Last Updated 06/24/2018

ACQUIRED VALVULAR DISEASE

Revised by V19 Cardio Group modified from Dr. Suzanne Cunningham

Introduction to Valvular Disease

Valvular disease is common in veterinary medicine, and some forms of acquired valvular heart disease lead to congestive heart failure (CHF) and early death. Possible causes of acquired valvular dysfunction include degenerative, infectious, traumatic, and neoplastic disease.

Acquired valvular disease is most commonly caused by degenerative mitral valve disease (DMVD)**,** also known as myxomatous mitral valve disease, which occurs in middle aged to older animals. Neoplastic, traumatic and infectious etiologies occur less frequently. Despite being relatively uncommon, infectious endocarditis resulting in valvular dysfunction is an important clinical entity, as it is often associated with bacteremia, sepsis, and a guarded to poor outcome (see Endocarditis).

Each disease process typically results in valvular thickening and loss of functional competence. The clinical signs, morbidity, and mortality associated with valvular disease depends on the degree of functional impairment, whether the process is acute or chronic, which valve is affected, and whether stenosis or insufficiency (regurgitation) has developed.

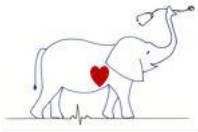
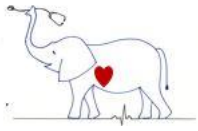
DEGENERATIVE MITRAL VALUVE DISEASE (DMVD) OF DOGS

- Also known as myxomatous mitral valvular degeneration (MMVD), endocardiosis (NOTE: **not** endocarditis!), acquired valvular disease, chronic degenerative valvular disease (CVD)

Description:

DMVD is the most common cause of congestive heart failure (CHF) in dogs. Amongst dogs with this condition, the mitral valve is typically the affected valve, followed by concurrent mitral and tricuspid involvement, sole tricuspid involvement, and aortic valve involvement. Chronic valvular disease can also be seen in species other than small companion animals; in older horses, chronic degeneration of either the aortic or mitral valves is a significant clinical problem.

- **Signalment:**
  - **Breed:** DMVD is most common in small breed dogs and has the highest prevalence in Cavalier King Charles Spaniels (CKCS), with 50% of CKCS affected by chronic valvular disease by 5 years of age, and over 90% affected by 10 years of age. This disease is also inherited in dachshunds. While it is less common to see clinical signs of valvular disease in large breed dogs, it does still occur and tends to be accompanied by concurrent systolic dysfunction.
  - **Sex:** There is an increased incidence in male dogs relative to females (1.5:1).
  - **Age:** DMVD is a slowly progressive disease and is generally *NOT* a disease of young animals. In the early stages, a mid-systolic click or quiet systolic murmur may be the only clinical signs. Clinical disease rarely develops before middle age, while decompensation and congestive heart failure typically do not occur until even later in

life. In CKCS, a more malignant course of the disease may be seen, wherein CHF develops at a younger age.

- **Etiology:** Unknown. Possibly related to dysfunctional valvular serotonin signaling, or disorders of collagen or glycosaminoglycan metabolism. There is a genetic basis predisposing to the disease.
- **Pathology:** DMVD is primarily a non-inflammatory process (called myxomatous degeneration or endocardiosis). Grossly, valve leaflets appear thickened and shortened with curled and nodular margins, and chordae tendineae may be thickened or ruptured. In chronic, severe mitral regurgitation, the left ventricle (LV) will be dilated and eccentrically hypertrophied. The onset of CHF is associated with chronic congestion of the lungs (left-sided CHF) or abdominal viscera (right-sided CHF).

Pathophysiology:

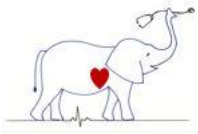
Valvular regurgitation leads to volume overload of the chambers receiving the regurgitant blood. Each time the heart contracts there is a forward fraction (the effective stroke volume), and a regurgitant fraction, which leaks back into the atrium and creates extra work for the heart. To maintain homeostasis compensatory mechanisms are activated, ultimately increasing both the effective circulating volume and cardiac preload. These mechanisms include:

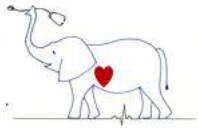
- Sodium and fluid retention via the **renin-angiotensin-aldosterone-system**
- Water retention via **ADH release**
- Systemic **sympathetic stimulation,** which constricts arterioles and veins, leads to inotropic and chronotropic responses, and facilitates fluid retention

Increased preload leads to increased stroke volume and, chronically, eccentric hypertrophy. Eccentric hypertrophy allows the heart to compensate for the added workload and temporarily keeps filling pressures within a tolerable range. Eventually increased filling pressures result in venous congestion and capillary fluid extravasation, causing clinical signs of CHF**.** Dilation of the heart also contributes to the disease process and increases wall stress within the dilated chamber(s). Though myocardial function is typically normal in early stages of the disease, myocardial failure may eventually occur.

With thickening of the mitral valve and the development of mitral regurgitation, there is progressive eccentric hypertrophy of the LV and progressive increases in left atrial size. As left atrial pressure increases the left atrium (LA) enlarges further, and the pressure rises in the pulmonary veins and is transmitted back to the pulmonary capillaries. Increases in pulmonary capillary pressure > 15 to 20 mm Hg results in fluid leak from the capillaries. Enhanced lymphatic flow removes some of the fluid, but eventually fluid accumulates in the pulmonary interstitium and alveoli, leading to overt pulmonary edema.

Infrequently, dogs will worsen suddenly after rupture of a major chordae tendinae, with a sudden rapid rise in LA pressure and severe pulmonary edema. Alternatively, due to chronic stretch on the LA wall, an endocardial split may develop. If a complete tear develops in the LA wall then blood will leak into the pericardial space and cause cardiac tamponade. In the latter stages of the disease, overt myocardial failure can develop, and histopathologic changes include myocyte loss, myocardial fibrosis, and arteriosclerosis of the small coronary arteries.



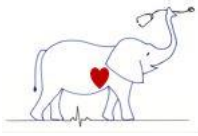
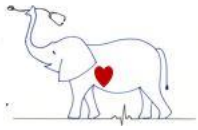


CLINICAL SYNDROMES

- **Cardiac Murmur and Heart Sounds**: Prior to the development of a murmur, a mid-systolic click associated with mitral valve prolapse may be audible. The classic murmur associated with DMVD is a left apical, systolic, regurgitant quality murmur. Typically dogs with clinically relevant DMVD have at least a grade III/VI murmur, and more often a grade IV-V/VI murmur. There is a rough correlation between murmur grade and severity of disease. A tricuspid or mitral regurgitation murmur of III/VI or louder is usually a good indication to perform additional testing (thoracic radiographs, echocardiography, or NT-proBNP testing) to evaluate condition severity.
- **Acute CHF** may be associated with rupture of chordae tendinae or an acute exacerbation of chronic CHF following some event. This is a cardiac emergency.
- **Chronic CHF** is slowly progressive and eventually terminal. After the onset of CHF survival time averages 6-12 months. CHF is normally left sided (from mitral regurgitation), but may be right sided (from tricuspid regurgitation) especially in cases of pulmonary hypertension.
- **Large airway compression:** In advanced DMVD, the LA may be large enough to compress the large airways. In patients presenting with cough, the clinician must determine whether the cough has been triggered by mechanical bronchial/tracheal irritation or pulmonary edema/CHF.This judgement is aided by thoracic radiographs and NTproBNP levels. Cardiac cough may be seen in any disease where the LA is enlarged, or in dogs with concurrent respiratory disease, and is not specific for DMVD.
- **Syncope:** Small-breed dogs with DMVD may experience vasovagal syncope at the onset of CHF. Syncope may also occur secondary to pulmonary hypertension, significant arrhythmias, or following a coughing spell (“tussive syncope” or “cough-drop syndrome”).
- **Endocardial split/Left atrial tear:** With mitral DMVD, chronic jetting of blood and severe elevations in LA filling pressure may lead to weakening/rupture of the atrial wall. If rupture occurs into the pericardium, it is an unusually a peracute cardiac emergency. This can lead to death: however, it is possible for the tear to clot and scar over such that many dogs who survive the acute episode do reasonably well.
    - Endocardial splitting may occur without complete rupture, or rupture may occur without bleeding into the pericardial sac, especially if the rupture occurs across the interatrial septum.

CLINICAL FINDINGS

- **History**: Varies with disease stage.
    - Animals may present for syncope, acute respiratory distress, cough, or in rare cases, sudden death. In many cases the murmur is noted during a routine examination by the primary care veterinarian.
    - One of the primary presenting complaints for DMVD is a deep, resonant cough, which may occur after exercise or may be more prominent at night due to pooling of fluid. Orthopnea may also occur during periods of recumbency.
    - With advancing disease, progressive exercise intolerance and increasing severity of respiratory signs may be noted.

- Late findings may include cardiac cachexia and progressive abdominal distention (right-sided CHF).

- **Physical examination** findings may include:
  - Respiratory signs: Increased respiratory effort, tachypnea, orthopnea, or hyperpnea (may be accompanied by anxiety and reluctance to lie down).
    - Coughing may be elicited by tracheal palpation or occur unprovoked.
    - Paroxysms of cough may end in swallowing or the production of a whitish, pinkish, or blood-tinged foam or froth (pulmonary edema).
  - Murmur: In this condition, murmur intensity is roughly correlated with the severity of disease.
    - Mitral regurgitation murmur: A systolic, regurgitant quality murmur typically localized to the left apex near the 5th intercostal space. As disease severity progresses, the murmur becomes louder, becomes more clearly holosystolic, and may radiate well to the right side of the chest.
    - Tricuspid regurgitation murmur: Systolic regurgitant quality murmur located on the right chest over the tricuspid valve. The intensity is typically less than that of the MR murmur, unless significant pulmonary hypertension is present.
  - Other auscultation findings:
    - Click: A mid-systolic click may be heard with early DMVD due to a prolapsed valve. Must be differentiated from an S3 gallop which can indicate heart failure
    - S1: often loud and snapping in mitral regurgitation
    - S2: may be prolonged or split due to abbreviation of LV ejection and premature aortic valve closure relative to the pulmonic valve
  - A precordial thrill may be present (murmur V/VI or VI/VI), and the ventricular apex beat is hyperdynamic and progressively shifts caudally with increasing disease severity.
  - Femoral pulses may be normal, prominent, or weak (if CHF). Pulse Rate and strength irregularities may occur in association with an arrhythmia. A “jerky” character may be noted due to shortened LV ejection.
  - Mucous membranes are pink in early stages but may progress to a muddy color with decompensation and cyanosis may be noted with acute fulminant left-sided CHF.
  - Right-sided CHF: Jugular venous distention and prominent systolic “V” wave, abdominal organomegaly, +/- ascites.
  - Severe disease: Loss of respiratory sinus arrhythmia and an elevated heart rate may be indicative of sympathetic stimulation and loss of parasympathetic tone.

- **Radiographs:** Findings on thoracic radiograph vary with the stage of disease. In early compensated mitral insufficiency, there is mild cardiomegaly with left atrial enlargement and minimal changes to the pulmonary vessels, and usually a normal radiographic lung pattern. As mitral regurgitation progresses, left ventricular and left atrial enlargement become progressive, leading to tracheal elevation (decreaed angle between the trachea and thoracic spine) and a decreased caudal cardiac waist on the lateral view. The pulmonary veins may

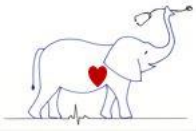
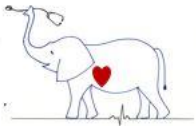
become distended. The onset of CHF, typically with the development of cough, tachypnea, and dyspnea, is associated with an increased interstitial lung pattern, marked LA enlargement, generalized cardiomegaly, pulmonary venous distension, and eventually overt alveolar pulmonary edema. Pulmonary edema is sometimes most evident on the DV view in the right caudal lung lobe. Some dogs develop signs of right-sided CHF such as enlargement of the caudal cava, ascites, pleural effusion, and hepatomegaly.

- **NT-proBNP:** There is progressive elevation of NT-proBNP in dogs with DMVD. There is minimal elevation early in the disease, and values are often in the normal range (< 900 pmol/L). Progressive cardiomegaly results in modest elevations of NT-proBNP. As dogs approach CHF, the NT-proBNP rises, and most dogs with a value > 1500 pmol/L will develop CHF in the next 6 to 12 months. At the time of CHF most dogs have an NT-proBNP > 2200 pmol/L, and many dogs have values > 3,000 pmol/L.

- **ECG:** Normal sinus rhythm or sinus tachycardia; typically, an absence of sinus arrhythmia in advanced disease. Some dogs have mild ST segment changes. Left ventricular enlargement pattern and P mitrale (left atrial enlargement) may be seen as cardiomegaly develops.
    - With disease progression and marked atrial enlargement, supraventricular arrhythmias such as atrial premature beats or atrial fibrillation may occur. Other potential arrhythmias include paroxysmal supraventricular tachycardia (SVT), ventricular premature depolarizations, or paroxysmal ventricular tachycardia.
- **Echocardiography:** Valvular thickening (sometimes more notable early at the anterior mitral leaflet); valvular prolapse during systole; increased fractional shortening; LV and LA enlargement
    - The degree of LA dilation is one of the most useful markers of disease staging, with more severe LA enlargement indicating more advanced disease.
    - With severe disease and chordae tendinae rupture the leaflet may “flail”- the tip of the leaflet everts completely back into the LA.
    - Color Flow Doppler can be used to examine the location and severity of mitral regurgitation.
    - Pulsed Wave Doppler can assess mitral inflow and tissue doppler patterns to estimate myocardial function and LV filling pressures.
- **Invasive methods** are no longer commonly used in practice, as echocardiography has provided a less invasive alternative of disease assessment.
    - Angiocardiography and cardiac catheterization: Demonstrate dilation of the LV and LA, regurgitation of contrast into the LA and/or increased LA and LV end-diastolic pressures.
    - The pulmonary capillary wedge pressure is a correlate of LA pressure and can be used to demonstrate the degree of pulmonary venous congestion.

DIFFERENTIAL DIAGNOSES

- **Upper airway disease/collapsing trachea** may present with signs of dyspnea and cough, which resemble DMVD. Both diseases are common in small breed dogs. However, an upper airway cough is typically described as having a "honking" character and is often associated with periods of excitement.

- **Pulmonary disease** may mimic CHF. Both disease states may include a history of coughing and interstitial or alveolar lung pattern on radiographs. With lower airway disease, pulmonary crackles are often auscultated, and a murmur may be present incidentally, which may lead to a misdiagnosis of left-sided CHF. The lack of a loud mitral murmur or significant left-sided cardiomegaly, especially coupled with a normal heart rate, should differentiate pulmonary disease from CHF. NTproBNP results may also provide helpful information, and would not be elevated in most forms of pulmonary disease.
- **Bacterial Endocarditis:** Mitral valve vegetations may appear similar on echo to valvular thickening due to DMVD. However, vegetative lesions are often more echodense and appear to oscillate independently of the valve. The majority of dogs with bacterial endocarditis appear severely systemically ill with evidence of sepsis.
- **Congenital heart diseases** may cause systolic murmurs (subaortic stenosis, pulmonic stenosis, PDA, ASD, VSD, mitral or tricuspid dysplasia.). Typically, these patients are evaluated early in life.

THERAPY AND MANAGEMENT

Typically, therapy is directed at alleviating the signs of CHF, since repair or replacement of the diseased valve is not commonly done, although certain individual surgeons have good luck with mitral valve repair using cardiopulmonary bypass. Significant hemodynamic benefit and improvement of clinical signs may result from medical and dietary therapy for CHF, and studies have demonstrated improved survival secondary to certain drugs. More complete treatment of CHF is outlined in a later section of the course, and therapy will be only briefly outlined here.

Treatment before the onset of CHF

- Pimobendan administration to dogs with at least a III/VI murmur plus evidence of moderate cardiac enlargement documented by echocardiography and thoracic radiographs can delay the onset of CHF and improve overall survival.

Acute CHF therapy

- Treatment goals are to relieve congestion and survive the episode. Diuretics, exercise restriction, and sometimes vasodilators (sodium nitroprusside or nitroglycerine) are used.

Chronic CHF therapy

- In chronic CHF therapy, the mainstays of treatment are diuretics, an ACE inhibitor, and pimobendan. Exercise limitation and dietary modification are also advised. A low salt diet aims to decrease preload by limiting salt and fluid retention. These drugs, and sometimes other drugs, are used to relieve signs resulting from heart disease (e.g., congestion, dyspnea, syncope, cough), to slow progressive cardiac enlargement, prolong survival, and maintain good quality of life.