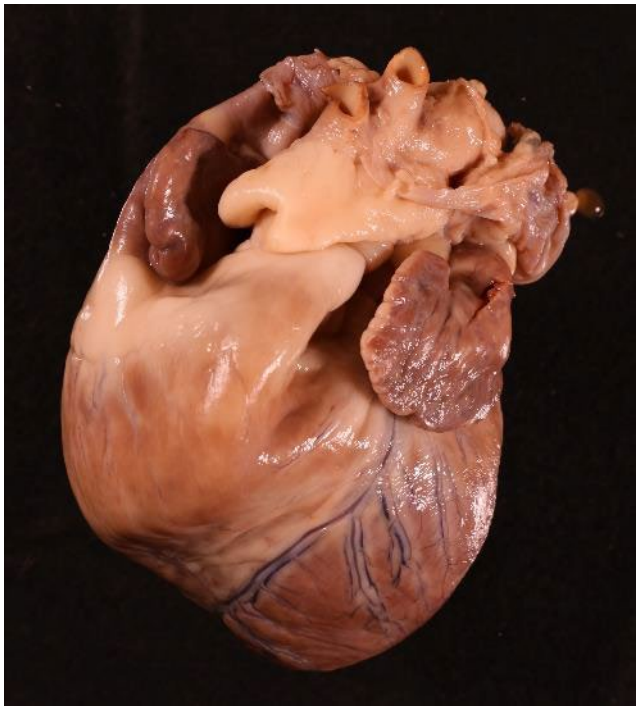


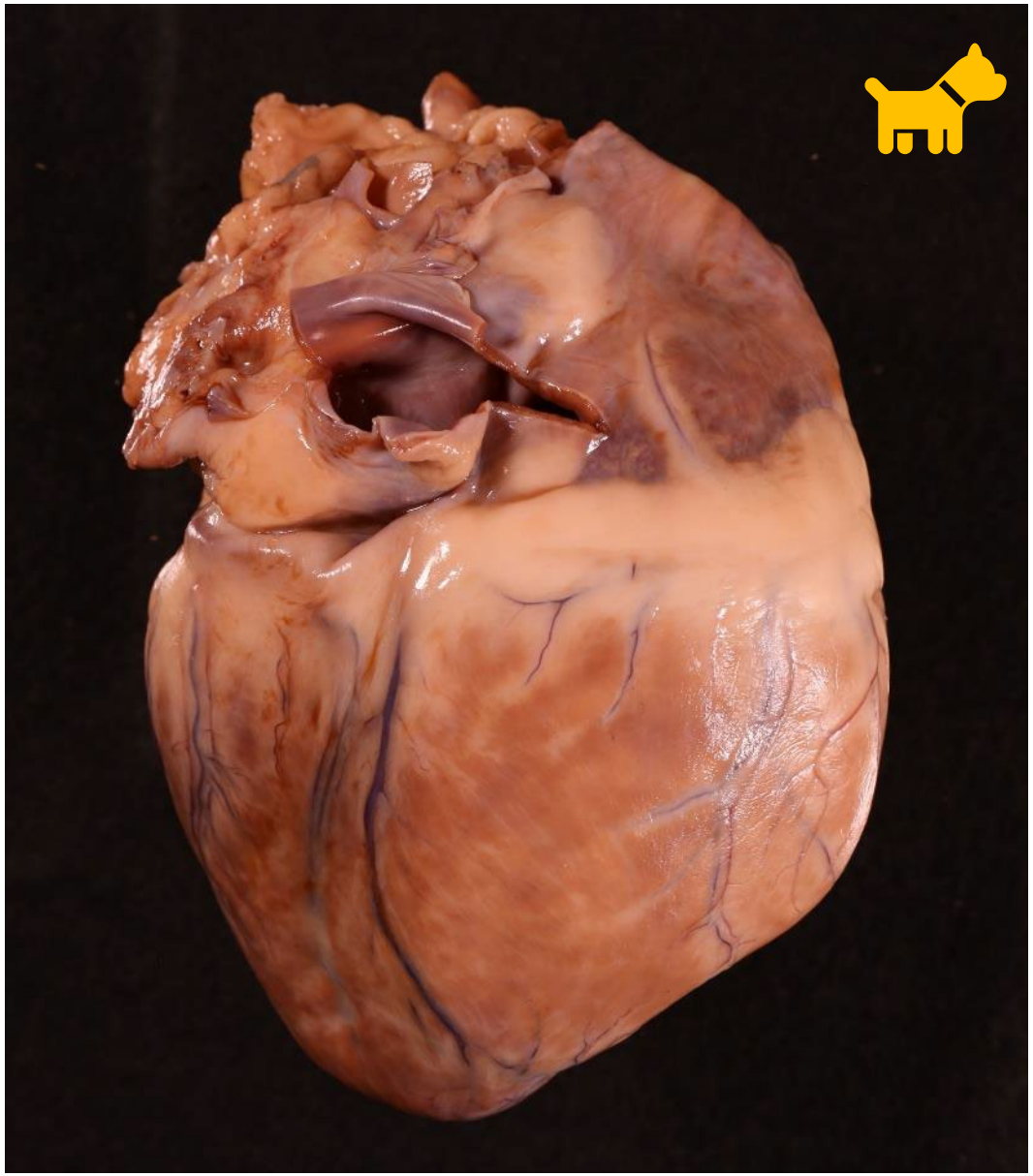


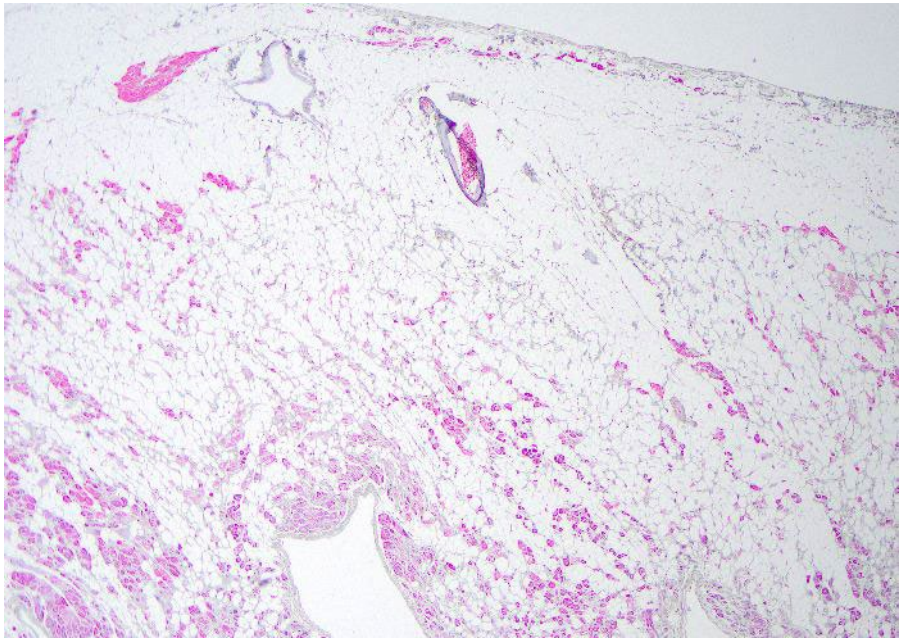


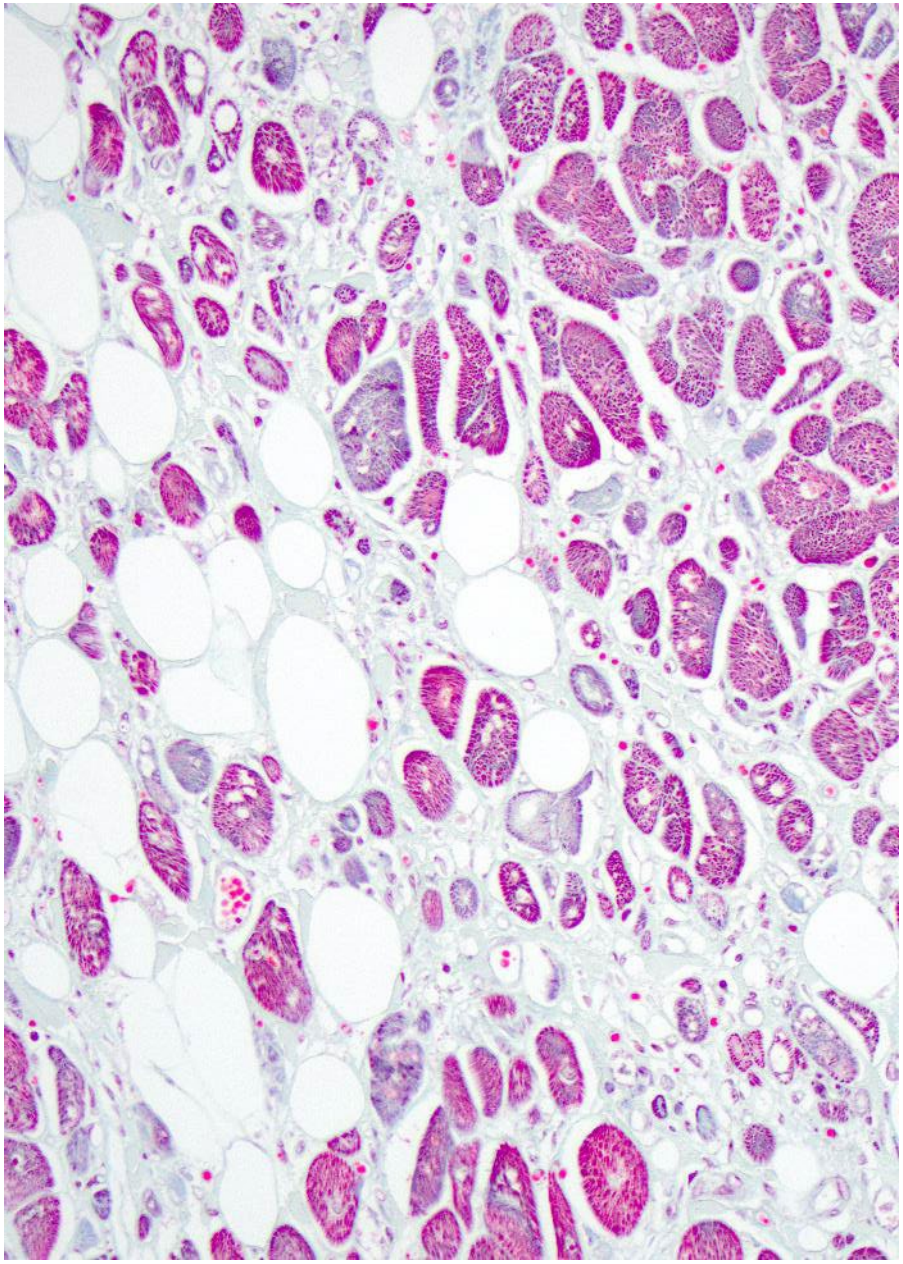


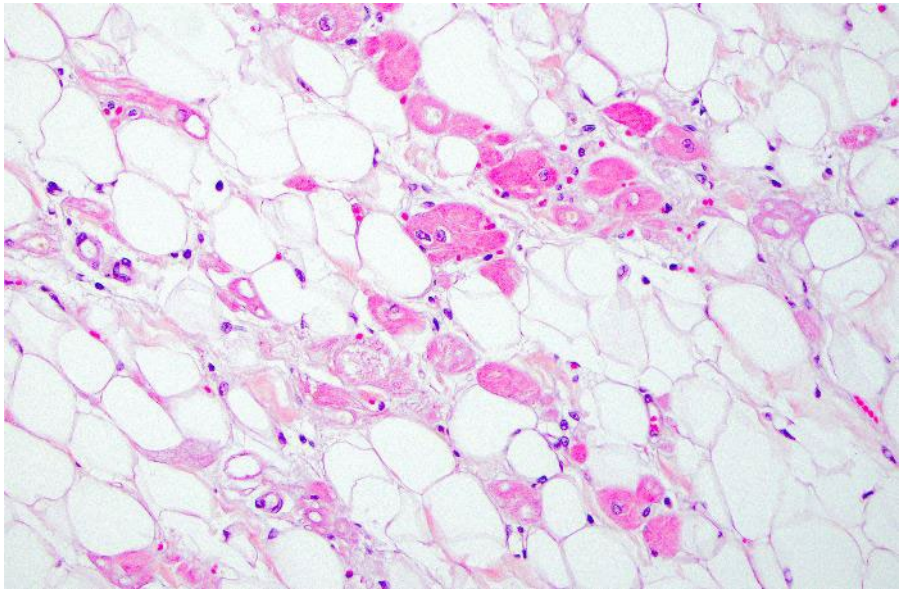


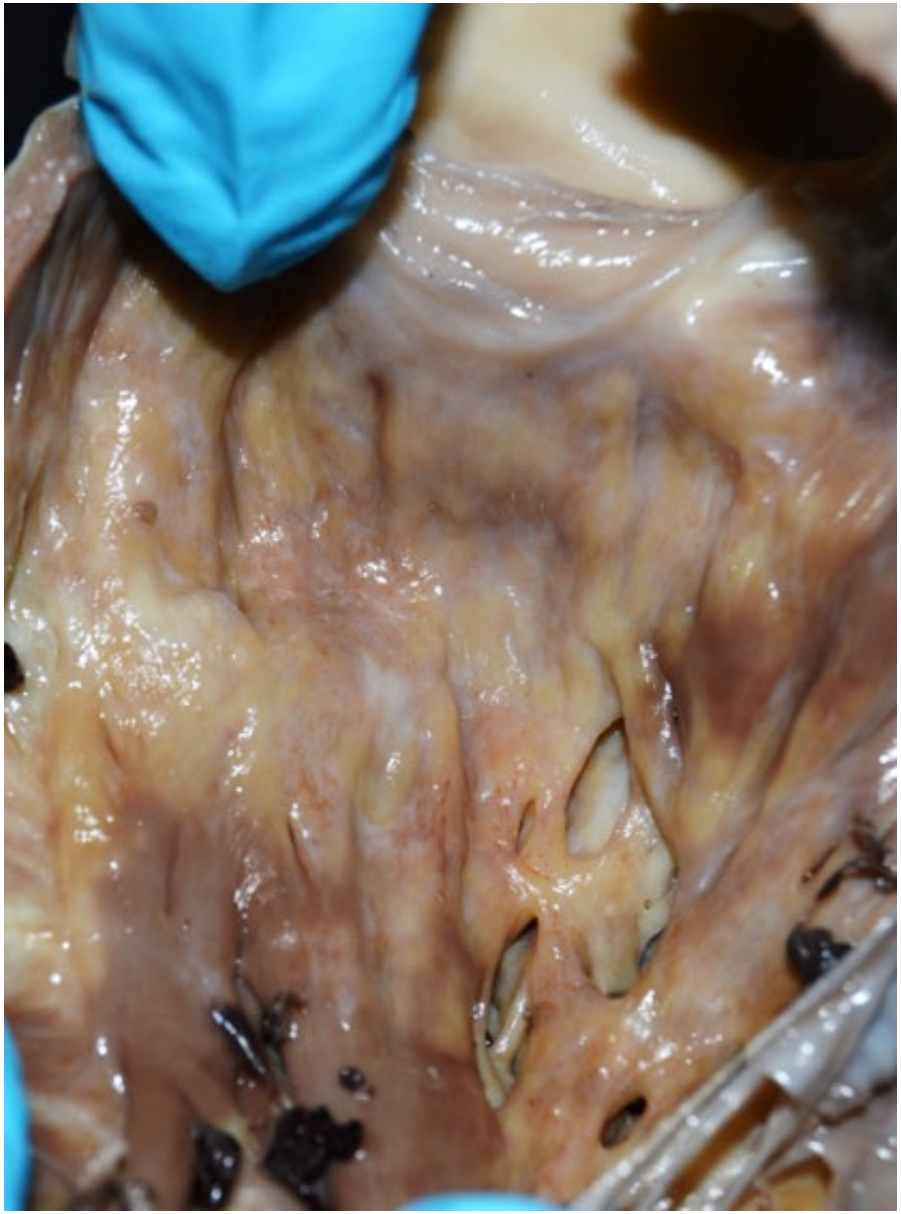


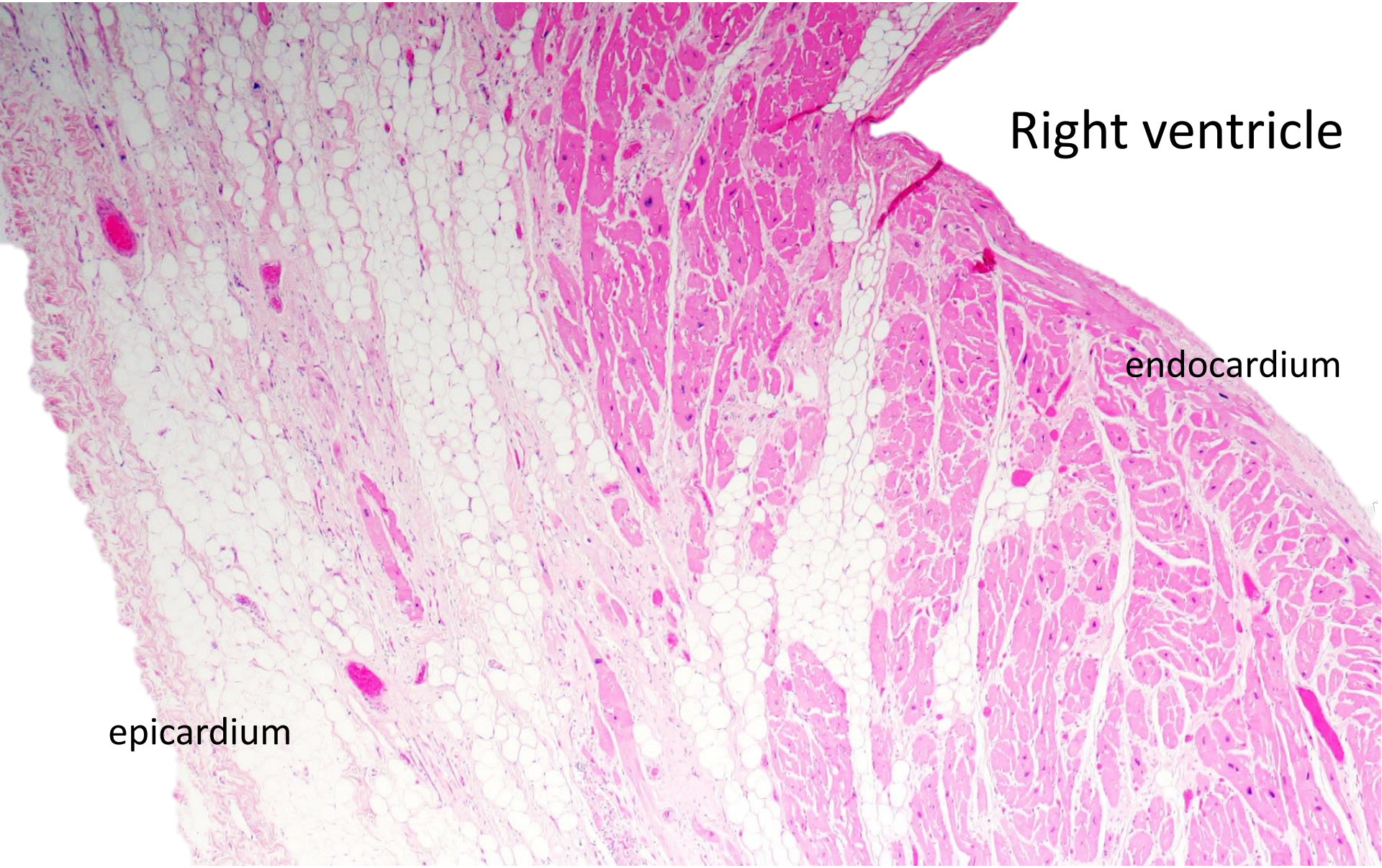


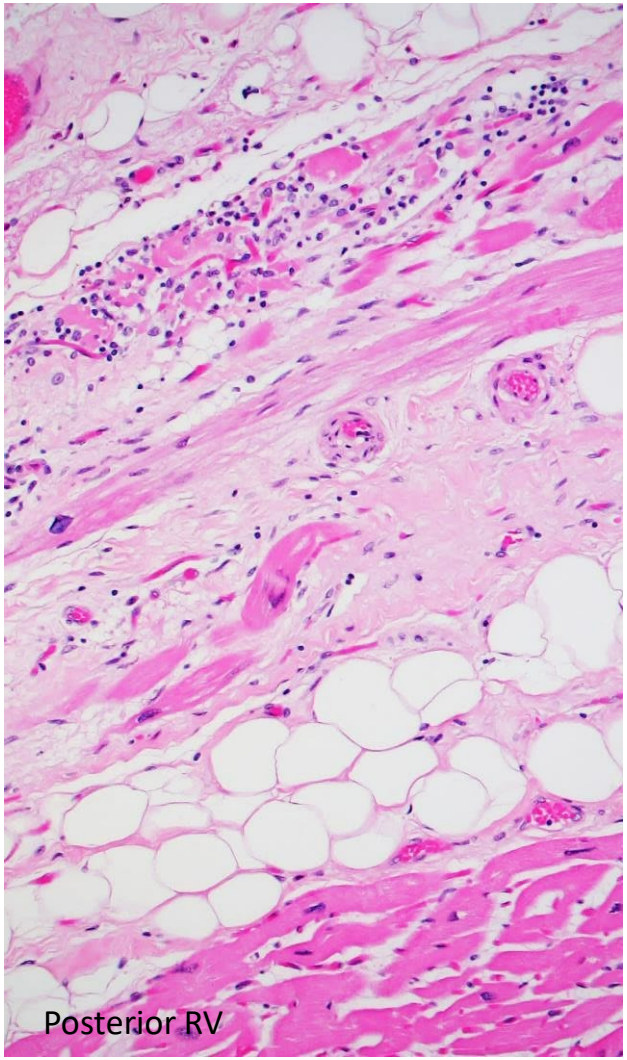


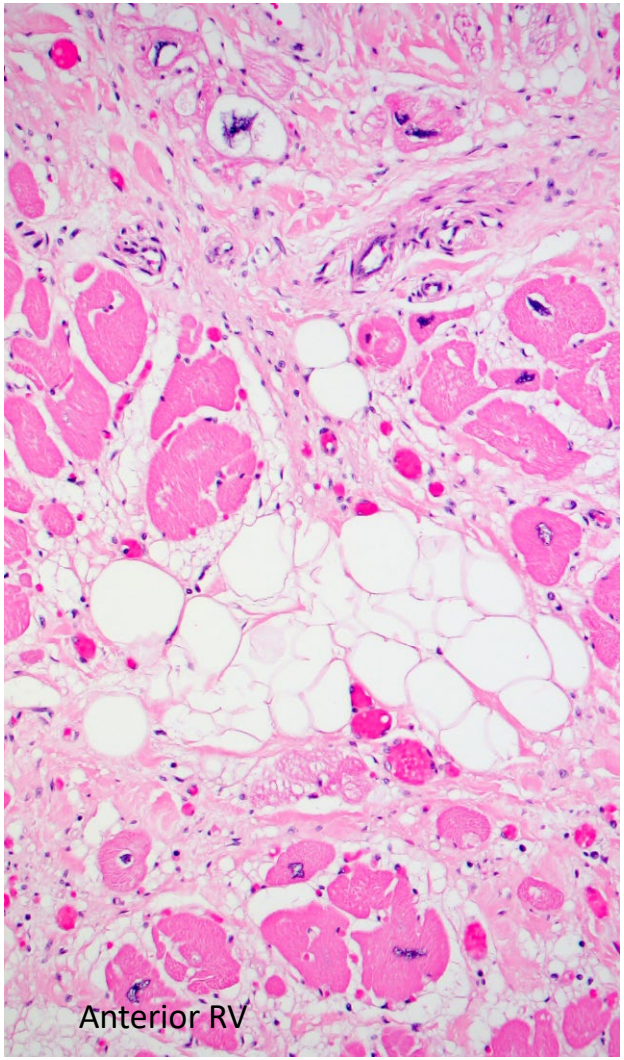


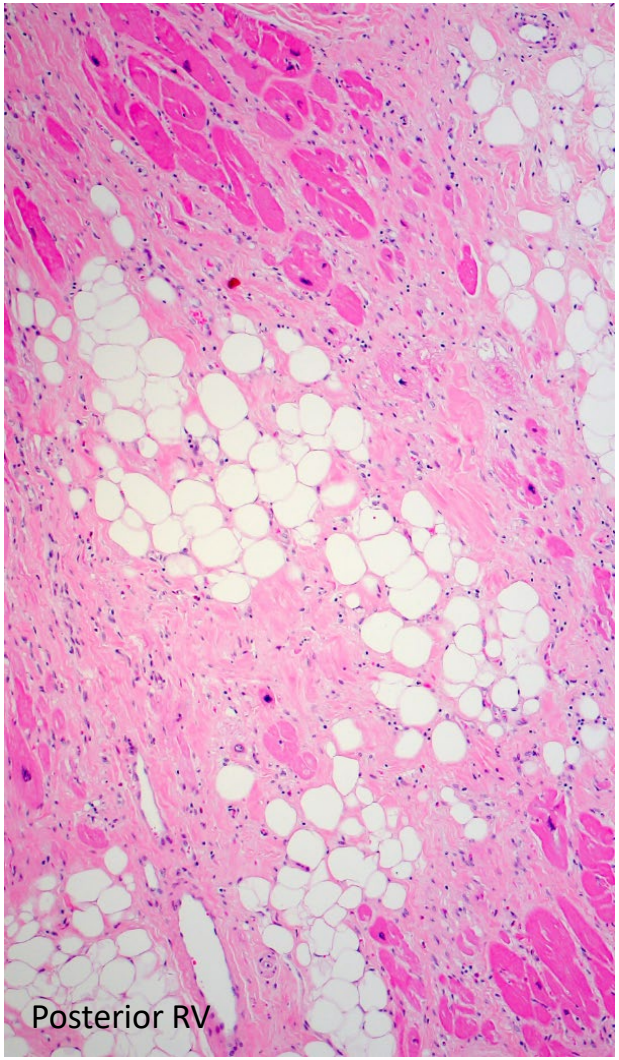






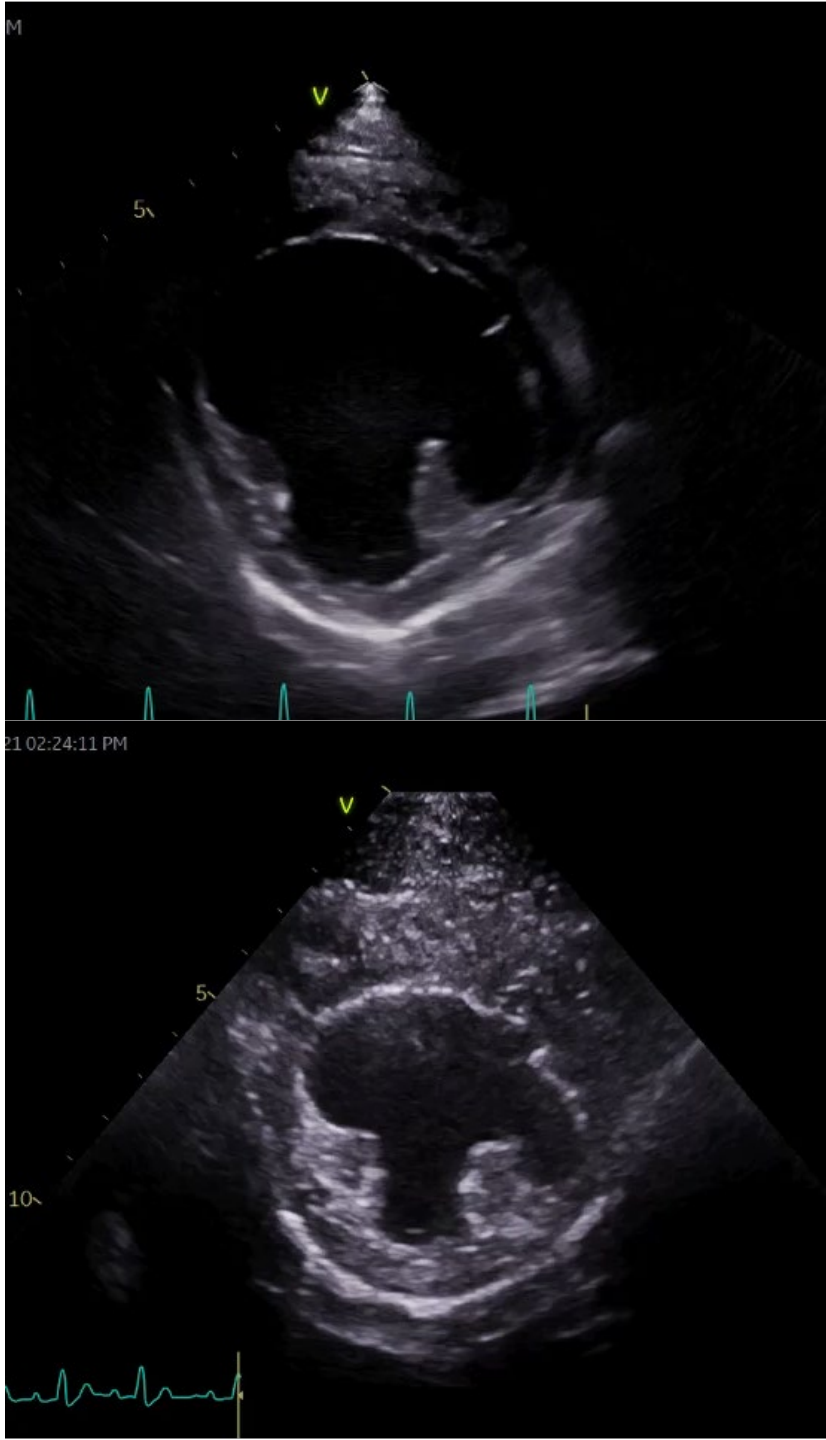

Posterior RV

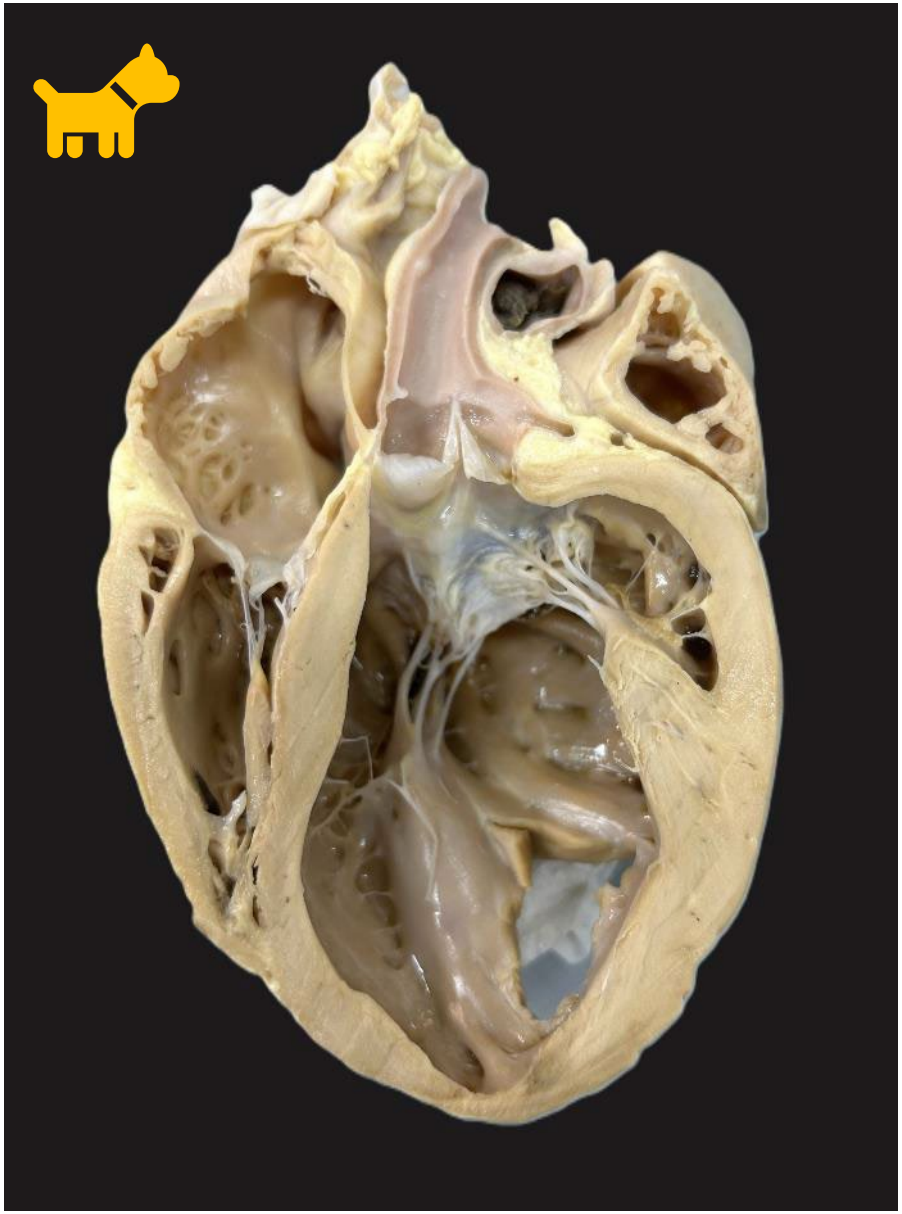

Anterior RV

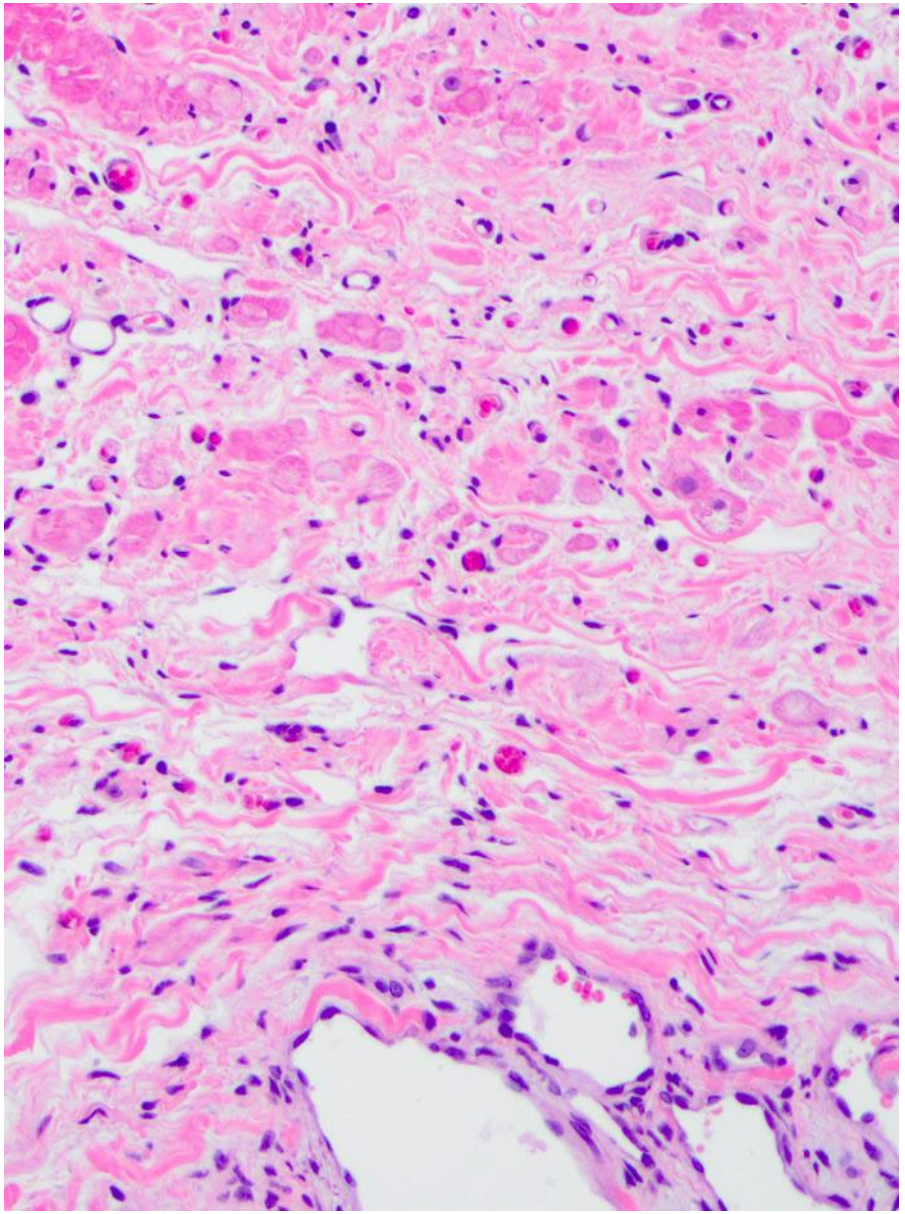

Posterior RV

DCM associated with certain diets

- Association between certain diets and DCM
  - High in peas, pea fractions, lentils, chick peas, sweet potatoes, potatoes or other uncommon sources
  - May be reversible if detected early
  - A small fraction of these diets led to taurine deficiency
  - If caught late, they might live longer than typical DCM
    - Still susceptible to arrhythmias and sudden death
    - Up to 50% still die of cardiac disease
    - LV contractile function might not recover for 2-3 years



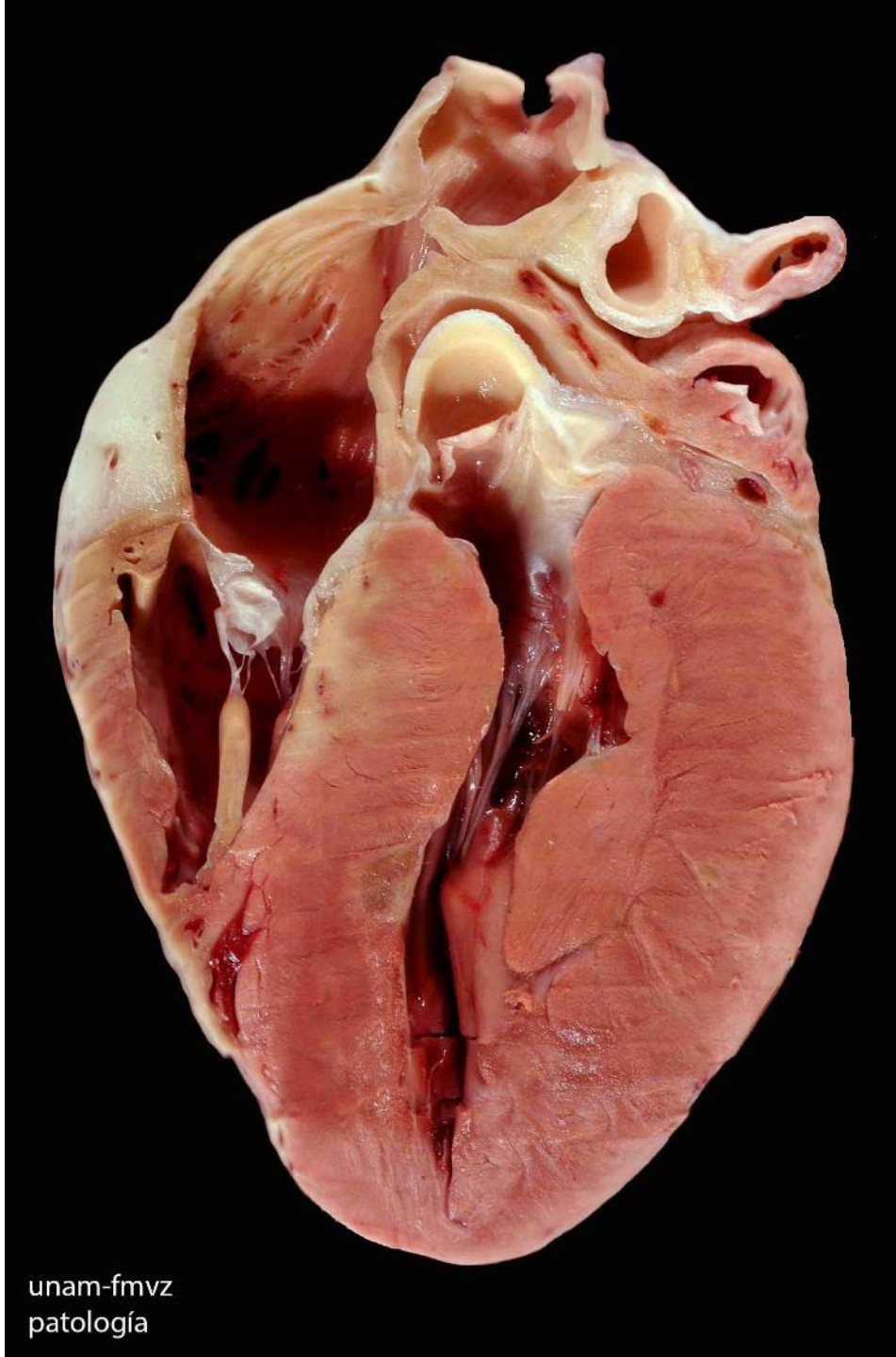


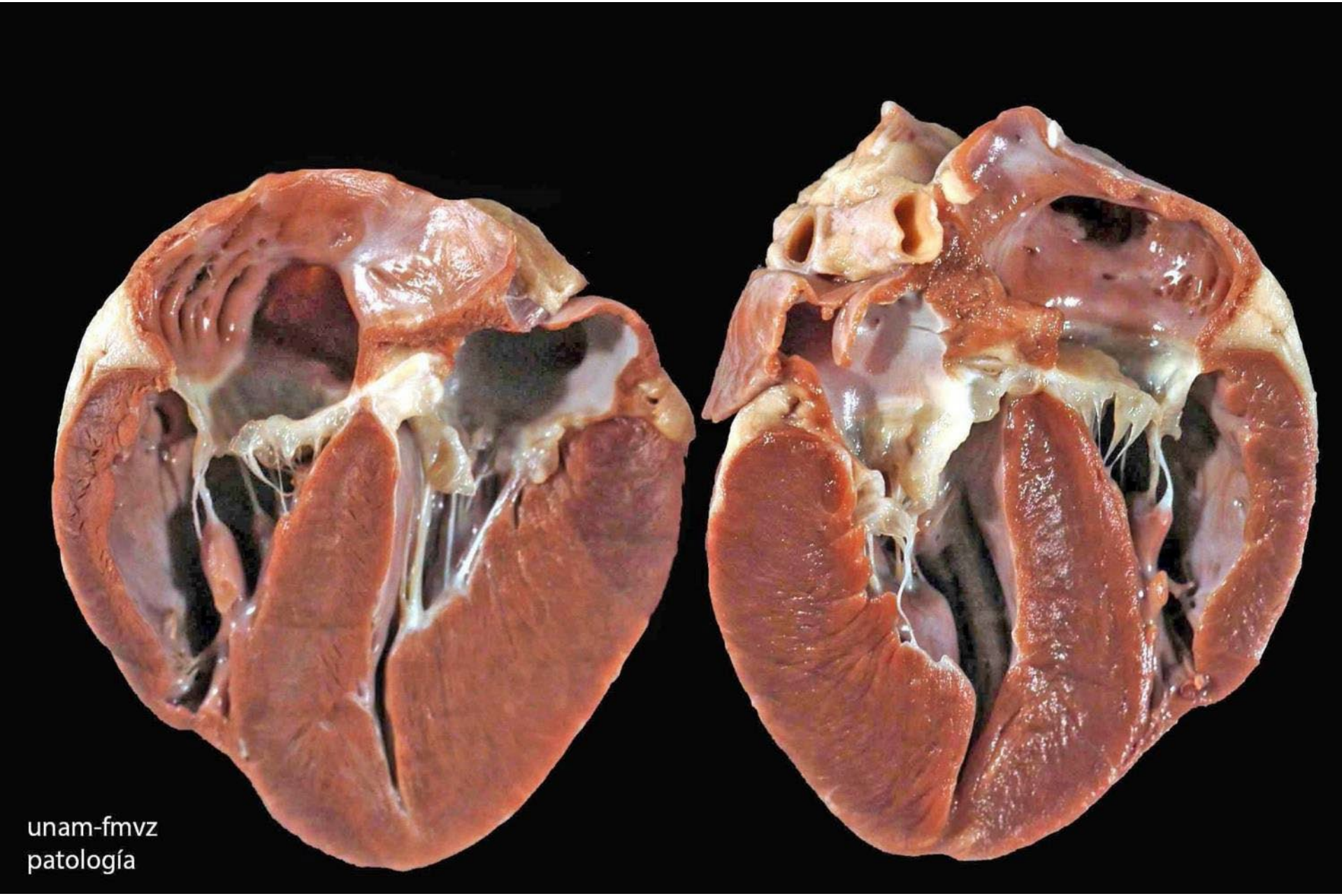


Canine hypertrophic cardiomyopathy

- Very uncommon
- German shepherd, Pointers, Dalmatians, Rottweilers; also small breeds
- Can result in sudden death or exercise intolerance or CHF
- Concentric LV hypertrophy
- Conduction abnormalities, 3º AV block, ventricular arrhythmias

- Diastolic filling is compromised





Feline cardiomyopathies

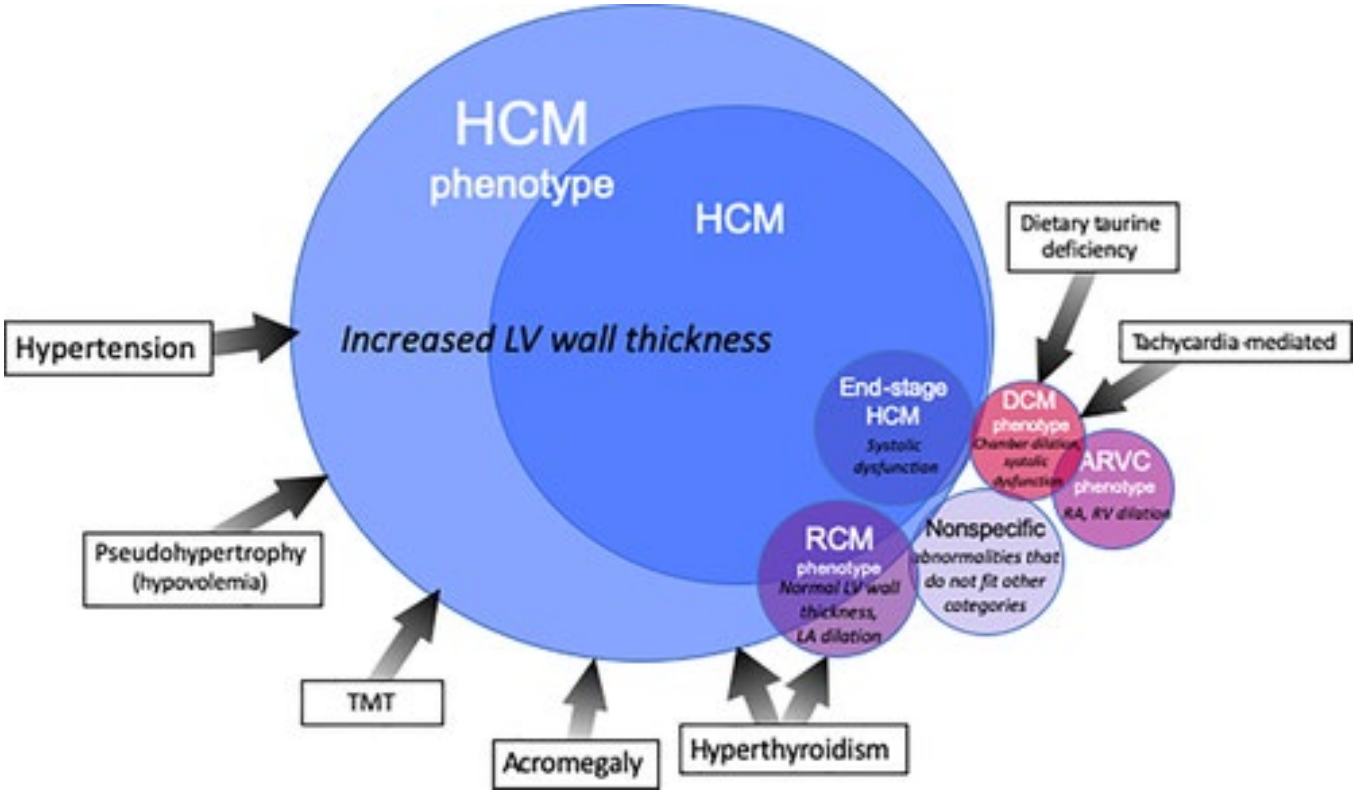


TABLE 3 Definitions of cardiomyopathy phenotypes. Cardiomyopathy is defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal in the absence of any other disease sufficient to cause the observed myocardial abnormality

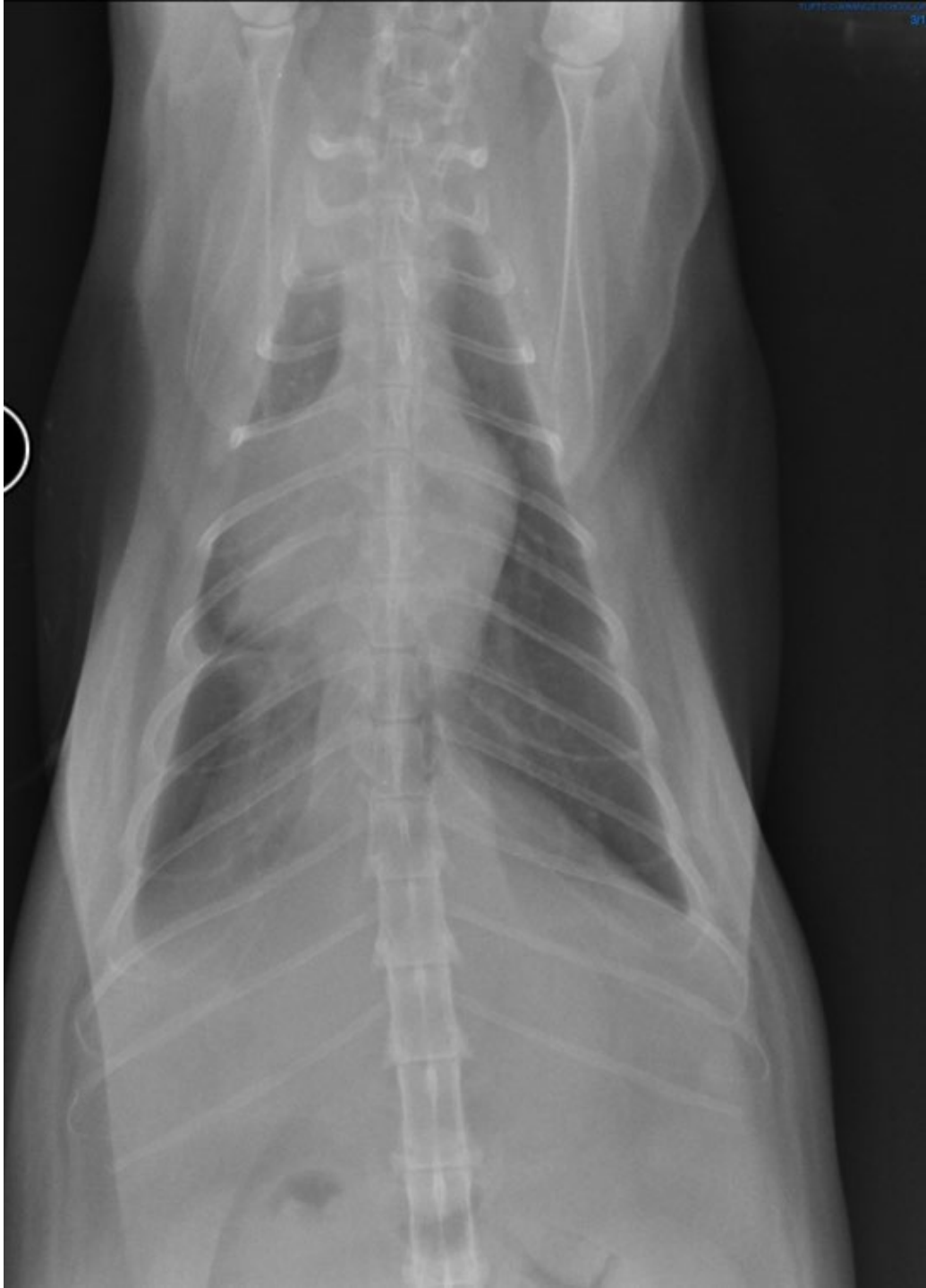
Phenotype	Definition
Hypertrophic cardiomyopathy (HCM)	Diffuse or regional increased LV wall thickness with a nondilated LV chamber.
Restrictive cardiomyopathy (RCM)	
Endomyocardial form	Characterized macroscopically by prominent endocardial scar that usually bridges the interventricular septum and LV free wall, and may cause fixed, mid-LV obstruction and often apical LV thinning or aneurysm; LA or biatrial enlargement is generally present.
Myocardial form	Normal LV dimensions (including wall thickness) with LA or biatrial enlargement
Dilated cardiomyopathy (DCM)	LV systolic dysfunction characterized by progressive increase in ventricular dimensions, normal or reduced LV wall thickness, and atrial dilatation.
Arrhythmogenic cardiomyopathy (AC), also known as arrhythmogenic right ventricular cardiomyopathy (ARVC; or dysplasia (ARVD)	Severe RA and RV dilatation and often, RV systolic dysfunction and RV wall thinning. The left heart may also be affected. Arrhythmias and right-sided congestive heart failure are common.
Nonspecific phenotype	A cardiomyopathic phenotype that is not adequately described by the other categories; the cardiac morphology and function should be described in detail

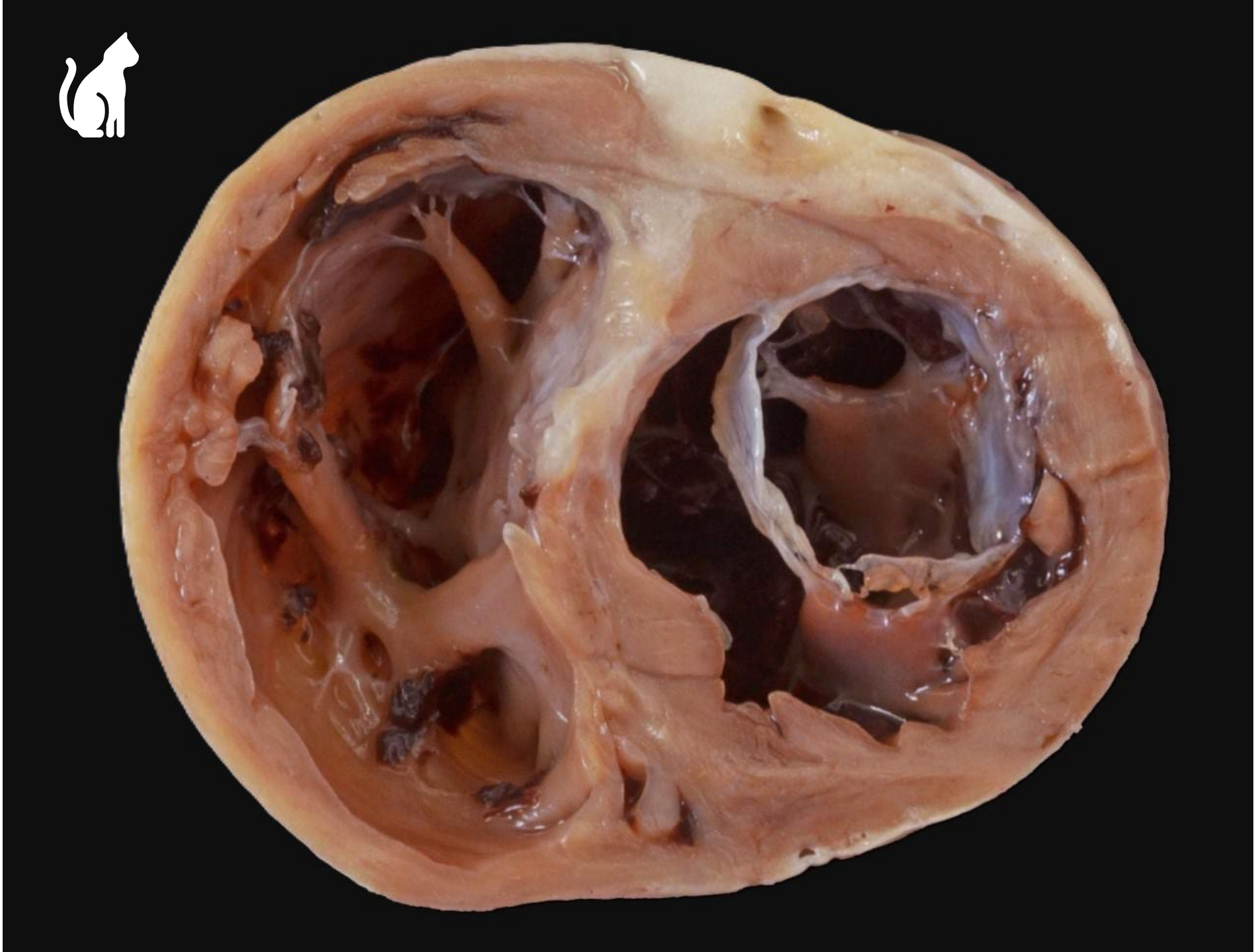
Luis Fuentes V, Abbott J, Chetboul V, et al. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. *J Vet Intern Med*. 2020; 34: 1062–1077.

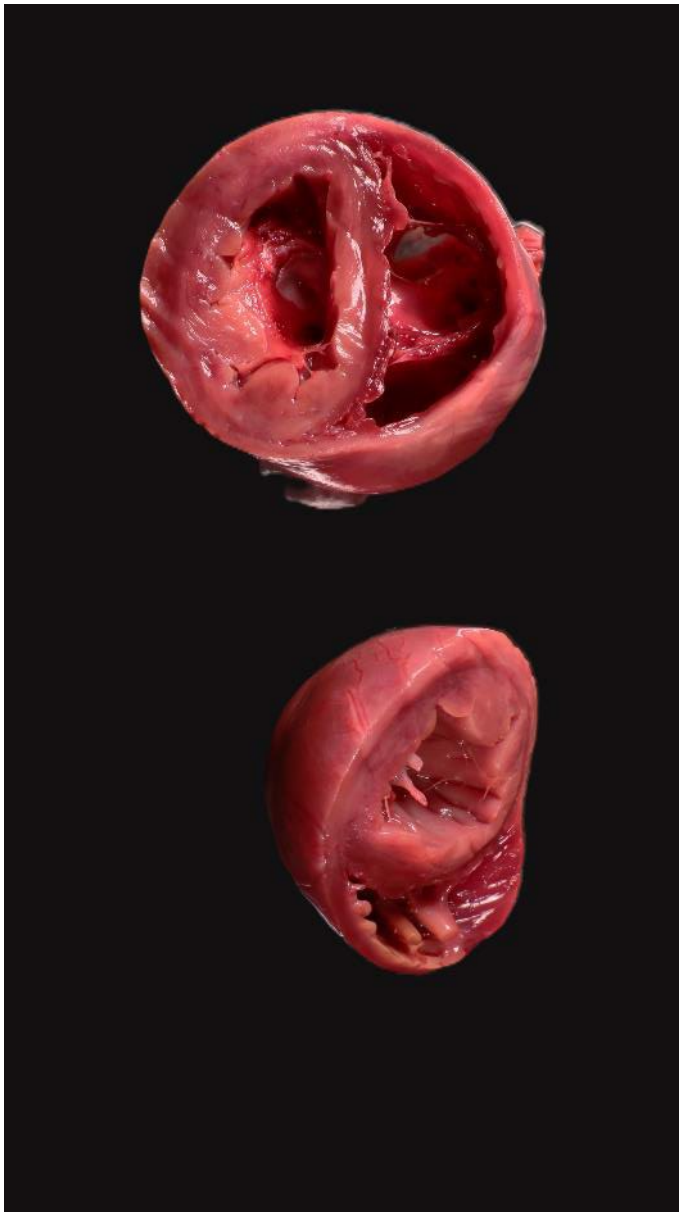
Feline dilated cardiomyopathy

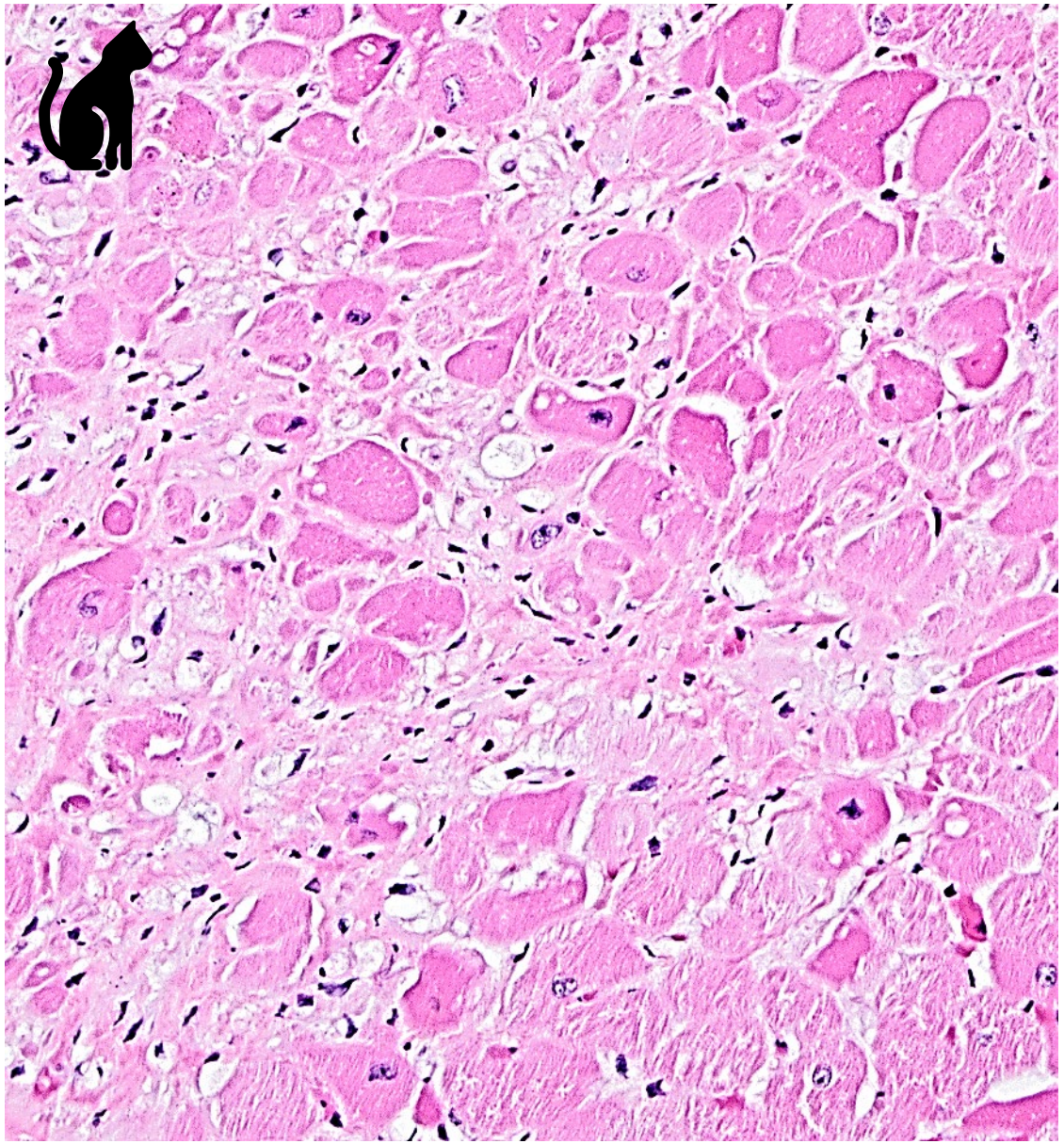
- Etiology unknown
- Dietary taurine deficiency in some cats
- Cytoskeletal protein abnormalities?
- Role for grain-free diets high in peas, lentils, chickpeas, sweet potatoes, potatoes??

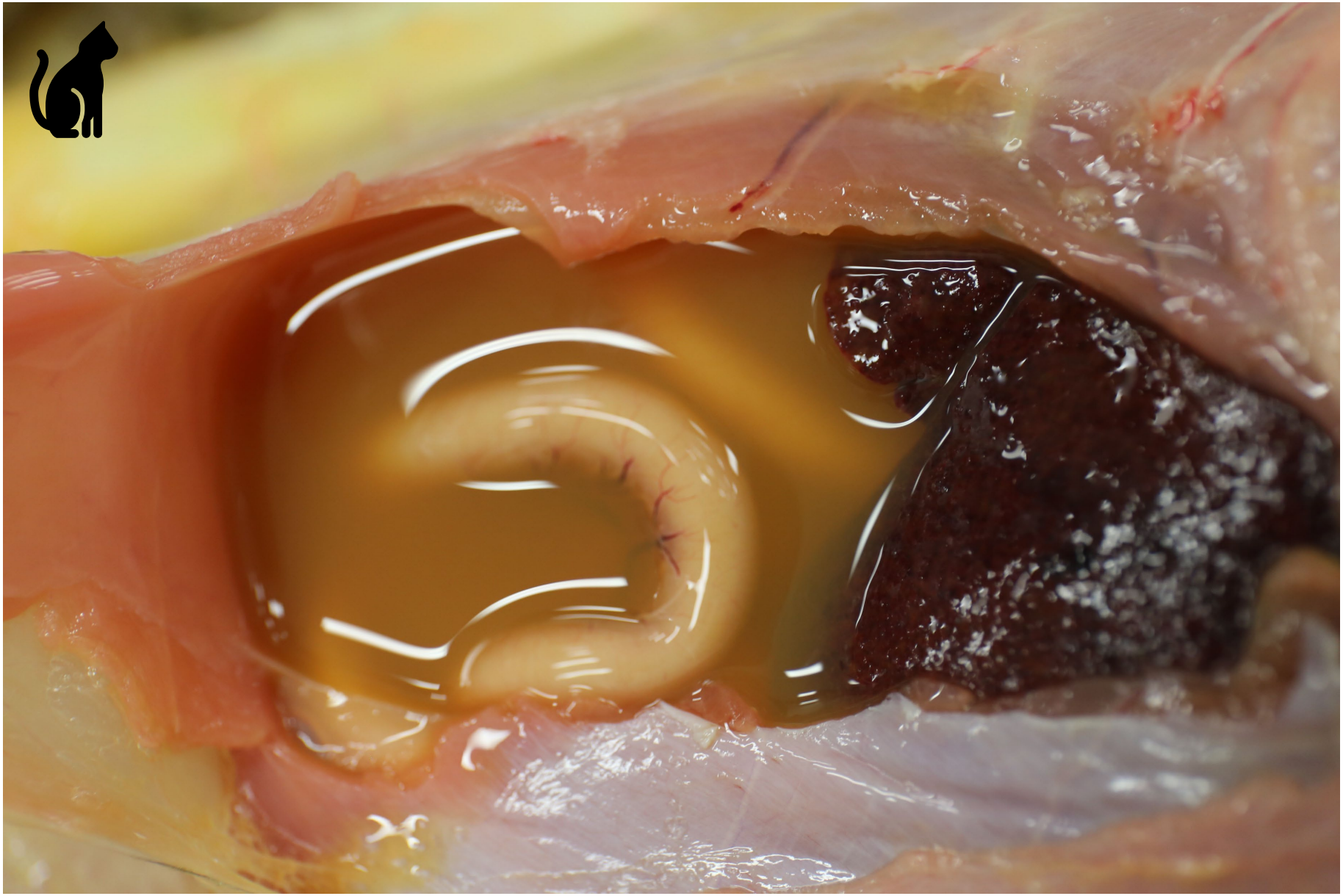
- Systolic and diastolic dysfunction
- Secondary mitral and tricuspid valve regurgitation
- CHF may be manifest with signs of left-sided or biventricular failure

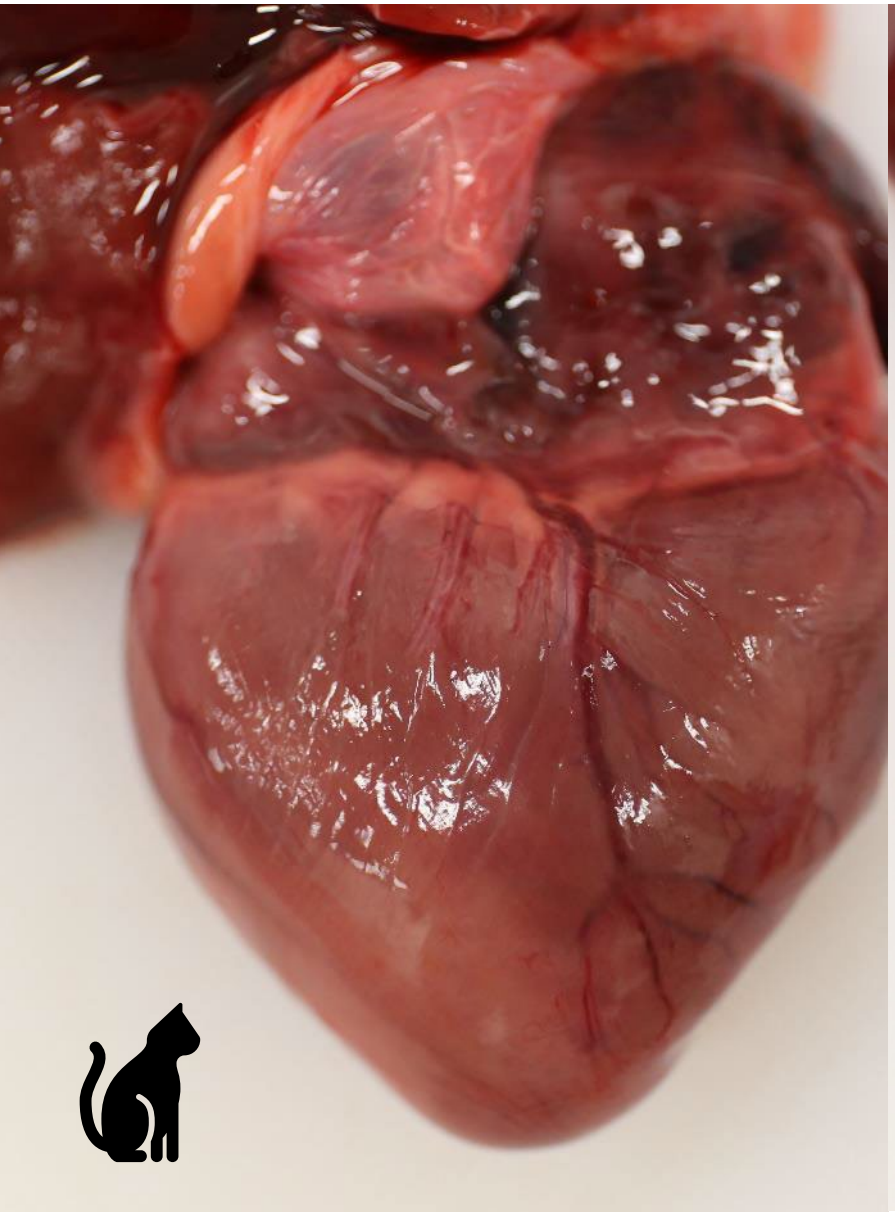


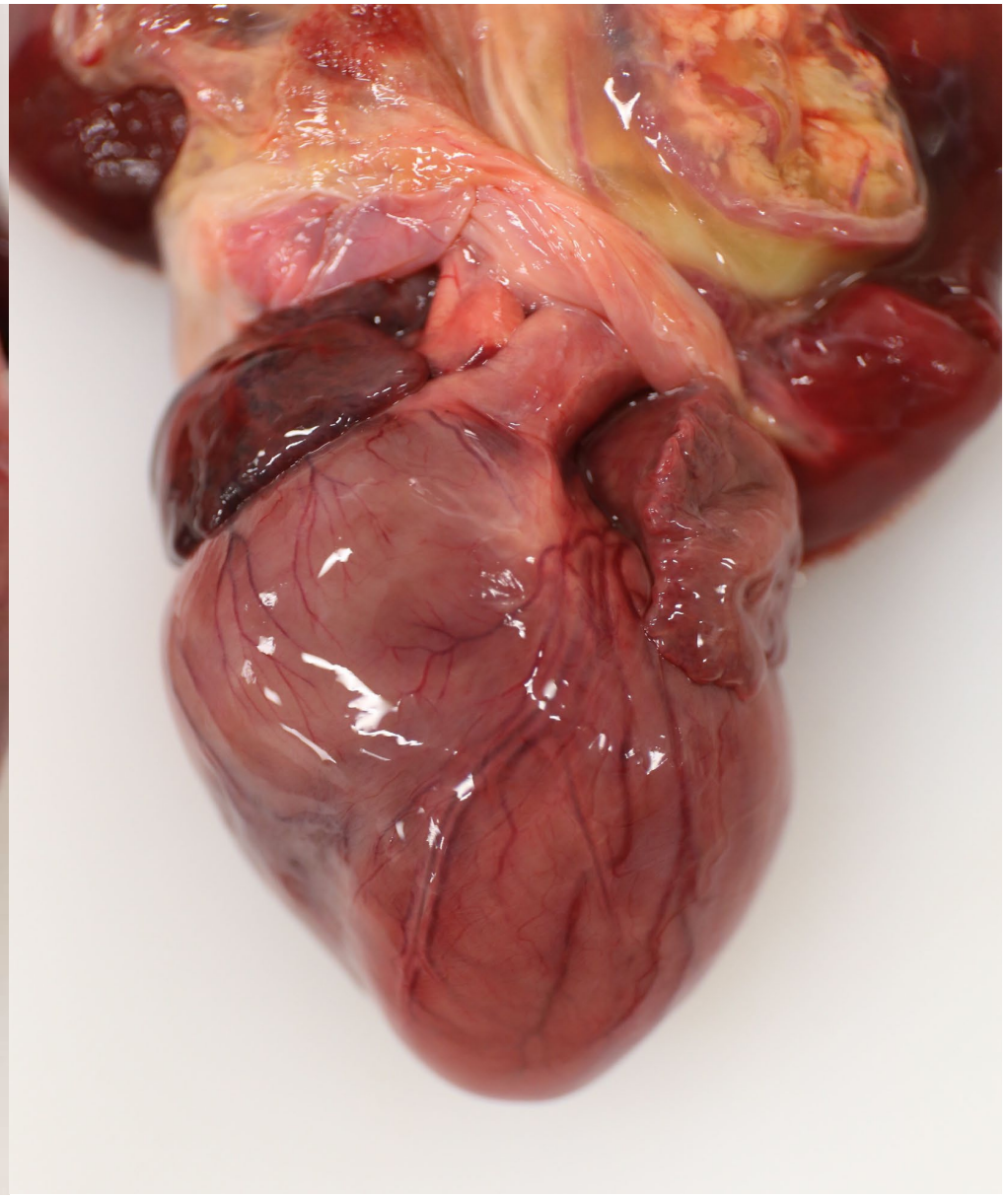


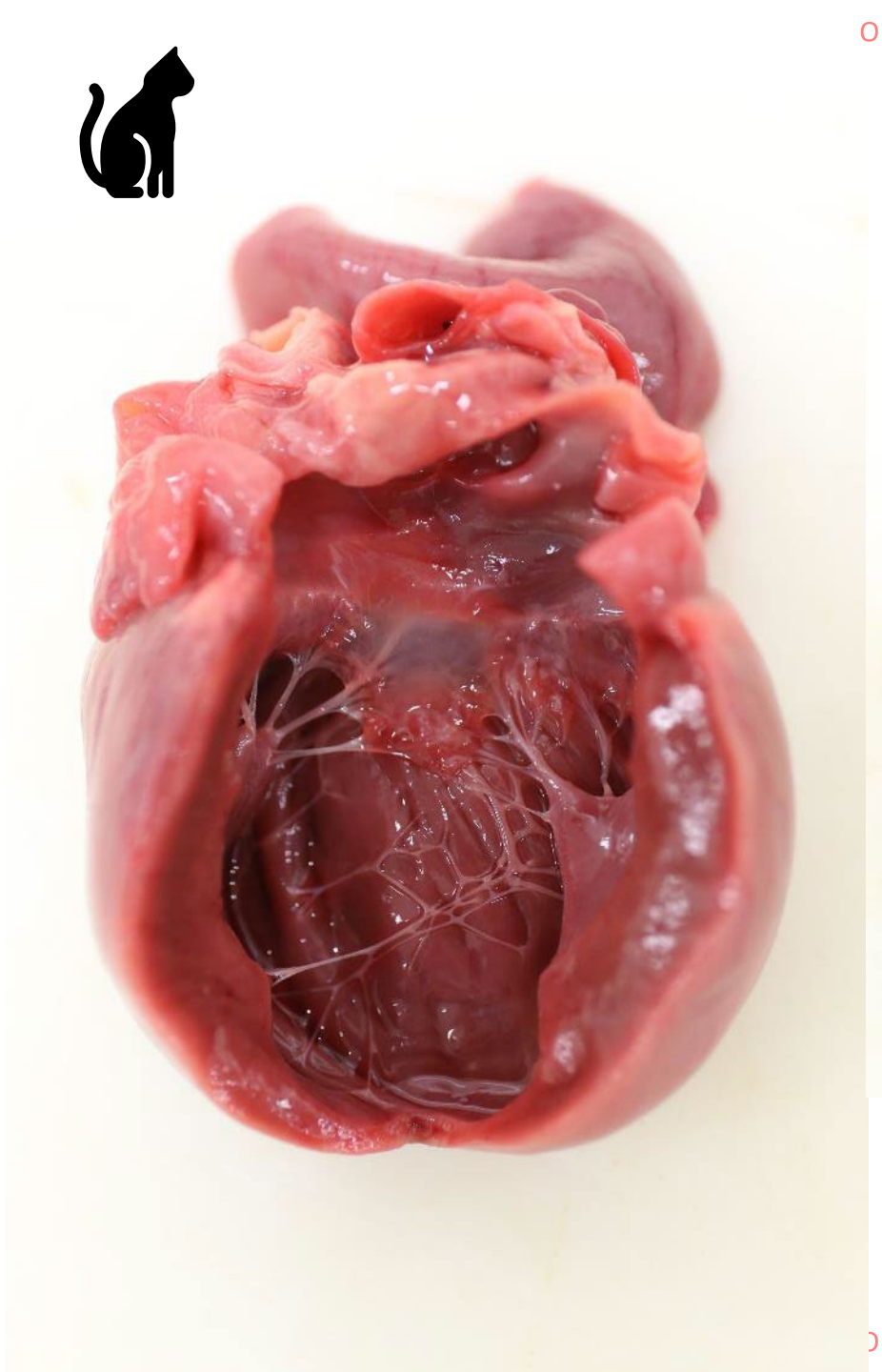


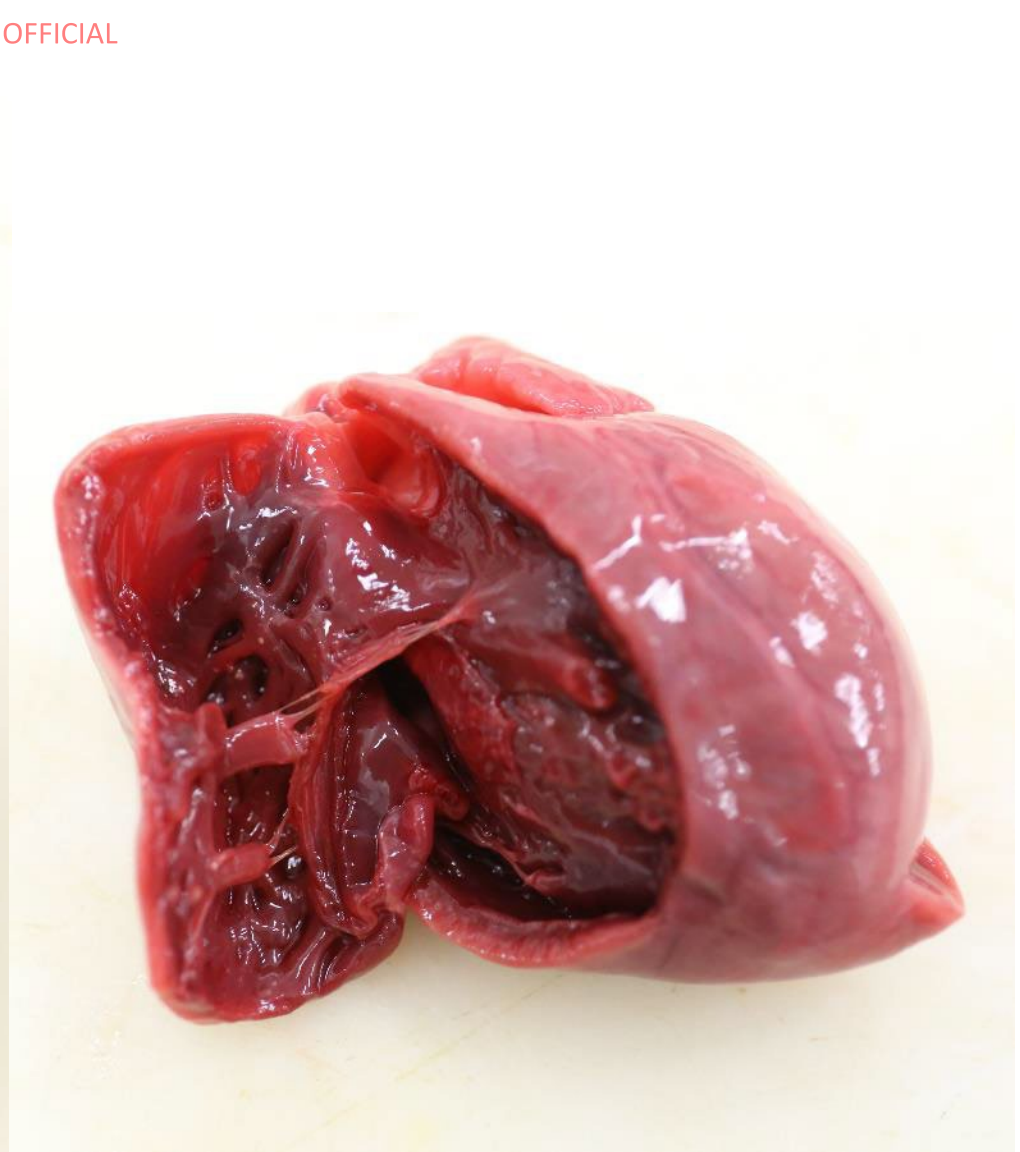


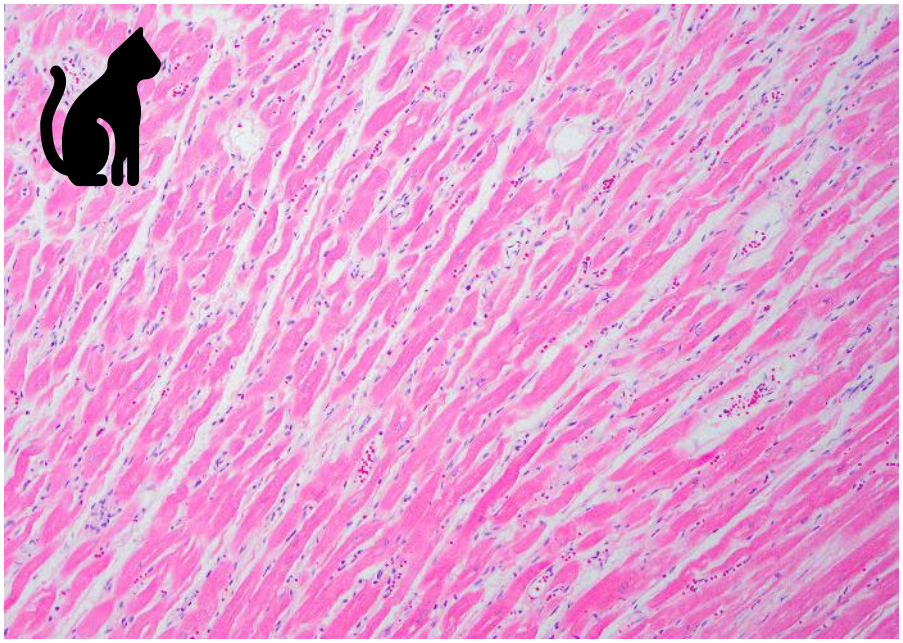


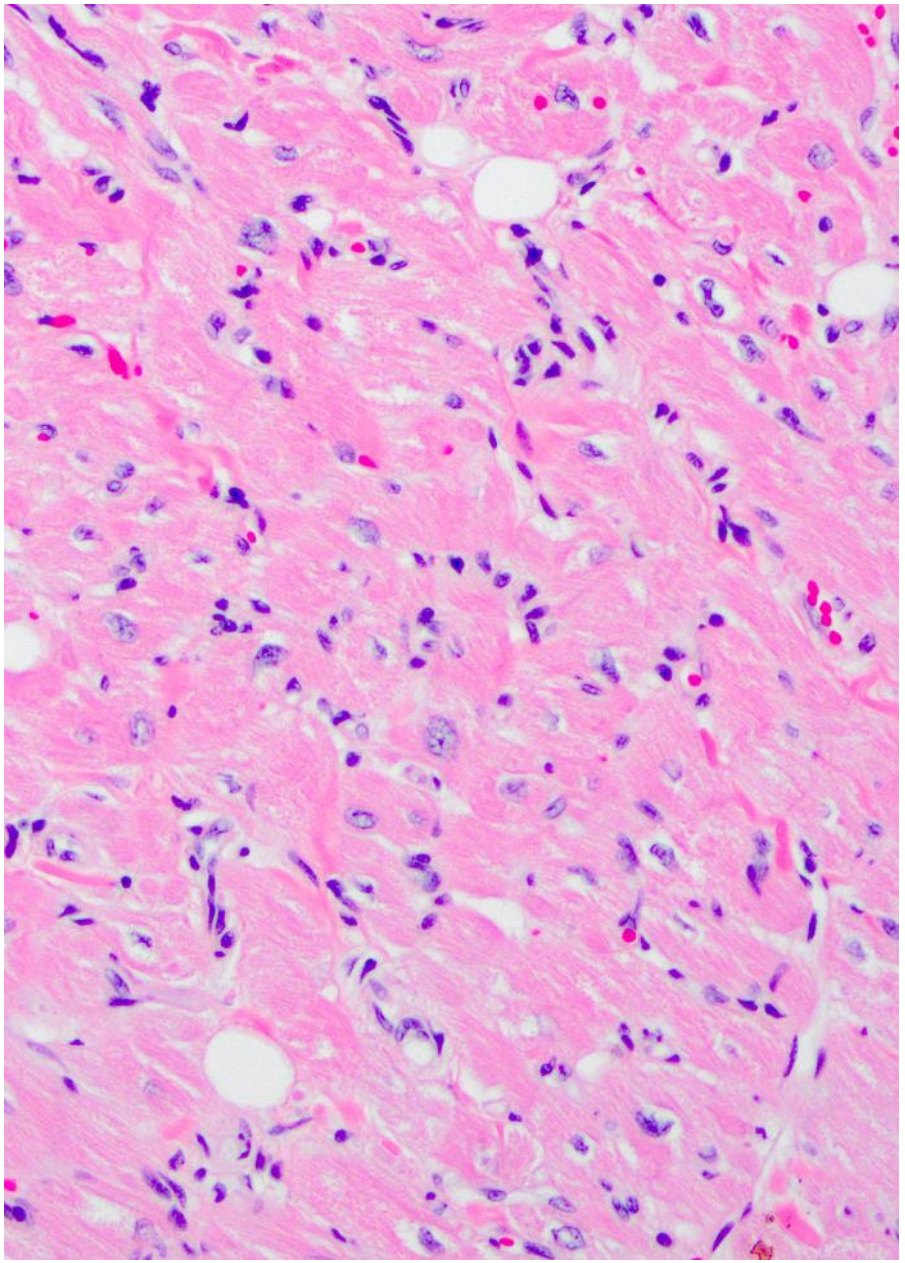


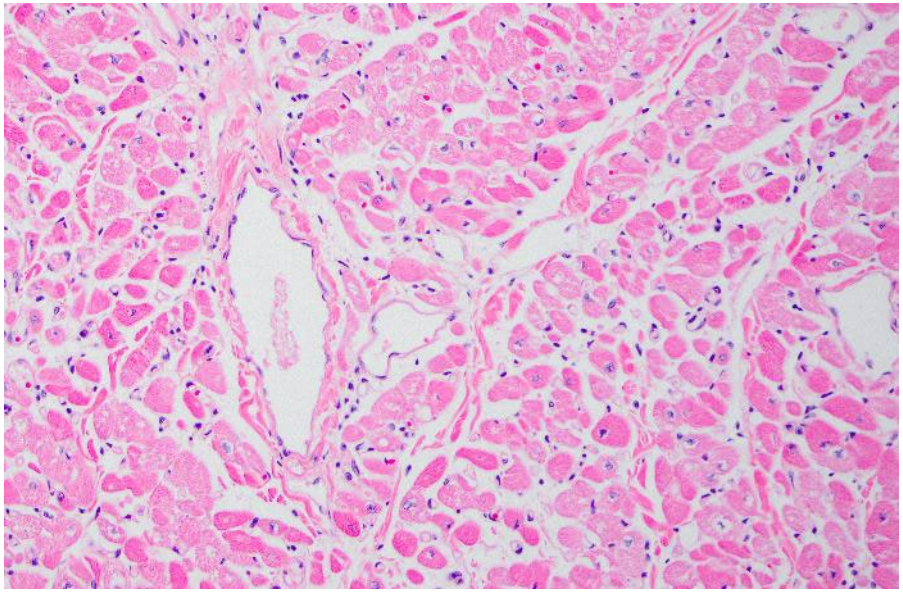


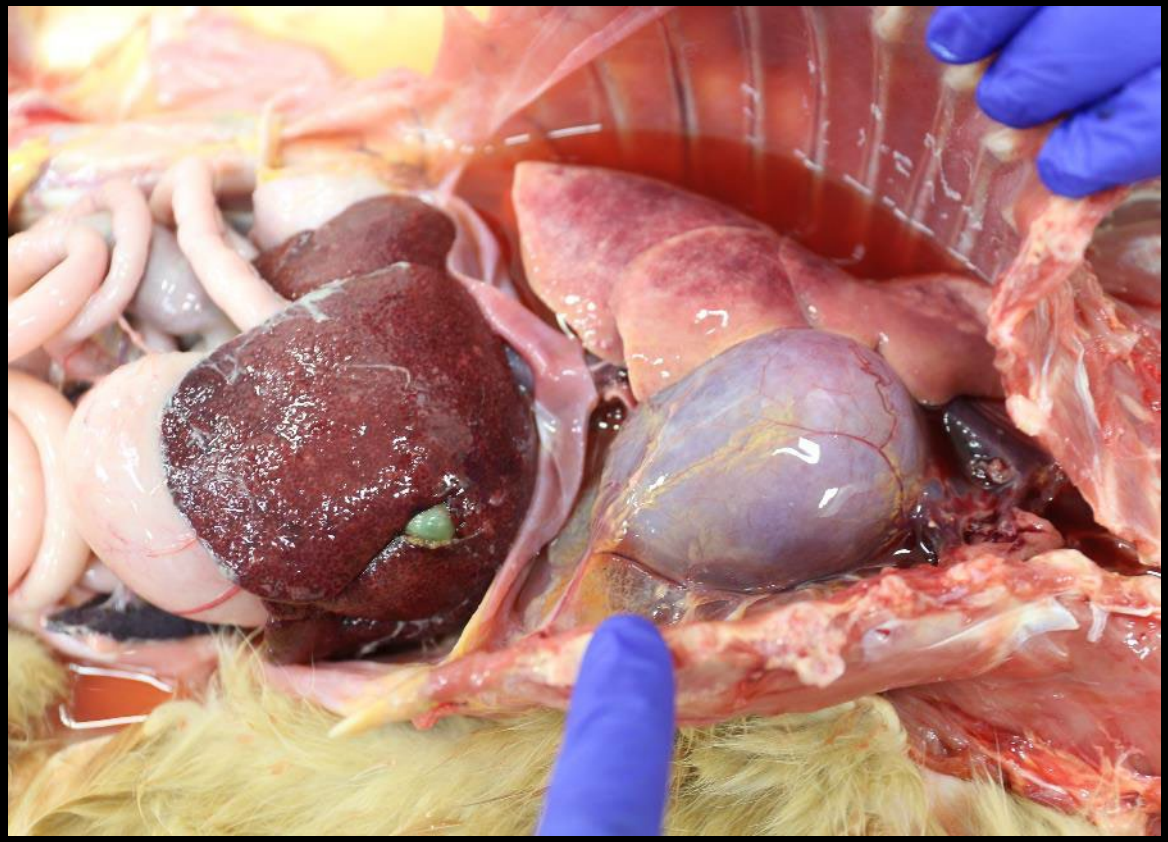


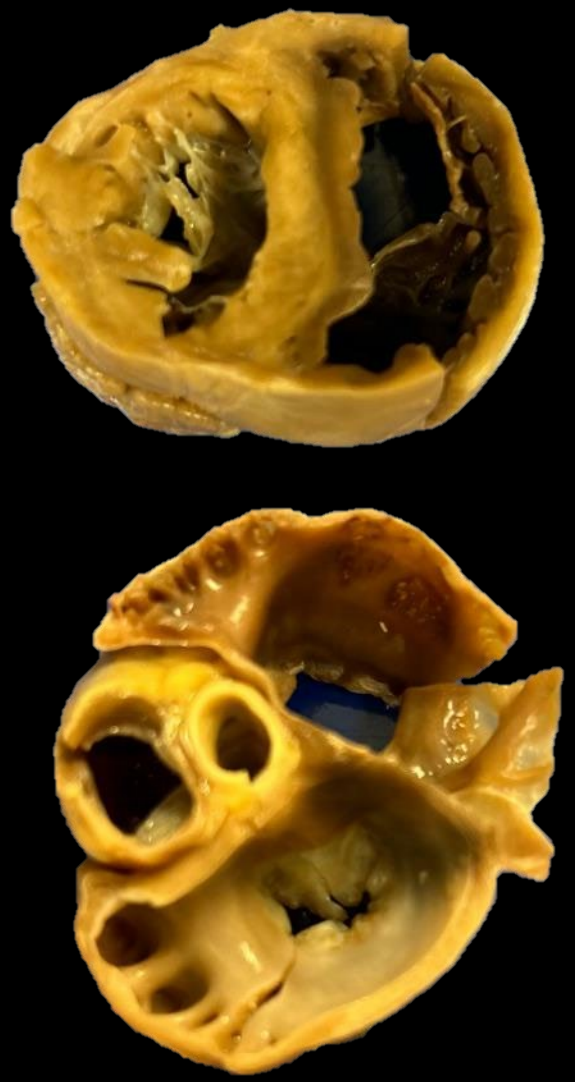


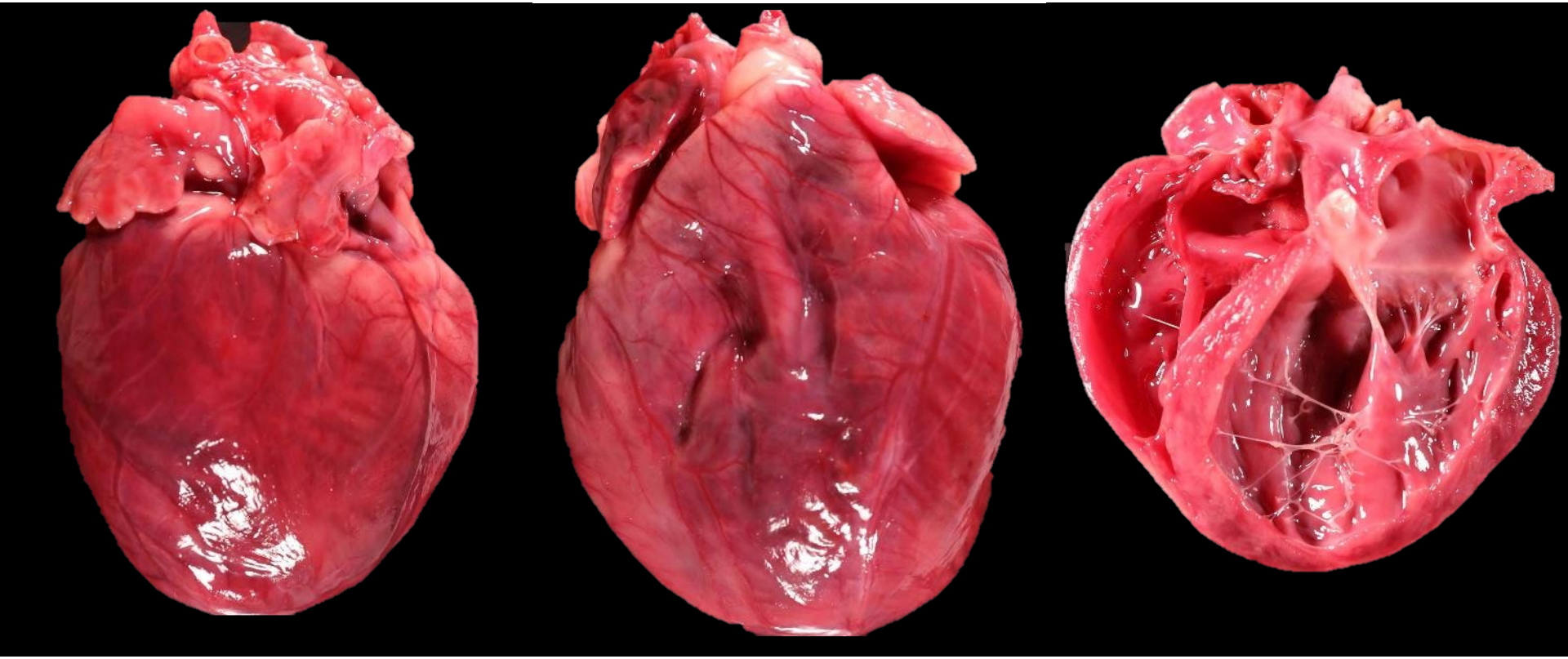




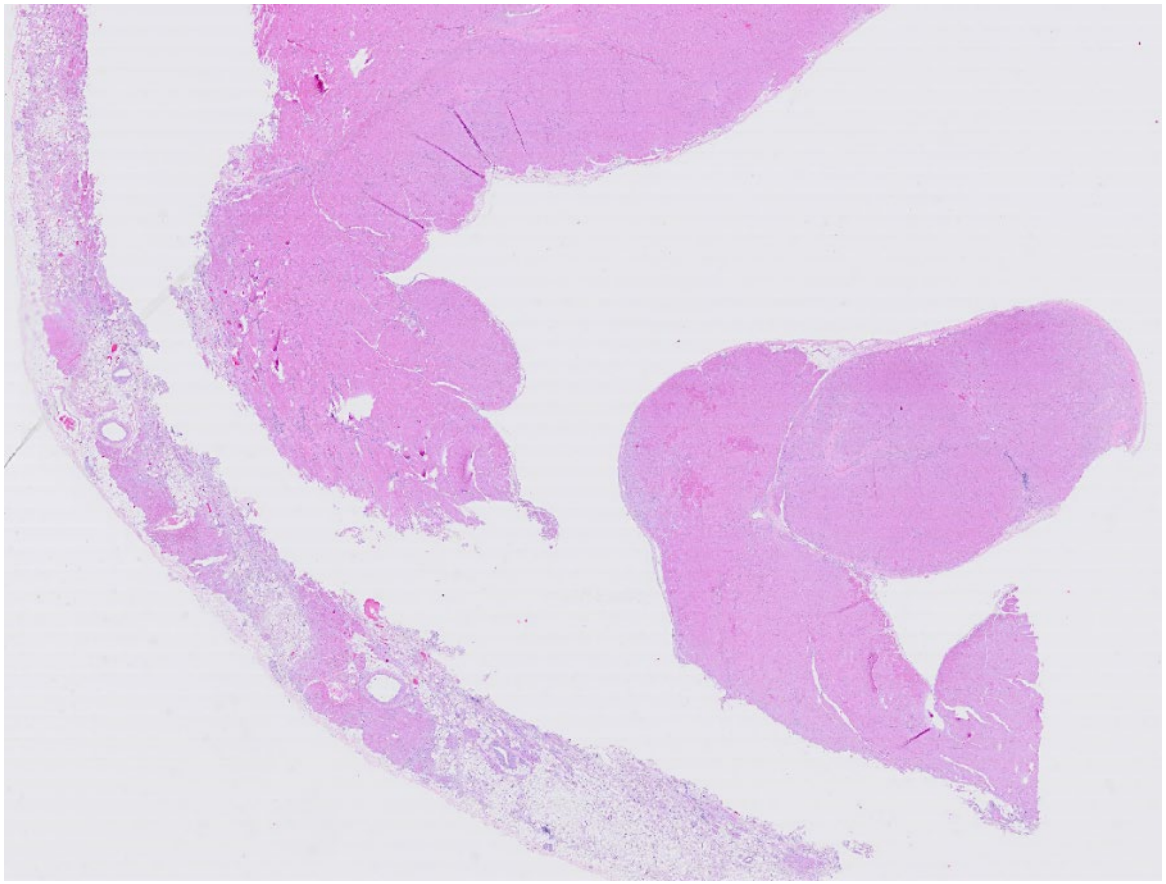




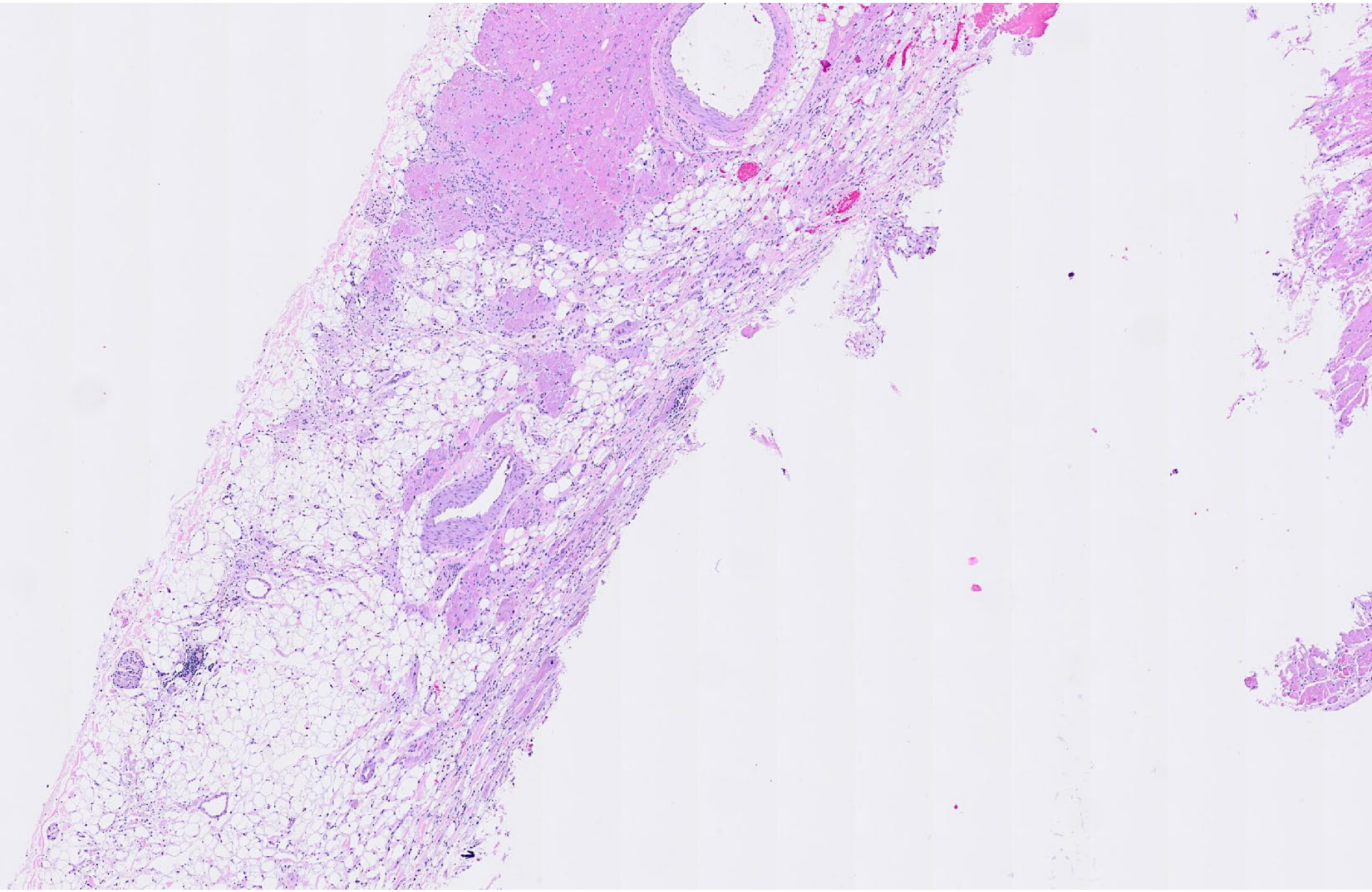


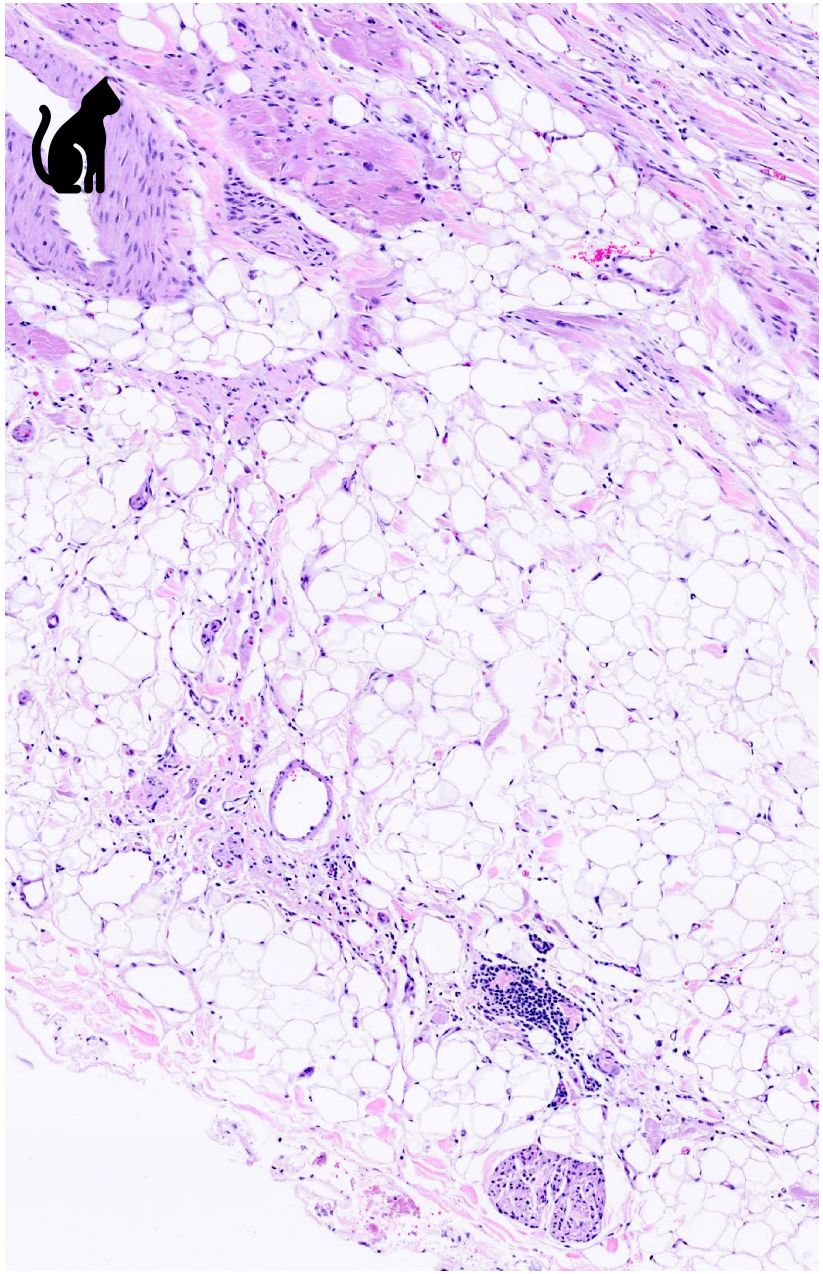


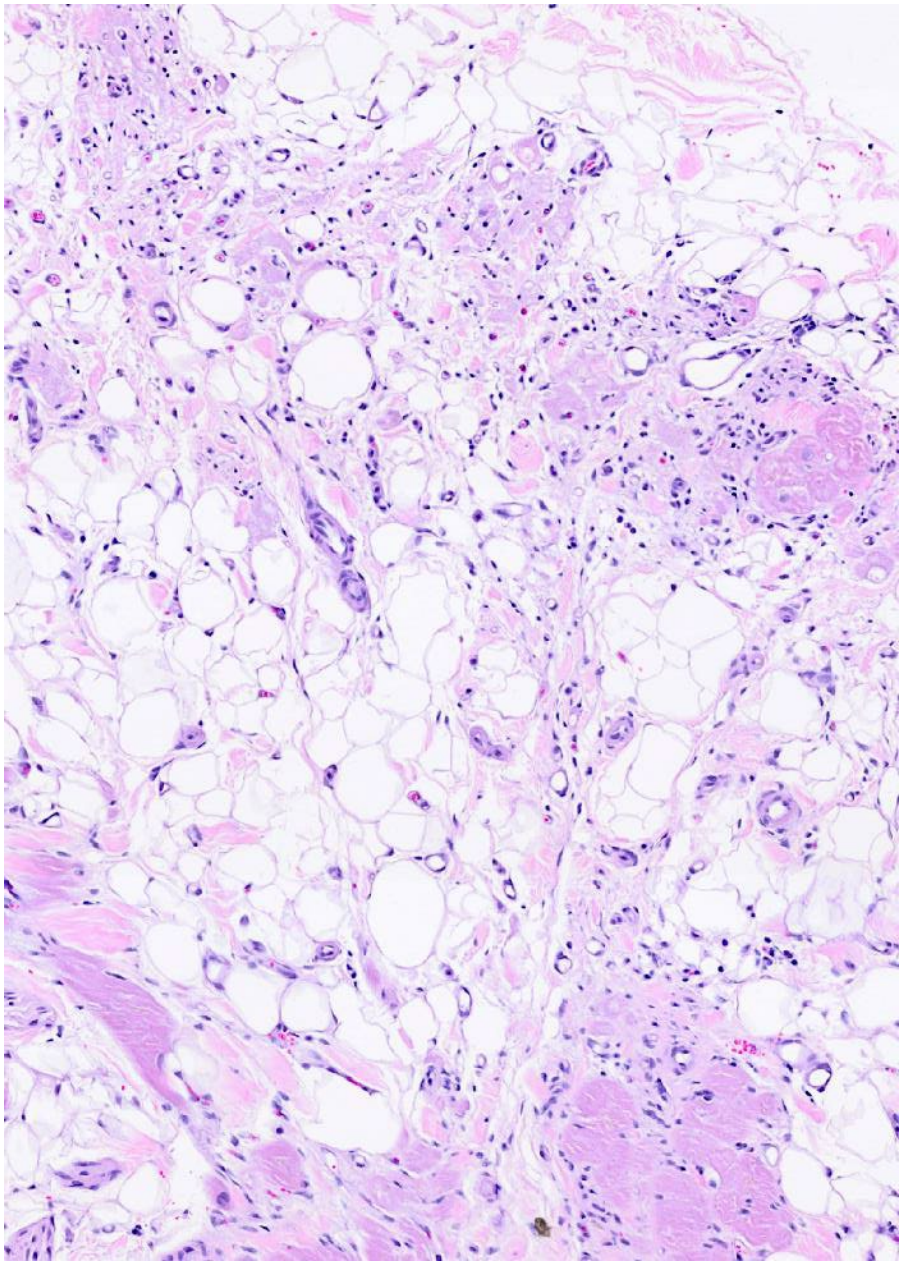
Feline arrhythmogenic right ventricular cardiomyopathy



- RV , RA enlargement
- Right-sided CHF
- Arrhythmias
- No cat families have been identified with ARVC, and no genetic analysis has been reported.

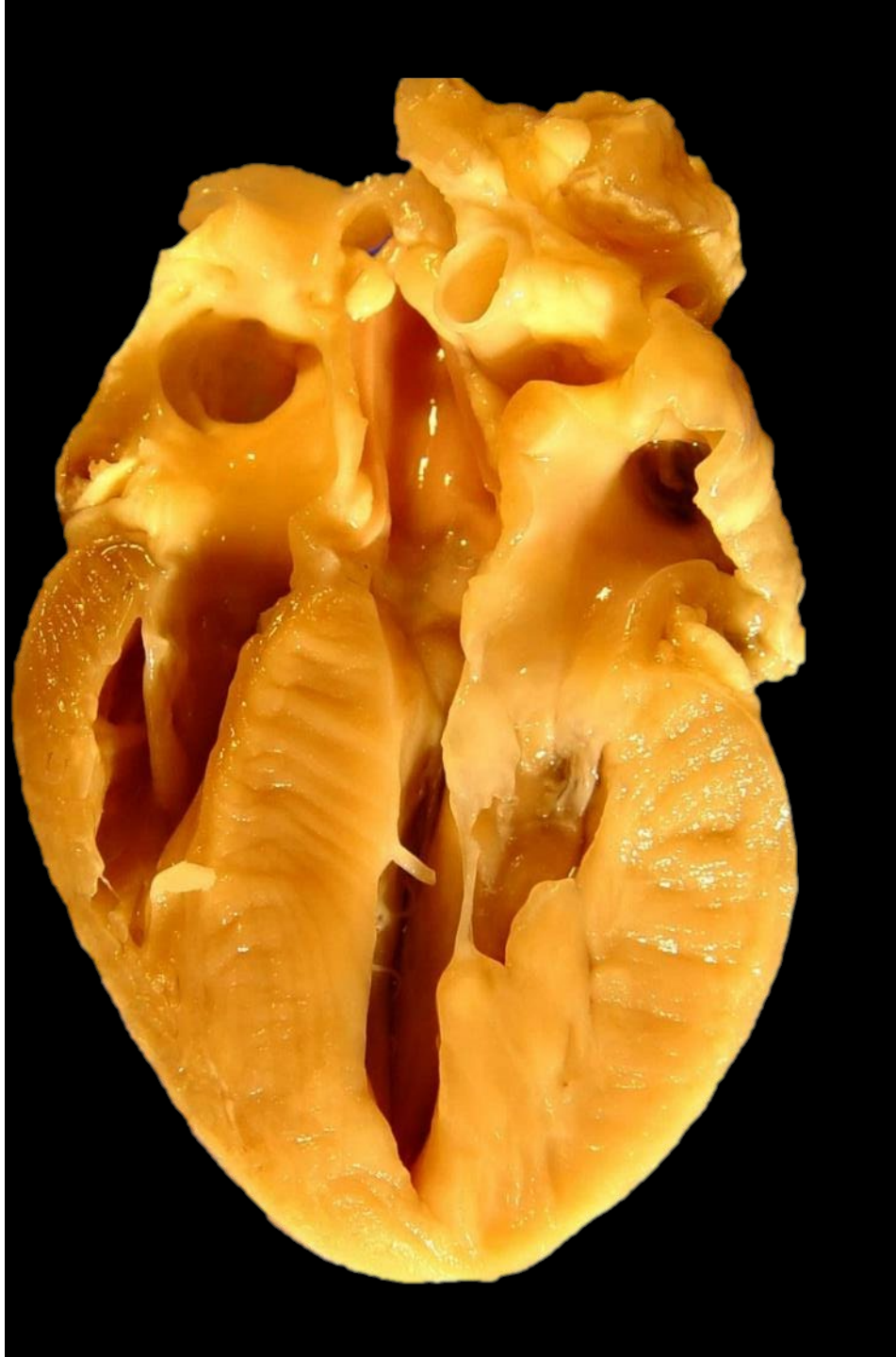






Feline hypertrophic cardiomyopathy

- Most common cardiovascular disease in the cat
- Most common feline cause of:
  - CHF
  - Arterial thromboembolism
  - Syncope
  - Sudden death
  - Unexpected anesthesia death



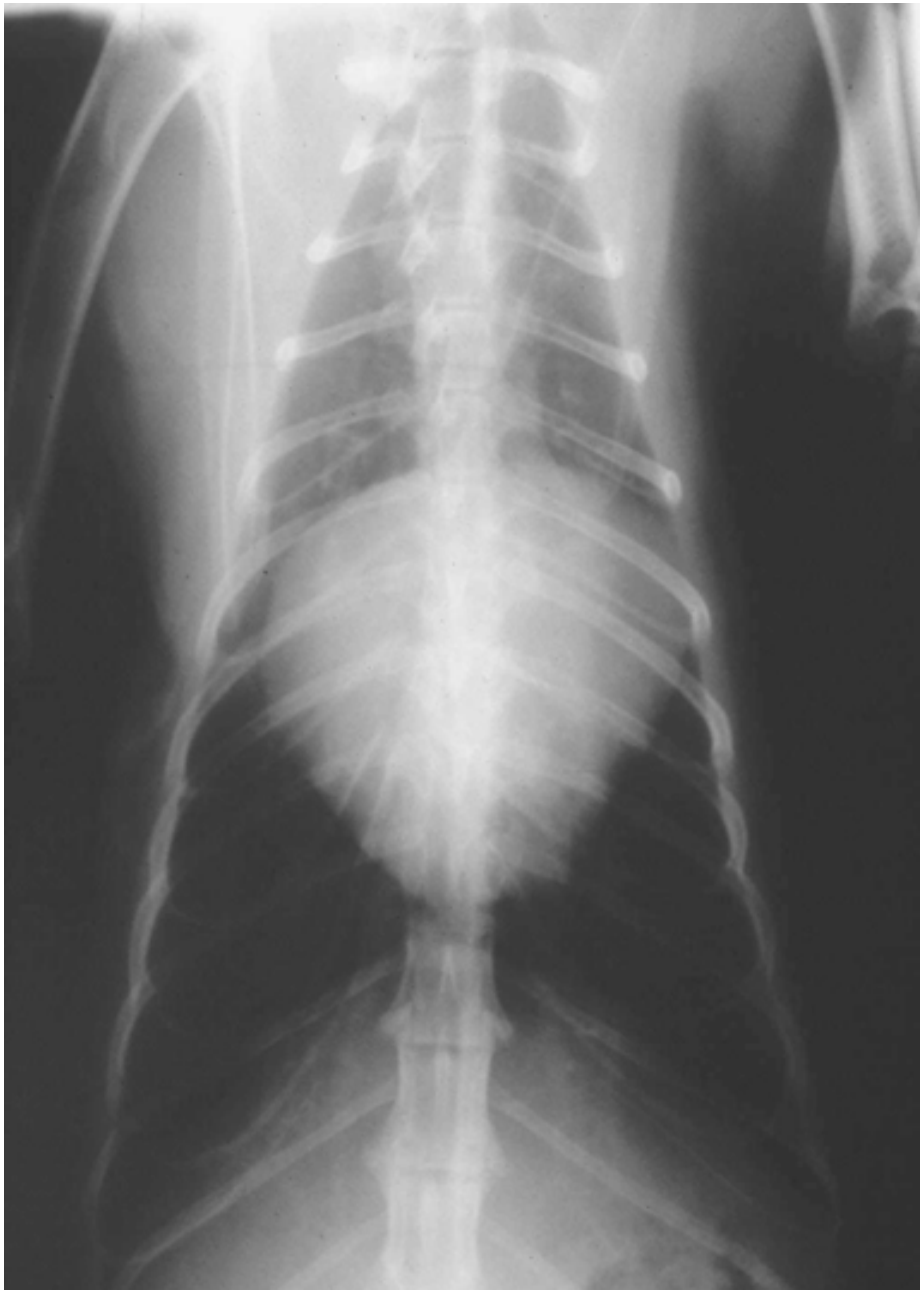
Some forms of feline HCM are genetic

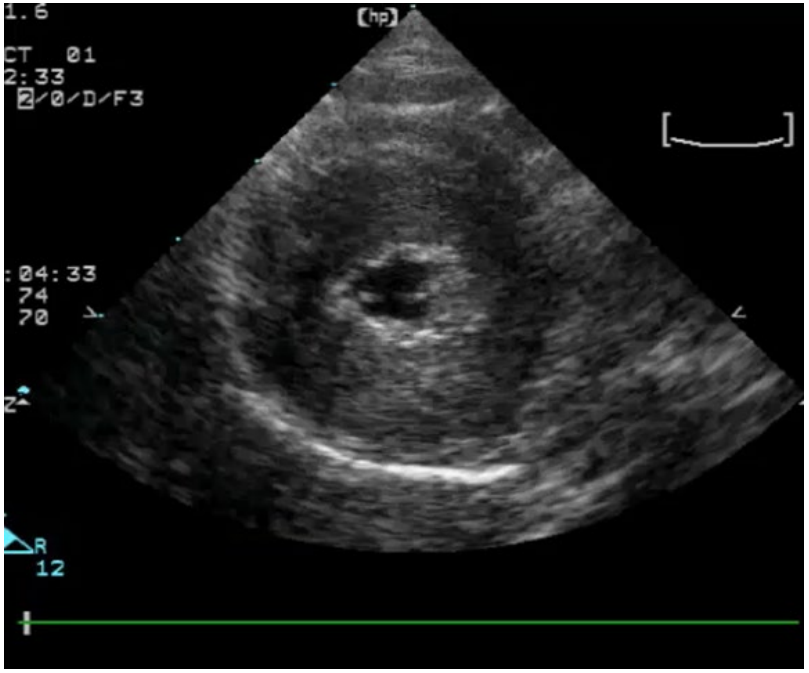
Mutations in sarcomeric proteins

- Myosin binding protein C in
  - Maine Coon cats, Ragdoll cats
    - Specific mutations: MYBPC3 [R818W] and MYBPC3 [A31P]
    - Other mutations: TNNT2 in Maine coon, ALMS1 in Sphynx

Cats without known genetic mutation develop HCM

HCM in non-breed cats, genetic pathologic variants are not detected

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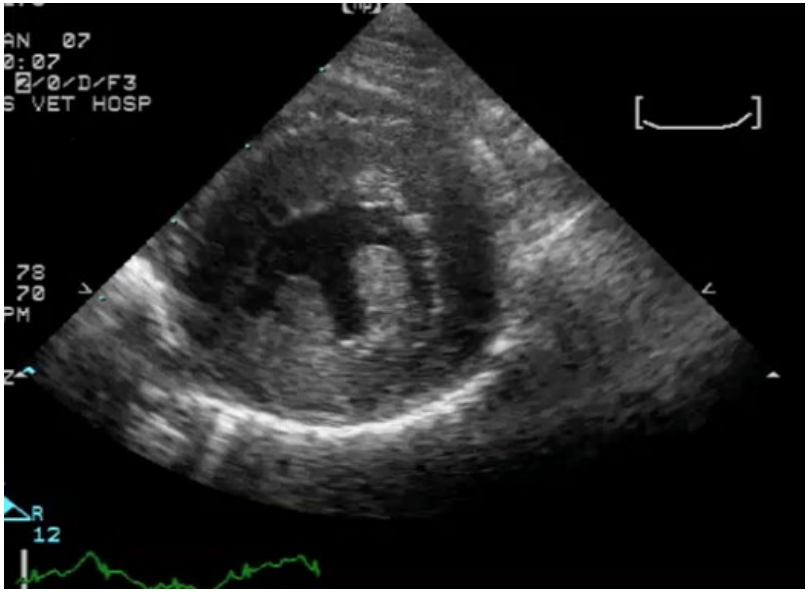
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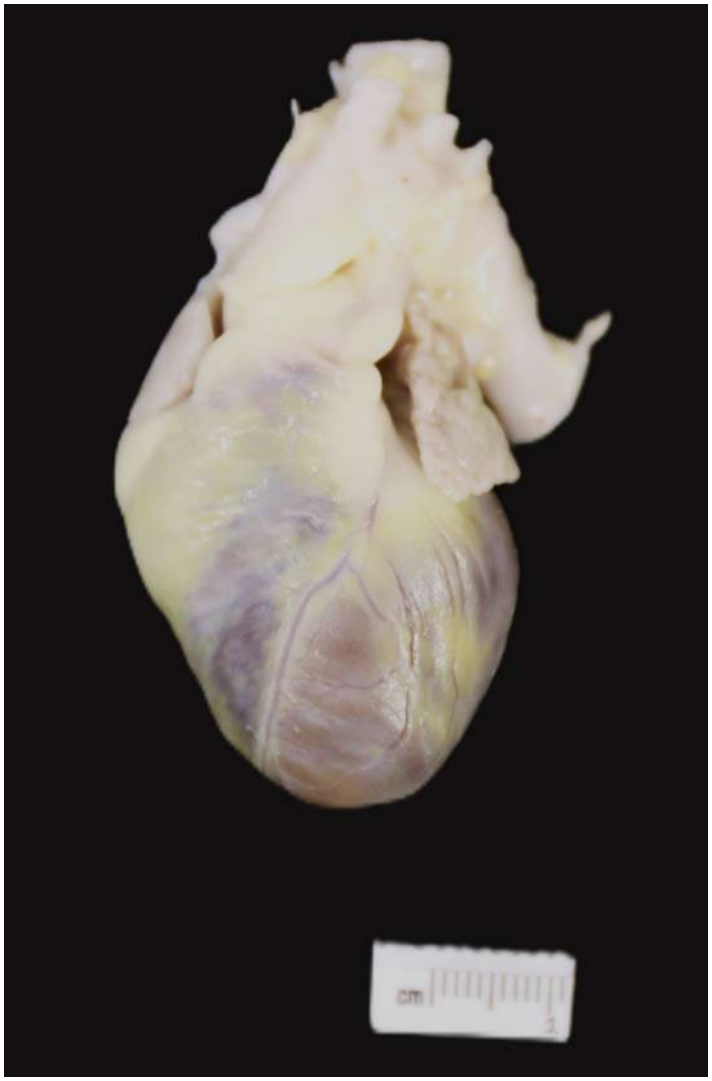
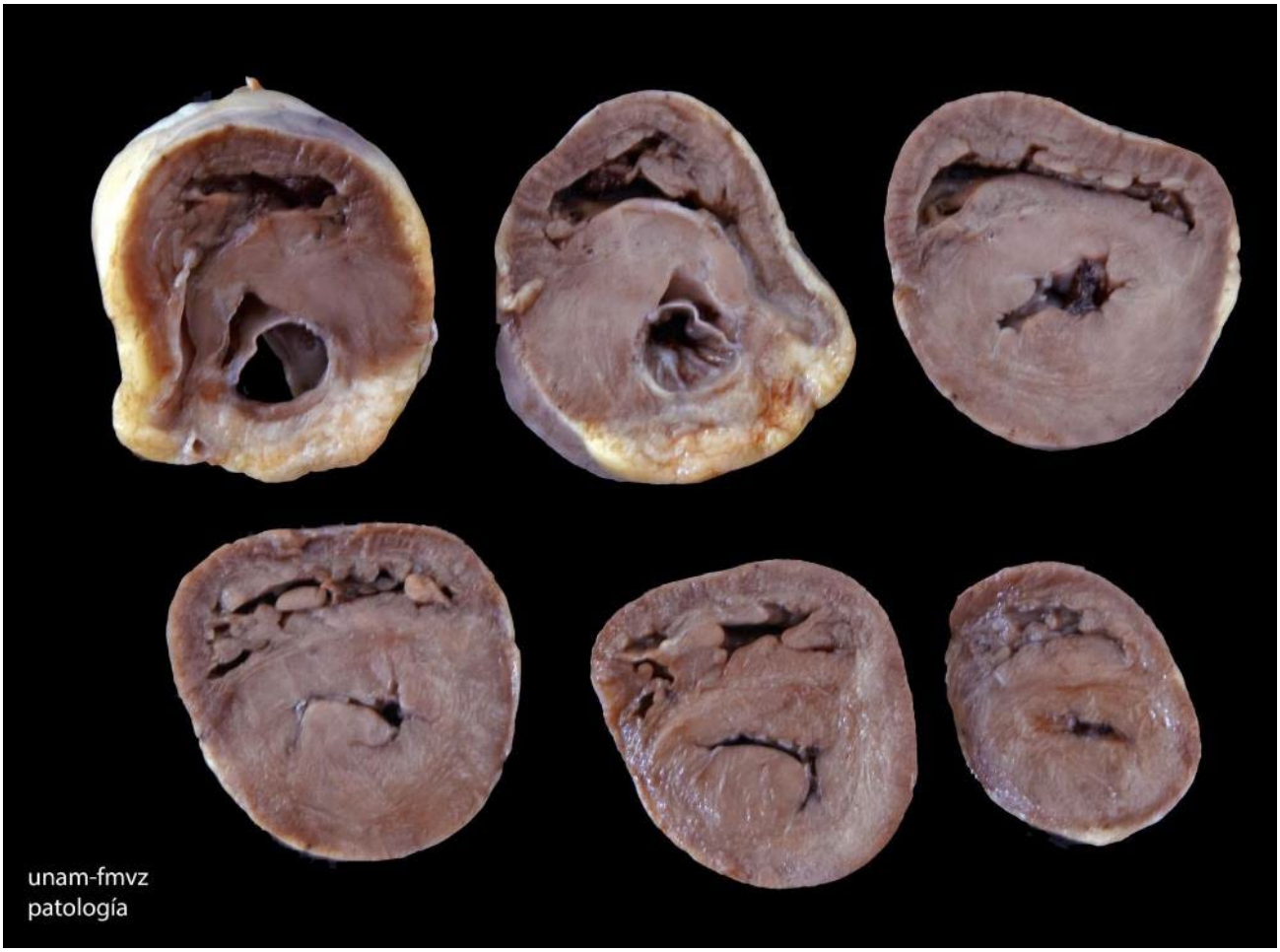
Hypertrophic Cardiomyopathy

- Concentric or asymmetric LV hypertrophy
  - ♥ Thickening of the LVFW and IVS
  - ♥ Small LV internal cavity
  - ♥ Papillary muscle hypertrophy
  - ♥ Myocardial fiber disarray
  - ♥ Fibrosis
  - ♥ Coronary arteriosclerosis
- Left atrial enlargement
- Right heart enlargement

- Decrease ventricular filling
- Decrease compliance—diastolic dysfunction

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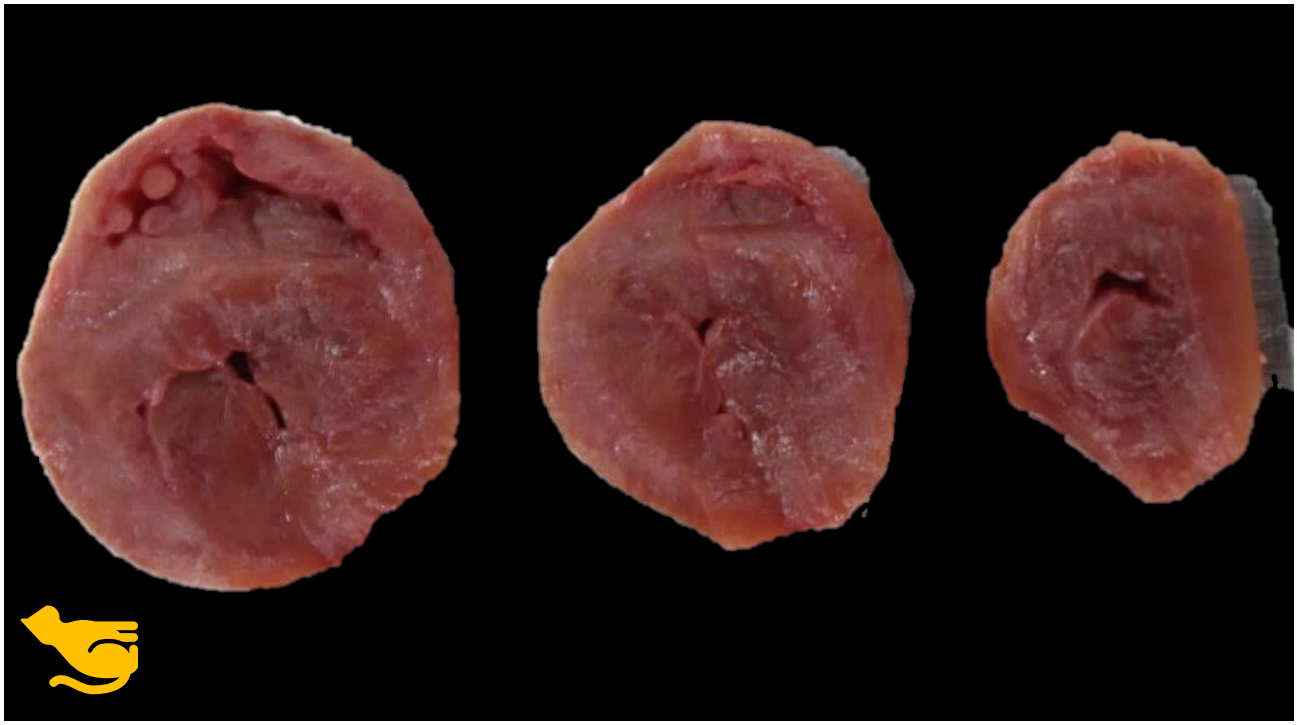
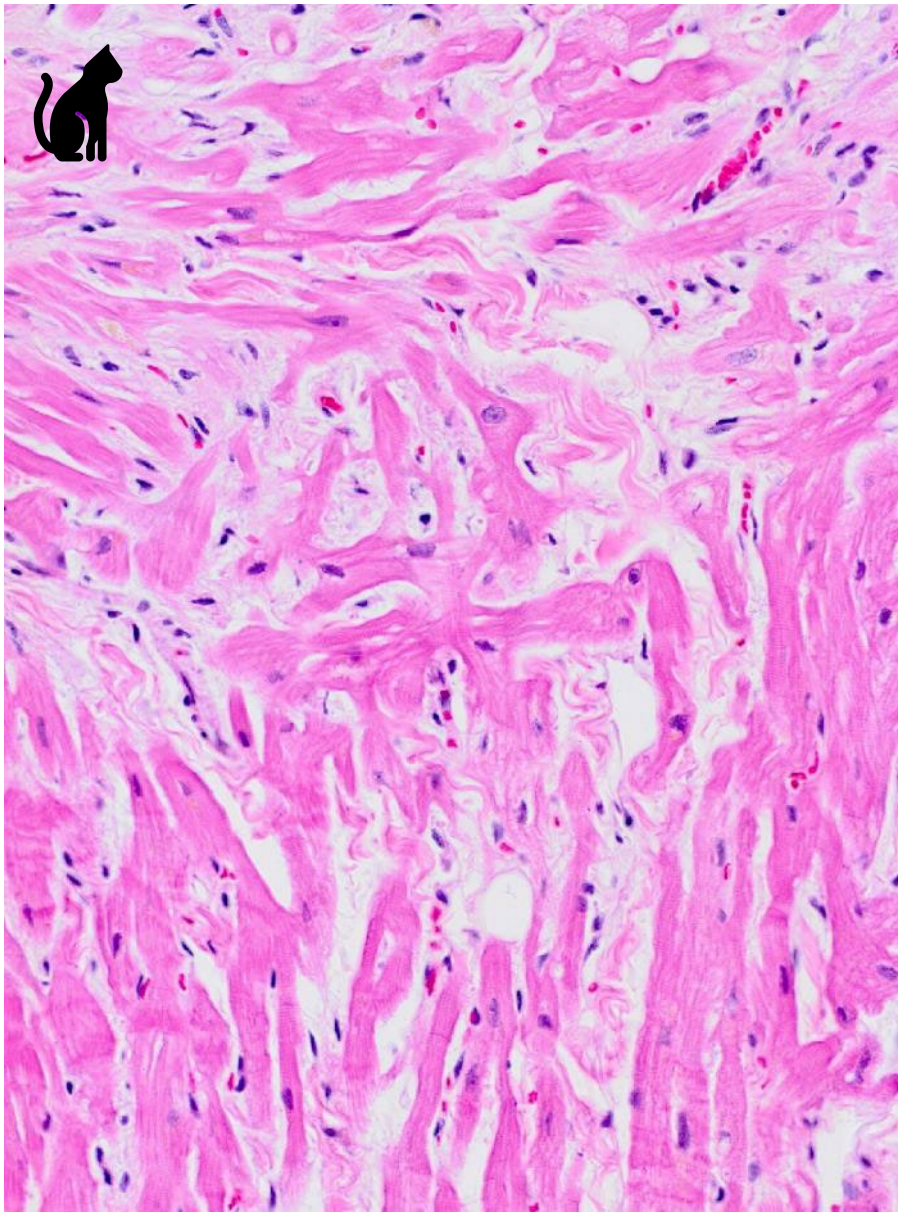
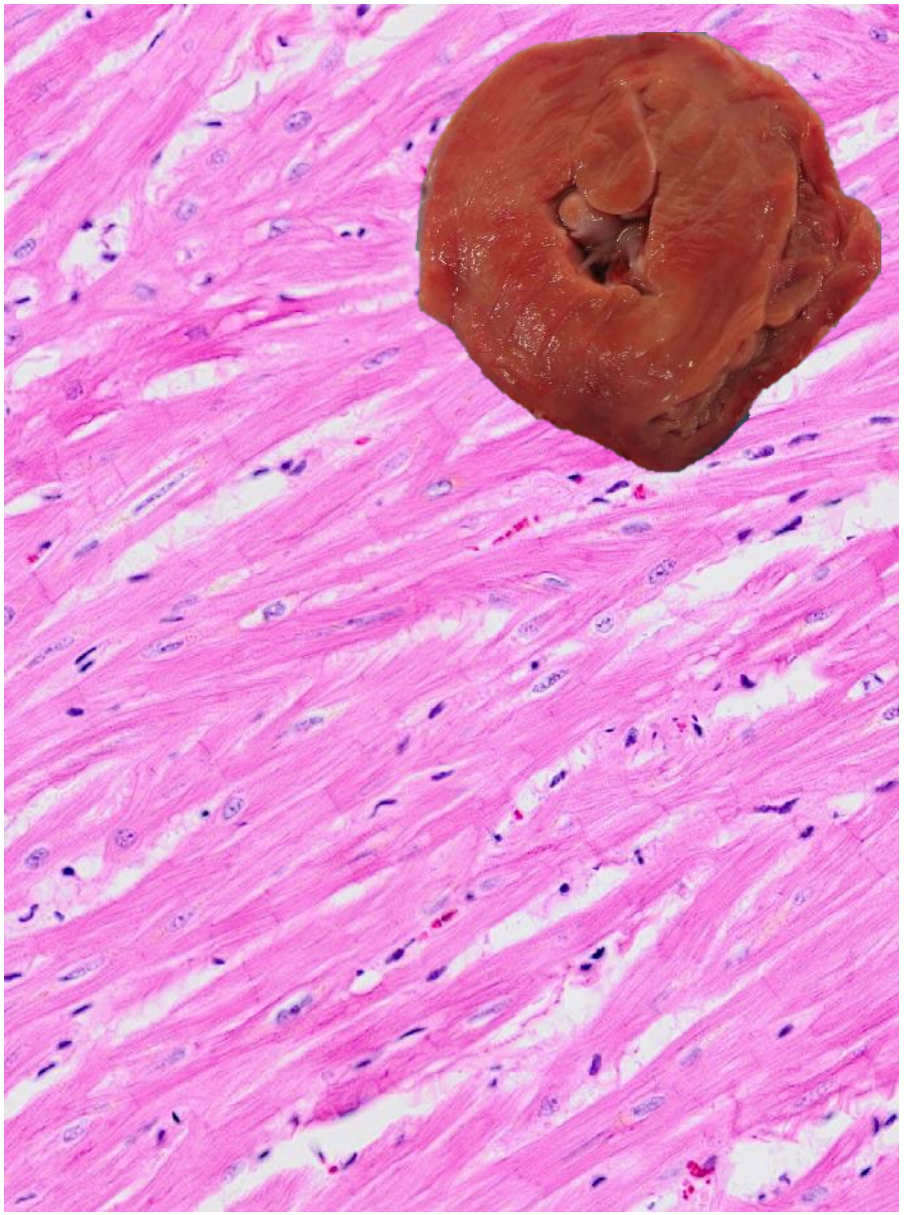


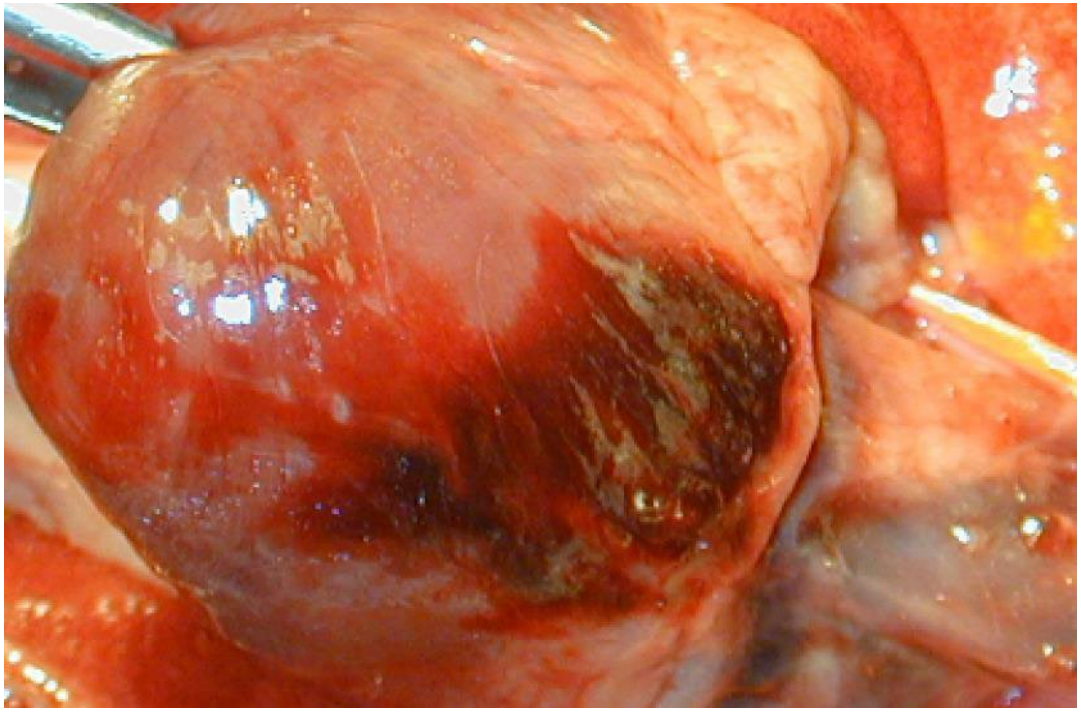




Arterial Thromboembolism

10-20% have atrial or caudal aortic thrombi

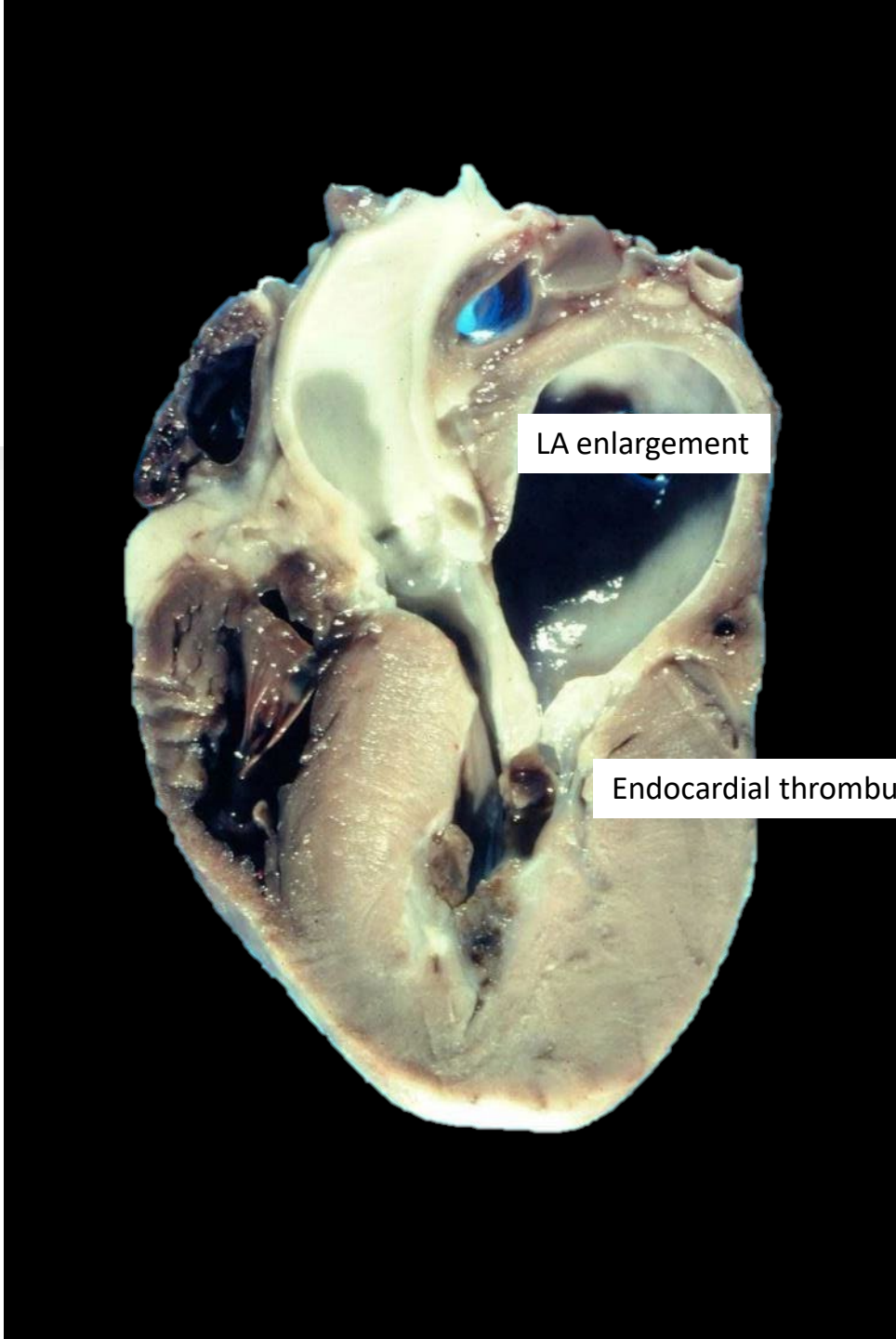
- Pelvic limbs – 85 to 90%
- Thoracic limbs – 5 to 10%
- Other sites:
  - Kidneys
  - GI tract
  - Brain
  - Heart
  - Lungs



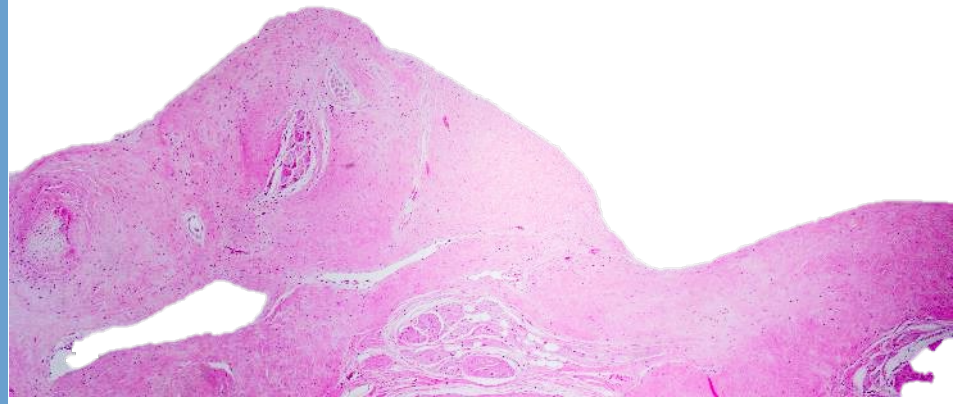
Restrictive cardiomyopathy

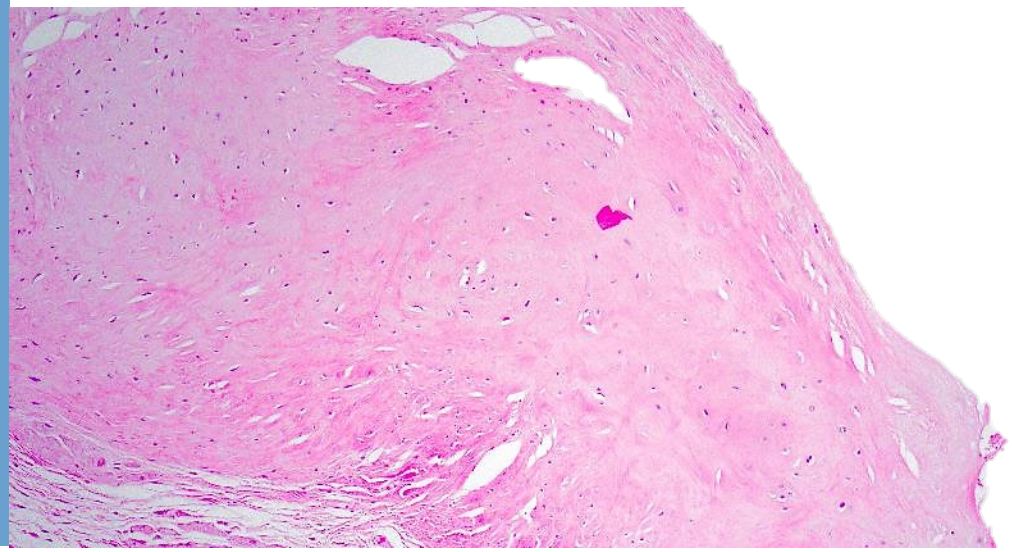
- Endocardial, subendocardial or myocardial fibrosis
- Endomyocardial fibrosis restricts LV diastolic filling and reduces the diastolic volume of one or both ventricles
- Systolic myocardial dysfunction (DCM) has occasionally been reported either in association with, or due to, RCM

- Endocardial fibrosis bridges papillary muscles
- Diffuse endocardial fibrosis
- LA enlargement
- Prone to ATE

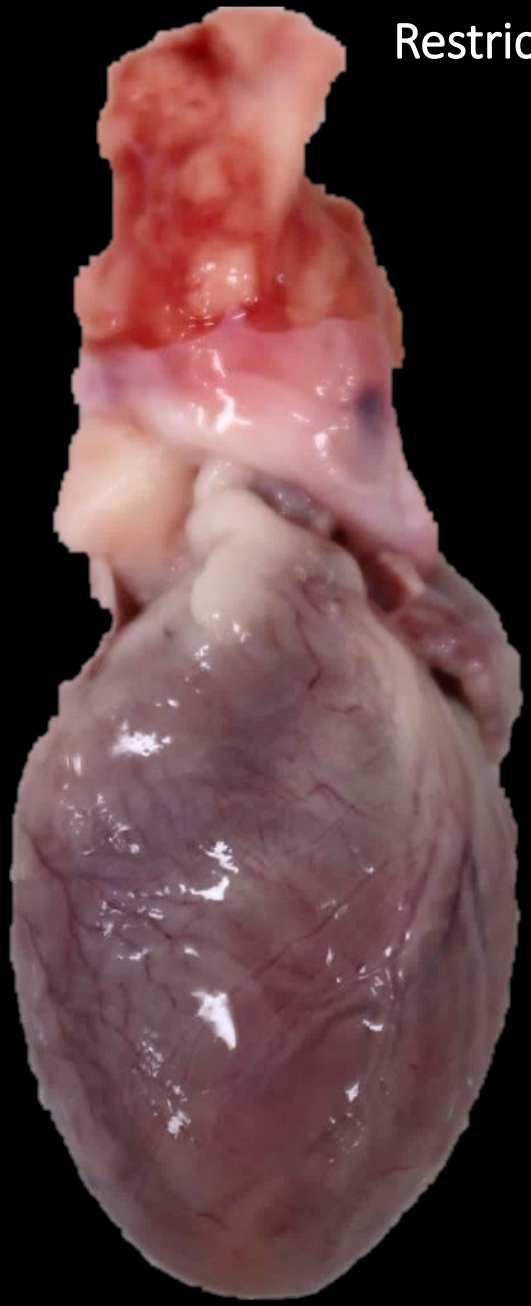


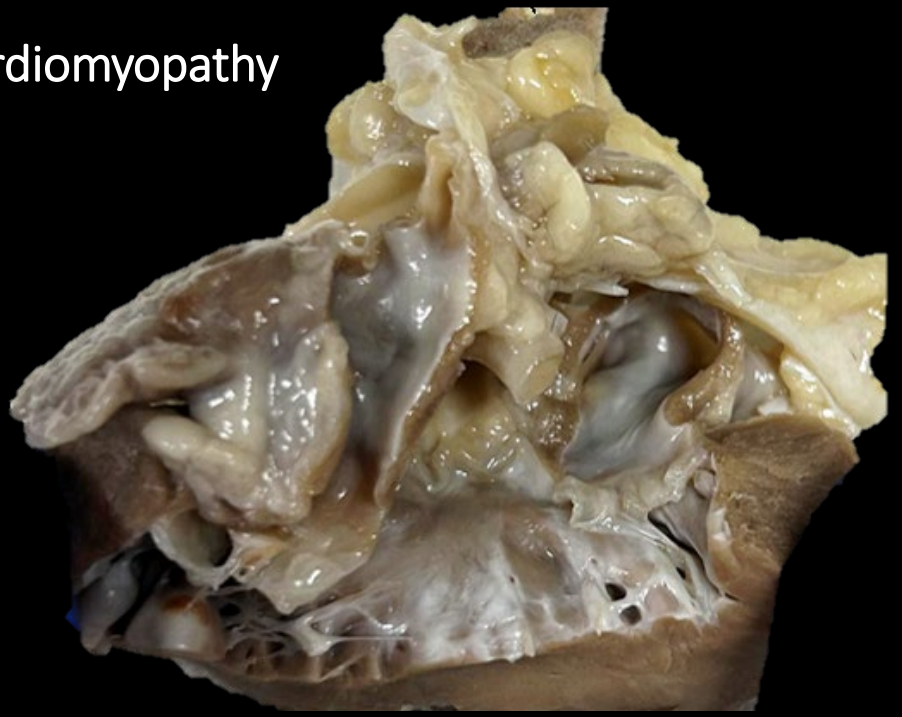
Restrictive cardiomyopathy

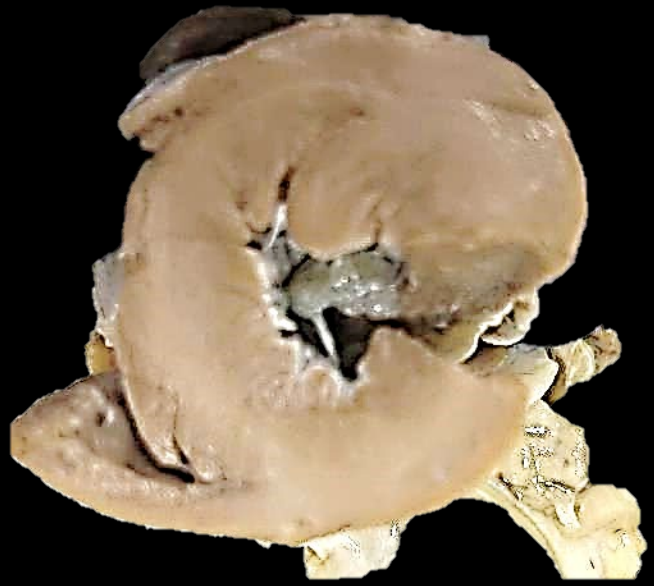


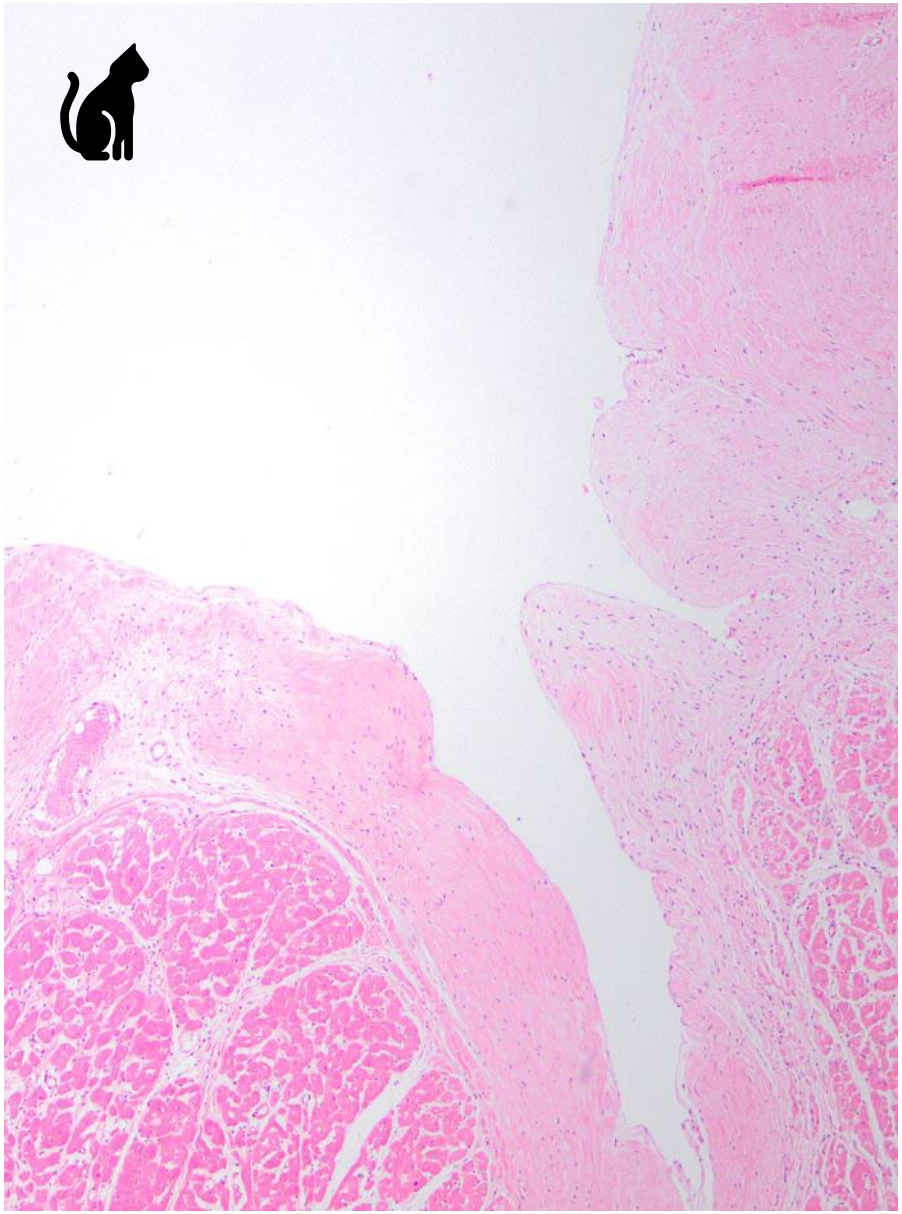


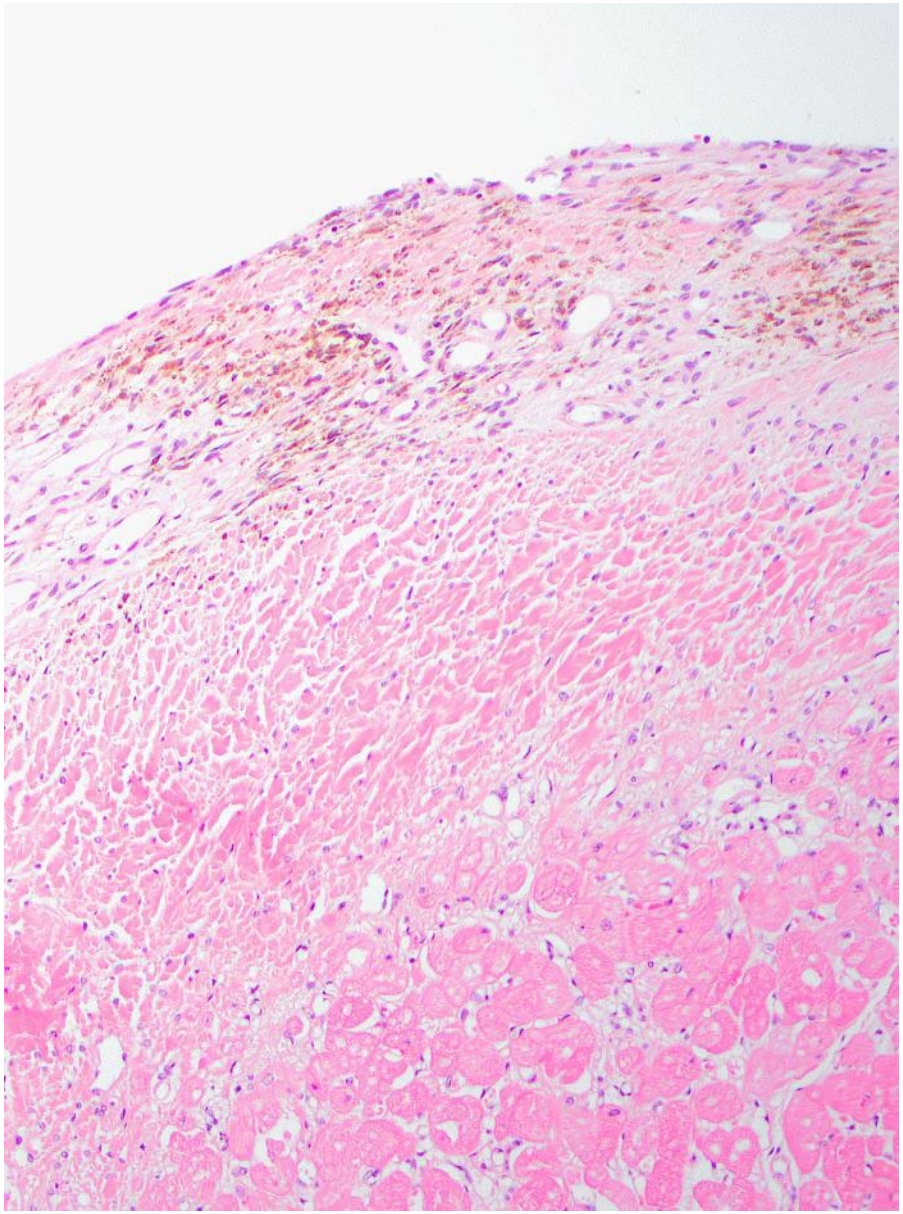
Restrictive cardiomyopathy



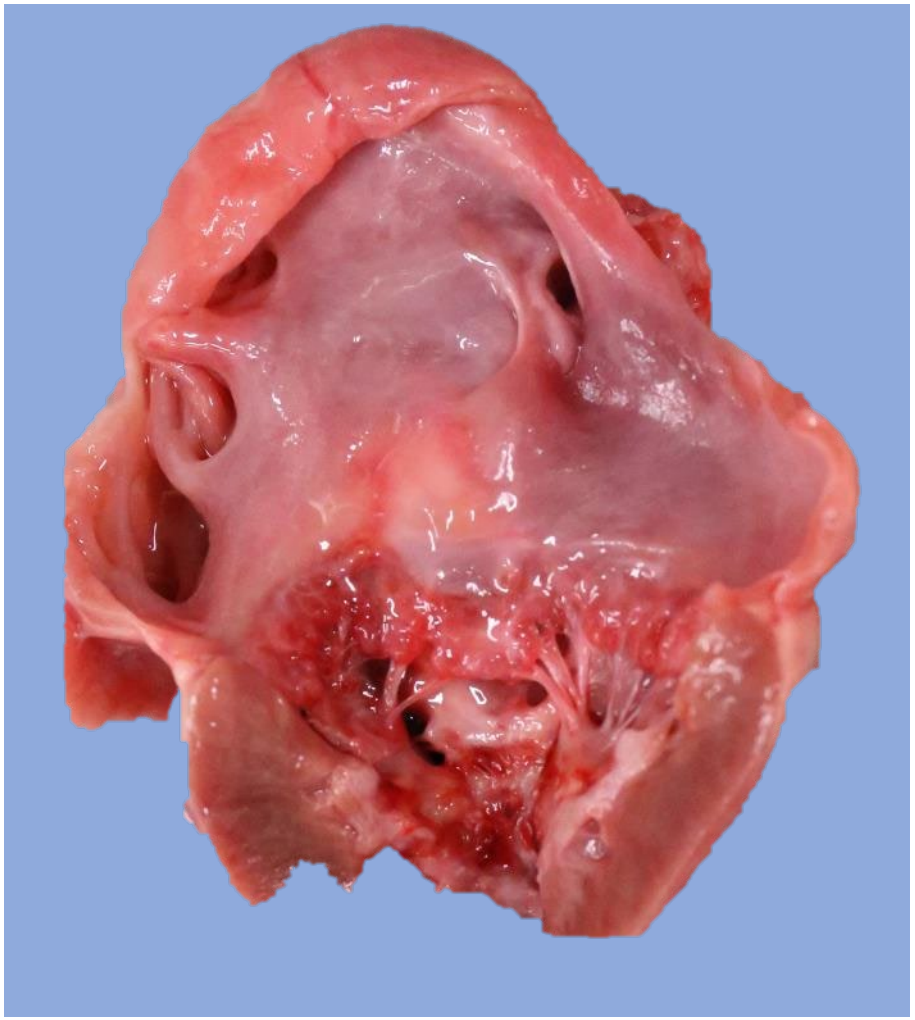


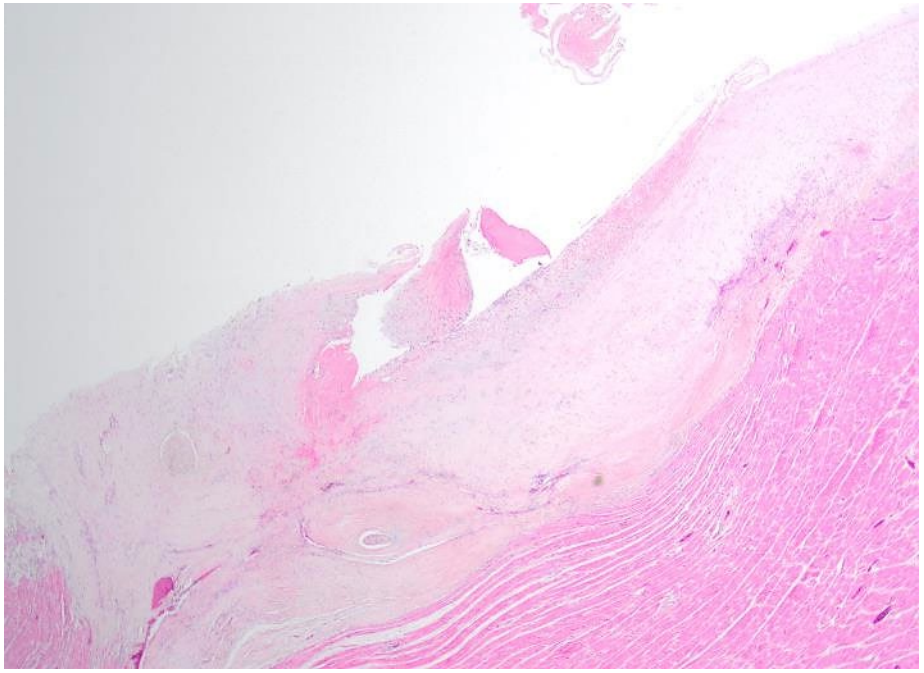


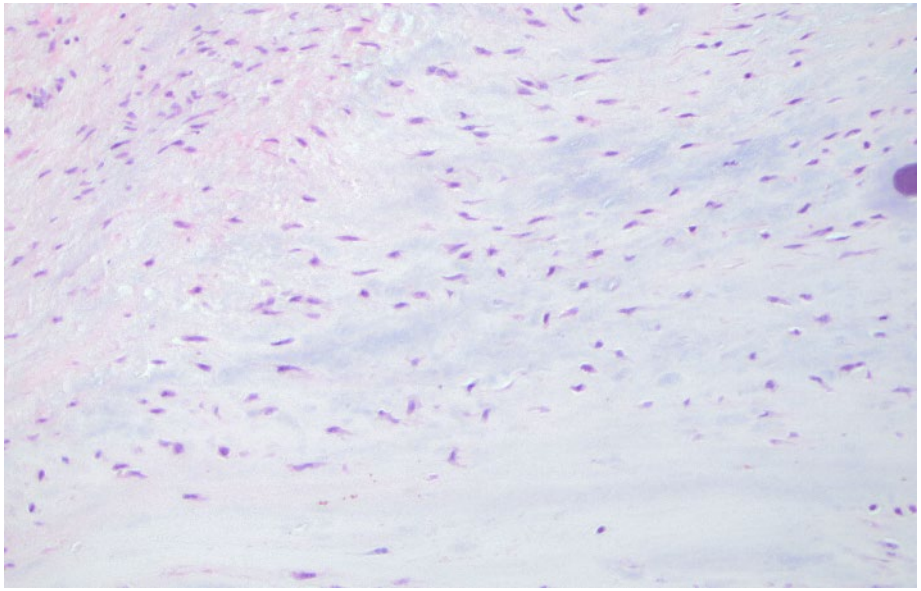




Restrictive cardiomyopathy

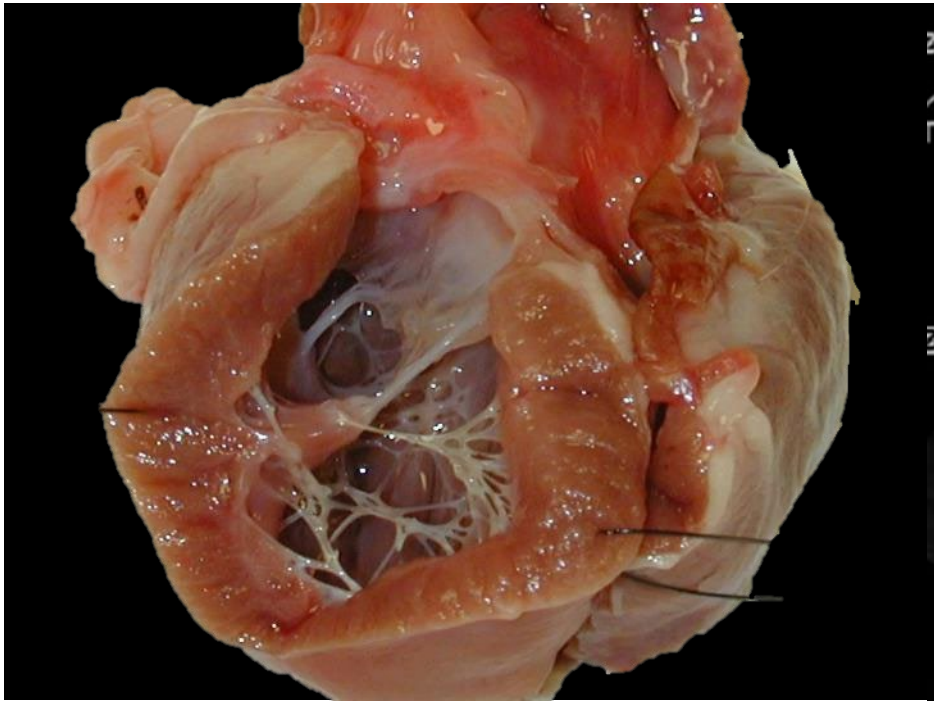


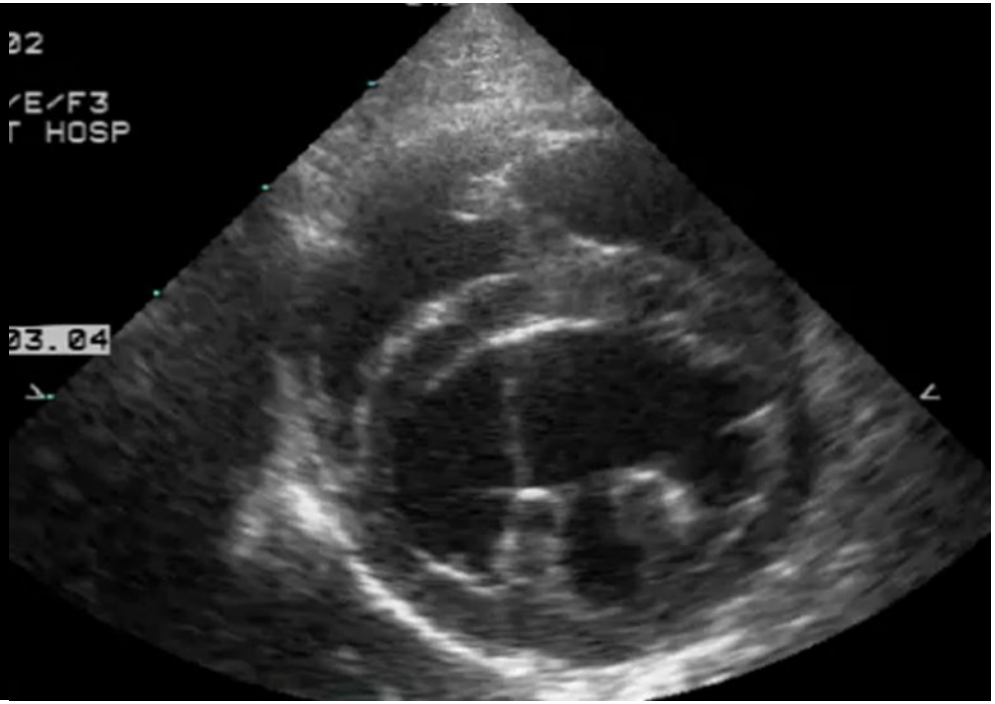


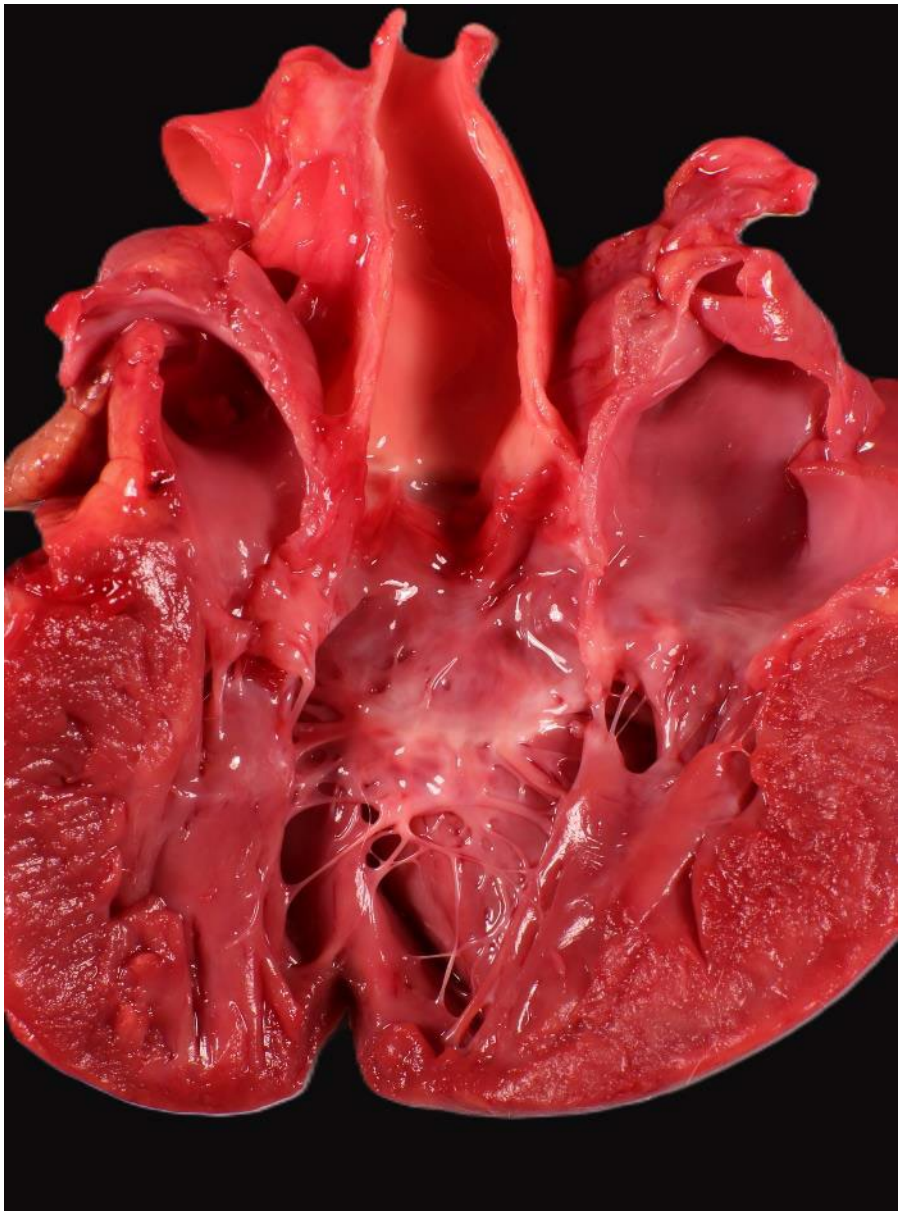


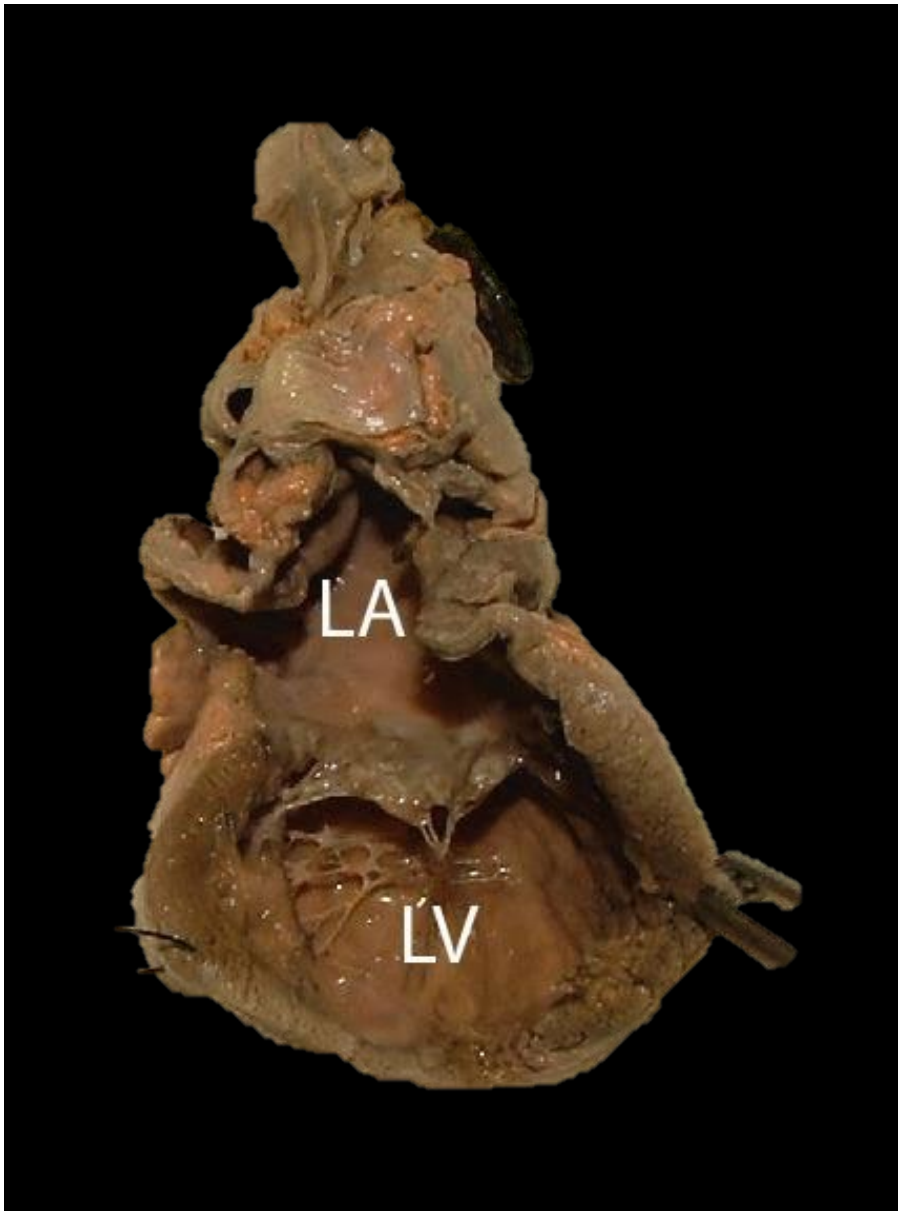
Excessive moderator bands

- Network of excessive moderator bands in the LV
- LV hypertrophy or dilation
- Likely represents a congenital defect
- Proposed to restrict cardiac filling

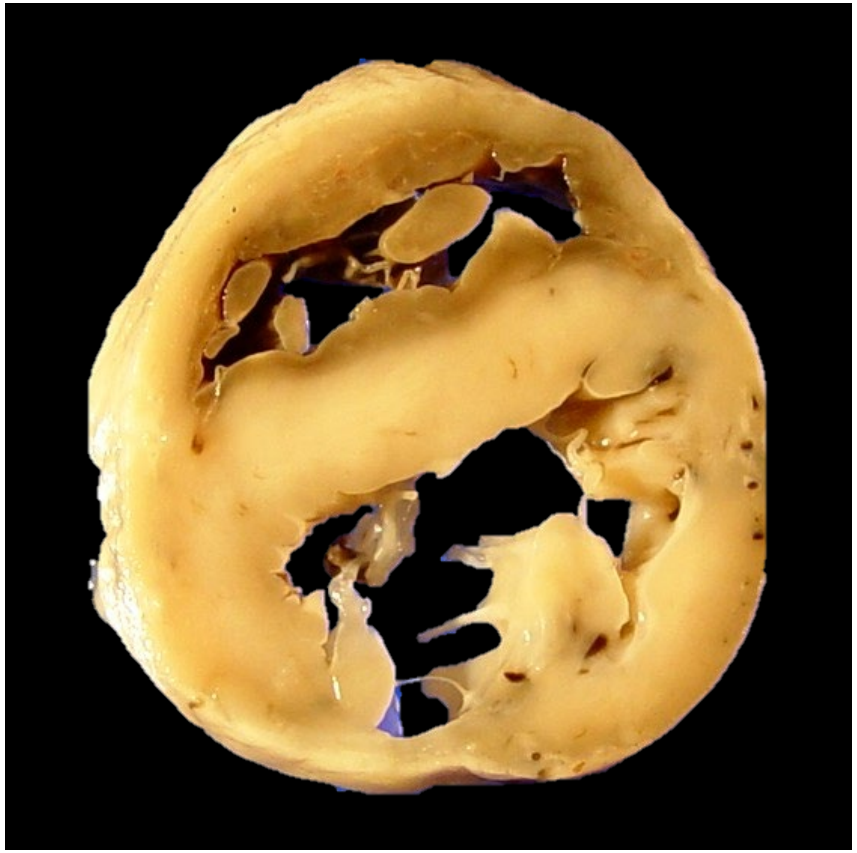








Thick, firm bands of tissue runs between the endocardial surfaces of the left ventricle
Collagen, myocytes, adipocytes, Purkinje cells, endothelium

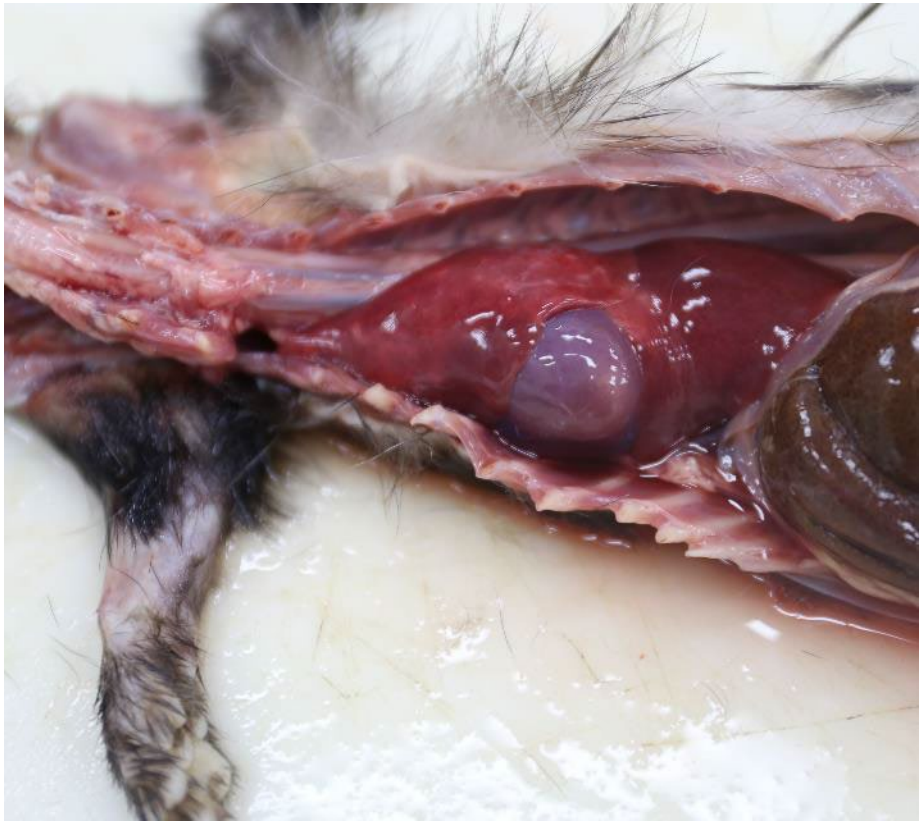


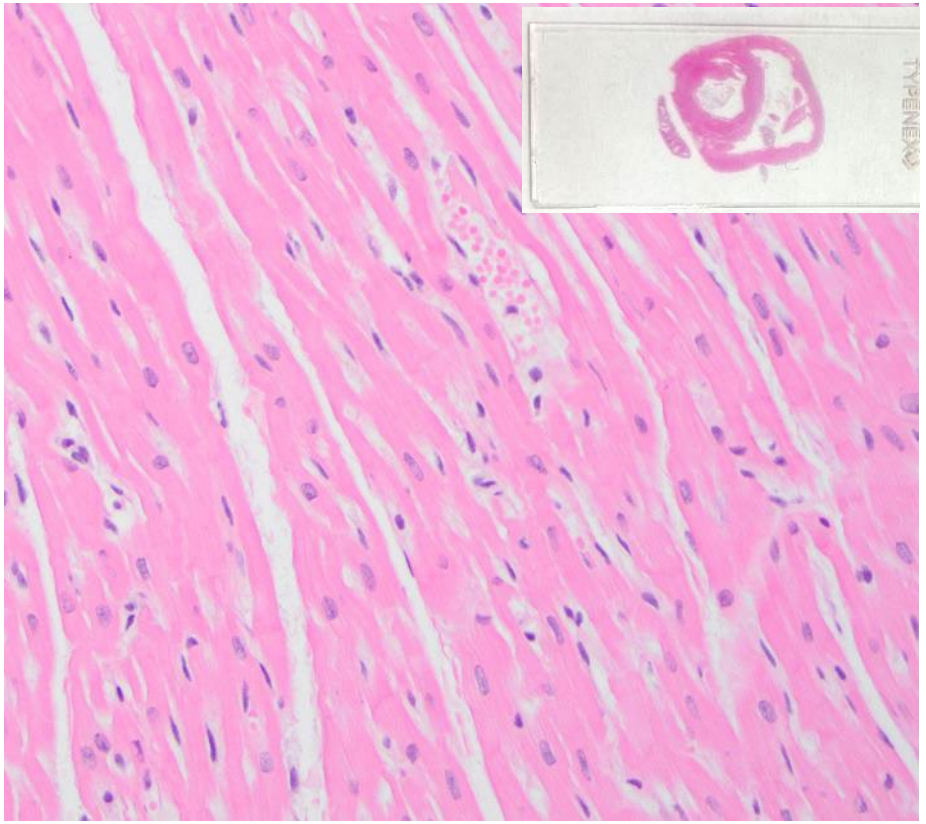
Nonspecific cardiomyopathy

- Do not fulfill diagnostic criteria for DCM and HCM
- No apparent pericardial, coronary, valvular disease, or systemic hypertension
- Myocardial disease that defies classification
  - Walls of variable thickness
  - Cavity may be dilated
  - May have reduced systolic function
  - Mild valvular regurgitation may be evident

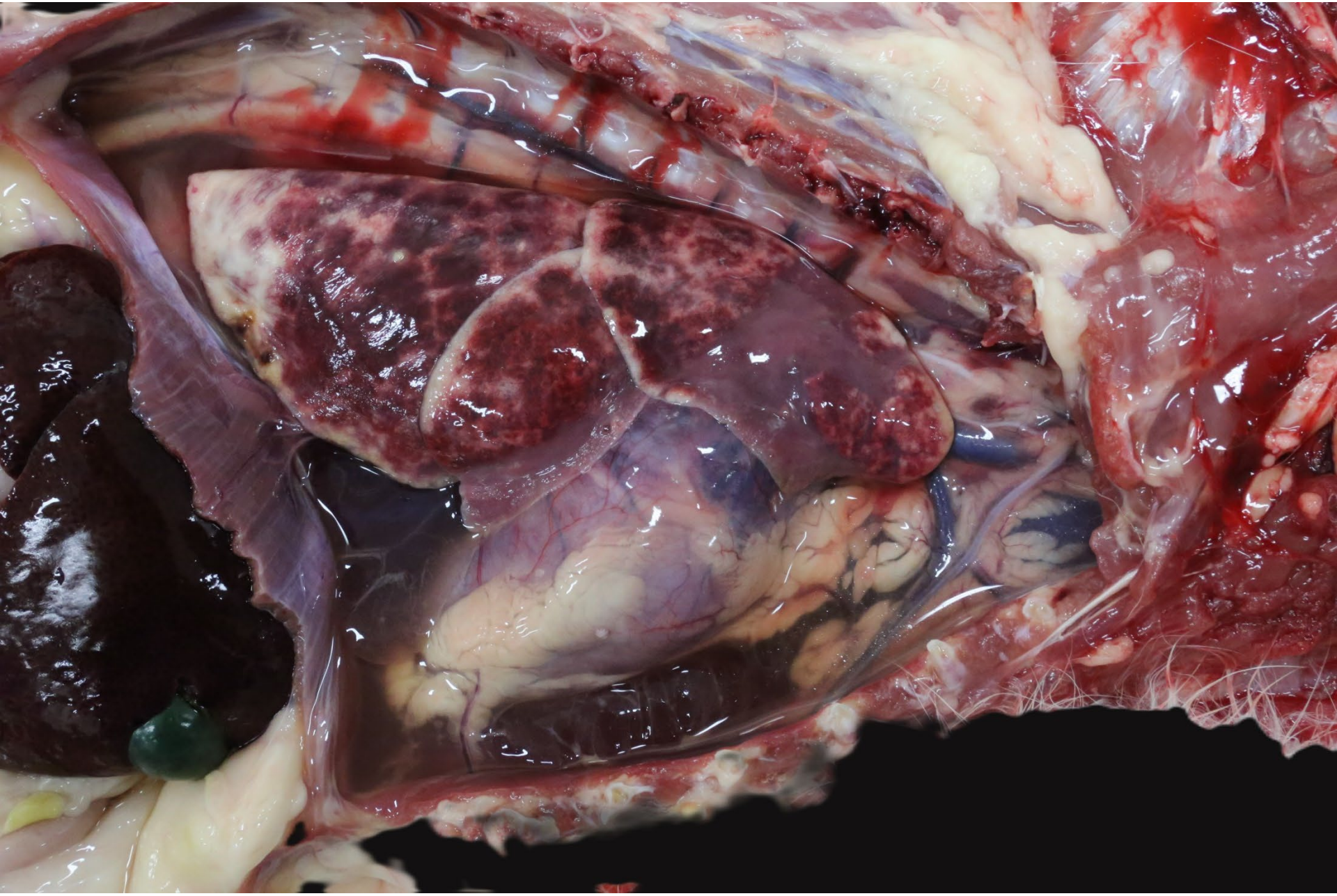
Ferret dilated cardiomyopathy

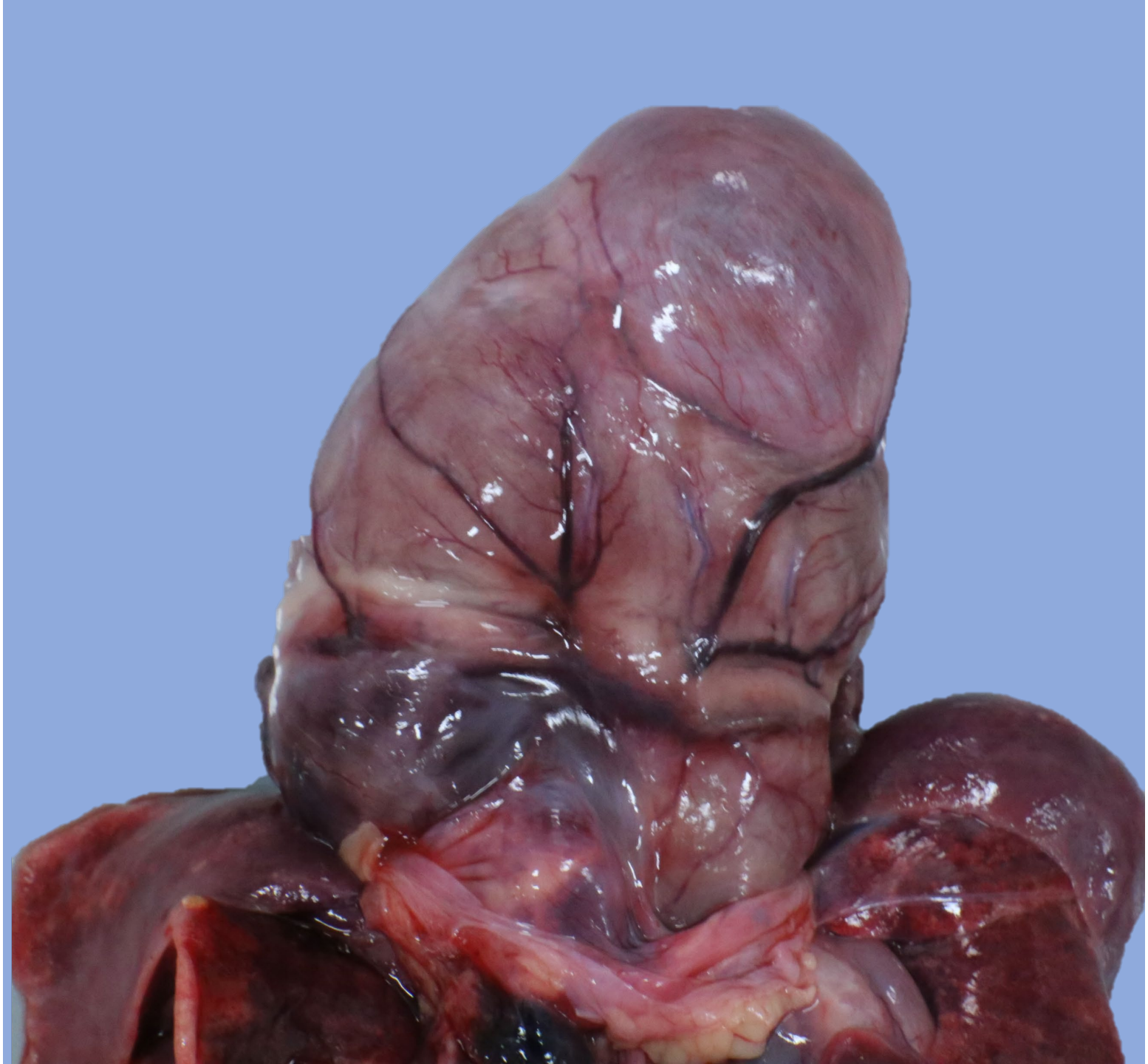
One of the most common acquired heart diseases in ferrets

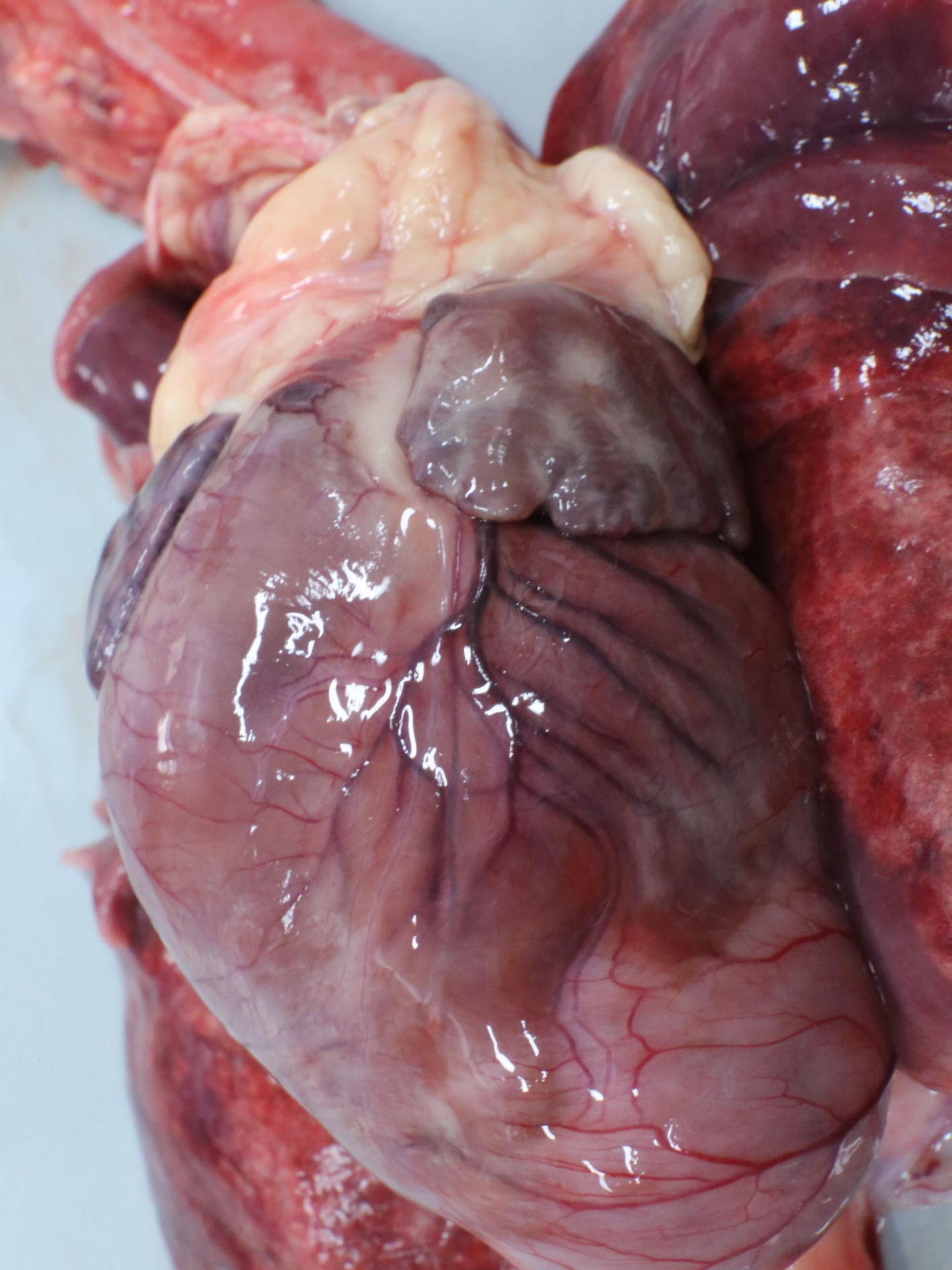


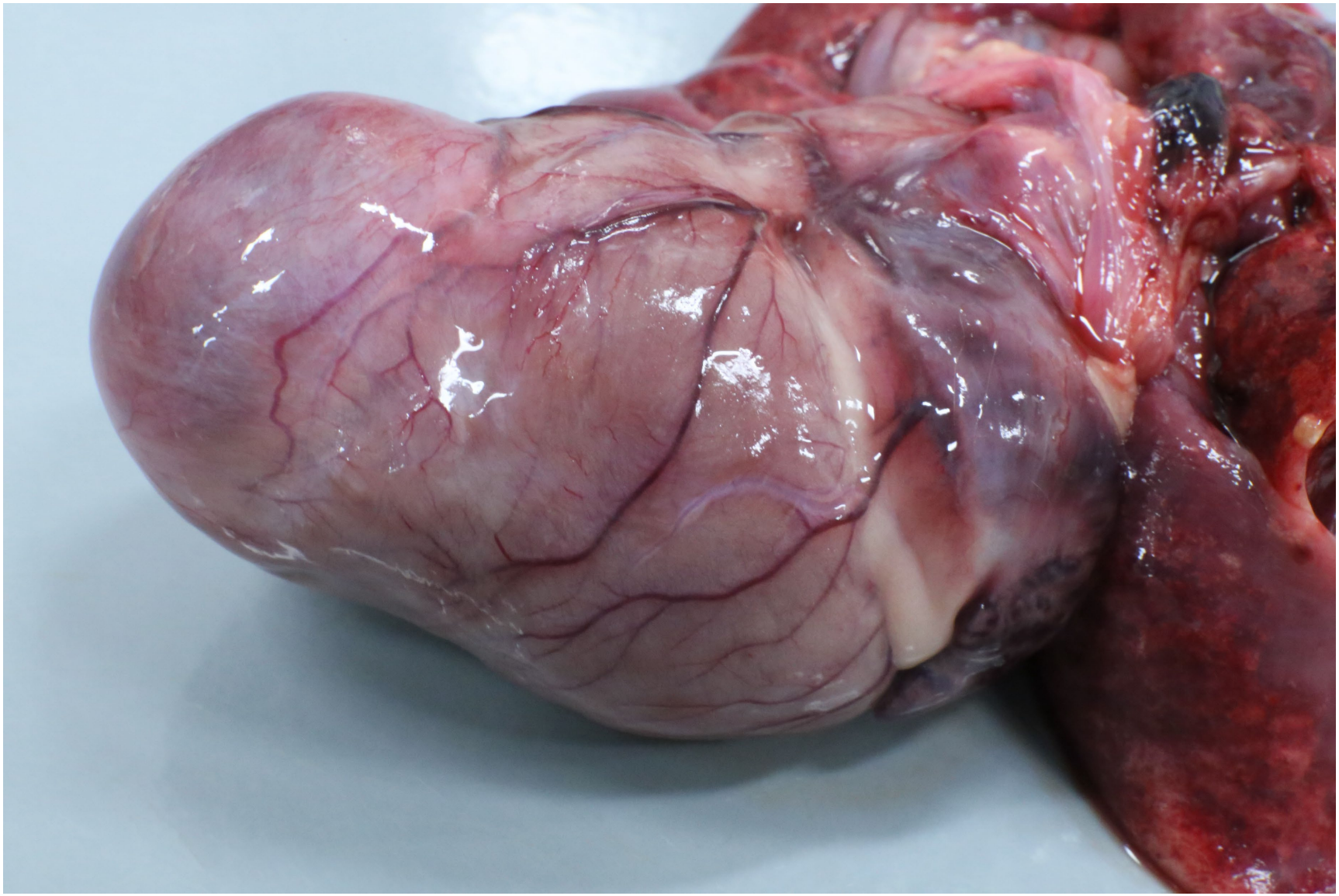


Rare cardiomyopathy in a cat









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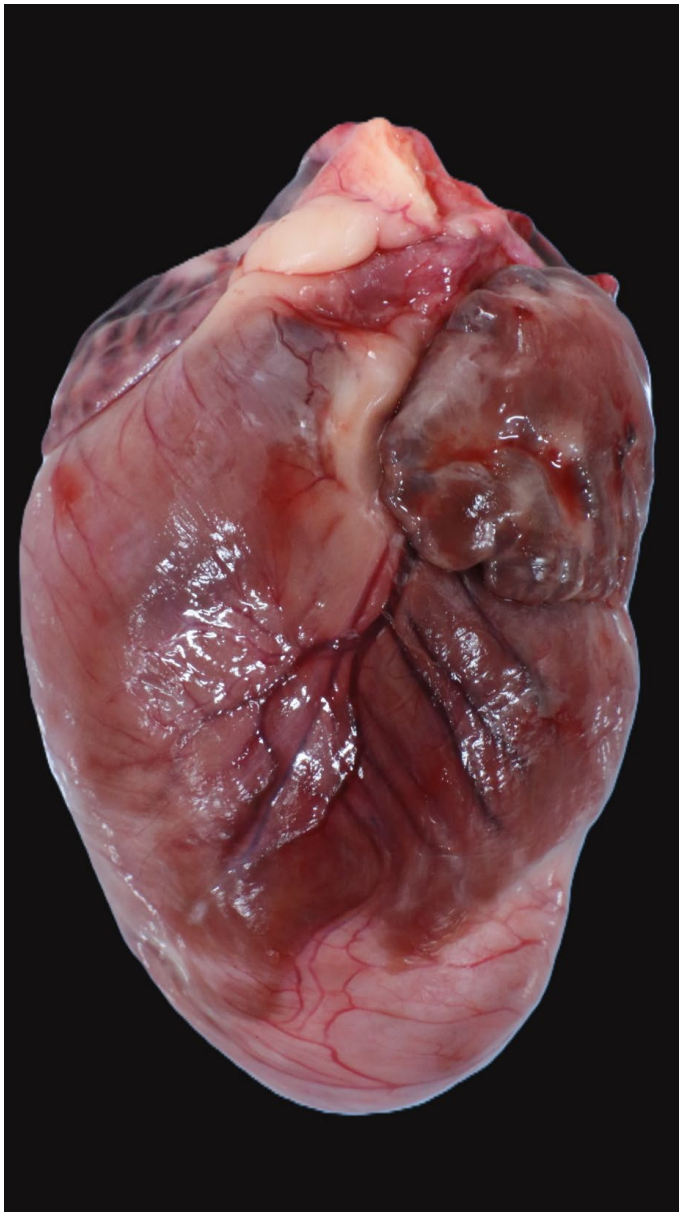
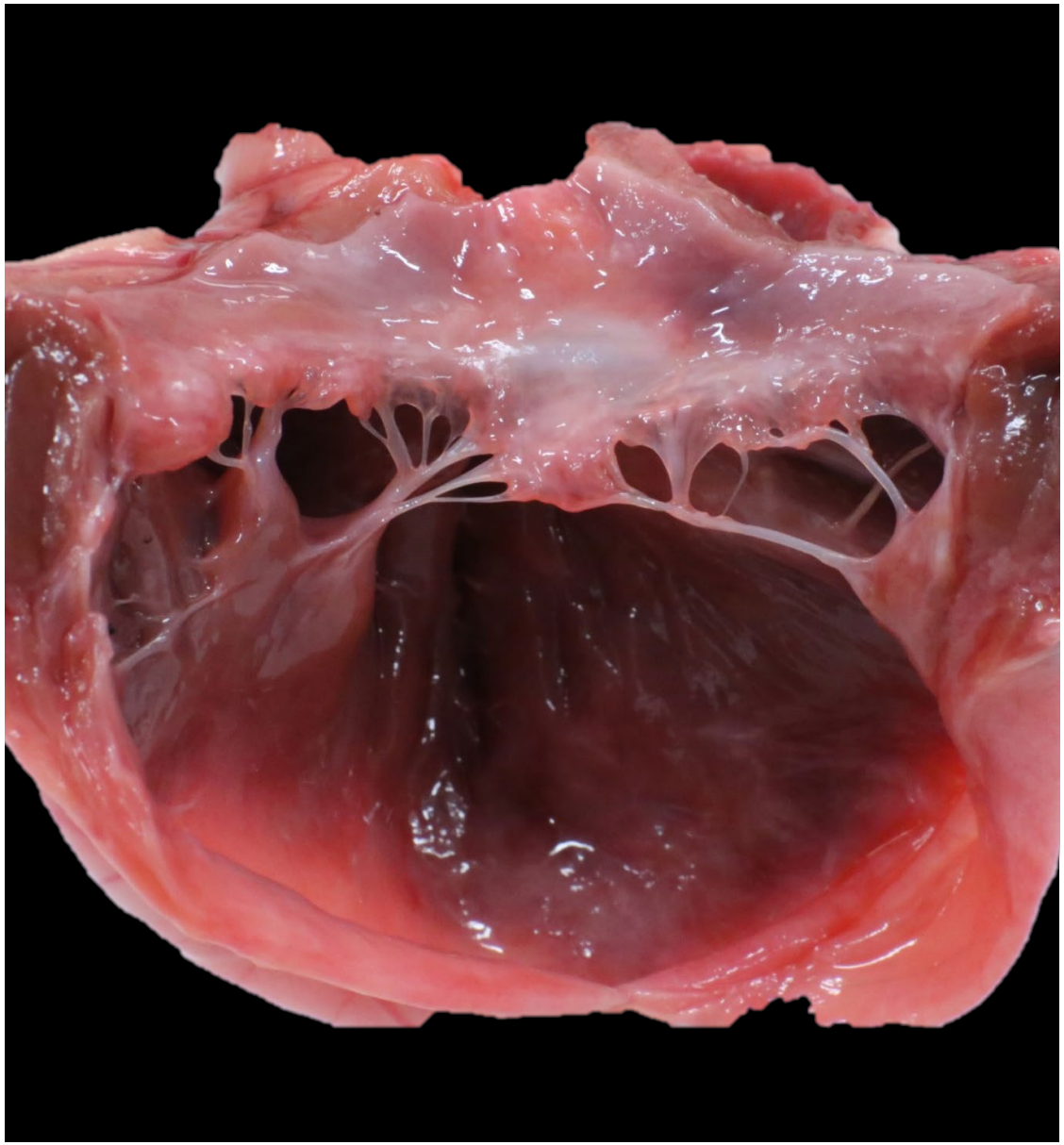
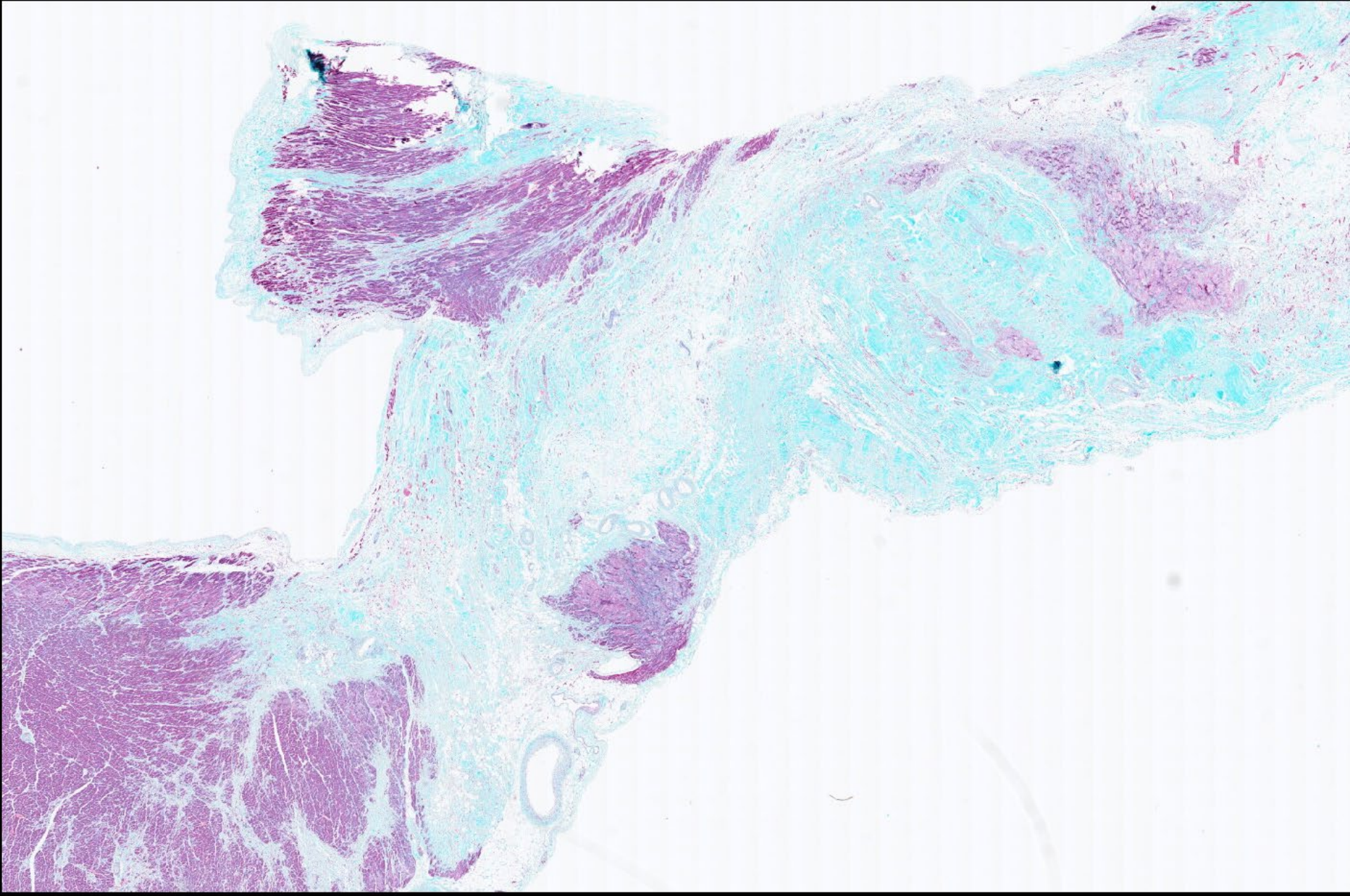
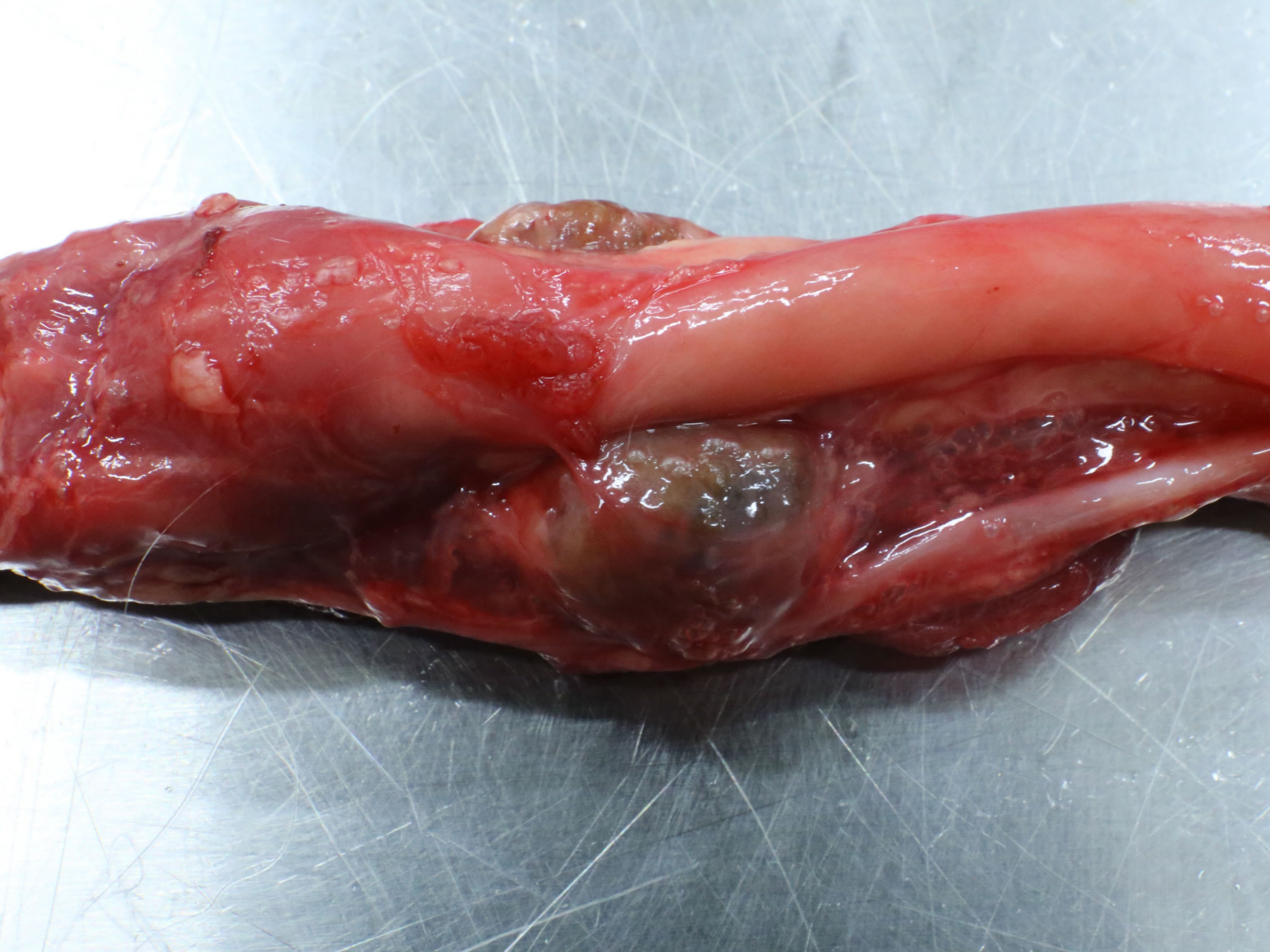
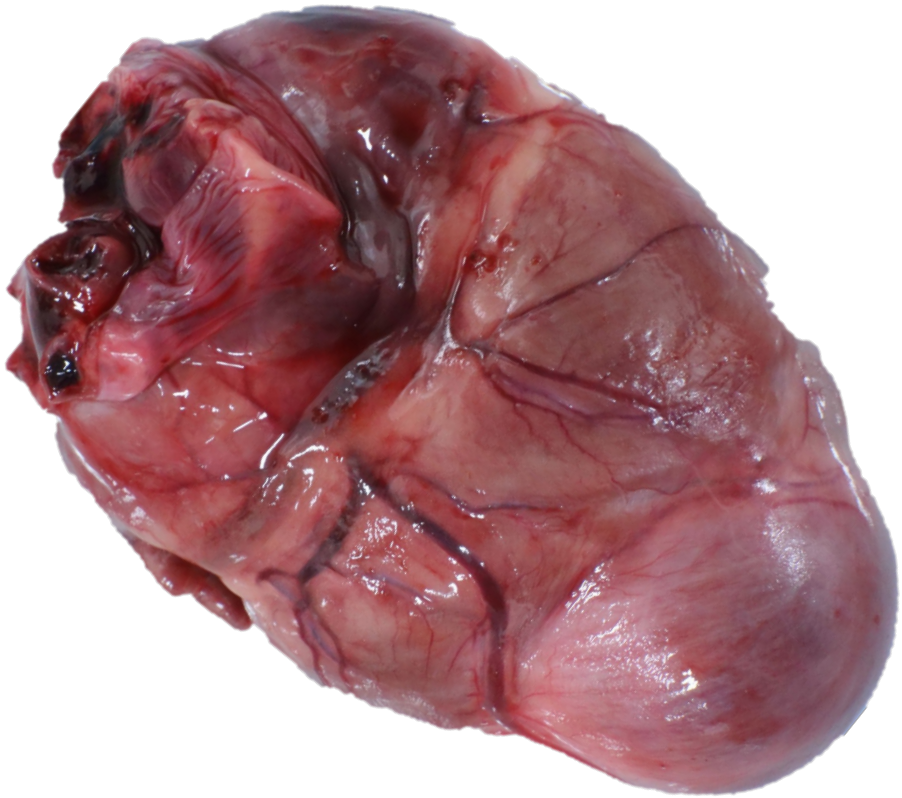








Takotsubo-like cardiomyopathy



The shape of the left ventricle becomes similar to the octopus trap (Tako-Tsubo)

Takotsubo cardiomyopathy

Etiology not fully understood

- Emotional and physical stressors
- Seizures
- Phaeochromocytoma
- Hyperthyroidism
- Surgery

Cathecolamine release:
Adrenergic cascade through the hypothalamic-pituitary –adrenal axis
Activation of the axis involves myocardial dysfunction induced by sympathetic hyperactivity
Increase myocardial catecholamine levels induce microvascular spasm and stunning

Myocardial stunning:
Rising cathecolamines levels act on beta-adrenergic receptors
Beta-adrenergic receptors have their highest concentration in the apex

Different morphological patterns:

- Apical ballooning
- Midventricular
- Basal
- Focal

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Xoloitzcuintle
Mexican hairless dog