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MANAGING FELINE HEART DISEASE-
AN EVIDENCE BASED APPROACH
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Overview
More than 95% of feline heart disease is caused by cardiomyopathy (CM). Many affected cats remain asymptomatic for life, although this percentage has never been clarified. The most common cause of symptomatic heart disease is diastolic heart failure. This results from diastolic dysfunction, the principal pathophysiologic consequence of a wide range of heart muscle disorders, most prominent of which are hypertrophic cardiomyopathy or restrictive cardiomyopathy.

Diastolic Dysfunction
Diastolic dysfunction is the principal pathophysiologic consequence of a wide range of phenotypically heterogeneous myocardial disorders. Hearts from cats with ventricular hypertrophy (HCM), and restrictive cardiomyopathy (RCM) are affected by complex intrinsic and extrinsic factors that affect left ventricular diastolic performance. Some of the better recognized factors include altered loading conditions; increased myocardial mass (hypertrophy); myocardial injury (inflammation, myocytolysis, necrosis) and repair (fibrosis, matrix changes); myocyte disorganization; and ischemia. These alterations promote ventricular stiffness and loss of compliance (diastolic dysfunction). Diastolic heart failure may result.

Diastolic Heart Failure
When alterations in diastolic function lead to increased left ventricular filling pressure and mean left atrial pressure, congestive heart failure may result. This clinical in which pulmonary edema occurs in the setting of abnormal diastolic function and relatively normal systolic function has been termed diastolic heart failure.

Screening for Heart Disease
Echocardiography is the gold standard for assessing cardiac structure and function. Thoracic radiography is important to help document the presence of heart failure as well as other non-cardiac conditions, but does not substitute for echocardiography. Electrocardiography is valuable in the face of arrhythmia, unfortunately, is insensitive for detecting the presence of heart disease. Noninvasive measure out blood pressure can be useful to detect the presence of systemic hypertension which could affect left ventricular wall thickness. Blood pressure assessment is particularly relevant in face of diseases known to raise blood pressure or effect heart structures such as chronic renal failure and hyperthyroidism. Certain clinical pathology tests such as serum T4 (in cats older than six years of age) may be relevant. While interesting information is emerging about biomarkers and heart disease, their use for cardiac screening has not yet been validated.

Management of Feline Heart Disease

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While the goal for managing heart disease is to reduce morbidity and mortality, there remain important gaps in our understanding of several critical areas. For example, etiopathogenesis of the cardiomyopathies is unresolved; clinical categorization of myocardial disease still requires refinement; the natural history of myocardial disease has not been established; and importantly, risk factors that predispose to morbidity and mortality remain to be identified.

Historically, in absence of prospective, randomized clinical trials in cats, treatment strategies have been extrapolated from human data, retrospective feline case studies, pharmacologic or physiologic studies of drug mechanisms in cats, and personal experience. Limitations of these approaches include lack of knowledge regarding drug efficacy and long-term treatment benefit.

Goals for Managing Heart Disease
The overarching goal when managing heart disease is to improve survival by reducing morbidity and mortality.

The Asymptomatic Cat

There is currently no evidence that treatment of asymptomatic cats prevents disease progression, reduces risk factors, or affects morbidity and mortality. Moreover, there is no data to guide whether therapies have to be implemented throughout the lifetime of an individual, or indicate when a particular drug should be given. Nevertheless, certain circumstances would appear to increase risk of cardiovascular morbidity.

Potential Risk Factors

In several conditions, substantial abnormalities involving myocardial structure or function appear to promote adverse outcome, thereby providing raison d'être for pharmacologic intervention. The following may warrant therapy, although efficacy remains to be proven.

Myocardial Infarction
In cats with myocardial infarction inferred by echocardiography, ACE inhibitors and beta-blockers may be justified. Rationale for ACEI therapy is based upon the potential of these agents to favorably influence ventricular remodeling and reduce mortality in people and in experimental animals. Rationale for beta-adrenergic blockers similarly include reduction of infarct size, myocardial oxygen utilization, and reduced mortality.

Tachyarrhythmia
Rapid tachyarrhythmias can reduce cardiac filling, promote ischemia, and result in hemodynamic instability. Sustained tachyarrhythmias are usually associated with myocardial disease with attendant cardiac remodeling (myocyte necrosis, fibrosis, inflammation, and interstitial matrix changes). Therefore, it is prudent to consider antiarrhythmic therapy in selected cases, particularly when the ventricular rate is rapid.

Massive Left Ventricular Hypertrophy (Severe HCM)
Although not confirmed, cats with greatly increased left ventricular mass (maximal diastolic septal or left ventricular wall thickness > 8mm) may be at increased risk for cardiovascular events.

**Syncope**
Recurrent syncope is a risk factor for sudden death in humans with HCM, and retrospective feline studies related syncope and poor outcome. In cats syncope can be associated with tachyarrhythmias, dynamic LV outflow obstruction, and ischemia (infarction). Symptoms can often be managed successfully with beta-blockers to reduce or abolish LV outflow tract obstruction.

**Spontaneous Echo Contrast (“Smoke”)**
Spontaneous echo contrast is associated with blood stasis. This finding is considered to presage thrombosis and is associated with increased thromboembolic risk. It should therefore warrant antiplatelet drugs (aspirin) and perhaps more aggressive therapies.

**“Malignant” Familial History of Sudden Death (High Risk Genotype)**
Pedigrees may be identified with a documented heritable pattern of HCM with severe morbidity and mortality (e.g., Maine coon cats, others). Early intervention with calcium channel blockers or beta-adrenergic blockers may be contemplated based on experimental considerations which hold that a pathway to the phenotypic expression of LV hypertrophy is influenced by triggers such as higher LV pressure and work load.

**Myocardial Failure**
In some HCM cats LV contractility is reduced (e.g., fractional shortening, 23-29%; LV end-systolic dimension, 12-15 mm) from acute or chronic myocardial infarction, myocarditis, and other causes of LV remodeling. Therapies include oral taurine supplementation, ACE inhibitors to counteract neurohormonal activation and reduce remodeling, and judicious beta-blocker therapy if myocardial infarction is suspected or with tachyarrhythmia.

**Arrhythmic Right Ventricular Cardiomyopathy**
Cats with advanced structural lesions (e.g., severe RV dilation, ventricular tachycardia) may be at risk for CHF. ACE inhibitors and potentially, antiarrhythmics (sotalol) should be considered.

**Managing Diastolic Heart failure**

**Acute CHF (Pulmonary Edema)**
Pulmonary edema is rapidly progressive and life threatening. Rapid resolution is the goal, and diuretics represent the cornerstone for acute, emergency management. Furosemide administered intravenously causes peak diuresis within 20- 30 minutes. It inhibits renal sodium tubular reabsorption or its accompanying anions; promotes brisk diuresis; and reduces vascular volume decreasing LV filling pressures (i.e., cardiac preload) and pulmonary congestion. Initial dosage is 1- 2 mg/kg IV every 30-60 minutes until dyspnea associated with congestion is reduced. Then, dosage frequency is reduced, typically to every 8-12 hours- or, the animal is changed to furosemide administration via constant rate infusion (ie, based upon estimated dose...
for 24 hours). Resolution of pulmonary edema may be enhanced by application of trans-dermal 2% nitroglycerin ointment, ¼ to ½ inch q 6hr. To reduce nitrate tolerance, alternate 12 hrs with and 12 hrs without nitroglycerine therapy. Supplemental oxygen (40-60% O$_2$-enriched inspired gas) may improve pulmonary gas exchange. Clinical improvement and resolution of congestion is indicated by reduced respiratory rate and work of breathing, resolved lung crackles, and radiographic clearing of alveolar infiltrates (usually by 24 to 36 hrs). Dehydration, azotemia, and hypokalemia can result from over-diuresis.

**Chronic Diastolic Heart Failure**

Chronic therapy is individualized to maintain a congestion-free state; prevent arterial thromboembolism; halt, slow, or reverse myocardial dysfunction (theoretically); promote enhanced quality of life; and prolong survival. Treatable and contributory diseases should be identified and managed (e.g., systemic hypertension, hyperthyroidism, and anemia). Therapy for each case must ultimately be individualized.

Furosemide is gradually decreased to the lowest effective dosage, typically, 6.25-12.5 mg q 12 - 24h). Some cats remain stable on 1- 2 mg/kg PO given every other day while in others, diuretics may be used twice weekly or even discontinued.

Ideally, treatment should be guided by clinical evidence that one or more drugs are safe and effective. The foundation of evidence-based medicine is randomized clinical trials designed to evaluate effects of specific therapies on morbidity and mortality. To help assess scientific data with an evidence-based perspective, one widely held technique qualifies clinical data according to four categories of evidence type (e.g., Type A evidence results from large, prospective, randomized, controlled clinical trials designed to assess treatment and outcome; type D evidence is anecdotal or personal experience).

Recently, data has been reported by the author from a multicenter, collaborative, feline heart failure trial designed as a prospective, blinded, controlled study study (Fox PR, for the Multicenter Feline Chronic Heart Failure Study Group. Prospective, double-blinded, multicenter evaluation of chronic therapies for feline diastolic heart failure: Interim analysis. J Vet Int Med 17:398, 2003). Cats recovering from first onset of diastolic heart failure were randomized into one of four treatment groups that received once daily administration of atenolol, dilacor, enalapril, or placebo. All cats received background therapy furosemide daily (6.25-12.5mg). Survival was statistically shorter in the beta-blocker group. There was no statistical difference in survival between cats who received placebo vs dilacor. Cats in the enalapril group did as well or better than the placebo group.

**Managing Systolic Heart Failure**

Historically, myocardial failure was most typified by reversible dilated cardiomyopathy associated with taurine deficiency. This condition was nearly eliminated in the late 1980s after a pet food companies reformulated diets to increase taurine content. However, cases are routinely encountered of idiopathic dilated cardiomyopathy that involve a number of different etiologies such as...
myocardial infarction, inflammation, or idiopathic causes. Case is usually present with effusions, hypothermia, and sometimes cardiogenic shock.

Acute management involves intensive care, administration of dobutamine (2-5 mcg per kilogram per minute constant rate infusion), judicious furosemide administration (often constant rate infusion), ACE inhibitor administration (enalapril, benazepril, ramipril, etc), physical removal of effusion when severe, and generalized supportive measures, including supplemental oxygen supplementation, care for preserving electrolyte balance, and assessment of renal function). While the role of pimobendan in acute management is unsubstantiated, many use it (0.625 mg q 12-24hr PO). Supplemental feeding via naso esophageal tube can be useful.

Chronic management includes the lowest effective dose of furosemide, spironoactone, ACEI, and either digoxin or pimobendan. Generally, long-term outlook is guarded.

**Recurrent Heart Failure**

Upward diuretic titration may be necessary with recurrent CHF. Diuretic resistance may occur as heart failure progresses, and cats with recurrent CHF are likely to benefit acutely from intravenous furosemide which has higher bioavailability. Addition of a second diuretic (e.g., thiazide-5 to 10 mg daily, or spironolactone- 12.5 to 25 mg daily) is reserved for cases of diuretic resistance. It is prudent to assess BUN, creatinine, electrolytes and blood pressure in anorectic cats. Enalapril is added to current therapy if not already in place. Addition of other drugs is contingent on individual needs and underlying disease.

**Thromboembolism**

Antiplatelet aggregating therapy may be considered when severe left atrial enlargement is present, when spontaneous echo contrast is evident in the LA or LAV, or when cats have had previous thromboembolic episodes. Aspirin may be used, dosed at approximately 80mg every three days. Other agents are presently under investigation such as clopidogrel (Plavix). Low molecular weight heparin drugs are added when cats have thromboembolic complications. Two particular agents, enoxaparin (Lovenox) and dalteparin (Fragmin), have received the most attention. Both drugs are expensive but appear to have a far greater safety margin than unfractionated heparin. Fragmin (100 U/kg q 12-24hrs SQ) or enoxaparine (1mg/kg q 12 hrs SQ) have been used relatively safely. This dose of fragmin, however, may be too little- or the frequency too low, to be efficacious. Administration rates of every 6 to 8 hours are generally impractical, however, for long term administration. Hyperkalemia can occur acutely as a result of re-perfusion injury. Continuous ECG monitoring is valuable during the first 3 days of hospitalization. Periodic evaluation of BUN and electrolytes are useful.