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
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†
- 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), pellagra, scurvy, selenium, carnitine, kwashiorkor
- Autoimmune/collagen
- Systemic lupus erythematosus
- 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
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 um in diameter with wavy appearance
  - Typically seen in giant breed DCM

From Keene
Attenuated wavy fibers

Normal

CardioRush
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)
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
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
Dobie with Osteosarcoma getting doxorubicin and serial radiography

Mild LAE and increased IS pattern
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
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
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

Plasma Concentration in pmol/L

- Significant heart disease unlikely
- Might have heart disease: More testing
- Heart disease likely present; if dyspnea then CHF likely

![CardioRush](CardioRush.jpg)
Canine NT-proBNP
Asymptomatic Doberman Pinscher
Does it Have or Will it Develop Occult DCM?
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
DCM Associated with Taurine Deficiency

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Testing performed at University of California, Davis
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

![ECG Diagram]

CardioRush
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
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
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
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