Cardiomyopathy

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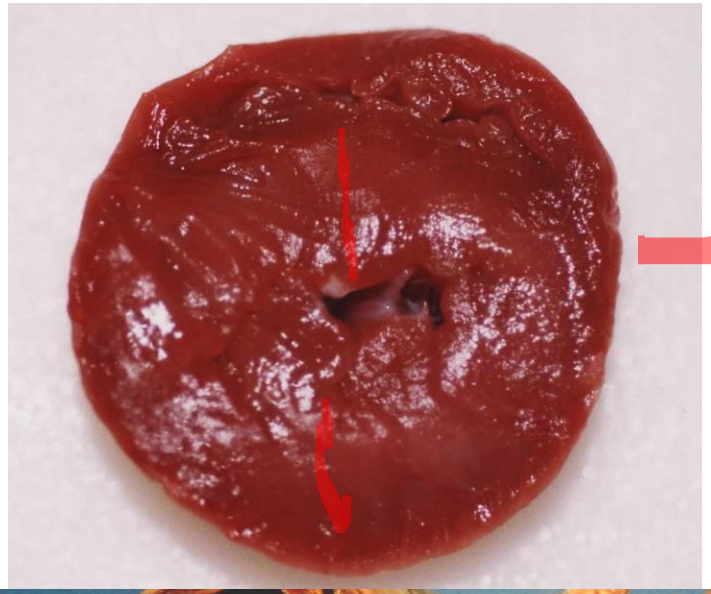
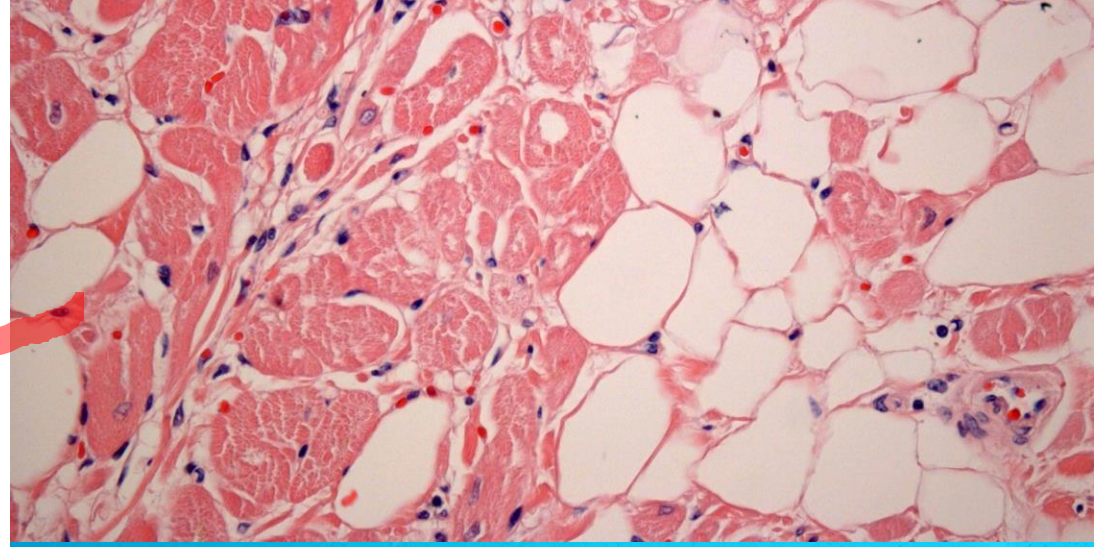
Cardiomyopathy

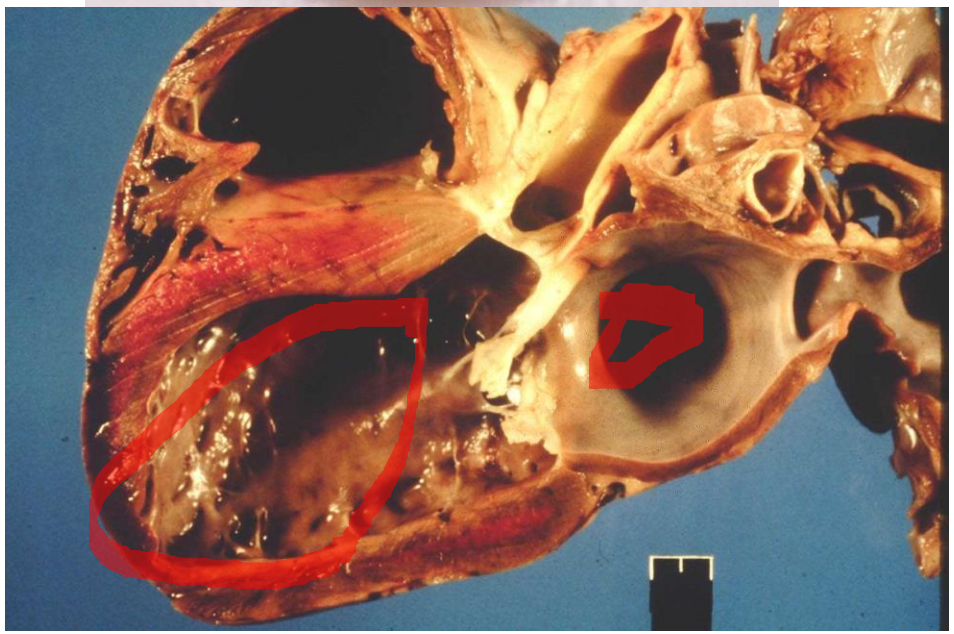
- A heterogeneous group of myocardial diseases associated with:
  - ♥ Mechanical dysfunction
  - ♥ Or Electrical dysfunction
  - ♥ Usually resulting in ventricular hypertrophy or dilatation
- Causes are frequently genetic
- Cardiomyopathies can be:
  - ♥ Confined to the heart or
  - ♥ Part of generalized systemic disorder
- Often lead to weakness, exercise limitation, syncope, progressive heart failure, or cardiovascular death

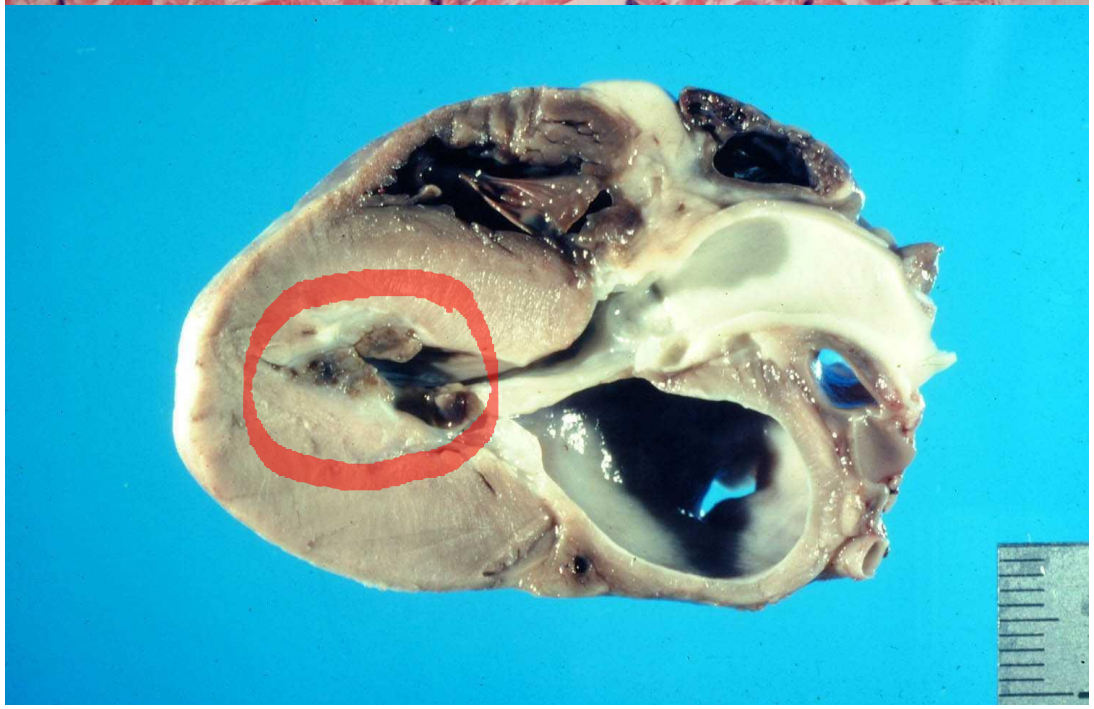
Anatomic and Hemodynamic Classification of Cardiomyopathy

- Dilated cardiomyopathy
  - ♥ Chamber dilation, thinned walls
  - ♥ Systolic (+/- diastolic) dysfunction
- Hypertrophic cardiomyopathy
  - ♥ Concentric hypertrophy, small cavity, +/- left ventricular outflow tract obstruction (LVOTO)
  - ♥ Diastolic (+/- systolic) dysfunction
- Restrictive cardiomyopathy
  - ♥ Endocardial fibrosis, LA enlargement
  - ♥ Typically diastolic dysfunction
- Arrhythmogenic right ventricular cardiomyopathy









Cardiomyopathy

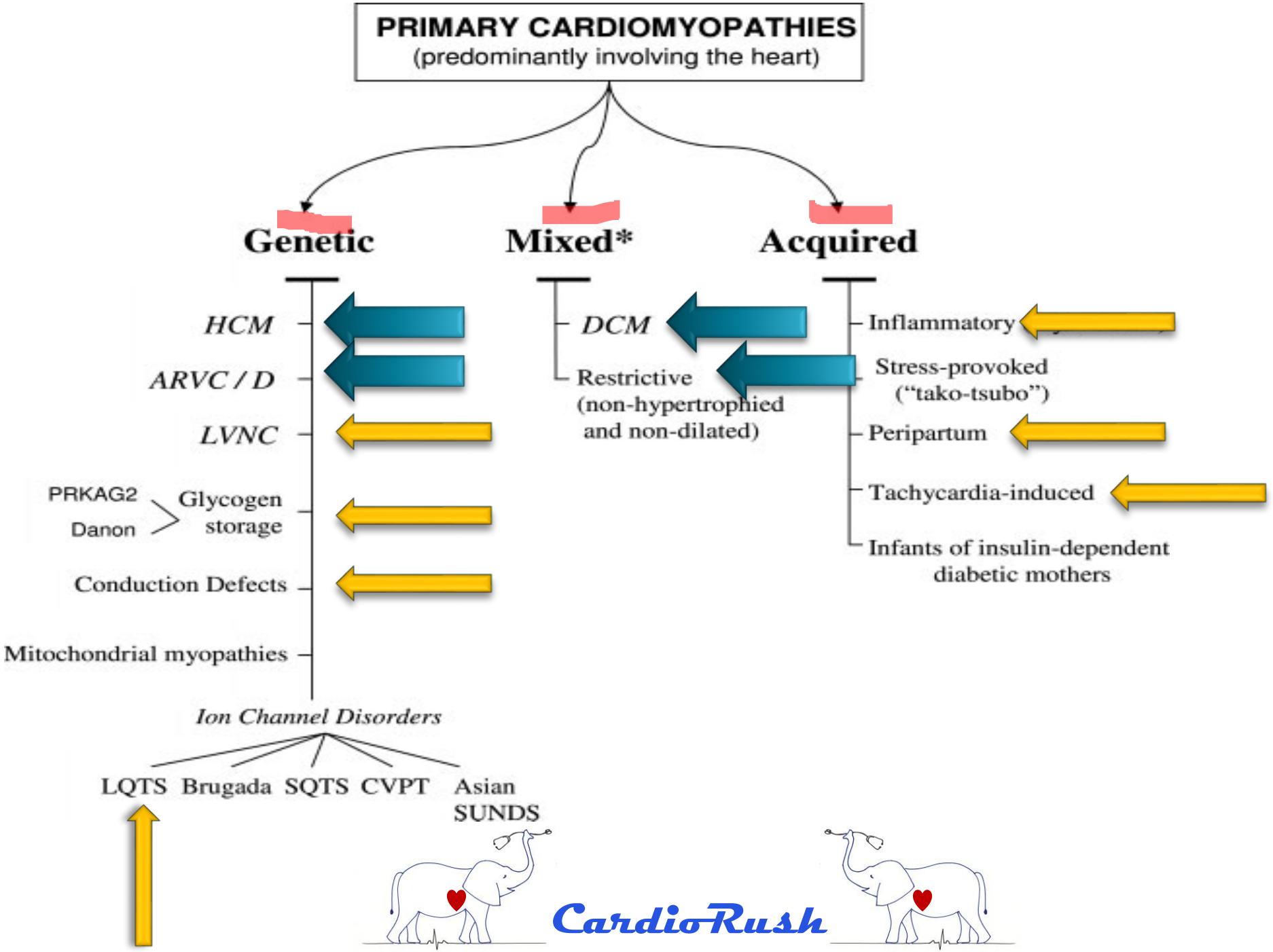
Primary (intrinsic) cardiomyopathy

- Myocardial disease primarily affecting heart
  - ♥ Genetic mutation is the cause for many
  - ♥ Also includes certain non-genetic or acquired

Secondary (extrinsic) cardiomyopathy

- Myocardial disease secondary to another identifiable systemic (multiorgan) disease
  - ♥ Ischemic cardiomyopathy
  - ♥ Doxorubicin cardiomyopathy

Alternative nomenclature: Doxorubicin-induced cardiotoxicity


PRIMARY CARDIOMYOPATHIES
(predominantly involving the heart)
Genetic
Mixed*
Acquired
HCM
ARVC / D
LVNC
PRKAG2
Danon
Glycogen storage
Conduction Defects
Mitochondrial myopathies
Ion Channel Disorders
LQTS
Brugada
SQTS
CVPT
Asian SUNDS
DCM
Restrictive (non-hypertrophied and non-dilated)
Inflammatory
Stress-provoked ("tako-tsubo")
Peripartum
Tachycardia-induced
Infants of insulin-dependent diabetic mothers
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Common Cardiomyopathies in Veterinary Medicine

- Hypertrophic cardiomyopathy
  - HCM vs HOCM (hypertrophic obstructive CM)
- Dilated cardiomyopathy (DCM)
- Restrictive cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy (ARVC)
- Myocarditis >>> DCM
- Tachycardia-induced cardiomyopathy

Secondary Cardiomyopathies

Vet Med in Green

Secondary Cardiomyopathies

Infiltrative*

Amyloidosis (primary, familial autosomal dominant†, senile, secondary forms)

Gaucher disease†

Hurler's disease†

Hunter's disease†

Storage‡

Hemochromatosis

Fabry's disease†

Glycogen storage disease† (type II, Pompe)

Niemann-Pick disease†

Toxicity

Drugs, heavy metals, chemical agents

Endomyocardial fibrosis

Hypereosinophilic syndrome (Löeffler's endocarditis)

Inflammatory (granulomatous)

Sarcoidosis

Endocrine

Diabetes mellitus†

Hyperthyroidism

Hypothyroidism

Hyperparathyroidism

Pheochromocytoma

Acromegaly

Cardiofacial

Noonan syndrome†

Lentiginosis†

Neuromuscular/neurological

Friedreich's ataxia†

Duchenne-Becker muscular dystrophy

Emery-Dreifuss muscular dystrophy†

Myotonic dystrophy†

Neurofibromatosis†

Tuberous sclerosis†

Nutritional deficiencies

Beriberi (thiamine), pallagra, scurvy, selenium, carnitine, kwashiorkor

Autoimmune/collagen

Systemic lupus erythematosis

Dermatomyositis

Rheumatoid arthritis

Scleroderma

Polyarteritis nodosa

Electrolyte imbalance

Consequence of cancer therapy

Anthracyclines: doxorubicin (adriamycin), daunorubicin

Cyclophosphamide

Radiation

Clinical Importance of Cardiomyopathy

- Cat – Most common cause of heart disease
  - ♥ 70-90% of all feline heart disease
- Dog – Second most common heart disease
  - ♥ 12-20% of canine heart disease
- Ferret – common heart disease
- Also known as a cause heart disease in horses, primates, hamsters, mice, rats, turkeys, cattle, sheep, goats, birds and Zoo ruminant species

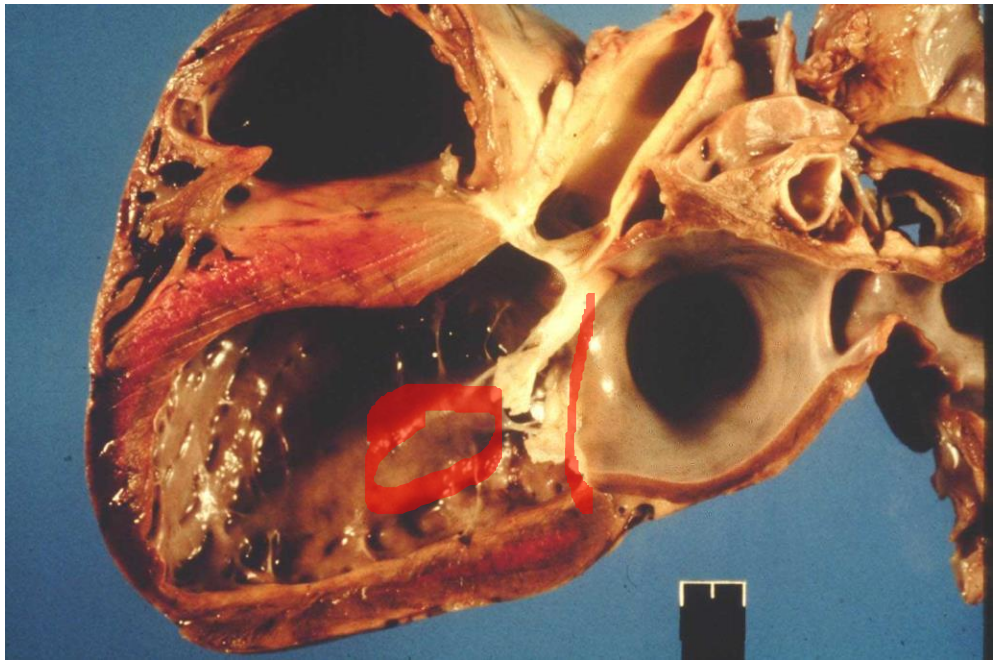
Clinical Manifestations of Cardiomyopathy

- Congestive heart failure
  - ♥ Dyspnea
  - ♥ Exercise intolerance
- Cardiac arrhythmias
  - ♥ Syncope, episodic weakness
  - ♥ Sudden death
- Thromboembolism
  - ♥ Acute lameness, other signs
  - ♥ Dyspnea

Canine Dilated Cardiomyopathy

Pathology – Most common findings

- Dilation of all 4 cardiac chambers
- Left heart changes may predominate
- Thinning of the IVS, LV and RV walls
- Atrophy of the papillary muscles
- Enlarged circumference to AV ring
- Ascites, pleural or pericardial effusion
- Pulmonary edema
- Hepatomegaly



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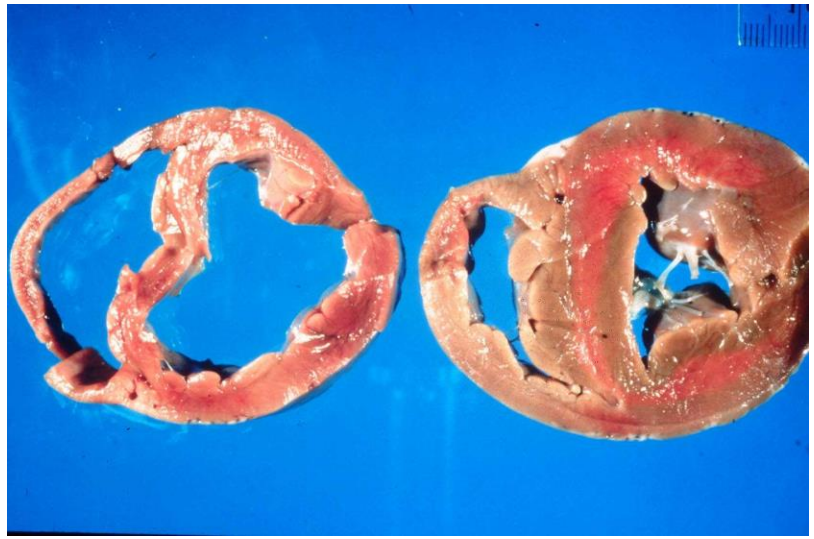
Canine Dilated Cardiomyopathy

Pathology

- Mild endocardial fibrosis
- Interstitial fibrosis and edema
- Focal regions of myocytolysis
- Mild mononuclear cell infiltrate
  - ♥ More in Boxers and Doberman
- Attenuated wavy fibers
  - ♥ Myocardial cells < 6 *u*m in diameter with wavy appearance
  - ♥ Typically seen in giant breed DCM



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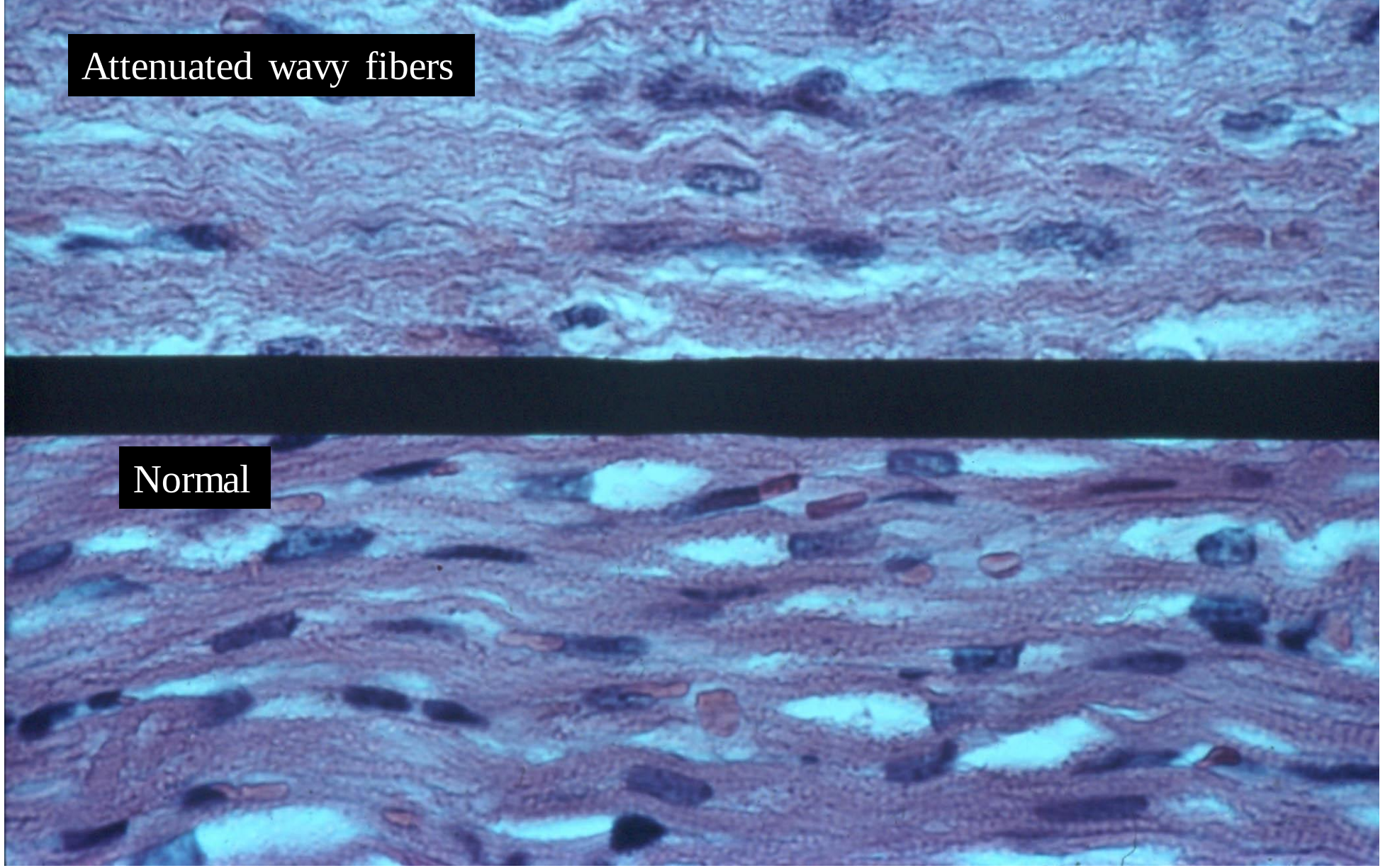
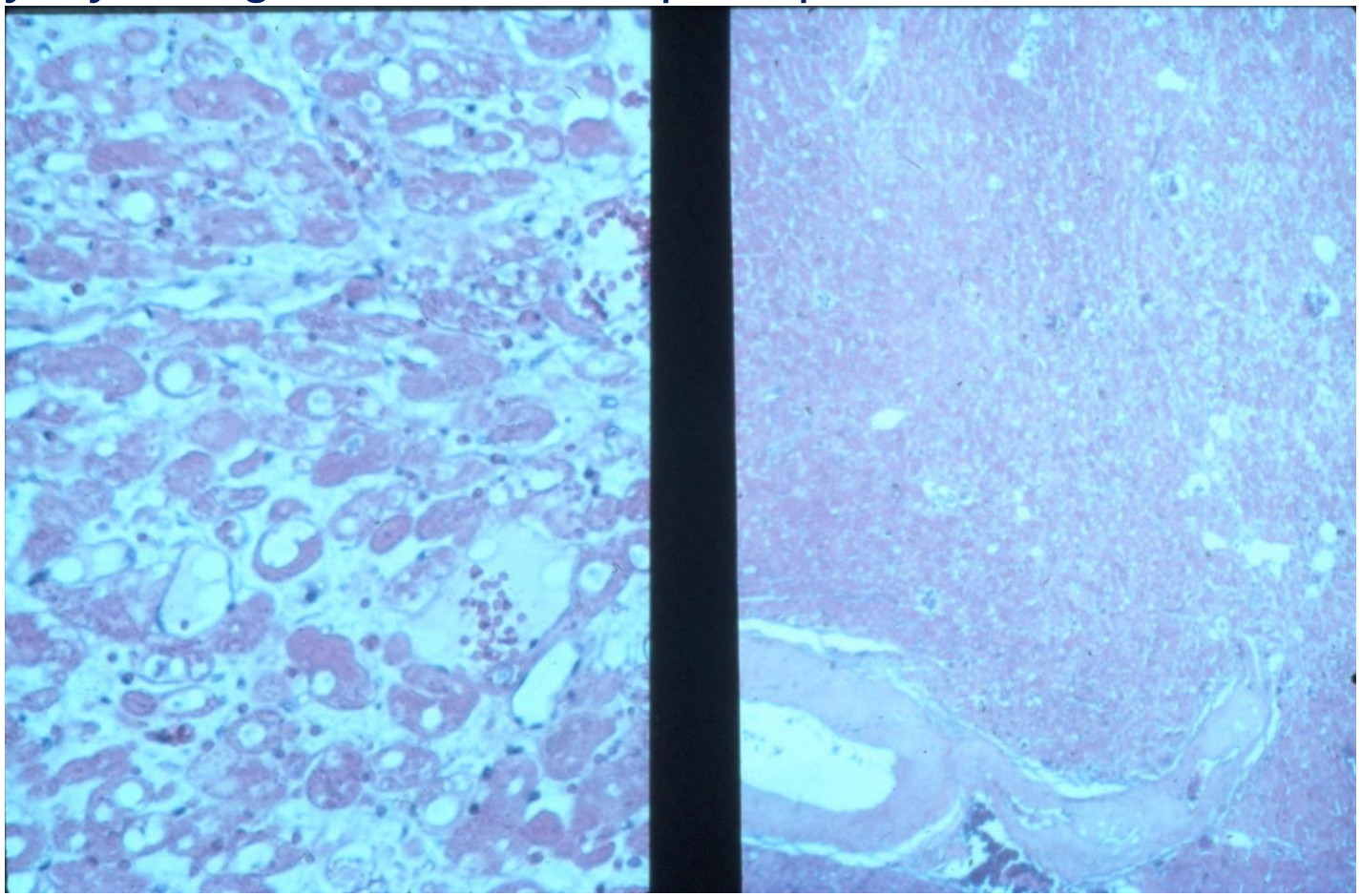
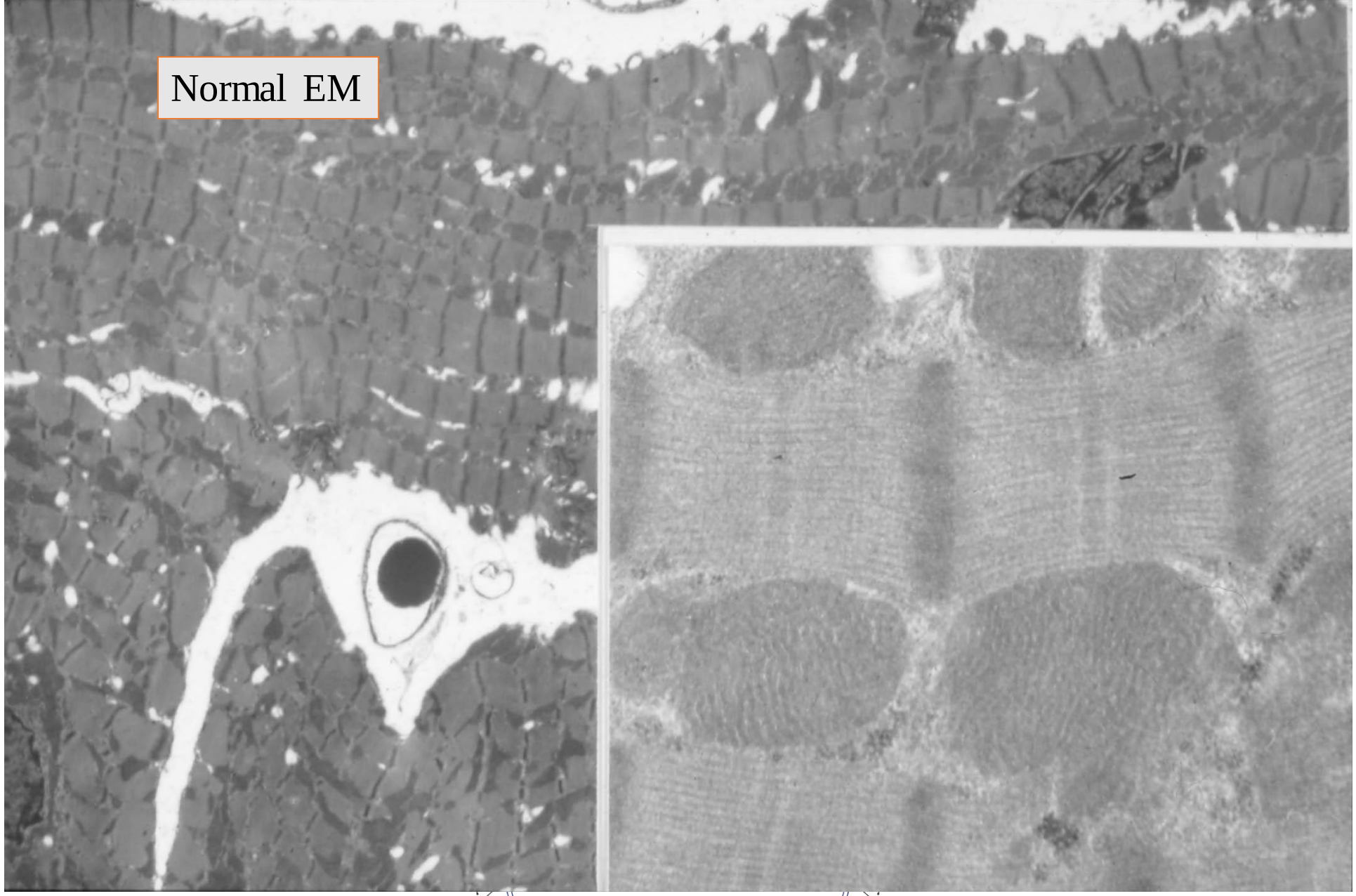


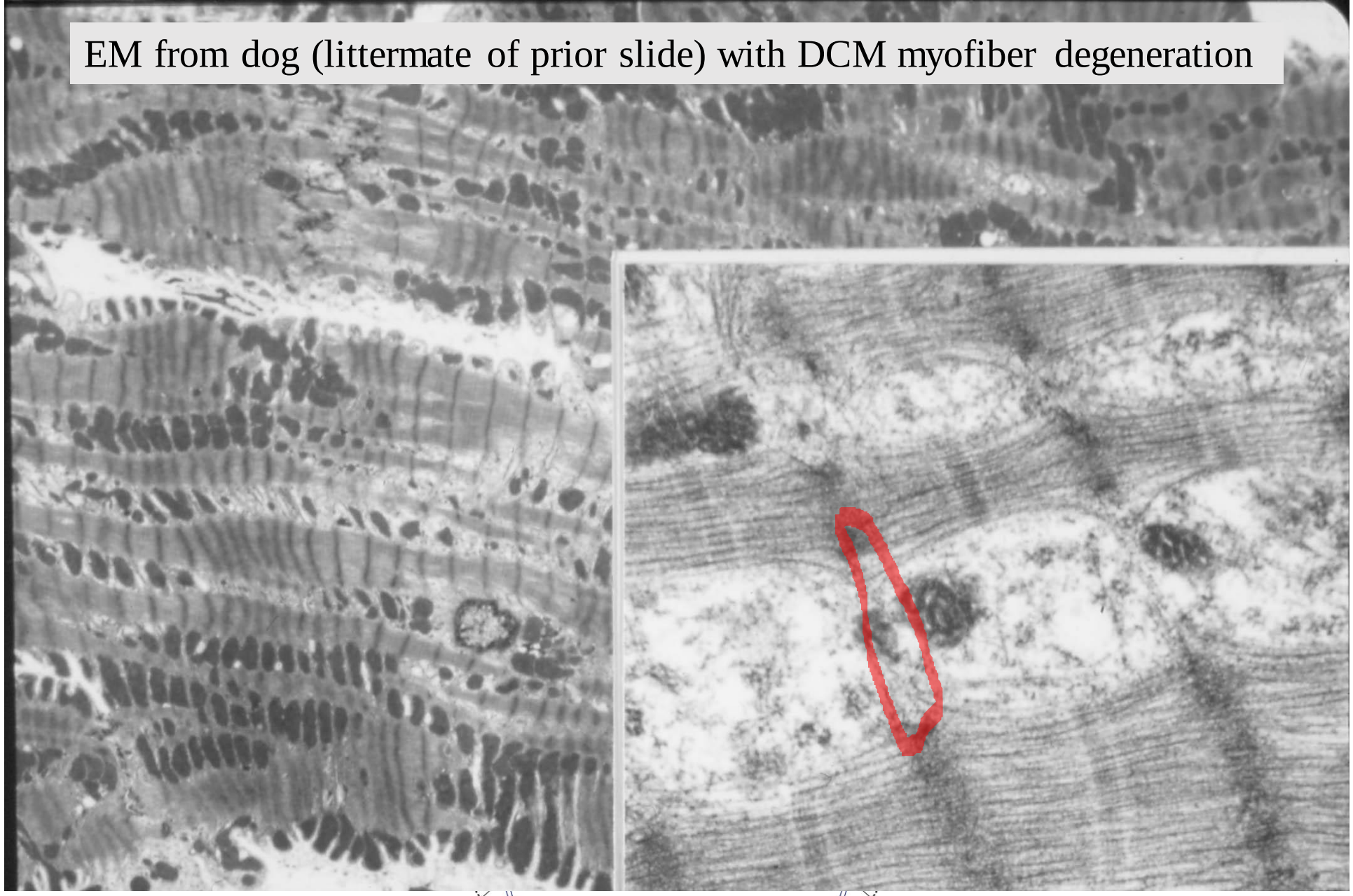
Histopathology Doberman DCM

Mild inflammation, myocyte degeneration and lipid replacement in LV

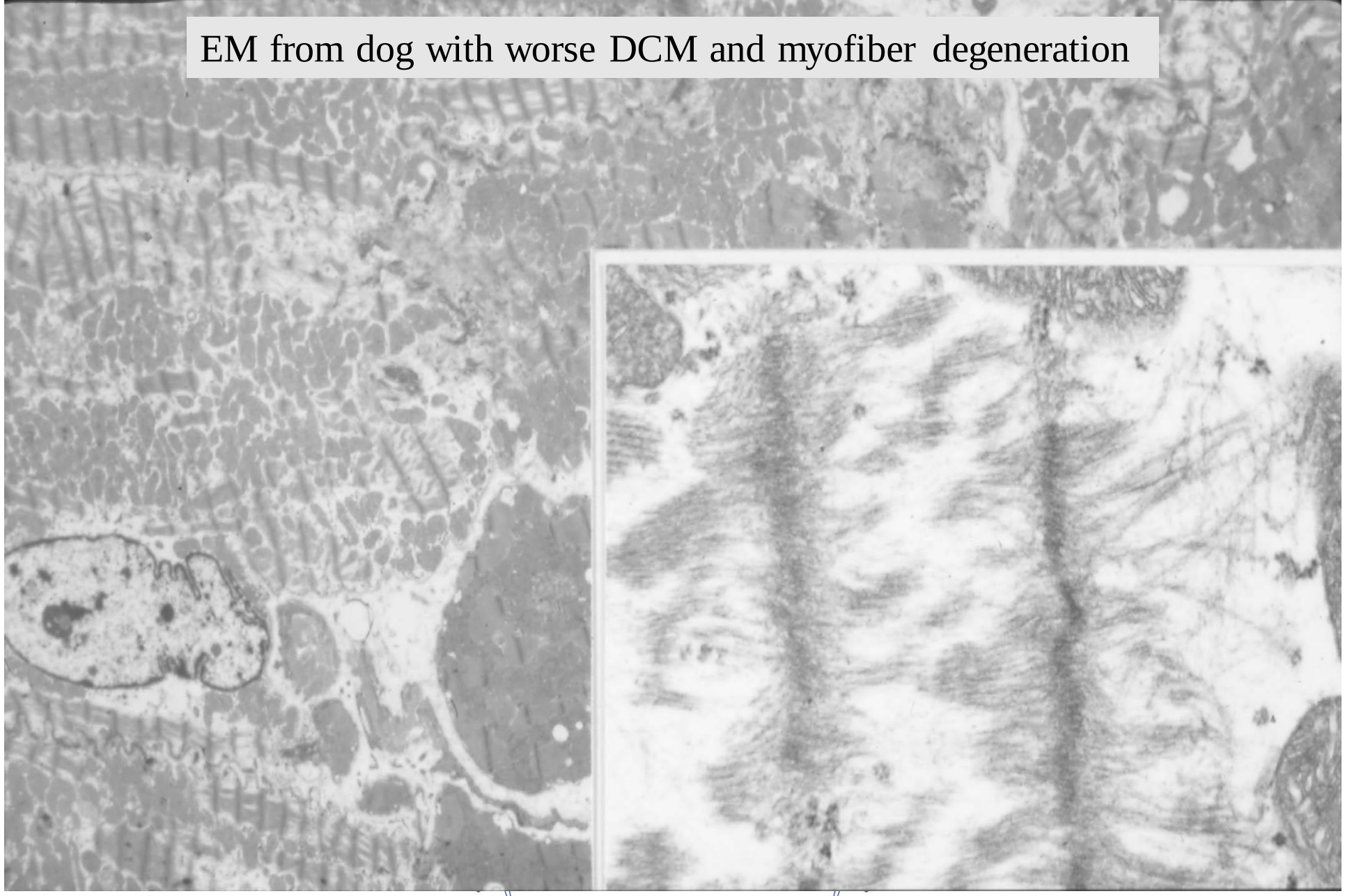




EM from dog (littermate of prior slide) with DCM myofiber degeneration



EM from dog with worse DCM and myofiber degeneration



Canine Dilated Cardiomyopathy

Pathophysiology

- Systolic dysfunction
  - ♥ Hallmark finding of the disease
- Diastolic dysfunction
  - ♥ Present in most cases with CHF
- Neuroendocrine compensatory responses
- Dilation leads to secondary mitral and tricuspid valve regurgitation
- CHF may be manifest with signs of left-sided, right-sided, or biventricular failure

Canine Dilated Cardiomyopathy

Etiology

- Heterogenous condition
- End-stage of myocyte damage/dysfunction
- Cytoskeletal protein mutations
  - ♥ Humans:
    - Calmodulin
    - Dystrophin
    - Vinculin
    - Metavinculin
    - Desmin
  - ♥ Boxers
    - Striatin and others (?)
  - ♥ Doberman pinschers
    - PDK4 gene
    - Dobie DCM 2 gene (titin or other?)
- Taurine? Carnitine? BEG diets?
- Co-Enzyme Q10?

Canine Dilated Cardiomyopathy

Signalment

- Large breed (Wolfhound, Dane, Newfoundland, German Shepherd dog, etc.)
- Doberman
- Boxer
- Cocker spaniel
- Dalmatian
- Portuguese water dog
- +/- Male > female
- Middle age or older (except PWD, and maybe pit bull)

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Canine Dilated Cardiomyopathy

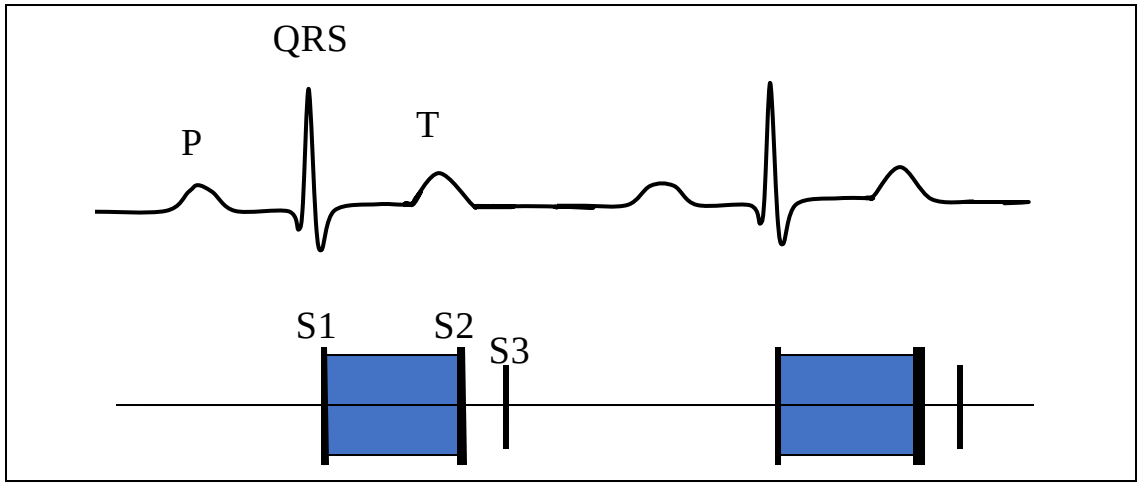
History

- Cough is variably present
- Dyspnea may be worse at night
- Syncope
- Weakness or collapse
- Anorexia
- Exercise intolerance
- Weight loss
- Sometimes misdiagnosed with “bronchitis” in last 3 weeks

Canine Dilated Cardiomyopathy

Cardiac Auscultation

- Soft (II-III/VI) systolic murmur - mitral or tricuspid
- Gallop (S3)
- Arrhythmia often present



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Canine Dilated Cardiomyopathy

Physical Examination - CHF

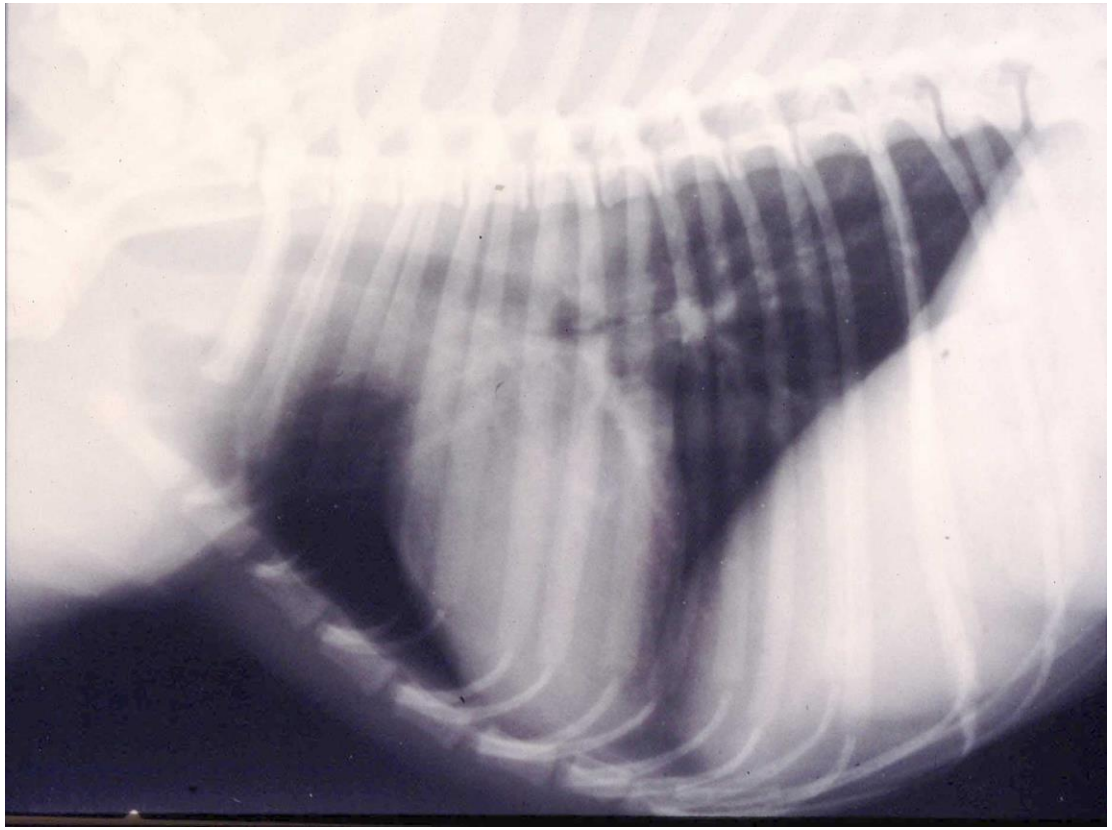
- HR variable; often faster if CHF or serious arrhythmia
- Pulmonary crackles, dyspnea, +/- dull ventrally
- Cough on tracheal palpation - brassy
- Arterial pulses weak
- Weak apex beat, +/- displaced caudally
- Jugular vein dist / H-J reflux (esp. ascites or pl eff)
- MM pallor, delayed CRT
- Weight loss, cool limbs, weakness, temp N or low

Canine Dilated Cardiomyopathy

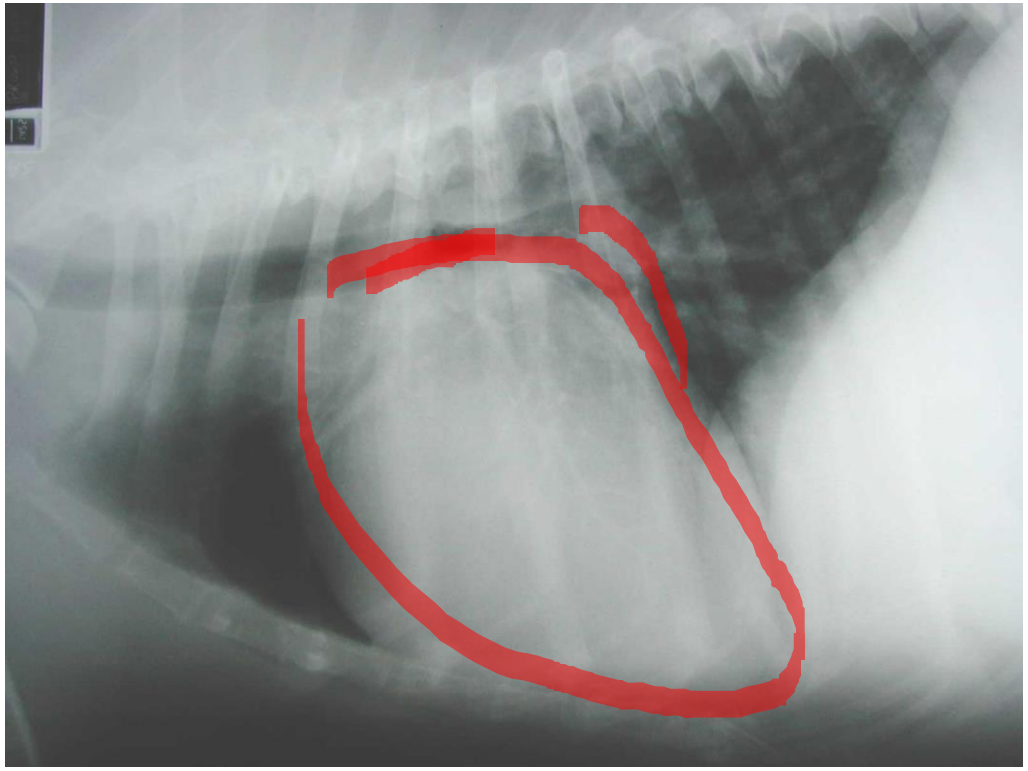
Thoracic Radiographs

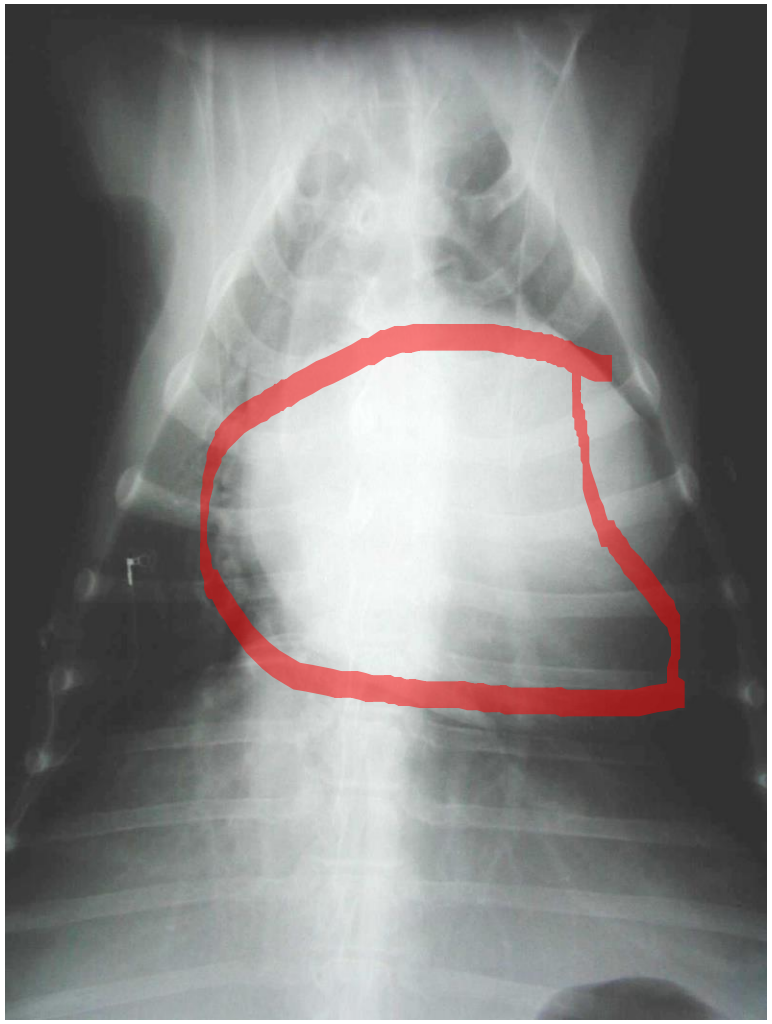
- Generalized cardiomegaly, tracheal elevation
- Left atrial enlargement
- Perihilar interstitial pattern, bronchial pattern, +/- alveolar infiltrates
- Variable vessel findings; veins > arteries
- +/- Enlarged caudal vena cava and liver
- Pleural effusion / pleural fissure lines
- VHS in deep-chested dogs (Doberman)

Normal for comparison

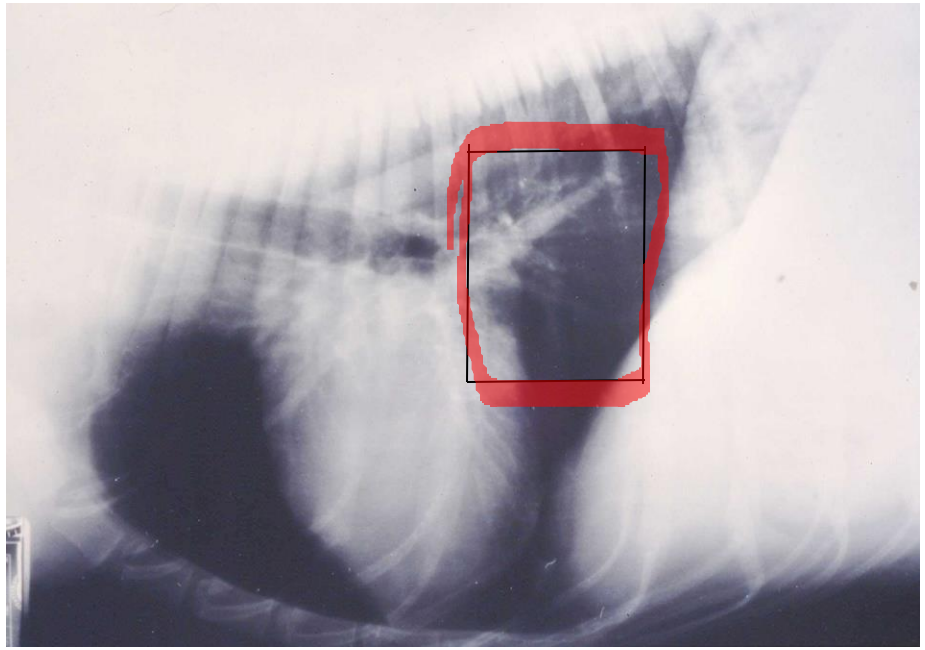


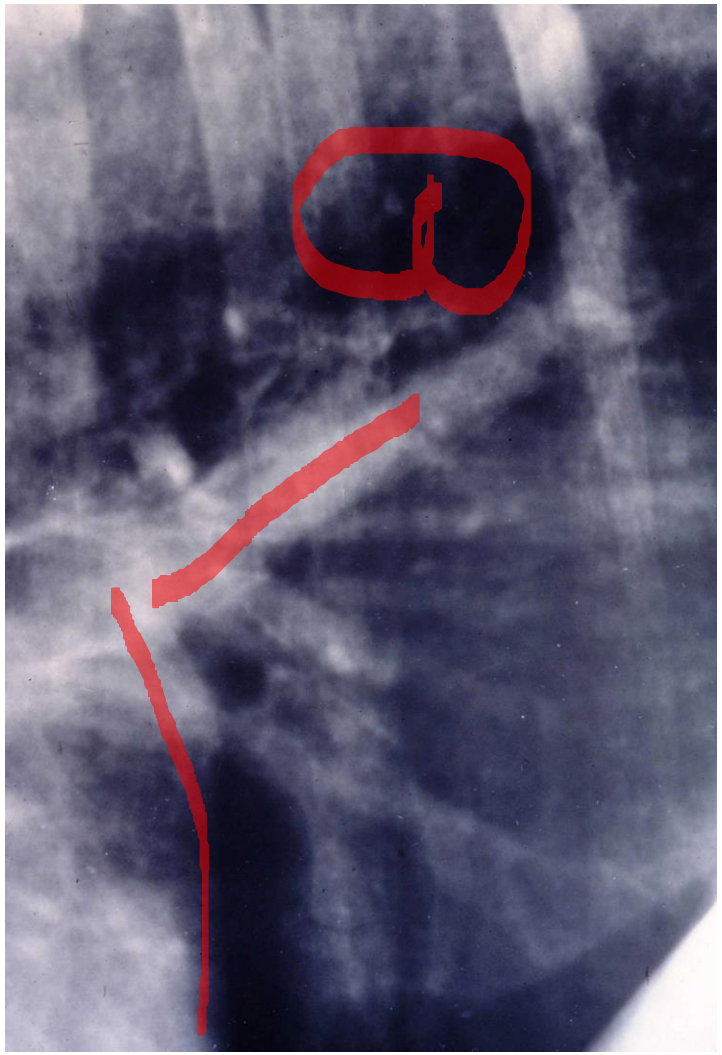
Cardiomegaly with DCM;
No CHF





Dobie with Osteosarcoma getting doxorubicin and serial radiography





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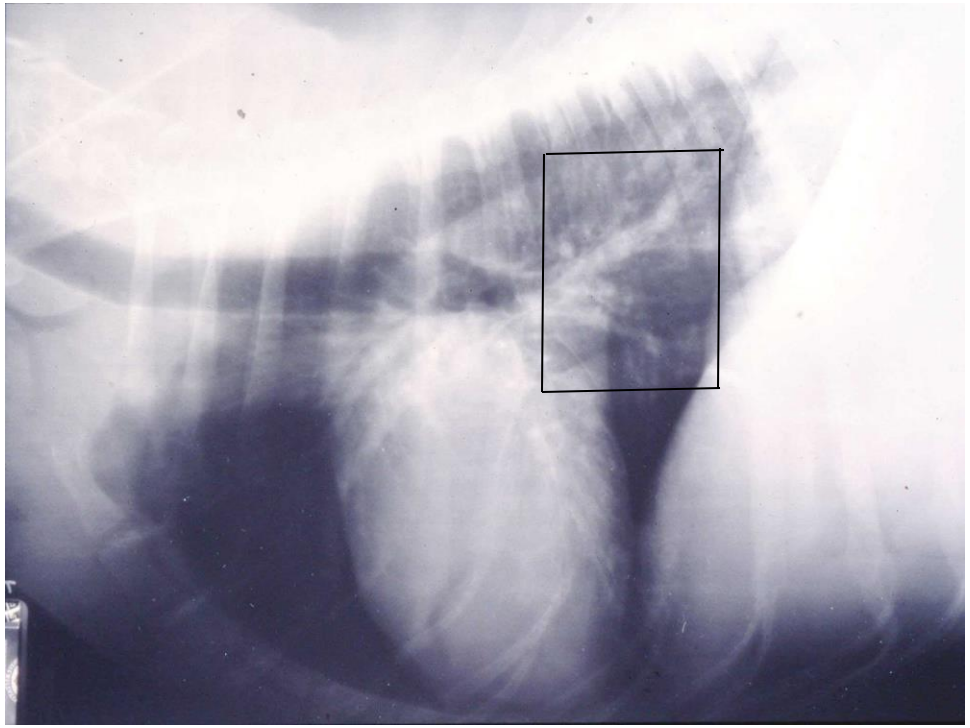

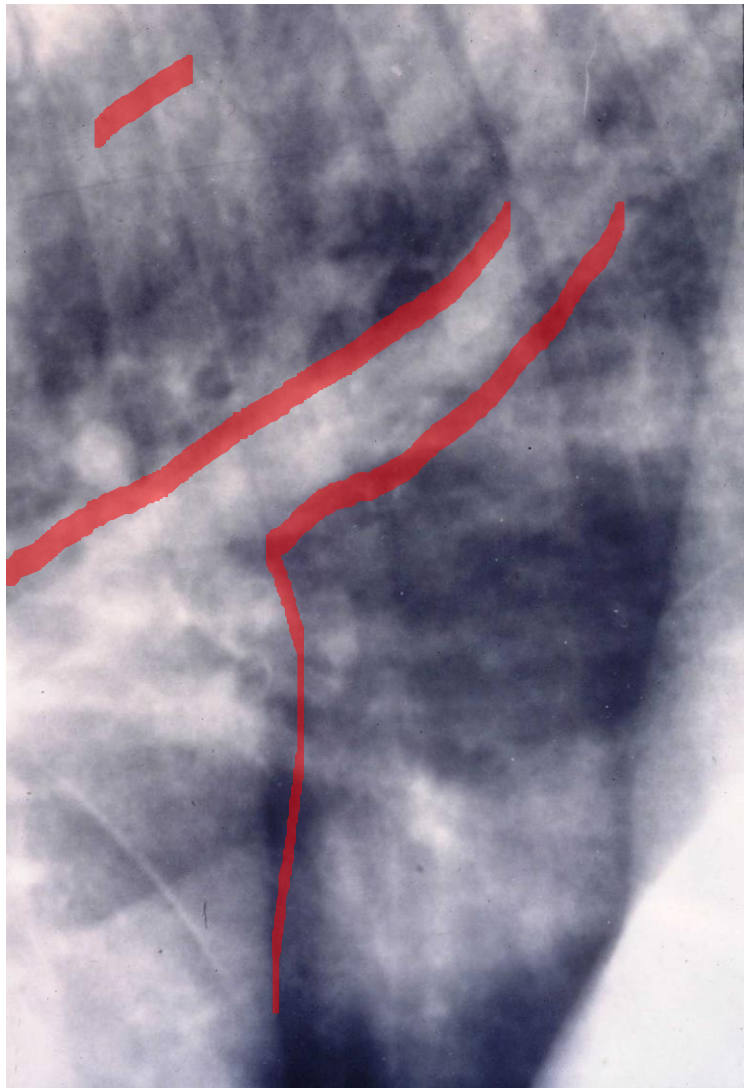

Mild LAE and
increased IS pattern

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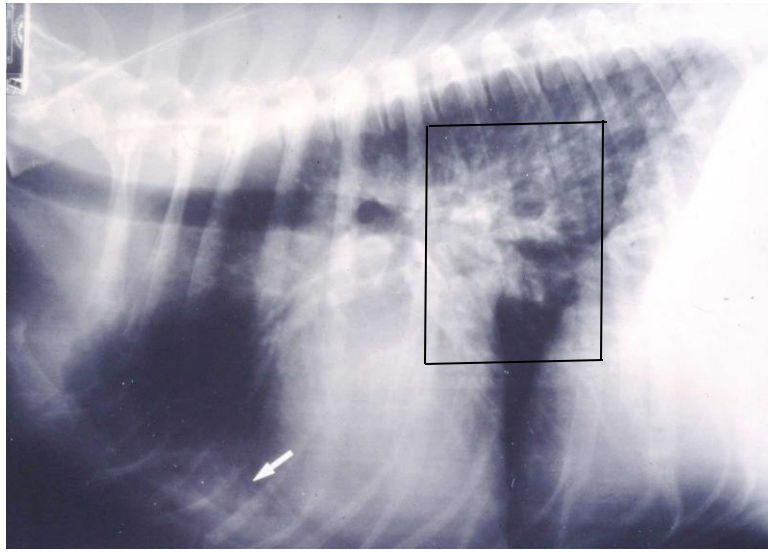
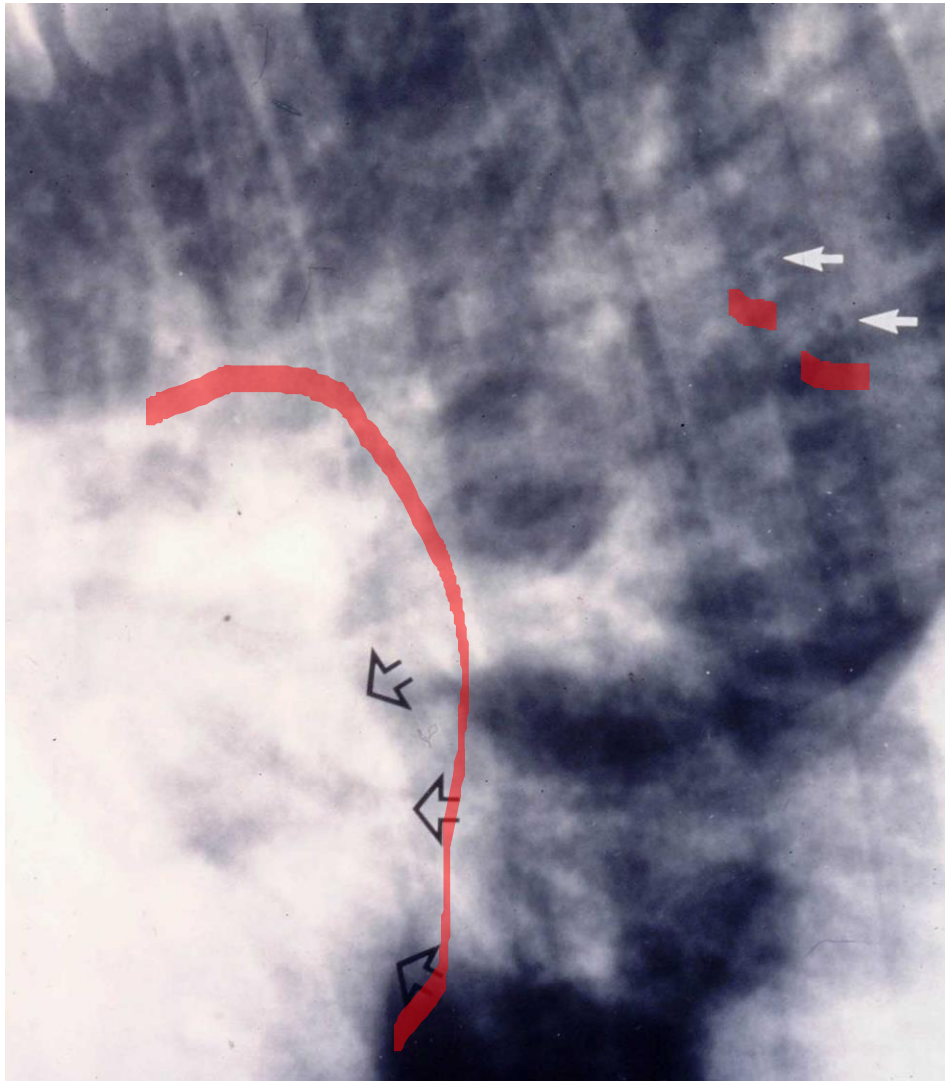
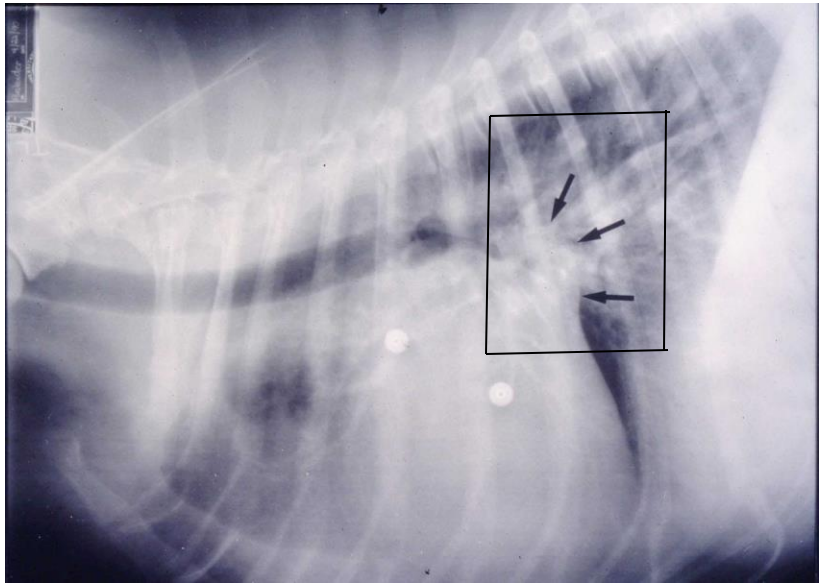
Dobie with Osteosarcoma getting doxorubicin and serial radiography





More LAE, worsening IS pattern and now bronchial pattern

CHF with small volume pleural effusion and air bronchograms (arrows)



Dobie with Osteosarcoma getting doxorubicin and serial radiography

Canine Dilated Cardiomyopathy

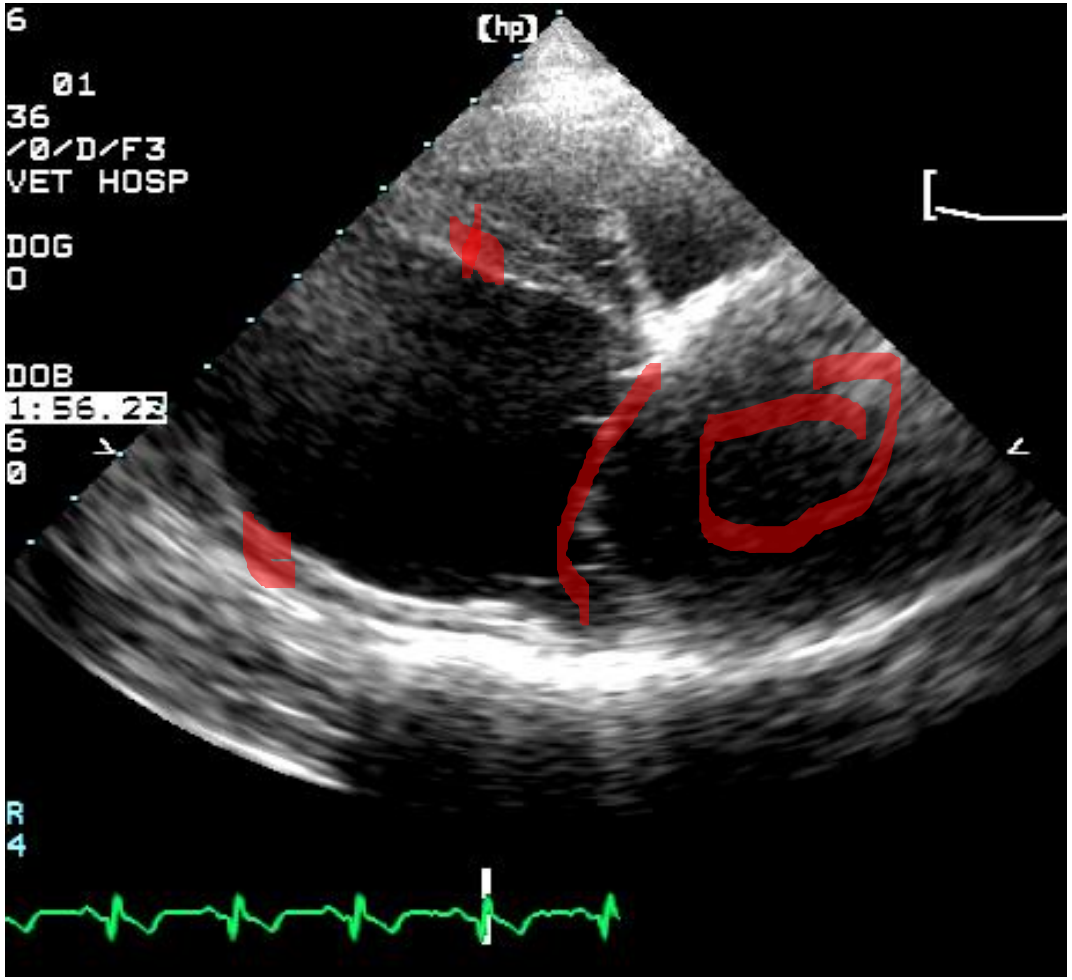
Electrocardiography

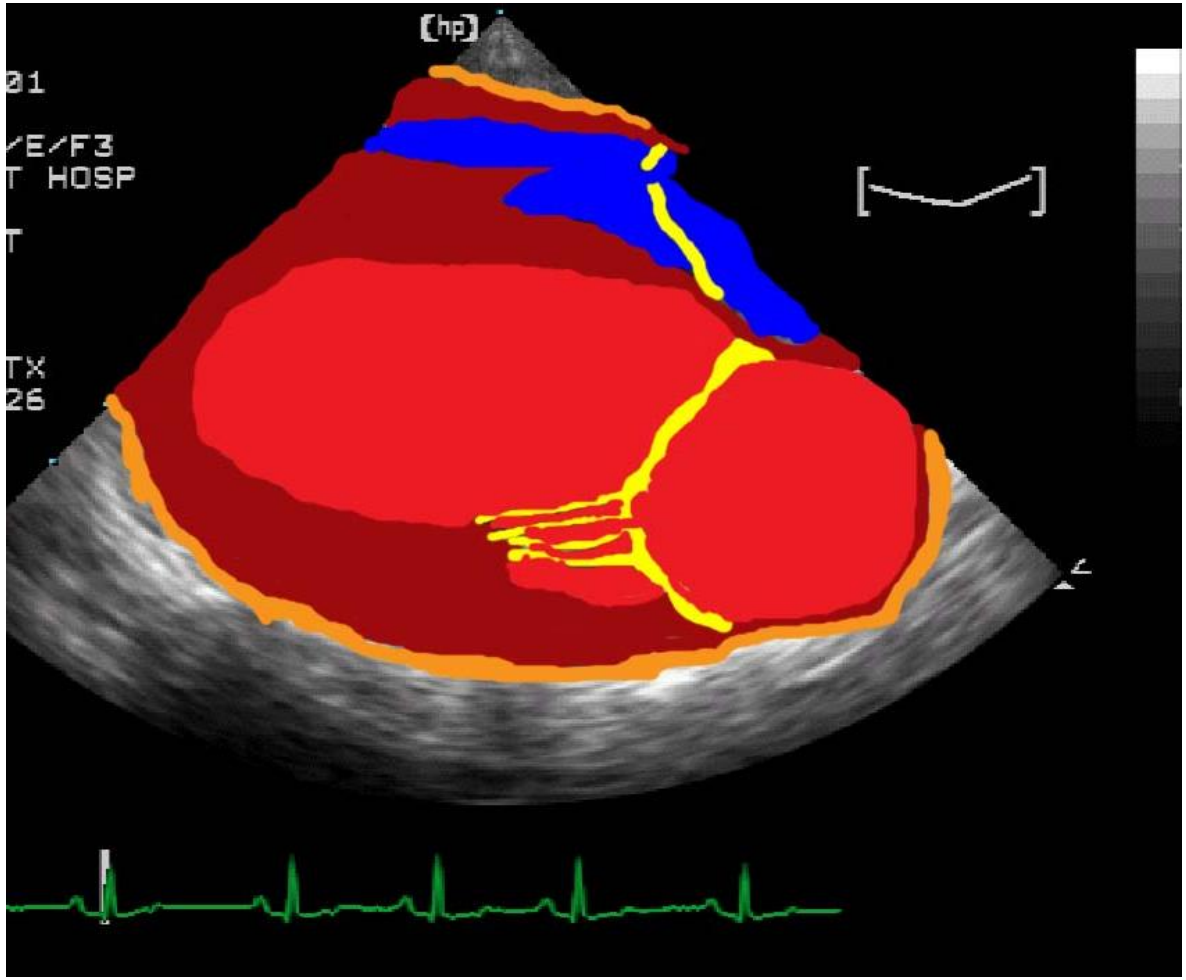
- Sinus rhythm / sinus tachycardia
- P-mitrale (left atrial enlargement)
- +/- Left ventricular enlargement pattern
  - ♥ less likely in Boxers, Dobies
- Atrial fibrillation - Giant breeds
- Ventricular arrhythmias - Boxers and Dobies
- APCs - Giant breeds, Wolfhounds, Cockers

Canine Dilated Cardiomyopathy

Echocardiography

- Dilation of all cardiac chambers, esp. LV
- Reduced fractional shortening (< 25%)
- LV walls are thinned
- Papillary muscles atrophied
- Left atrial enlargement if CHF
- Poor aortic root motion on m-mode
- Mitral and tricuspid regurgitation





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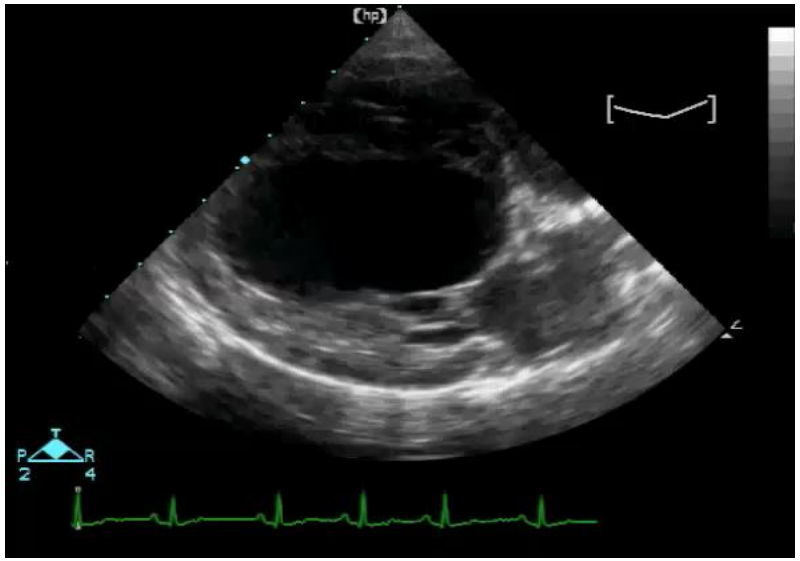

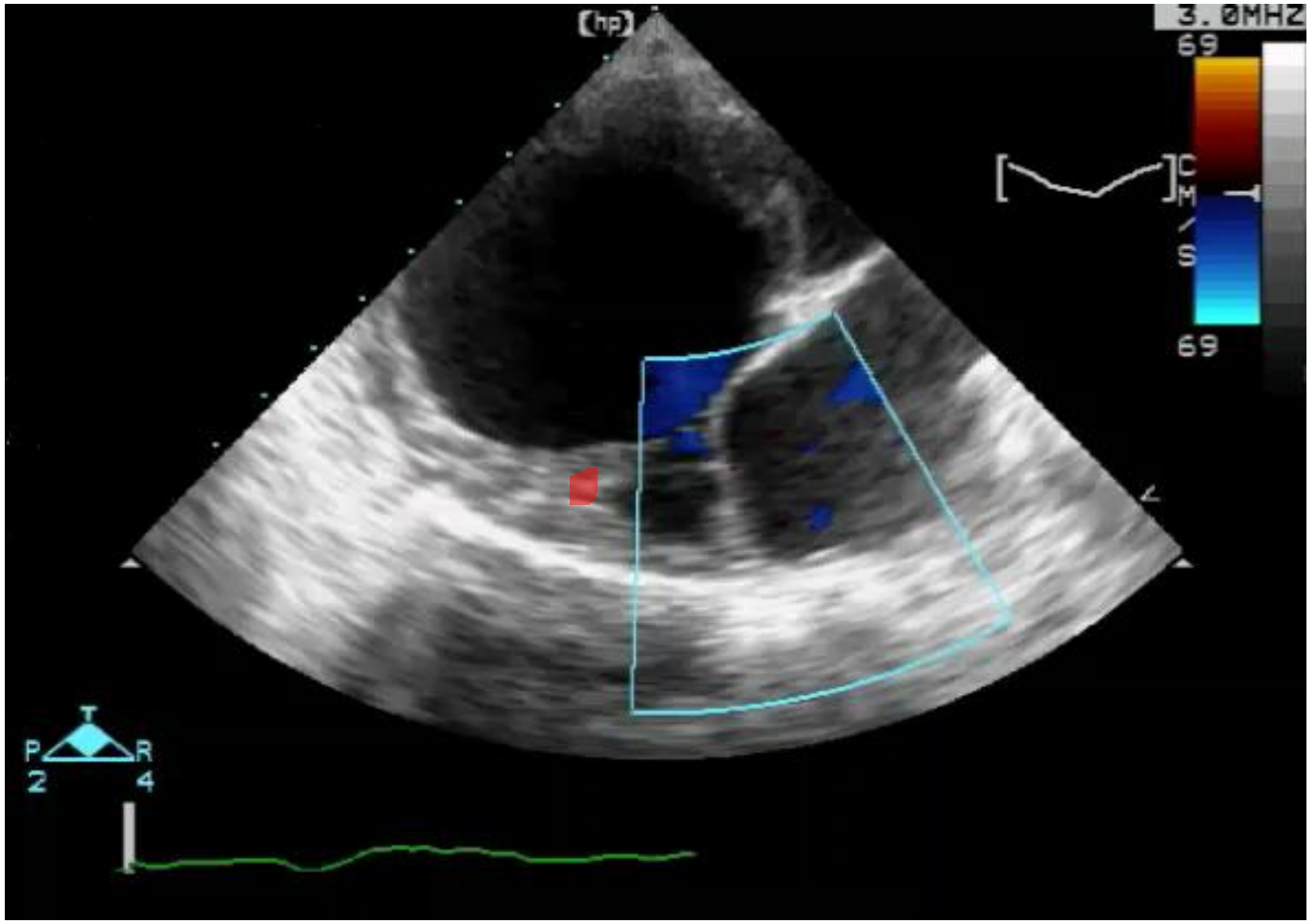

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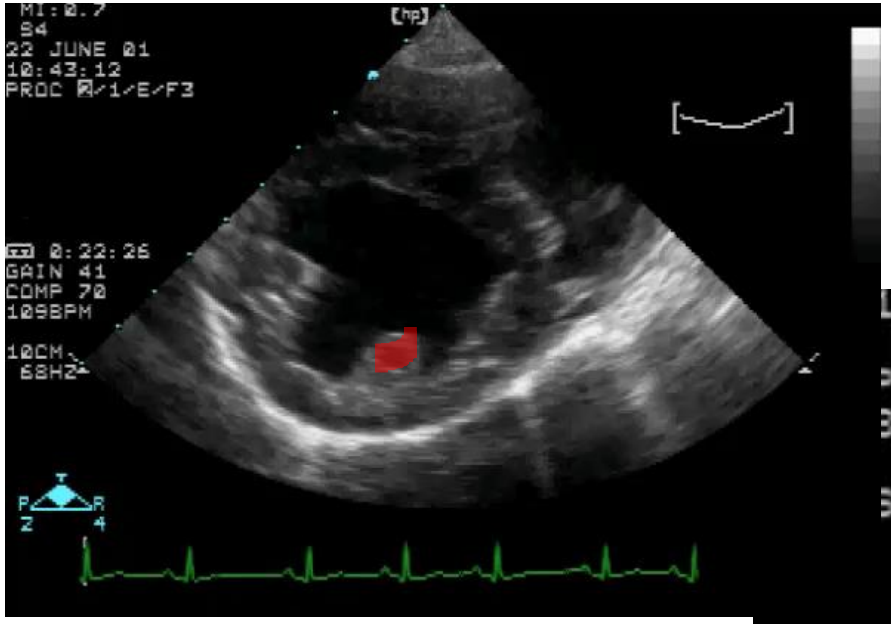
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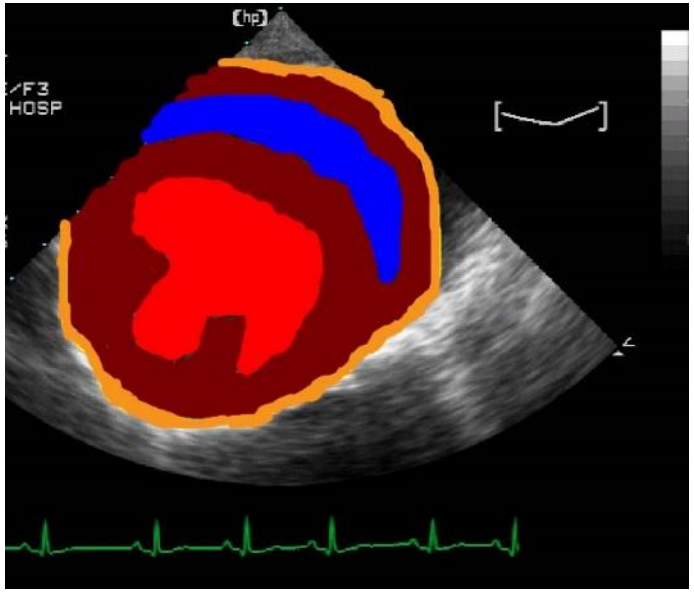
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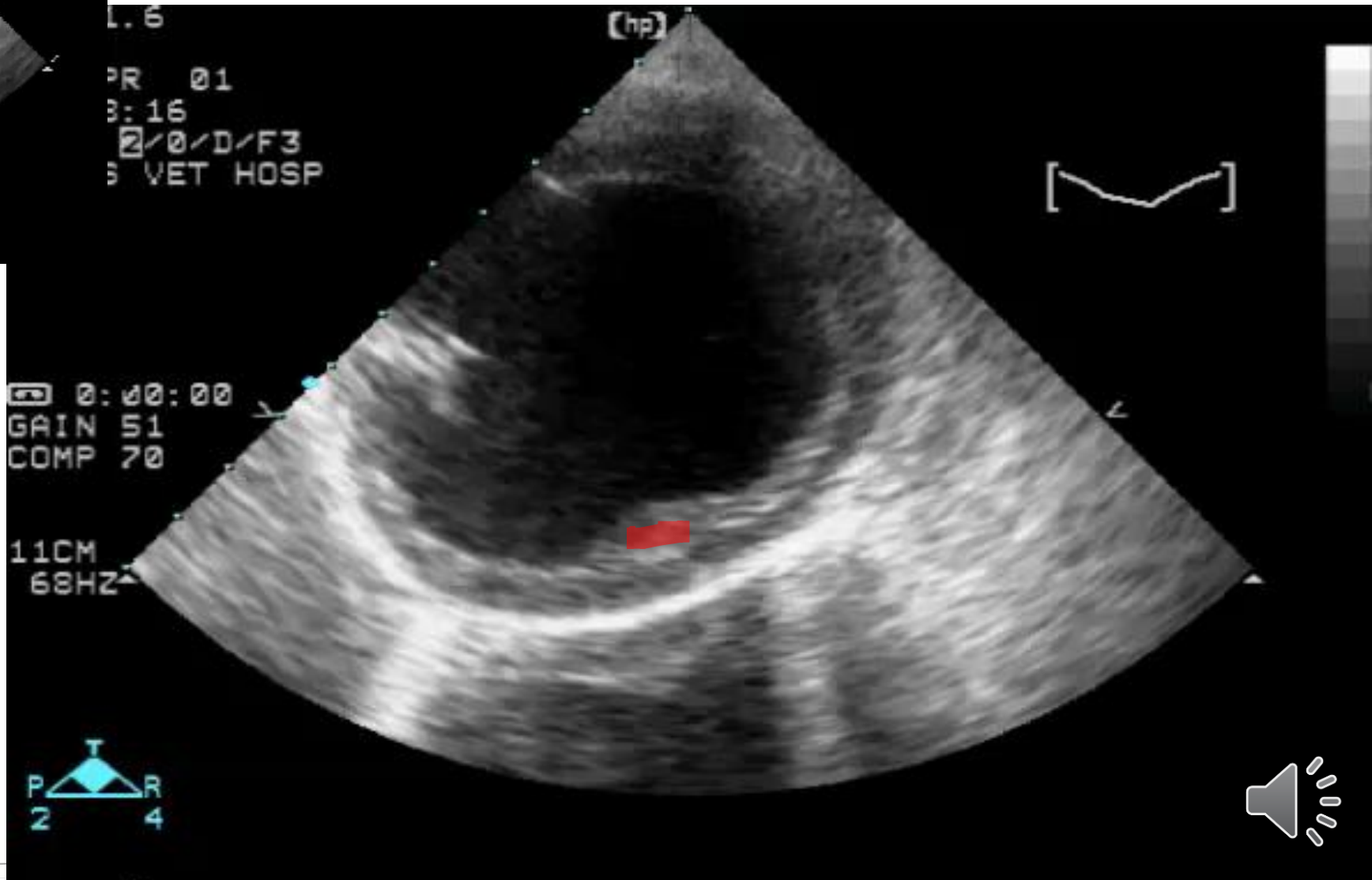
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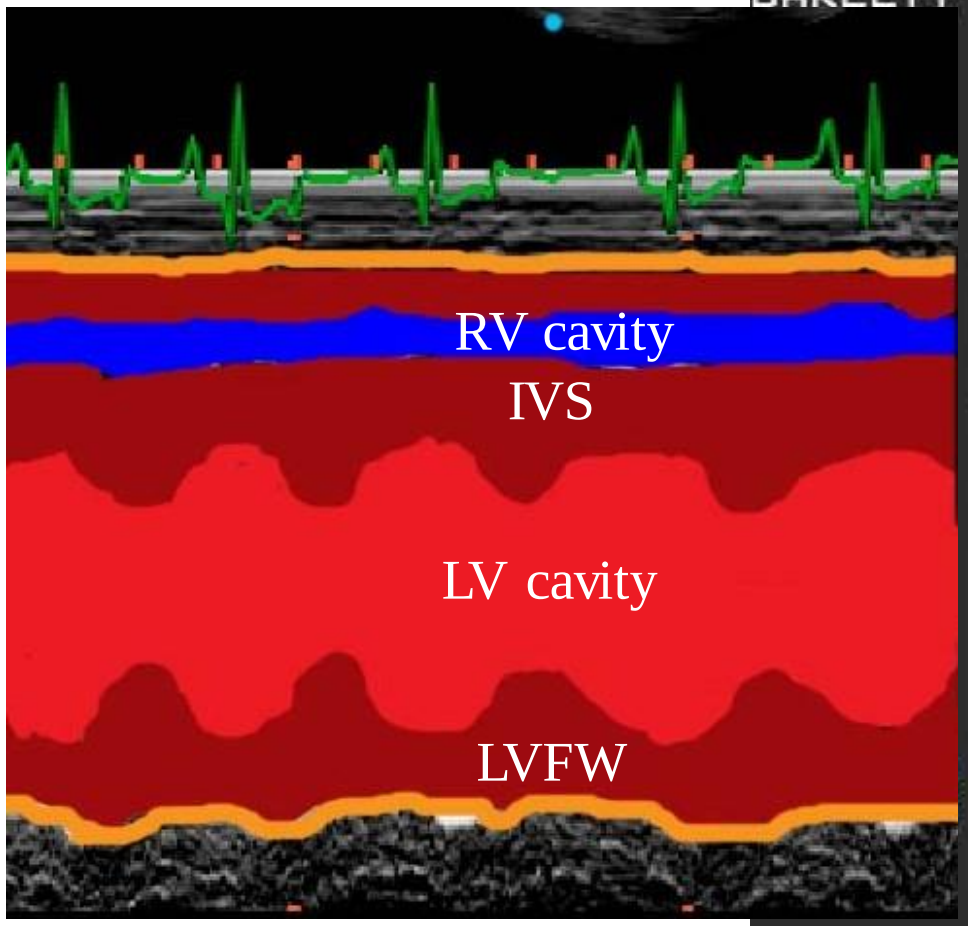
RV cavity
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LV cavity
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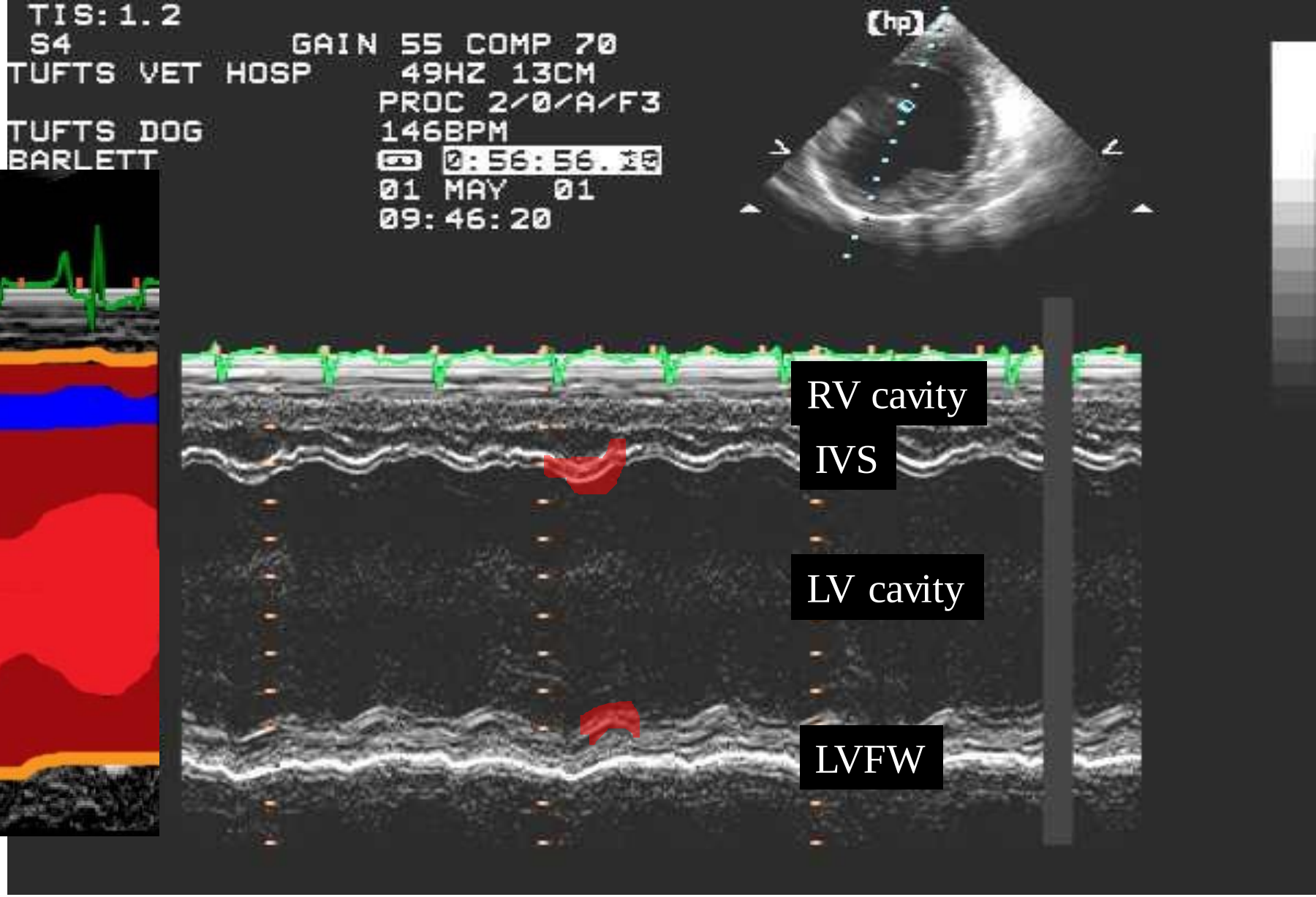
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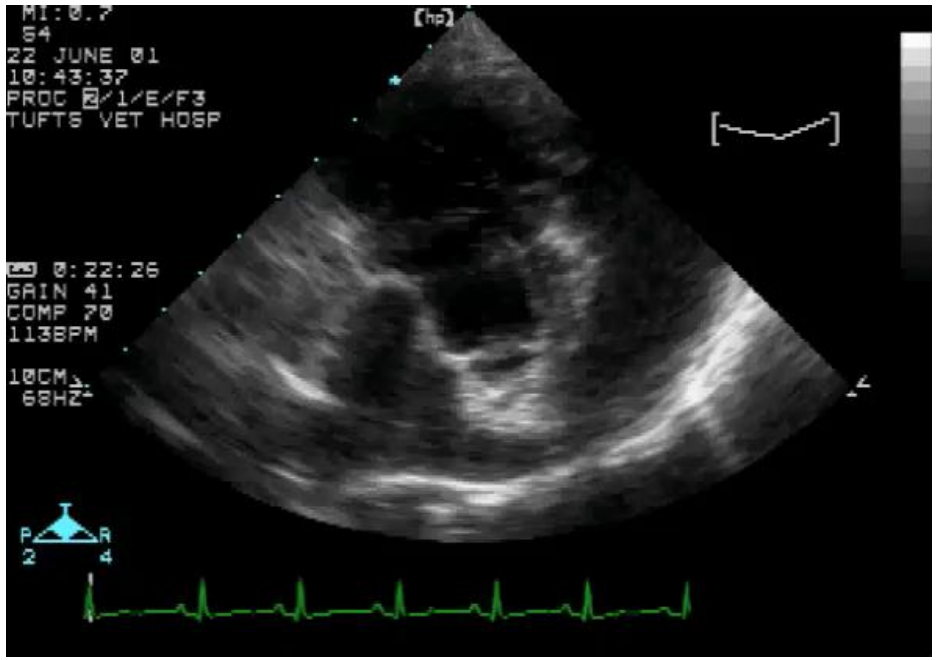
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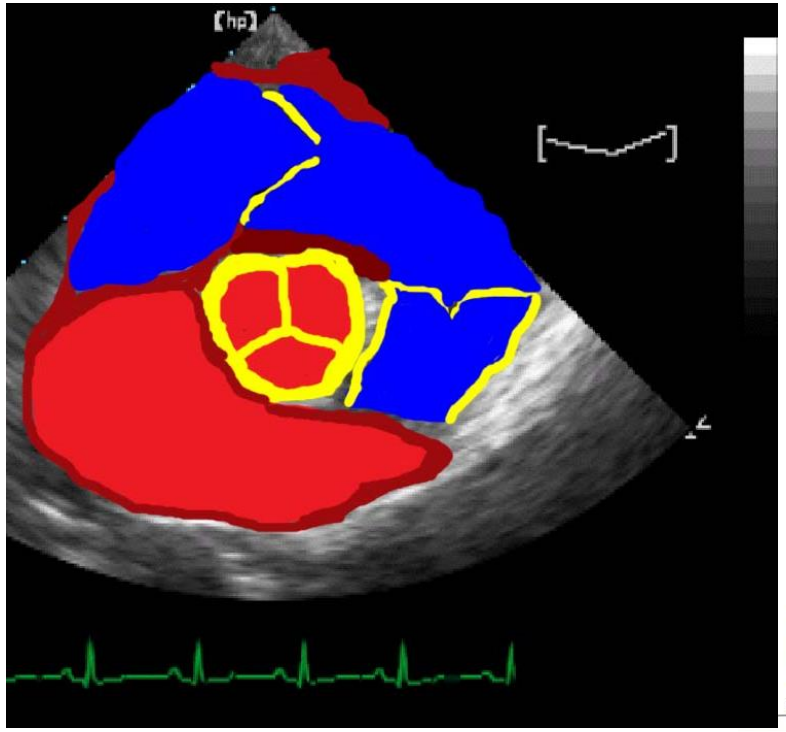
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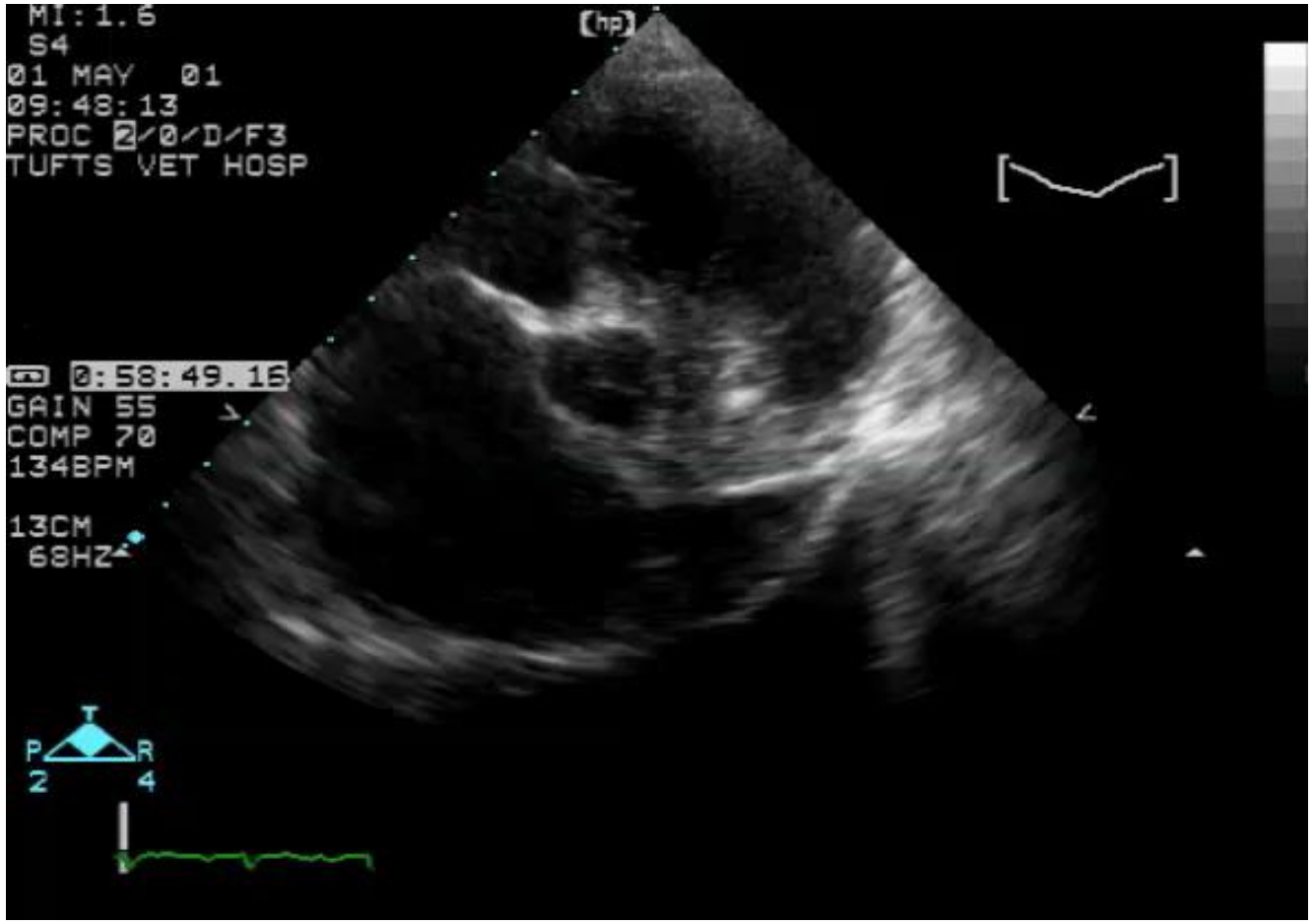
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Canine Dilated Cardiomyopathy

Laboratory / Additional Testing

- CBC usually not helpful
- Chemistry profile for baseline renal and lytes
  - ♥ Hepatic congestion - increased LE's
  - ♥ Pre-renal azotemia
- Urinalysis ideal
- Confirm heartworm status
- Plasma and WB taurine concentrations (?)
- Blood pressure
- NT-proBNP – elevated if CHF; often elevated before CHF

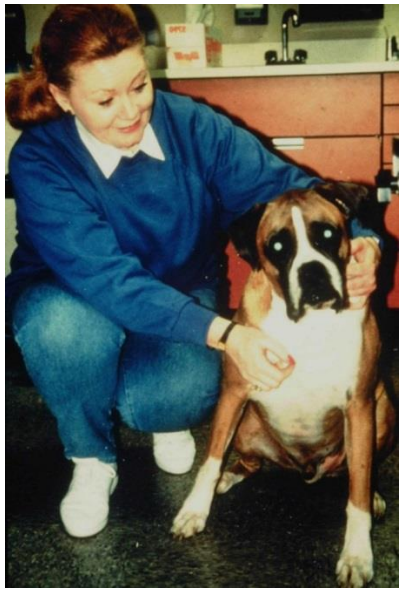
Canine Dilated Cardiomyopathy

Chronic management

- Furosemide - Lowest possible dose
- ACE inhibitor
- Pimobendan
- Spironolactone
- +/- Digoxin – Conservative; usually only if atrial fibrillation
- +/- Beta-blocker?
- Torsemide? Sildenafil? Amlodipine?
- Taurine? - Blood levels
- Carnitine? - Cockers and Boxers?
- Co-enzyme Q-10?
- Diet – Change if on high pea or lentil diet
- Exercise limitation

Canine Dilated Cardiomyopathy

Syndromes



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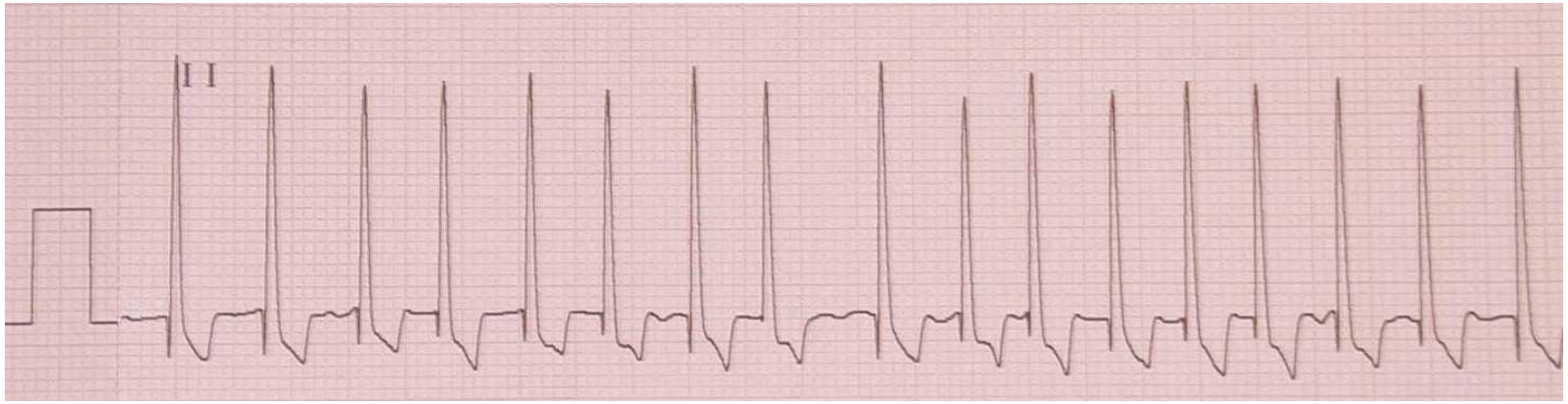
Dilated Cardiomyopathy of Giant Breed Dogs

- Left heart failure or biventricular failure
- Atrial fibrillation is common
- Sudden death is possible
- Survival often 6 months or less if CHF
- Asymptomatic with arrhythmia alone - often a prolonged survival (Lone atrial fibrillation?)



Dilated Cardiomyopathy of Irish Wolfhounds

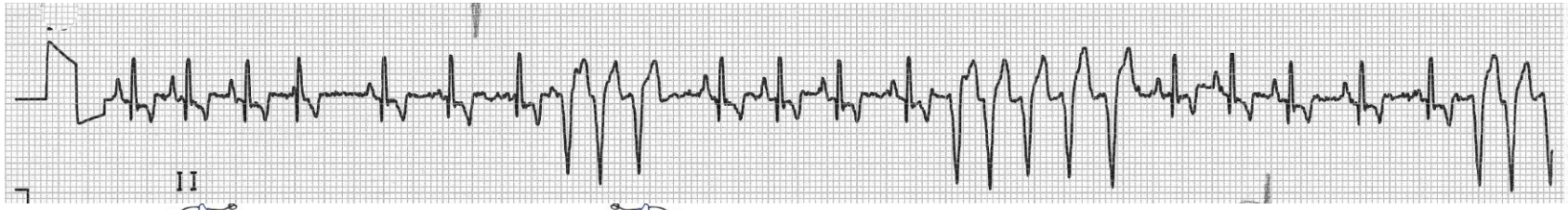
- Pleural effusion predominates when CHF develops, often with chylothorax
- Up to 50% of “normal” dogs have a CV abnormality
- Fractional shortening is higher than many dogs with DCM and CHF
- Atrial fibrillation is common when CHF develops
- Disease can be slowly progressive
- Controversy over progression of “Lone A-fib” cases to DCM
  - A portion of these will progress to DCM
- Pimobendan may slow progression of disease

Dilated Cardiomyopathy of the Newfoundland

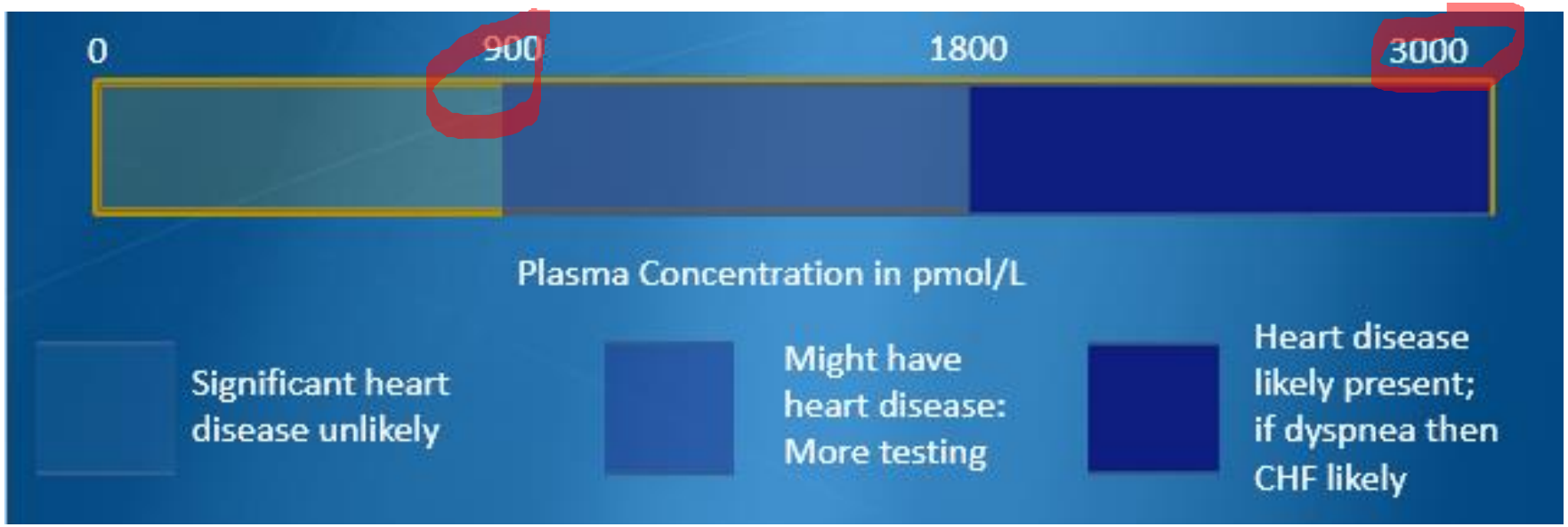
- Typically middle age or older
- Some “normal” dogs have fractional shortening between 20-28%
  - Normal male LVIDd < 5.5 cm, normal female LVIDd < 5.0 cm
- Atrial fibrillation is common
- Sudden death less common than other breeds?
- Taurine deficiency if eating certain diets
- Refractory CHF is the most common cause of death/euthanasia

Doberman Pinscher Cardiomyopathy

- Occult cardiomyopathy
  - ♥ Ventricular arrhythmias
  - ♥ LVIDd > 4.6 cm
  - ♥ LVIDs > 3.8 cm
  - ♥ Simpsons method for LV volumes and ejection fraction
  - ♥ Between 45-63% of Dobermans have DCM
- 40 to 50% with DCM may die suddenly
- Ventricular arrhythmias/ventricular fibrillation
- Cardiogenic shock
- Specific genetic tests



Canine NT-proBNP



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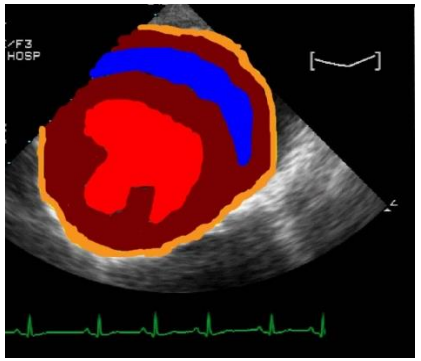
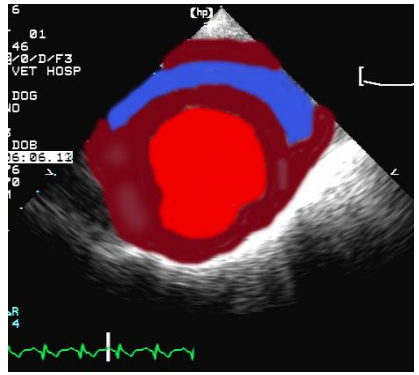
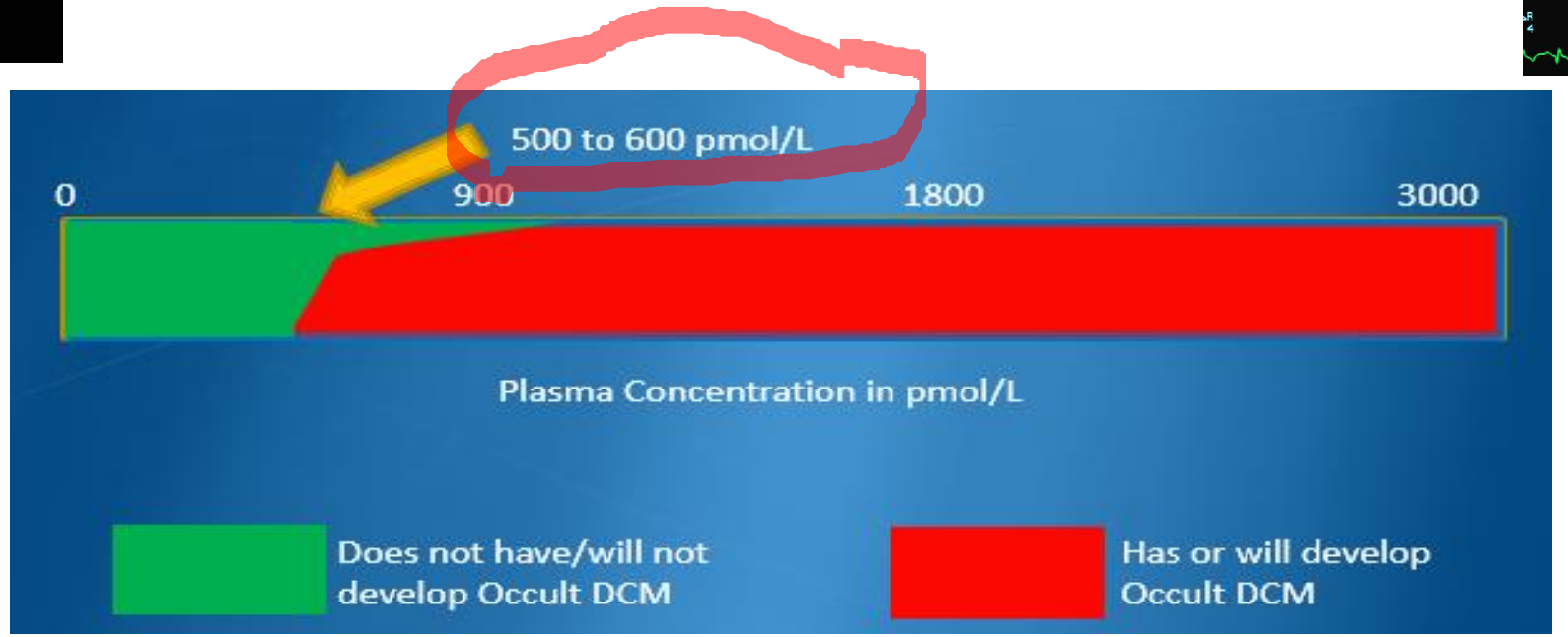
Canine NT-proBNP

Asymptomatic Doberman Pinscher
Does it Have or Will it Develop Occult DCM?







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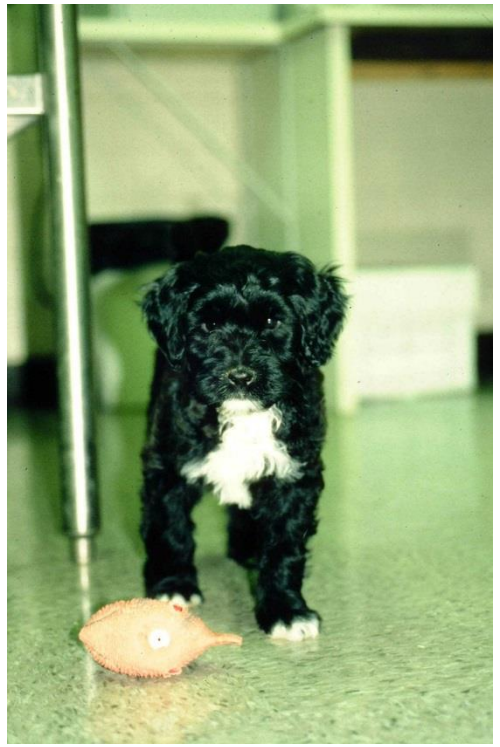
English and American Cocker Spaniel Cardiomyopathy

- Average age 6-10 years (range 10 mo-13 years)
- Nearly equal male : female ratio
- ECG - LVE pattern with tall R wave, APC's are common
- Generalized cardiomegaly with pulmonary edema
- Many have low plasma or whole blood taurine concentrations
- Taurine and carnitine supplementation can result in clinical and echo improvement in some dogs

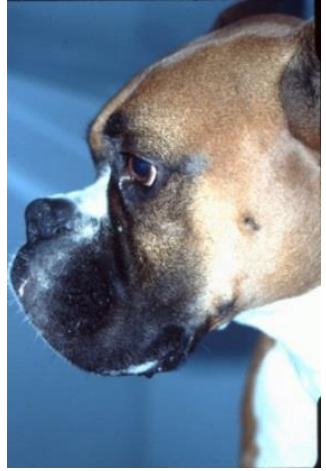
Juvenile DCM in Portuguese Water Dogs



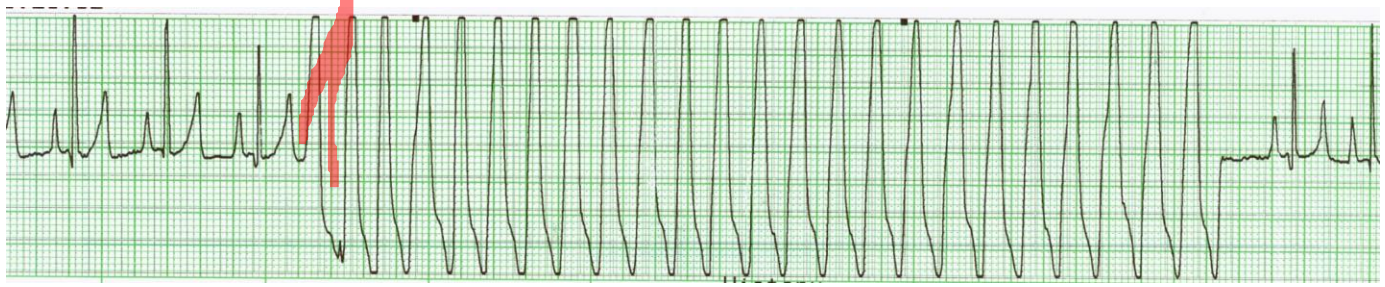
- Sudden death and peracute CHF
- 5 weeks to 3-4 months of age
- Necropsy / echo findings = typical DCM
- Conflicting reports about the role of taurine
- Genetic mutation – Chromosome 8
- Arrhythmias infrequent, soft murmur or gallop
- Pulmonary edema, hepatomegaly
- Some with normal echo at 6 weeks of age developed DCM before 6 mo of age

Boxer Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy



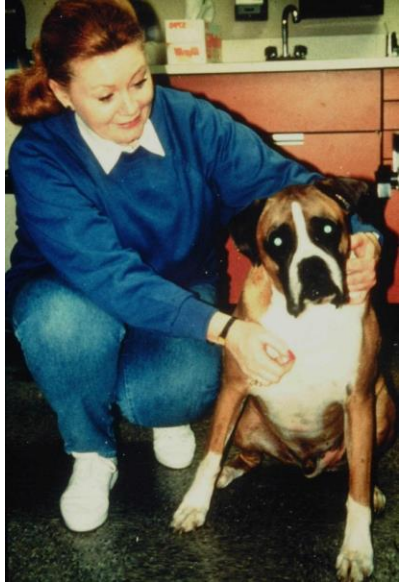
- Average age 8 years (range 0.5-15 years)
- Nearly equal male : female ratio
- Sustained, rapid (300-400/min) ventricular tachycardia
- VPC's often have LBBB pattern (positive in Lead II)
- ECG - Often low voltage, wide QRS, wide P wave
- Ryanodine receptor: Striatin mutation in some; esp DCM



Boxer Cardiomyopathy

Arrhythmogenic Right Ventricular Cardiomyopathy

Boxer ARVC



- Sudden death due to ventricular arrhythmias
- Sudden death more likely than CHF
- Dysfunctional ryanodine receptor
- Atrial fibrillation less common, worse prognosis
- Sotalol often effective for ventricular arrhythmias
- Mexiletine and atenolol or mexiletine and sotalol combinations are also often effective
- Myocarditis, apoptosis, adipose tissue and fibrous tissue replacement in RV
- Holter useful to search for asymptomatic individuals: Suspect >100 VPC/24 hours is affected

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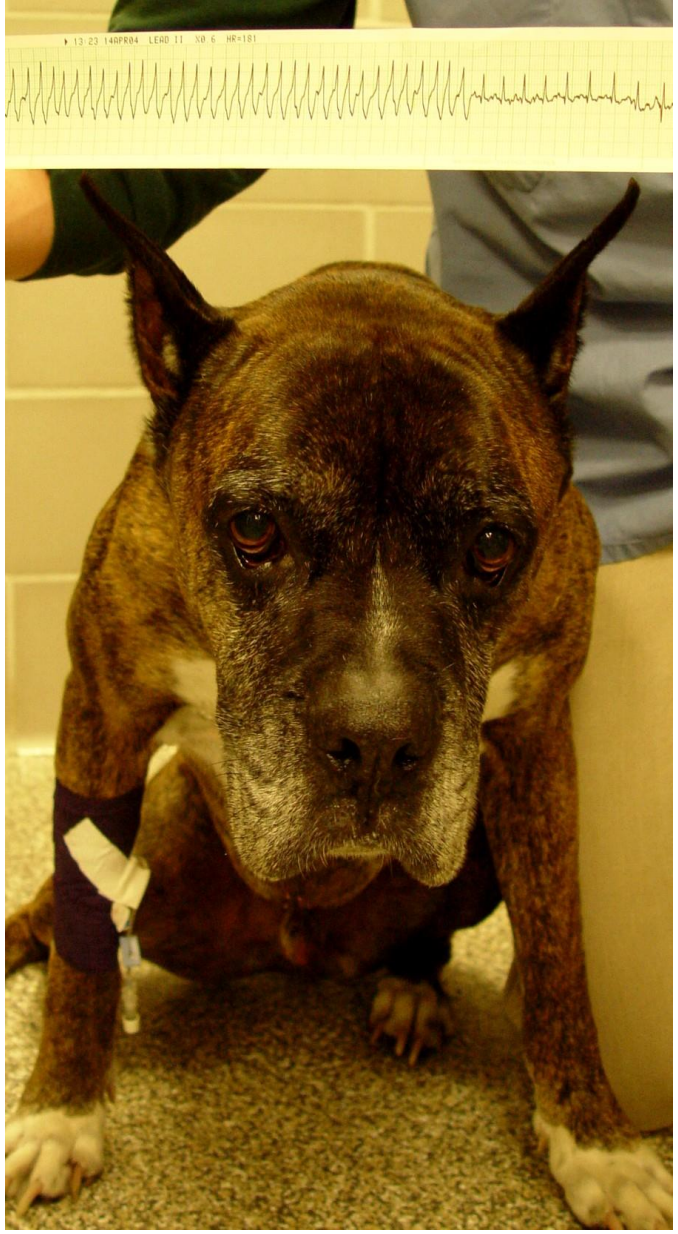

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DCM Associated with Taurine Deficiency

Idexx VetConnect - TAURINE (WHOLE BLOOD)

12/22/2015 05:49 AM

Requisition #	20928750		
Accession #	R0878482		
Unit Title	TAURINE (WHOLE BLOOD)		
TAURINE	52CL	200 - 350 NMOL/ML	
Comment	[redacted]	[redacted]	

CANINE WB TAURINE REF. RANGE 200-350Testing performed at University of California, Davis

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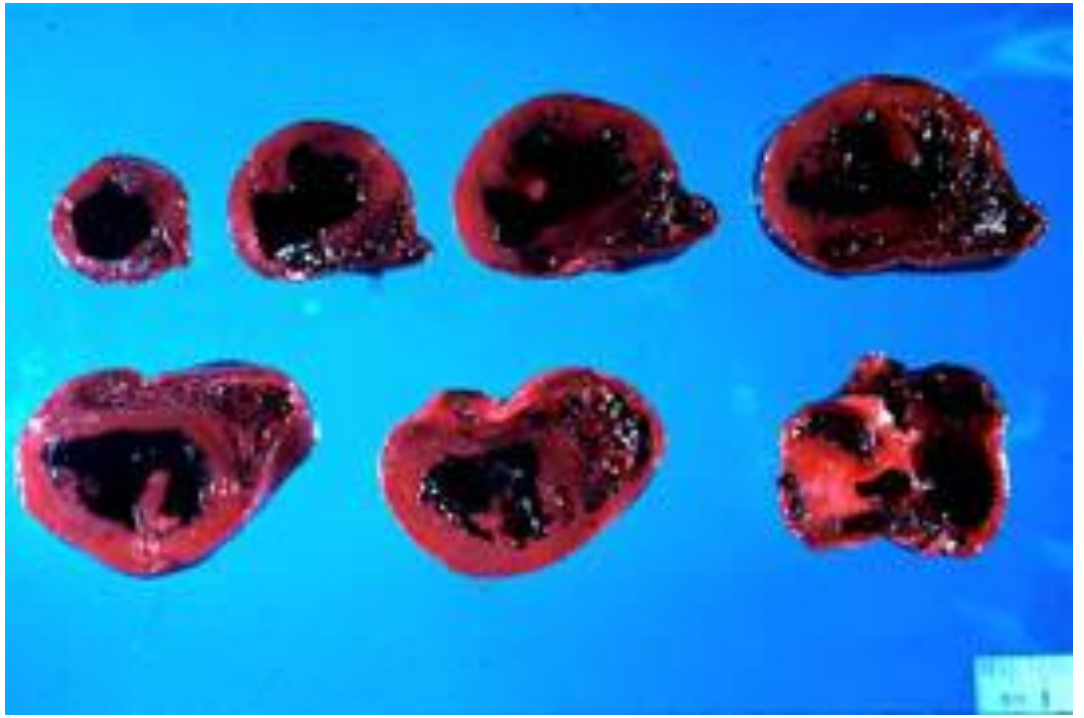
DCM associated with certain diets

- Association between certain diets and DCM
  - ♥ High in peas, lentils or other uncommon sources
    - ♥ Sometimes advertised as Grain Free diets
    - ♥ May have exotic ingredients (Kangaroo? Others?)
  - ♥ May be reversible if caught early
  - ♥ A small fraction of these diets resulted in taurine deficiency
  - ♥ If caught late they might live longer than typical DCM
    - ♥ Still susceptible to arrhythmias and sudden death
    - ♥ LV contractile function might not recover
    - ♥ LVIDd and LVIDs and LA size might get smaller

Feline Dilated Cardiomyopathy

Pathology

- Dilation of all 4 cardiac chambers
- Thinning of the IVS, LV and RV walls
- Atrophy of the papillary muscles
- Enlarged circumference to AV ring
- Pleural effusion +/- ascites
- Pulmonary edema
- Hepatomegaly



Feline Dilated Cardiomyopathy

Pathology and Pathophysiology

- Mild endocardial fibrosis
- Interstitial fibrosis and edema
- Focal regions of myocytolysis
- Mild mononuclear cell infiltrate
- Systolic and diastolic dysfunction
- Neuroendocrine compensatory responses
- Secondary mitral and tricuspid valve regurgitation
- CHF may be manifest with signs of left-sided or biventricular failure

Feline Dilated Cardiomyopathy
Etiology

- Heterogenous condition
- Dietary Taurine deficiency in some cats
- Cytoskeletal protein abnormalities?

Feline Dilated Cardiomyopathy

Signalment

- 5 months to 16 years
- No sex predisposition
- Burmese
- Siamese
- Abyssinian

Feline Dilated Cardiomyopathy

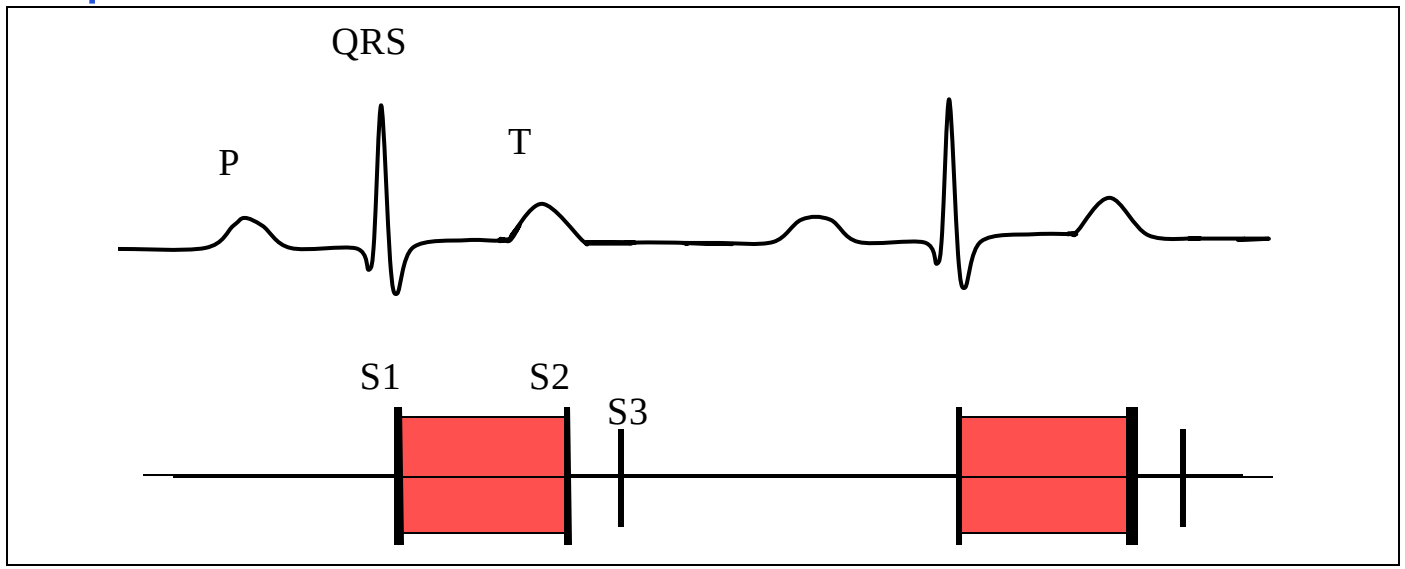
History

- Anorexia, lethargy for 1-3 days
- Hiding under the bed
- Vomiting
- Dyspnea
- Weakness or collapse
- Lameness from arterial thromboembolism
- +/- Weight loss
- Cough is uncommon

Feline Dilated Cardiomyopathy

Cardiac Auscultation

- Soft (I-III/VI) systolic murmur – mitral, tricuspid, or stenal location
- Gallop (S3)
- Arrhythmia often present



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Feline Dilated Cardiomyopathy

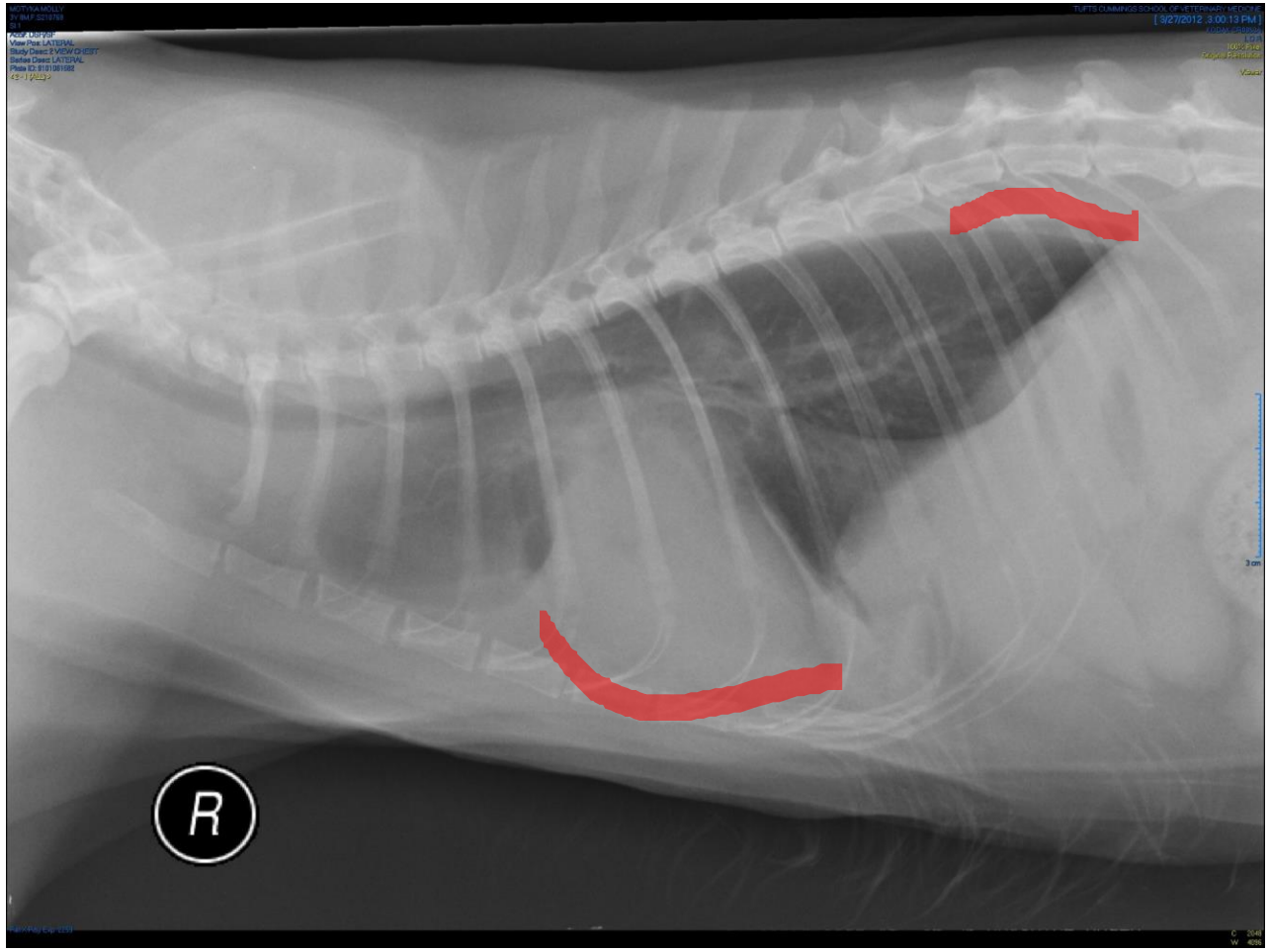
Physical Examination

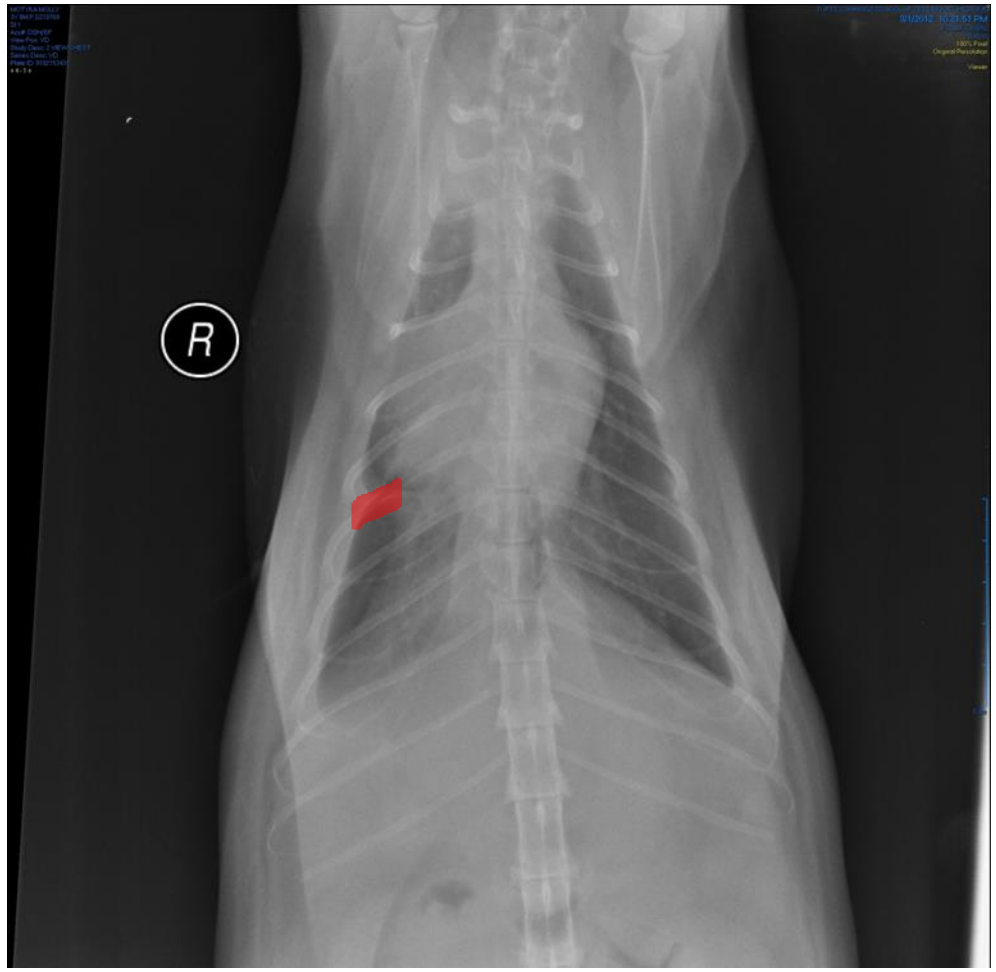
- Normothermic or hypothermic
- Weak arterial pulses
- HR variable – 120-150/min if hypothermic
- Dyspnea, dull ventrally, +/- crackles
- Arterial pulses and apex beat weak
- Jugular vein dist, + H-J reflux, hepatomegaly (esp. if pleural effusion)
- MM pallor, delayed CRT
- Weight loss, cool limbs, weakness

Feline Dilated Cardiomyopathy

Thoracic Radiographs

- Generalized cardiomegaly +/- tracheal elevation
- Pleural effusion / pleural fissure lines
- Perihilar interstitial pattern +/- alveolar infiltrates
- Variable vessel findings; often both veins and arteries enlarged
- +/- Enlarged caudal vena cava and liver
- Rarely ascites





Cardiomegaly and pleural effusion

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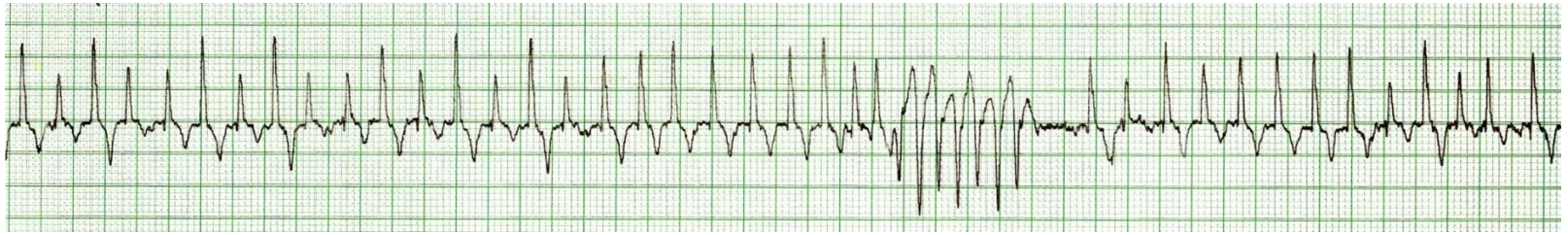
Feline Dilated Cardiomyopathy
Electrocardiography

- Sinus rhythm or relative bradycardia
- P-mitrale (or pulmonale) (left atrial enlargement)
- Left ventricular enlargement pattern
  - ♥ Tall R wave Lead II
- Ventricular arrhythmias
- APCs or atrial fibrillation
- AV block



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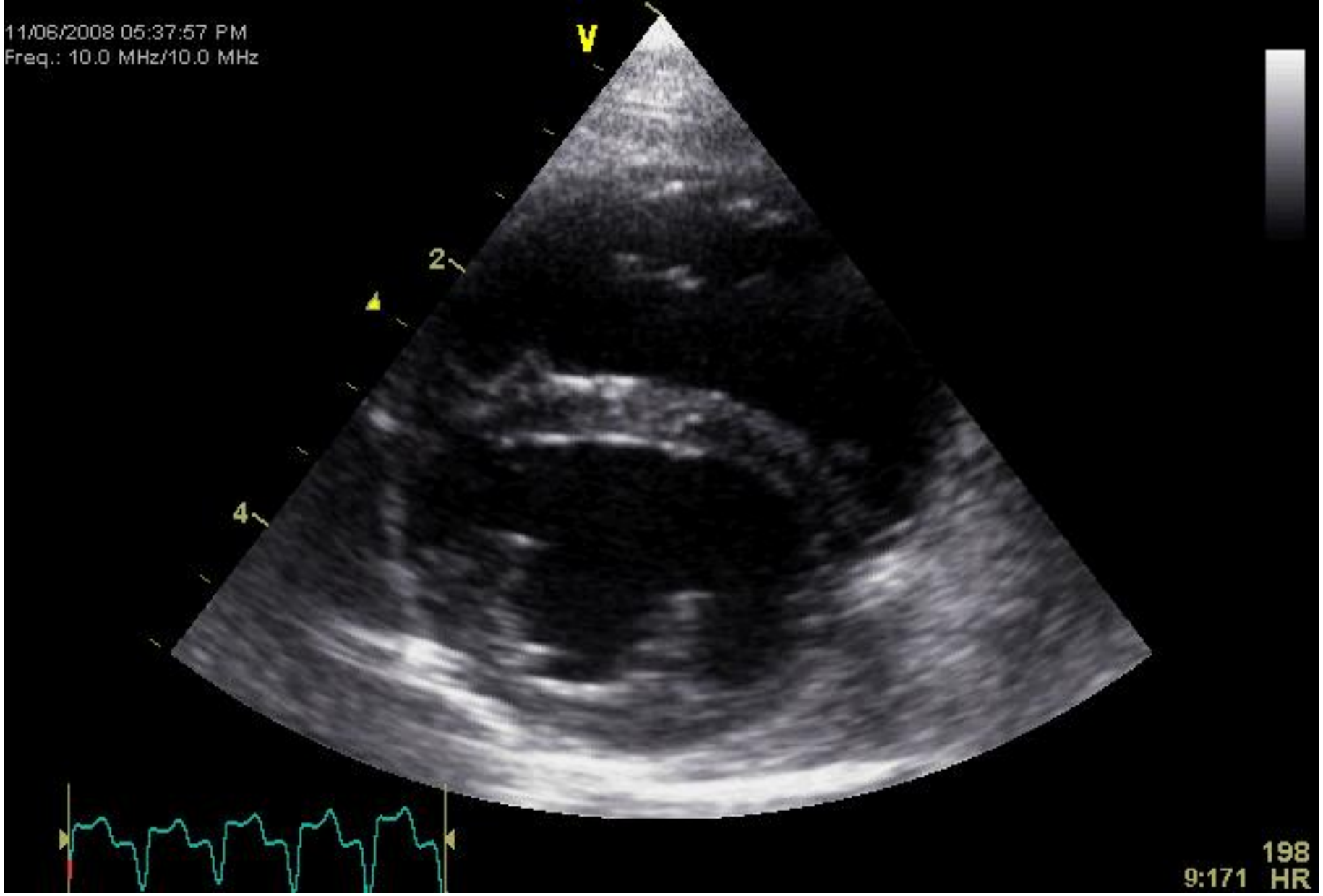
Feline Dilated Cardiomyopathy
Echocardiography

- Dilation of all cardiac chambers, esp. LV
- Reduced fractional shortening (< 28%)
- LV walls are thinned
- Papillary muscles atrophied
- Left atrial enlargement if CHF
- Poor aortic root motion
- Mitral and tricuspid regurgitation



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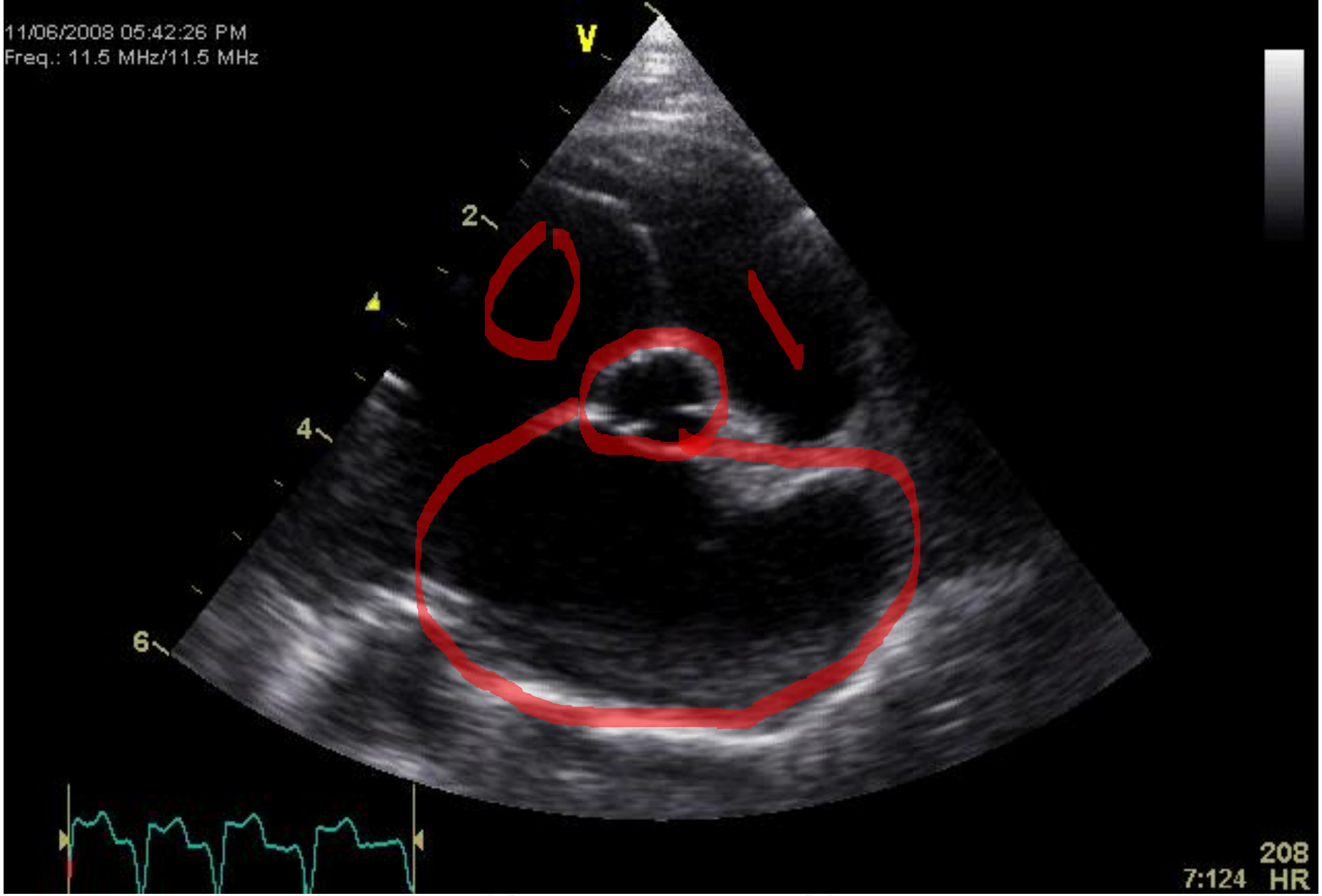

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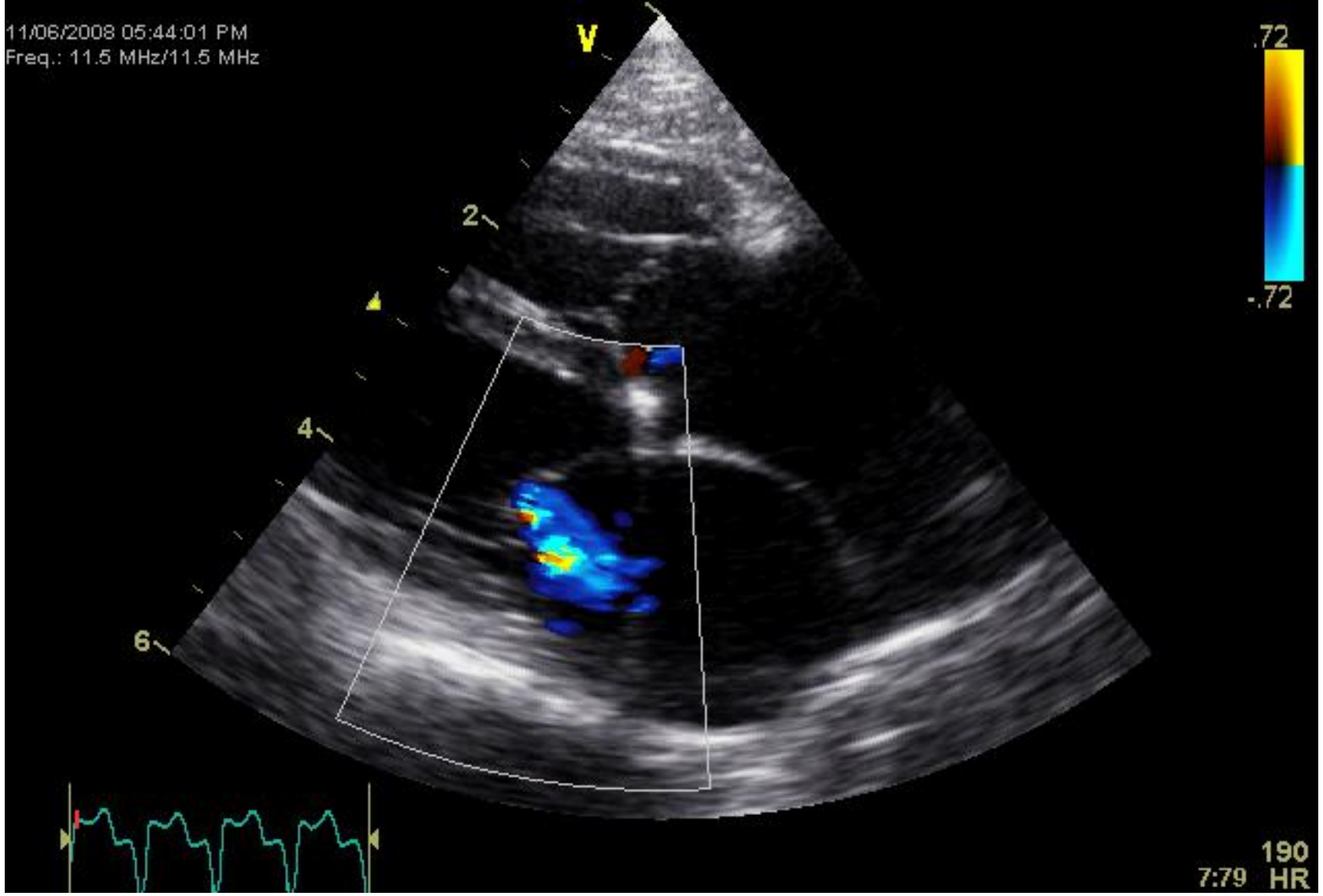

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Feline Dilated Cardiomyopathy
Laboratory / additional testing

- CBC - normal or mild leukocytosis
- Chemistry profile for baseline renal and electrolytes
  - ♥ Hepatic congestion - increased LE's, esp. AST, ALT
  - ♥ Pre-renal azotemia
- Plasma and whole blood taurine concentrations
  - Low in a small proportion of cats
- NT-proBNP – typically elevated
- Blood pressure – may be low

Feline Dilated Cardiomyopathy

Management

- CHF
  - ♥ ACE inhibitor
  - ♥ Furosemide - Lowest dose to control congestion
  - ♥ Pimobendan
  - ♥ Diet and Exercise restriction
- Other therapies:
  - ♥ Taurine
    - ♥Get blood levels
    - ♥250 or 500 mg BID
  - ♥ Dobutamine?
  - ♥ Digoxin?
  - ♥ Prevention of ATE

Equine Dilated Cardiomyopathy

- Uncommon disorder
- Monensin exposure a cause, or other toxins in some cases
- Cardiac murmur and loud gallop
- Atrial fibrillation in many cases
- If CHF, usually see biventricular failure manifest as peripheral edema, jugular vein distention
- ACE inhibitor? Effectiveness?
- Furosemide, Digoxin, Hydralazine
- Can they be ridden?

Ferret Dilated Cardiomyopathy

- One of the reported forms of cardiomyopathy in ferrets
- Often have CHF
- Typical radiographic and echocardiographic findings

Feline Arrhythmogenic Right Ventricular Cardiomyopathy

- Severe right heart enlargement
- Arrhythmias not as big a feature of the disease?
- Right-sided CHF signs
- Often poor prognosis once diagnosed