

## FELINE CARDIOLOGY

John D. Bonagura, DVM, DACVIM

Cardiovascular diseases are common in cats.<sup>1-3</sup> Myocardial disorders are the major cause of heart failure and thromboembolism, with idiopathic hypertrophic cardiomyopathy the most important of the primary myocardial diseases.<sup>4-7</sup> Extensive myocardial fibrosis leading to a restrictive cardiomyopathy or right ventricular cardiomyopathy is now recognized on a regular basis in mature cats. Conversely, dilated cardiomyopathy is rare today because feline diets are supplemented with taurine. Nonsuppurative myocarditis is identified sporadically in cats; however, the diagnosis is difficult and often based on suspicion (or necropsy). The cardiac manifestations of, hyperthyroidism, hypertension, and anemia are well known in this species, but these conditions must be distinguished from primary cardiomyopathies as management and prognoses differ. Primary acquired valvular disease is very rare in cats. Functional murmurs are common, including those related to ejection of blood into the dilated aorta found in older cats. Herein is a summary of clinical aspects of the most important of the feline myocardial diseases.

### **HYPERTROPHIC CARDIOMYOPATHY**

Feline hypertrophic cardiomyopathy (HCM) is characterized by hypertrophy of the left ventricle that cannot be unexplained by congenital heart disease, hypertension, or an endocrinopathy.<sup>4,5</sup> The condition is genetic in a number of breeds. The hypertrophy in cats is typically concentric, including the entire left ventricle. Regional hypertrophy however is also common, often involving the upper septum, ventricular free wall, or the papillary muscles. In most cases of symptomatic HCM the left atrium is dilated. Mitral regurgitation may be evident due to papillary muscle hypertrophy or accelerated blood flow in the left ventricular outlet that leads to mitral valve - septal contact (systolic anterior motion). Atrial and systemic thrombi are often encountered in this disease. Small vessel coronary artery disease has been reported in some cats, as well as areas of myocardial fibrosis and infarction. The natural history of feline HCM is quite variable and can benign or lethal. Clinical signs are explained by left-sided congestive heart failure (CHF), complications of thromboembolism, outflow tract obstruction, or arrhythmias.

**Clinical Pathophysiology** - The cause of CHF in cats with HCM is thought to involve mainly ventricular diastolic dysfunction.<sup>4,5,8,9</sup> Abnormalities of ventricular filling are characterized by either abnormal myocardial relaxation (an active, oxygen-dependent process) or reduced left ventricular compliance (distensibility). These problems are related to abnormal cardiac muscle, myocardial ischemia or oxygen imbalance (reduced delivery relative to demand), increased chamber stiffness (thick wall to lumen ratio), and myocardial fibrosis. Higher than normal pulmonary venous and left atrial pressures are required to fill a stiff ventricle, predisposing to pulmonary edema. A vigorous atrial contraction may be needed for maintain ventricular preload; accordingly, the development of atrial fibrillation can be disastrous, causing severe CHF. The roles of myocardial ischemia and of stress (sympathetic activity) in the pathogenesis of diastolic dysfunction require further study. It is well known, however, that stress predisposes affected cats to CHF. Certainly protracted tachycardia increases myocardial oxygen demand, decreases coronary perfusion time, and elevates left atrial pressure. These factors may explain the sudden development of left-sided CHF (flash pulmonary edema) so often observed in this disorder.

Cats with HCM may also suffer from abnormal ventricular systolic function.<sup>4,10</sup> Dynamic and labile pressure gradients between the left ventricle (LV) and aorta are often found as blood is ejected rapidly across a bulging ventricular septum. Increased systolic pressure in the LV may stimulate further hypertrophy and predispose to ventricular subendocardial ischemia. These systolic gradients are due to the combination of septal hypertrophy and mitral-septal contact. The latter stems from systolic anterior motion (SAM) of the mitral valve that begins once ejection has been initiated. The presence of significant SAM is invariably associated with

mitral regurgitation (MR). Mitral incompetency also can be traced to geometric changes in the left ventricle, papillary muscle dysfunction, or possibly atrial dilatation.

**Clinical features** - Male cats are predisposed. Young cats (5 months to 6 years of age) are often affected, though cats of any age may have HCM. Breeds at risk include the Maine coon cat<sup>10b</sup>, Persian cat, Ragdoll cat, and probably other breeds as well. The possibility of HCM may be prompted by auscultation of a cardiac murmur or gallop sound in a cat that has no other signs of heart disease.<sup>2,4,11</sup> When symptomatic, most cats are presented for tachypnea and dyspnea, attributable to CHF with pulmonary edema or pleural effusion. Stress, fever, moderate-to-severe anemia, thyrotoxicosis, anesthesia, or fluid therapy may precipitate congestive heart failure. Urgent presentation may follow arterial thromboembolism to the terminal aorta. More subtle or vague are signs related to embolism of the right forelimb or cerebrum. Sudden death is reported infrequently, and is likely to develop from a coronary embolus, a ventricular arrhythmia, or if signs of CHF are unrecognized and the cat succumbs to hypoxia. Nonspecific signs such as lethargy or anorexia are less common.

Typical physical examination features of HCM include various combinations of the following: gallop, murmur of MR (along the left apical, sternal border), arterial thromboembolism, pulmonary edema or biventricular CHF (pleural effusion). When present, the systolic murmur can vary, often increasing in intensity with higher heart rates. This finding suggests dynamic outlet obstruction and SAM are present. The apical impulse can be prominent. Arrhythmias can occur but are not common. Arterial blood pressure is normal.

Laboratory tests can be useful.<sup>2,3,5,12</sup> The ECG may be abnormal but results are inconsistent. Increased amplitude R-waves in lead II or a left axis deviation compatible with concentric hypertrophy or left anterior fascicular block may be observed. Radiographs can be normal, but in advanced cases demonstrate cardiomegaly (elongation) and left atrial enlargement (most evident as an auricular bulge on the VD view). Prominent pulmonary vascular patterns may indicate pulmonary hypertension secondary to elevated left ventricular diastolic pressure. Increased lung densities are compatible with pulmonary edema. Pleural effusion is common in acute CHF and in chronic, longstanding cases of heart failure. Routine CBC and clinical chemistries are unremarkable in most cases unless there is thromboembolism or intercurrent disease. Serum thyroxine is normal.

Hypertrophic cardiomyopathy is characterized echocardiographically by increased ventricular thickness (generally 6 mm or more), normal to decreased intraluminal size, and normal or increased systolic shortening fraction.<sup>3,5,10,10b,12</sup> However, 2D echo may show regional LV hypertrophy that is not homogeneous; thus, over-reliance on one measurement (i.e. the LV wall between the papillary muscles) is discouraged. In some cats there is prominent ventricular septal hypertrophy with varying obstruction of the LV outlet. In others, prominent papillary muscles are observed (representing an early sign of HCM in some cats). The size of the left atrium bears prognostic significance as it usually relates to the severity of diastolic failure or MR, and can predict the risk for CHF and thromboembolism. In chronic HCM, LV contractility may decrease, the chamber can dilate, and there may be evidence of progression to restrictive disease (see Restrictive Cardiomyopathy below). Systolic anterior motion of the mitral valve is observed quite often and increases in severity with increased sympathetic tone. Doppler studies may demonstrate abnormal relaxation or compliance of the LV, mitral regurgitation, or high velocity LV outflow caused by dynamic obstruction.

**Drug Therapy for Hypertrophic Cardiomyopathy** - A number of cardiovascular drugs are used in the management of feline HCM. These drugs may also be of value for treatment of other feline CV disorders. It is emphasized that there are no large, controlled studies that indicate a superior treatment for asymptomatic disease, for cats with recurrent bouts of CHF, or for advancing heart failure. Prevention of arterial thromboembolism is a persistent problem. Pharmacologic therapy of cats with HCM generally may include combinations of furosemide,

diltiazem, a beta-adrenergic blocker, an angiotensin converting enzyme inhibitor, or drugs that impair coagulation. Relevant clinical pharmacology of these drugs in cats is discussed below.

*Beta adrenergic blockers* (atenolol 12.5 mg PO once or twice daily or propranolol 2.5 - 5 mg PO, t.i.d.) are most often used to block the adverse effects of sympathetic efferent traffic on the heart.<sup>13</sup> Once daily atenolol often controls heart rate at <150/minute for almost 24 hours, though pharmacokinetic studies suggest that b.i.d. treatment may be better. Beta-blockers prevent sinus tachycardia and prolong diastole, increasing time for both coronary and ventricular filling. Myocardial oxygen demand is reduced through decreases in heart rate, contractility, and blood pressure. Beta blockade is especially helpful for reducing pressure gradients caused by dynamic left ventricular outflow obstruction. Once can administer the ultra-short beta-blocker, esmolol, at an initial 0.5 mg/kg loading followed by a 0.1 mg/kg/minute infusion as a provocative treatment during Doppler examination of the LV outlet. A simpler approach is to administer 12.5 mg of atenolol orally and repeat the Doppler study in 1-1/2 to 2 hours later. The murmur of mitral regurgitation when caused by SAM of the valve may partially abate with beta blockade. In a small European study, beta blockade with propranolol was associated with regression of LV hypertrophy, but this has not been a consistent finding. Unfortunately, the net effect of beta blockade on diastolic function in cats with HCM is unknown. The direct effect on myocardial relaxation is unfavorable; however, indirect effects, such as reduced myocardial oxygen demand, decreases in intraventricular gradients, and prolongation of diastole also should be important and could benefit diastolic function. Adverse effects include severe sinus bradycardia (examination HR < 100/min), depression, and precipitation of CHF. Owing to the nonspecific blocking effects of propranolol, it is not recommended in cats with uncontrolled pulmonary edema or in cats with arterial thromboembolism until collateral circulation has been restored.

*Diltiazem*, a calcium channel antagonist, is a popular drug for chronic management of HCM based on the clinical report of Bright et al.<sup>8,9</sup> Calcium channel blockers are thought to improve left ventricular relaxation. The precise mechanism for this benefit has not been elucidated. Indirect effects, by reducing blood pressure and reflexively increasing sympathetic tone, could be involved. Alternatively, myocardial perfusion may increase with diltiazem since the drug is a coronary vasodilator and also decreases resting heart rate, though not as effectively as a beta-blocker. Overall, diltiazem should reduce myocardial oxygen demand by decreasing heart rate, contractility, and blood pressure. Effects on reducing dynamic outflow tract gradients have been disappointing at the doses commonly used. Though the chronic administration of diltiazem has been reported to decrease LV hypertrophy in cats with *very severe* HCM, we rarely observe regression even after prolonged therapy with diltiazem, especially in the typical case. Overall, diltiazem is usually preferred in our practice when a cat has *already experienced* CHF, or when a cats has moderate to severe LV hypertrophy and left atrial dilatation as demonstrated by echocardiography. Diltiazem is also reasonable therapy for the cat with HCM and concurrent atrial fibrillation. Preparations of diltiazem vary and include: (a) diltiazem (30 mg tablet; ¼ tablet PO tid); (b) Dilacor XR brand of diltiazem (note: the 240 mg Dilacor XR capsule is opened to reveal four – 60 mg drug tablets which are split into halves using a pill cutter; the dose is 30 mg once or twice daily); or (c) Cardizem CD brand (120, 180, 240 mg capsules; compounded in capsules or in a palatable syrup to provide 30 mg once daily). Anorexia, skin reactions and erythema/edema have been observed in some cats receiving this drug. Depression, weakness, and hypotension may indicate sinus bradycardia, AV block, or arterial vasodilation from too high a dose or sensitivity to the drug (e.g., in older cats with inherent AV conduction disease). A *combination* of atenolol and diltiazem may be considered in cats with HCM and dynamic LV outflow tract obstruction (30 mg Dilacor in PM; 6.25 to 12.5 mg atenolol in the AM); however, heart rate and blood pressure should be monitored with this combination therapy because of the combined effect of these drugs on heart rate, contractility and blood pressure.

*Furosemide* is the initial treatment of choice for cats with pulmonary edema (2 – 4 mg/kg IV

or IM as an initial dose; thereafter, 1 – 2 mg/kg IV, IM, SQ q8-12h for 24 to 48 hours). Oral therapy is prescribed for home care of cats that have experienced pulmonary edema; however, the maintenance dosage is often titrated down to a relatively low 1 – 2 mg/kg every second to third day. This can be accomplished over a period of two to three weeks. In some cases, furosemide can be discontinued completely. Conversely, doses of 2 mg/kg, b.i.d. to t.i.d., or higher, may be needed to treat progressive pulmonary edema or pleural effusion in cats with chronic CHF. These problems are detected by having clients monitor exercise activity and resting respiratory rate and through periodic examinations and thoracic radiographs. Dietary sodium restriction can be combined with furosemide provided the cat will eat a new diet. Efficacy of diuretic therapy is monitored using respiratory rate, level of activity, thoracic examination, and the chest radiograph. Overzealous diuresis can be detected by periodic measurement of blood pressure, serum BUN, creatinine and electrolytes. Azotemia, hypokalemia, and hyponatremia are very common in cats taking furosemide on a daily basis. Mild to moderate azotemia (e.g. BUN 40 to 70 mg/dl) is not necessarily an indication to alter furosemide therapy in a cat with persistent fluid accumulation because the edema is likely to worsen if furosemide dosage is decreased. In contrast, the dose of furosemide should be reduced in the cat with azotemia and a completely clear chest cavity to prevent unneeded volume contraction.

*Angiotensin converting enzyme inhibitors* such as enalapril (Enacard) and benazepril (Lotensin) can be administered for recurrent or progressive pulmonary edema or pleural effusion at a dosage of 0.25 to 0.5 mg/kg q24h. Whether or not the angiotensin inhibitors will reduce myocardial hypertrophy in this disease is unknown, but clinically these drugs seem to benefit the fluid accumulation of CHF. Therapy is monitored by measuring arterial blood pressure indirectly and with periodic monitoring of renal function and serum sodium and potassium. Angiotensin inhibition, when combined with diuretic or aspirin therapy, can cause acute renal failure that is reversible with fluid therapy or discontinuation of drug therapy. If systolic blood pressure (the easiest to measure indirectly) is < 85 mmHg, or if BUN increases significantly above pretreatment levels, the dose of enalapril, furosemide, or both should be reduced by 33 - 50%.

*Nitrates* (nitroglycerine ointment, 1/4 cutaneously, once or twice daily) may be used for hospital therapy of CHF in conjunction with furosemide and oxygen administration. Nitrates may also be used for home care of cats, particularly if the cat experiences unexplained bouts of dyspnea or the client has trouble medicating their pet.

*Digoxin* is rarely used in cats with HCM. There are no data supporting use of cardiac glycosides in this disease. The principle indications for digoxin would be development of atrial fibrillation (given with diltiazem or a beta-blocker) or when there is CHF associated with echocardiographic evidence of progressive left ventricular systolic failure and cardiac dilatation. Digoxin is eliminated by renal mechanisms and the elimination  $T_{1/2}$ , even in healthy cats, is very long (often 2 to 3 days). Digitalization in cats is initiated at a dose of 1/4 of a 0.125-mg Lanoxin tablet every 48 hours. A serum digoxin concentration is measured about 14 days later with the blood sample drawn 10-12h post treatment. A trough serum concentration between 1 and 1.5 ng/ml is the therapeutic goal.

*Anti-thrombotic drug therapy* can be prescribed in an attempt to reduce the chance of arterial thromboembolism.<sup>14,16</sup> There are no prospective studies demonstrating efficacy of any treatment. Empirically two approaches have developed. Aspirin (1 baby aspirin or 1/4 of an adult aspirin every 3 days) or Warfarin (Coumadin, starting at 1/2 of a 1 mg tablet daily) may be prescribed to inhibit thrombogenesis. *Aspirin* may inhibit platelet function in some cats. The dose is probably critical, but good guidelines are lacking. Anorexia, vomiting, and gastric erosions are potential complications of therapy. *Coumadin* represents a more aggressive approach to treatment for cats with severe atrial dilation, prior embolization, or other risk factors (e.g. atrial fibrillation).<sup>15</sup> Since Warfarin initially enhances coagulation, co-therapy with heparin (100 IU/kg, subcutaneously) should be given for the first 48 – 72 hours. A

baseline one-stage prothrombin time (PT) should be obtained. It has been recommended to calculate the international normalization ratio (INR) to achieve a value of between 2.0 to 3.0 (with the blood sample drawn about two hours post-treatment). The INR = (patient PT ÷ control PT)<sup>ISI</sup> where ISI = international sensitivity index of the thromboplastin used in the PT assay. The control value is obtained from a control *population* (not a single cat!). The validity of using this approach in cats has not been completely determined, but it represents the most rationale approach thus far presented. Do not use Warfarin with aspirin, and consider other drug interactions. Should bleeding occur at any body site or in the litter box, immediately discontinue therapy, and re-establish the INR at 2.0 to 3.0. Vitamin K therapy is used to treat a bleeding diathesis.

**Treatment Approaches** - *There are no data that indicate any substantial benefits of therapy in asymptomatic cats with HCM.* Increasingly, cats with asymptomatic or mild HCM and normal left atrial size are left untreated. Many show little progression of disease at follow up. Thus, in the asymptomatic cat, the veterinarian could reasonably consider prescribing no therapy, or empirically a beta-adrenergic blocker, or diltiazem. Some clients will indicate that their cat is more active when receiving therapy, but this may simply represent a placebo effect. Beta-blockers are recommended by many in the setting of moderate to severe LV outflow tract obstruction, and atenolol is most often prescribed for this purpose. Marked left ventricular hypertrophy, especially with concurrent left atrial dilatation, suggests significant diastolic dysfunction or mitral regurgitation, and diltiazem is usually prescribed. Anticoagulant therapy may also be recommended especially when there is left atrial dilatation (see below). Initially cats with asymptomatic disease are examined by repeated thoracic radiographs or by echocardiography every 3 to 6 months. The echo has the advantage of providing objective measures of wall thickness and left atrial size, and a Doppler study can be used to document reduction in dynamic obstruction and associated MR should these flow disturbances be present at initial examination. Thereafter, the stable cat is seen every 6 to 12 months. In many cases, the disease is quite stable, and there is little justification for excessive re-evaluation after the one-year follow up.

**Management of Acute Heart Failure** in cats with HCM is a challenge. Initial efforts are directed at improving tissue hypoxia, relieving stress, and reducing the venous and pulmonary capillary pressures. Thoracocentesis is performed if there is a large pleural effusion. Intubation and artificial ventilation best manage impending respiratory arrest. Fortunately most cats can be managed medically. The cat is placed at rest, oxygen (40 – 50%) is administered by cage oxygenator, and sedation is given if necessary (butorphanol – 0.15 mg/kg mixed with acepromazine - 0.05 to 0.1 mg/kg subcutaneously). Furosemide is administered and once diuresis occurs the dose is reduced as previously described. Nitroglycerin (2%) ointment is also administered q12h when there is moderate to severe pulmonary edema. Treatment is continued for 24 to 72 hours. Subsequently, oxygen is withdrawn, nitrate ointment is discontinued, and the dosage of furosemide is lowered and titrated to the severity of pulmonary edema or pleural effusion. Many cats develop hypokalemia and pre-renal azotemia during such intensive therapy. Mild cases need not be treated, but if the cat refuses to eat and drink after 24 to 36 hours of therapy, judicious fluid therapy (e.g. 20 ml/kg/day) and potassium supplementation (IV or oral) will be needed.

**Chronic management of CHF** in cats with HCM often involves home therapy of furosemide, diltiazem, and a treatment to prevent thromboemboli. If the dosage frequency of furosemide is more than 1 mg/kg once daily, I add enalapril 0.25 mg/kg daily for 2 weeks with an intent to increase the dose to 0.5 mg/kg daily if blood pressure, renal function, and electrolytes are adequate. Initial re-

evaluation is in one to two weeks, then again in one month. Periodic re-evaluations (at least every three to six months for two years) are recommended and include history and examination, ABP measurement, thoracic radiographs, serum biochemical profile, and often a focused, recheck echocardiogram. The timing of specific examinations depends on clinical circumstances and economic considerations.

**Treatment and Prevention of Arterial Thromboembolism** - While some reports have indicated the importance of collateral vasoconstriction and the value of inhibiting platelet-derived vasoconstrictors, there are no controlled studies demonstrating improvement of collateral flow with therapy in spontaneous cases. Surgery generally has been avoided since these cats usually have DIC and many develop (or have) lung edema after anesthesia (though there have been some surgical successes following embolectomy). A significant number of cats (about 40%) with HCM will walk within three weeks of the thrombotic event provided heart failure is controlled and the limbs undergo spontaneous revascularization.<sup>16</sup> Sufficient time (at least one week) should be allowed for improvement. Severe ischemic muscle necrosis does develop in some cases, and these cats are usually euthanized. The cat with a single functionless or edematous limb may do well after limb amputation, but this is rarely recommended or requested.

The initial treatment of cats with involves analgesia and sedation with butorphanol (0.2 - 0.3 mg/kg SQ q8h combined with acepromazine 0.1 mg/kg; a 10 cm<sup>2</sup> fentanyl patch; 25 ug/hr release may also be considered but will not work as quickly as butorphanol). The acepromazine + butorphanol combination is effective sedation/analgesia for the cat in distress. Sodium bicarbonate (1 mEq/kg, IV over 10 -20 minutes) is sometimes administered at first presentation as there may be metabolic acidosis and/or hyperkalemia from muscle necrosis and reperfusion. Heparin may be administered to prevent further thrombosis (200 to 300 I.U./kg, is administered IV, then subcutaneously at 200 I.U./kg every 8 hours for 48 - 72 hours). Beta-blockers, especially propranolol, should be avoided until the cat is walking without difficulty. If CHF is controlled, maintenance fluid therapy is administered (with furosemide) to maintain urinary output and prevent hyperkalemia. Excitement has waned for IV streptokinase (90,000 I.U. IV over 30 min followed by 45,000 I.U./hour for 3 -6 hours) and IV tissue plasminogen activator (0.25 to 1 mg/kg/hour to a total dose of 1 to 10 mg/kg) as these expensive treatments are difficult to control and carry a very high mortality rate.<sup>14</sup> Reperfusion -be it spontaneous or induced by a thrombolytic drug -can lead to fatal hyperkalemia from rapid reperfusion of necrotic muscles.

*Prevention of thromboemboli* is recommended when there is atrial enlargement. When the left atrium is enlarged (>16 mm on 2D echo) aspirin is prescribed every three days. Warfarin is recommended when the cat has one of the following: (a) prior documented thromboembolism; (b) a left atrial dimension exceeding 20; (3) evidence of spontaneous echocardiographic contrast (smoke) in the left atrial cavity; or (4) atrial fibrillation. One must have a cooperative client for Warfarin therapy to succeed.

### **FELINE RESTRICTIVE CARDIOMYOPATHY**

Feline restrictive cardiomyopathy (RCM) has also been called intermediate cardiomyopathy and endomyocardial fibrosis.<sup>1,5,17,18</sup> The pathogenesis of these lesions is undetermined. Antecedent myocarditis seems a likely, though unproven, initiating cause. Restrictive cardiomyopathy in some cats clearly represents a late stage of hypertrophic cardiomyopathy complicated by myocardial failure or myocardial infarction. A variety of necropsy lesions have been observed in cats demonstrating clinical features of restrictive cardiomyopathy. Left ventricular endomyocardial fibrosis may be patchy, multifocal, or diffuse in distribution. The left ventricle may be mildly or regionally hypertrophied, mildly dilated, or normal in size. Often there is regional thinning or infarction of the left ventricular free wall or left ventricular apex interspersed with focal or regional wall hypertrophy. Prominent papillary muscle

hypertrophy or fibrosis is evident in some cats. Extreme endocardial fibrotic scarring is occasionally evident, and can involve the mitral valve apparatus, cause mid-ventricular constriction or stenosis, or obliterate the left ventricular apex. A common feature is striking biatrial dilation. Systemic thromboemboli are common and left atrial and ventricular mural thrombi may be observed. Histologic lesions include endocardial thickening, endomyocardial fibrosis, myocardial interstitial fibrosis, myocyte hypertrophy, and focal myocytolysis and necrosis. Arteriosclerosis of intramural coronary arteries may be recognized.

**Pathophysiology** - The pathophysiology of RCM in the cat is unresolved. Echocardiography generally demonstrates a low normal to mildly reduced shortening fraction (ejection fraction). When decreased ejection fraction is present, it is probably caused by a loss of functional myocardium, and the systolic dysfunction may progress over time. Regional left ventricular wall dysfunction may be observed, characterized by diminished left ventricular free-wall thickening and excursion. Doppler studies may demonstrate mitral insufficiency, but the regurgitation is usually mild. Because the abnormalities of ejection fraction and mitral valve function do not sufficiently explain the marked left atrial dilation characteristic of this disease, it is assumed that impaired left ventricular distensibility is the principal pathophysiologic disorder. Myocardial or endomyocardial fibrosis is the most likely explanation for this diastolic dysfunction. Myocardial ischemia, relaxation abnormalities, cardiac arrhythmias, or ventricular dilation can further impair ventricular diastolic function. Progressive increases of left atrial pressure develop to fill the stiff left ventricle and thereby predispose the cat to elevated pulmonary venous pressure and pulmonary edema. One can also speculate that the marked left atrial dilation and fibrosis increase the resistance to right ventricular ejection. These factors probably lead to chronic pulmonary hypertension and cause the progressive enlargement of the right side of the heart and contribute to the elevated central venous pressure that is so often observed in advanced cases. Pulmonary edema, pleural effusion, and hepatic congestion are typical manifestations of CHF, and can be explained by the aforementioned cardiac lesions along with neurohumoral and renal compensations activated in response to limited cardiac output. Stasis of blood in a dilated left atrium undoubtedly predisposes affected cats to atrial thrombi and systemic thromboembolism.

**Clinical findings** - Most cats with RCM are middle aged or older though young cats have also been recognized with this condition. History and clinical signs of RCM are similar to those described above for HCM. Examination of the cat with RCM can reveal a variety of physical manifestations. The most consistent auscultatory finding is a gallop sound, indicative of ventricular diastolic dysfunction. A soft to moderately loud systolic murmur of mitral or tricuspid regurgitation may be detected near the left or right sternal borders, but is not always evident. Premature ventricular or atrial beats may be heard, leading to an irregular rhythm and arterial pulse. The femoral pulse is otherwise normal or slightly reduced in amplitude. Palpable hepatomegaly or pleural effusion with elevated jugular venous pressure or prominent jugular pulsations is suggestive of concurrent right ventricular failure. Pulmonary edema or pleural effusion is most often manifested as tachypnea, though orthopnea, respiratory distress, and cyanosis may develop in severe cases of CHF. Thoracic auscultation is variable but careful auscultation may reveal loud bronchial sounds, fine crackles, or a fluid line. Blood pressure is usually normal. Signs of aortic thromboembolism may be evident.

Diagnostic studies are helpful in recognizing heart disease and establishing the diagnosis of RCM. The electrocardiogram is frequently abnormal. Ventricular enlargement and myocardial disease can be manifested as a widened QRS complex ( $> .04$  sec); increased amplitude R-waves ( $> .7$  mV) in leads II, aV<sub>F</sub>, or III; splintered R-waves, right axis deviation, or left bundle branch block; and ventricular extrasystoles. Atrial enlargement is characterized by widened ( $> .035$  sec) or tall ( $> .2$  mV) P-waves, atrial ectopic rhythms, or atrial fibrillation. Thoracic radiographs are often impressive and characterized by left atrial dilation and cardiac elongation that is typical of left ventricular enlargement. The cardiac apex can be pointed or rounded. Some cats manifest astounding left atrial enlargement which, on the lateral

projection, can be seen to separate the mainstem bronchi and create a convex dorsocaudal border. Some cases demonstrate a valentine-shaped heart reminiscent of HCM. Pulmonary hypertension may be evident radiographically as dilation of both lobar arteries and veins. Interstitial and alveolar infiltrates indicative of pulmonary edema or bilateral pleural effusions indicate the development of CHF. Left ventricle angiography is rarely performed, but can delineate a number of anatomic lesions: marked left atrial dilation, mild left ventricular dilation, and irregular filling defects of the left ventricular lumen seem most characteristic of this disease. In some cases, the left ventricular cavity is distorted by fibrotic papillary muscles, endocardial plaques, or prominent moderator bands; midventricular cavity obliteration may be evident.

The most characteristic echocardiographic feature of RCM is marked left atrial or biatrial dilation. The left ventricle, in typical cases of RCM, is neither as hypertrophied nor as dynamic as that observed in HCM. In contrast to cats with dilated cardiomyopathy, ventricular shortening fraction is either normal or just mildly reduced (generally > 25%) and the mitral opening (E point) to septal distance is minimally increased. However, marked regional wall dysfunction may be noted, most often affecting segments of the left ventricular free wall. Two-dimensional echo examination may reveal a ventricle that is mildly dilated just below the mitral valve; yet, apically the left ventricle may appear hypertrophied and the papillary muscles thick or rigid. Discrete thinned areas of ventricular atrophy, infarction, or scar may be imaged. Focal or diffuse, subendocardial, hyperechoic wall segments probably denote fibrosis or endomyocardial plaques. In extreme cases of endocardial fibrosis, imaging of the mid to apical left ventricular lumen may demonstrate thickened, hyperechoic, fibrous tissue that bridges the septum, papillary muscles or free wall; obliterates the apical left ventricular cavity; or confers an appearance of diminished systolic motion or restricted filling. Prominent left ventricular moderator bands (false tendons) also may span portions of the lumen. Left atrial or ventricular mural thrombi are observed infrequently. The right ventricle is often dilated in symptomatic cats, but is otherwise devoid of structural lesions. Doppler studies can indicate atrioventricular valve regurgitation but it is rarely severe. Owing to the rapid feline heart rate, Doppler assessment of diastolic function is sometimes difficult, but can demonstrate a restrictive LV filling pattern with rapid deceleration time and small A-wave. When congestive heart failure has developed, pleural and pericardial effusions will usually be present. The pericardial effusion can be substantial, but decreases markedly, following successful treatment of heart failure.

Clinical laboratory studies of cats with RCM are not specific and most abnormalities are attributable to CHF, diuretic therapy, or thromboembolism. A plasma or whole blood taurine should be measured since decreased concentrations have been noted in some cats and could contribute to reduced myocardial contractility. Analysis of pleural effusates indicates a transudate, modified transudate, or chyle. The predominant cells present are macrophages, mesothelial cells, and small lymphocytes unless there is chylothorax, in which case, well-preserved neutrophils may be more numerous.

**Therapy of Restrictive Cardiomyopathy** - Respiratory distress in this condition is attributed to pulmonary edema, pleural effusion, or both, and initial treatment should be directed accordingly. When pleural effusion is present and sufficient to cause atelectasis, thoracocentesis should be performed while the cat rests in sternal recumbency. A sample of the effusate should be retained for chemical and cytologic analysis. Pulmonary edema can be severe in some cats with RCM. Initial therapy includes supplemental oxygen, furosemide (2-4 mg/kg IM or IV q 8h), and 2% transdermal nitroglycerine paste (1/4 inch, topically q12h). Once diuresis has been observed the diuretic dose is decreased (1-2 mg/kg, subcutaneously q8-12h). Following initial diuresis, the cat should be given fresh water, ad libitum. Should water be refused or continual weight loss occur, maintenance IV or subcutaneous fluids should be given (40-50 ml/kg/24h of 0.45% NaCl - 2.5% dextrose solution; add 8-12 mEq Kc per 500 cc fluid). In cats with aortic thrombosis, both serum potassium and renal function should be monitored at least daily and more often if thrombolytic therapy is given. Liquid nutritional support given by an indwelling nasogastric tube may be considered if anorexia persists, however, most cats begin to eat following effective resolution of CHF. Systemic thromboembolism is managed as described previously for feline HCM.

Chronic therapy of the cat with RCM is centered on medical management of CHF and

prevention of thromboembolism. Drugs used in management of CHF have been discussed previously. A sodium-restricted diet should be dispensed if it is eaten. We have had the best results in treating CHF using a combination of furosemide, enalapril and digoxin. The daily furosemide dosage depends on the severity of fluid accumulation and must be individualized. Initial doses between 1-2 mg/kg q12h are reasonable; however, doses as high as 4-mg/kg q8h have been tolerated. The angiotensin converting enzyme inhibitors have been used frequently in cats with RCM. The initial dosage is low (0.25 mg/kg, PO, q 24h), but can often be increased to as high as 0.5 mg/kg q12h. Aspirin (1 baby aspirin every 3 days) or Coumadin (starting at 0.5 mg daily) may be prescribed to inhibit thrombogenesis. Should progressive pleural effusion develop, despite digoxin, furosemide, and enalapril therapy, the clinician can perform thoracocentesis and then consider one or more of the following strategies for refractory CHF: 1) increase the enalapril to a maximal dosage of 0.5 mg/kg q12h; 2) increase furosemide to 4 mg/kg q8h; 3) add nitroglycerine paste at a dose of 1/4 inch topically, q12h; or 4) add spironolactone (2 – 4 mg/kg PO daily); or 5) substitute one oral furosemide treatment for a subcutaneous injection two or three times weekly. The cat should be reassessed in 3 to 7 days by clinical examination and by radiography. Should each of these treatments fail, euthanasia should be considered.

The value of other treatments such as diltiazem or beta-blockers in feline RCM is unresolved. Rutin is prescribed when there is evidence of recurrent pleural effusion with chylothorax. Treatment of complicated and rapid ventricular tachycardia in cats with RCM is problematic. Propranolol (2.5-5.0 mg q8h) or procainamide (1/4 of a 250 mg capsule mixed in the food q8h) have been used, but negative inotropic effects, client and patient compliance, and lack of efficacy studies suggest that such treatments be reserved for symptomatic (i.e. syncopal) patients or those with dangerous ventricular arrhythmias.

The long-term prognosis of RCM is guarded and quite variable. Some cats have been successfully managed for CHF for over two years and such cases have been rewarding to clients and clinicians alike. One-year survival is not uncommon following onset of heart failure. Unfortunately, relentless CHF, refractory pleural effusion, or systemic thromboembolism each present formidable obstacles to long-term survival.

### **OTHER MYOCARDIAL DISEASES**

Dilated cardiomyopathy, is recognized by echocardiographic demonstration of reduced left ventricular shortening (ejection) fraction, absence of ventricular wall thickening, and absence of congenital or valvular cardiac disorder.<sup>4,5,19-22</sup> Congestive heart failure and thromboembolism are consequences of this disorder that is very uncommon in cats because feline rations are now supplemented with taurine. Previously, deficiency of this amino acid accounted for the large number of cases of dilated cardiomyopathy in the cat. Sporadic cases of dilated cardiomyopathy still occur, possibly a consequence of myocarditis. Cats with dilated cardiomyopathy are evaluated for taurine deficiency (particularly at-risk breeds include the Burmese, Abyssinian, and Siamese) and treated with taurine (250 to 500 mg twice daily for 12 weeks). Heart failure is managed with furosemide, digoxin, and enalapril or benazepril.

Hyperthyroid heart disease is common<sup>23-25</sup> and leads to biventricular hypertrophy with the left ventricle becoming quite thickened in chronic cases. While hyperthyroidism remains an important differential diagnosis for other forms of cardiomyopathy, affected cats infrequently develop CHF because veterinarians are now very cognizant of this disorder. If the thoracic radiographs show only mild to moderate cardiomegaly, further studies are unlikely to add to the management of the disorder and treatment of the hyperthyroidism is pursued with no additional cardiac medication prescribed. Infrequently, biventricular CHF develops in cats with moderate to severe cardiomegaly and evidence of reduced global left ventricular systolic function. This situation is managed medically, with furosemide, enalapril, and methimazole. Once the cat is stable, it should be referred for treatment with I<sup>131</sup> or possibly ultrasound-

guided injection of a unilateral tumor with ethyl alcohol. The cardiac manifestations of thyrotoxicosis usually abate following definitive treatment of hyperthyroidism (except for those with overt cardiac failure or those with true intercurrent hypertrophic cardiomyopathy). Thromboembolism is exceedingly rare in isolated thyrotoxic heart disease. Cardiac disease and clinical signs can be partially controlled with atenolol (6.25 to 12.5 mg, PO, once daily) in cats with long-standing thyrotoxicosis that cannot be managed definitively and cannot tolerate methimazole or carbamazepine.

Hypertensive heart disease should be included in the differential diagnosis of any cat with a gallop, murmur, or echo-proven left ventricular hypertrophy.<sup>26, 27</sup> The clinical condition can resemble mild HCM. Heart failure and thromboembolism are rare. Diagnosis is generally straightforward if the clinician obtains a device to measure ABP. Treatment is directed at controlling hypertension, progressive renal injury, and preventing ocular complications. Amlodipine (Norvasc - 1/4 of a 2.5-mg tablet once or twice daily; increase dosage as needed up 1/2 tablet t.i.d.) seems to be the current medication of choice for controlling hypertension in cats. Beta-blockers or angiotensin converting enzyme inhibitors are reasonable alternatives though not as effective. Furosemide is also indicated in short-term hospital therapy of cats with retinal hemorrhage/detachment.

Acromegaly and growth hormone excess have been incriminated as causes of feline heart disease.<sup>28</sup> Cats with diabetes and other signs of acromegaly should be considered as potential candidates for this syndrome. For optimal management, a specialist in internal medicine or endocrinology should be consulted.

Nonsuppurative myocarditis occurs sporadically in cats.<sup>5</sup> The cause is unknown. Some cats are presented for ventricular arrhythmias, while others develop fulminant heart failure, restrictive cardiomyopathy (chronic, healing phase), or thromboembolism. The diagnosis is difficult and often based on suspicion. Since myocardial biopsy is difficult in cats, and enzyme changes nonspecific, the diagnosis is usually tentative or may be made at the necropsy table.

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