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Chapter

150 Cardiomyopathy

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OVERVIEW

The left and right ventricles are capable of undergoing significant morphologic change in response to stresses and stimuli. Reaction to increased volume or pressure work frequently leads to chamber dilatation and hypertrophy, along with alterations in the cytoskeletal matrix of the ventricle. Myocardial and chamber responses develop with chronic valvular heart disease, cardiac shunts, systemic and pulmonary hypertension, thyrotoxicosis, and chronic anemia. These responses to stress are directed by various neural, hormonal, and genetic messages acting on the myocardium. These signals influence genetic expression in the cardiomyocyte and interstitial cells, and remodel the ventricle.

"Cardiomyopathy" refers to disease of the myocardium and, by extension, the cardiomyocyte and the supporting collagen and interstitial matrix. Idiopathic or primary cardiomyopathies are those that cannot be explained by a malformation, acquired cardiac lesion, dysrhythmia, or coronary artery disease. Many idiopathic cardiomyopathies are genetic diseases. A more expansive definition of cardiomyopathy accepts that some myocardial diseases can be explained by other disorders, and in such cases, the term *secondary cardiomyopathy* can be used. When myocardial failure develops from chronic volume or pressure overload of the ventricle, the term *cardiomyopathy of overload* has been proposed to explain the remodeling associated with increased ventricular work.

Although there are many known causes of cardiomyopathy, most cases in cats and dogs are idiopathic and thought to represent a genetic disorder. This is particularly true of dilated cardiomyopathy in dogs and hypertrophic cardiomyopathy in cats. What stimulates these genetic factors to cause heart muscle disease is poorly understood, and most cases of cardiomyopathy are irreversible and progressive. But there are special examples that demonstrate that some cardiomyopathic states can be postponed, arrested, or even reversed. For example:

- Chronic tachyarrhythmias cause a cardiomyopathy with loss of myocardial contractility that is reversible if the arrhythmia is resolved.
- Taurine deficiency in cats is a classic example of a reversible dilated cardiomyopathy.
- Regression of left ventricular hypertrophy may occur after successful treatment of systemic hypertension or hyperthyroidism.

Cardiomyopathies often are classified by the postmortem anatomic appearance of the left (or right) ventricle and by the correlative echocardiographic features of ventricular anatomy and function. The most important forms of cardiomyopathy can be classified as follows (see Table 150-1):

- ***Myocarditis*—**An inflammation of the heart muscle observed most often in cats. It may be responsible for premature ventricular complexes, sudden death, or progressive heart failure.
- ***Dilated cardiomyopathy (DCM)*—**A dilated, poorly contracting left ventricle (LV) usually associated with development of congestive heart failure (CHF), cardiac arrhythmias, and sudden death. DCM is a common disease of dogs but is very uncommon in cats.
- ***Hypertrophic cardiomyopathy (HCM)*—**A thickening of the LV walls of unknown or genetic cause and displaying considerable phenotypic heterogeneity. HCM is mainly a disorder of cats and often leads to cardiac murmurs, CHF, or thromboembolic disease.
- ***Restrictive cardiomyopathy (RCM)*—**A heterogeneous and poorly characterized disorder defined by extensive fibrosis in the LV. It is encountered mainly in mature or older cats and is a recognized cause of arrhythmias, CHF, and arterial thromboembolism.
- ***Right ventricular cardiomyopathy*—**A disorder that affects mainly (or initially) the right ventricle resulting in either CHF or ventricular arrhythmias.
- ***Unclassified cardiomyopathy*—**Primary LV diseases that are not easily classified as HCM, DCM, or RCM. Some cases are probably related to myocardial infarction.
- ***Cardiotoxicity*—**The heart also can be damaged by a number of cardiotoxins, some of which are listed in Table 150-1. The outcome of cardiotoxicity is often an arrhythmia, conduction disturbance, sudden death, or development of a secondary dilated cardiomyopathy.

Table 150-1. CAUSES OF CARDIOMYOPATHY (CM)

Disorder*	Feline	Canine
Myocarditis		
Noninfective	Idiopathic	Idiopathic
	Thymoma (immune-mediated)	Trauma
Infective	Toxoplasmosis	Bacterial
	Feline infectious peritonitis?	Parvovirus
		Distemper virus
		Systemic mycoses
		Lyme carditis (*Borrelia*)
		Chagas disease (*Trypanosoma cruzi*)
Dilated CM (DCM)‡	Taurine deficiency	Idiopathic†
	Idiopathic	Carnitine or Taurine deficiency
	Potassium iodide toxicity	Breed-"specific" DCM†
	Hyperthyroidism	Doberman pinscher
	Sustained ventricular or supraventricular tachycardia	Boxer dog
		Cocker spaniel
	Chronic hypokalemia (causes taurine deficiency?)	"Giant" purebred dogs
		Springer spaniel muscular dystrophy
		Sustained ventricular or supraventricular tachycardia
Hypertrophic CM	Idiopathic† (familial?)	Idiopathic
Left ventricular concentric hypertrophy	Acromegaly (rare)	Hypertension
	Hypertension†	Hyperthyroidism (iatrogenic)
	Hyperthyroidism†	
Restrictive-intermediate CM	Idiopathic*	
Arrhythmogenic right ventricular cardiomyopathy	Idiopathic	Boxer dog (genetic)†
		English bulldog (genetic?)†
Cardiotoxicity	Sodium iodide	Catecholamines including brain-heart syndrome and pheochromocytoma
		Doxorubicin
		Digitalis purpurea (foxglove) and *Strophanthus* spp.
		Toad (*Bufo*) toxicity
		Chocolate toxicity

*Both primary (idiopathic) and secondary causes of cardiomyopathy are considered here.
†Most important types.
‡Also see infective and noninfective myocarditis because DCM can develop secondary to severe inflammatory disease.

This chapter will next describe the clinical features of feline cardiomyopathies and the therapy of related complications. Following this is a consideration of canine DCM and arrhythmogenic cardiomyopathy.

FELINE HYPERTROPHIC CARDIOMYOPATHY

Overview and Pathophysiology of Feline HCM

- Feline idiopathic HCM is characterized by hypertrophy and thickening of the left ventricle unexplained by congenital heart disease, systemic hypertension, or an endocrinopathy.
- The condition is genetic in a number of feline breeds, including the Maine coon cat, Persian cat, and the Ragdoll. Thus far, one sarcomeric mutation has been identified.
- The pattern of ventricular hypertrophy in this disease is variable as demonstrated at necropsy or by 2D echocardiography.
  - Symmetrical concentric hypertrophy of the LV walls and papillary muscles is considered typical of feline HCM, but there is substantial variation in the location and severity of hypertrophy in this disease.
  - The main histologic finding is of myocardial cell hypertrophy with fiber disarray. Small, intramural coronary arteries are often narrowed. Microscopically, there is fibrosis between myocytes. Focal areas of infarction or inflammation may be observed.
  - The left atrium (LA) is usually dilated and the wall may be hypertrophied from increased pressures needed to fill the LV. Atrial or auricular clots are found attached to the chamber wall in some cases.
- The natural history of untreated feline HCM is quite variable following a benign or lethal course; a brief or protracted clinical disease; and sometimes remarkable recovery from life-threatening complications. Some cats remain asymptomatic for many years before succumbing (if ever) to the disease.
- Clinical signs in HCM are explained by left-sided CHF, complications of arterial thromboembolism (ATE), LV outflow tract obstruction, or arrhythmias capable of causing syncope or sudden cardiac death.
- The differential diagnosis for the clinical signs of HCM in cats is extensive (Tables 150-2 and 150-3),

Table 150-2. DIFFERENTIAL DIAGNOSIS OF FELINE CARDIOMYOPATHY AND HEART FAILURE*

Other Causes of Dyspnea/Tachypnea
Airway obstruction
Nasopharyngeal polyp
Laryngeal paresis
Tracheal or esophageal foreign body, neoplasm, granuloma, abscess
Mediastinal masses
Lymphoma or thymoma
Primary bronchopulmonary disease
Bronchial asthma/bronchitis
Lungworms and lung flukes
Pneumonia (viral, bacterial, fungal, toxoplasmic)
Neoplasia
Aspiration
Pulmonary vascular disease/embolism
Heartworms/spontaneous worm death
Noncardiogenic pulmonary edema
Electrocution
Trauma (shock lung)
Anaphylaxis
Trauma
Diaphragmatic hernia
Pulmonary hemorrhage/edema
Pneumothorax
Hemothorax
Pleural effusion
Pyothorax
Hemothorax
Feline infectious peritonitis (FIP)
Lymphoma-associated effusion
Chylothorax
Hyperthermia/fever
Anemia
Methemoglobinemia
Acetaminophen toxicity
Cetacaine
Abnormal ventilatory pattern
Metabolic acidosis
Central nervous system disease
Other Causes of Acute Lameness/Paresis/Gait Abnormality
Musculoskeletal pain or injury
Bite wounds
Hypokalemia (weakness)
Peripheral neuropathy
Related to diabetes mellitus
Spinal cord disease
Injury
Neoplasia
FIP infection
Extradural mass/granuloma
Urinary obstruction
Causing abdominal pain and reluctance to move
Other Causes of Cardiac Murmurs/Gallops/Arrhythmias/ Cardiomegaly
Congenital heart disease
Especially spetal defects and mitral valve dysplasia
Congenital peritoneopericardial-diaphragmatic hernia
Bacterial endocarditis
Pericarditis
FIP infection
Idiopathic
Bacterial
Neoplastic
Lymphoma
Mesothelioma
Cardiac neoplasia
Lymphoma
Cor pulmonale
Heartworms
Severe chronic respiratory disease
Chronic degenerative valvular disease (mitral, aortic)
Dilation of the aortic root with aortic regurgitation
Cardiac arrhythmias (primary electrical disturbances)
Chronic bradyarrhythmias
Atrioventricular block in aged cats
Tachyarrhythmias and premature complexes
Sedatives, tranquilizers, anesthetic drugs
Chronic or severe anemia
Hyperthyroidism
Acromegaly
Systemic hypertension
Chronic renal disease
Hyperthyroidism
Idiopathic
Electrolyte abnormalities
Hyperkalemia
Urinary obstruction
Hypokalemia
Renal disease

*The most common clinical presentations of feline cardiomyopathy are dyspnea from congestive heart failure, rear-limb paresis from aortic thromboembolism and inactivity. The veterinarian often detects a murmur, gallop rhythm, arrhythmia, or cardiomegaly during examination.

and includes congenital heart disease, myocarditis, and other forms of primary cardiomyopathy (RCM, DCM). When an echocardiogram demonstrates thickening of the LV, specific disorders causing LV hypertrophy must be excluded including

- Mitral valve malformation causing dynamic obstruction of the LV outflow tract with secondary hypertrophy.
- Congenital aortic or subaortic stenosis.
- Hyperthyroid heart disease (thyrotoxicosis).
- Hypertensive heart disease.
- Focal basilar septal hypertrophy associated with aortic dilatation (aortoannular ectasia).
- Acromegaly (growth hormone excess).

- The *pathophysiology* of feline HCM (Figure 150-1) is relevant to the diagnosis and drug therapy of this disease. The presumptive cause of CHF is ventricular diastolic dysfunction, because most cats with HCM have a normal to hyperdynamic LV ejection fraction.
  - Diastolic dysfunction is the inability to fill the left ventricle with normal LA pressures.
  - Early diastolic dysfunction is characterized by abnormal myocardial relaxation with a vigorous LA contraction to support late diastolic filling. This situation is associated with the atrial (S4) gallop so often detected in these cats.
  - Progressive ventricular disease is associated with reduced chamber compliance with loss of passive

Table 150-3. COMMON FELINE CARDIAC DISEASES

Disorder	Necropsy and Echo (Anatomic Diagnosis)	Typical Clinical Problems	Etiologic diagnosis
Pericardial effusion and pericardial disease	• Peritoneopericardial diaphragmatic hernia (PPDH) • Secondary to CHF • Infection (including FIP) secondary to infection • Neoplastic related (LSA) • Echo: echo-free space around heart; +/− mass lesions; often observe *left*-sided cardiomyopathy; Liver and fat in PPDH	• Unexplained cardiomegaly (PPDH) • CHF as a cause of PE • CHF as consequence of PE and cardiac tamponade • Systemic illness (infection, neoplasia)	• Congenital (?genetic)—PPDH • Infectious (coronavirus) • Lymphosarcoma • Immunosuppression (?)
Septal defects—VSD, ASD, ECD	• Ventricular or atrial septal defect • AV valve malformation (ECD) • Echo: above lesions with volume overload of affected chambers	• Systolic heart murmur • Cardiomegaly • CHF • Cyanosis (reversed shunt)	• Congenital • Genetic?
Dilated cardiomyopathy (DCM) *phenotype*	• Cardiac chamber dilatation (typically left sided chambers +/− right sided) • Echo: cardiac dilatation & loss of myocardial contractility	• CHF—left-sided; biventricular • Arterial thromboembolism • Arrhythmias • Sinus bradycardia • Hypotension • Soft heart sounds • Secondary AV valvular regurgitation	• Idiopathic DCM • Taurine deficiency DCM • Moderate to severe anemia • Fulminant myocarditis
Hypertrophic cardiomyopathy (HCM) *phenotype*	• Left ventricular hypertrophy that is concentric or regional • Focal septal LVH (aged cats; dilated aortic root) • Echo: LV hypertrophy; variable; possible LA dilation	• Abnormal auscultation: heart murmur, gallop, arrhythmia • Thyroid adenoma in cases of hyperthyroidism • Target organ injury: brain, eyes, kidneys, and heart in systemic hypertension	• *Primary* HCM: genetic or idiopathic cardiomyopathy
Restrictive cardiomyopathy *phenotype*	• Left ventricular endomyocardial fibrosis or myocardial fibrosis (multifocal or generalized) • LV wall infarction • Echo: Marked bi-atrial dilatation; variable LV anatomy, wall motion, and systolic function	• Abnormal auscultation: gallop, arrhythmia, heart murmur • CHF—biventricular • Chylothorax (from CHF) • Arterial thromboembolism • Arrhythmias • Sudden cardiac death	• Idiopathic RCM • Antecedent myocarditis • Chronic HCM with myocardial injury from coronary thromboembolism, coronary vascular disease, or neurohormonal injury
Unclassified or "Intergrade" cardiomyopathy	• Left ventricular myocardial disease with variable morphologic characteristics with Echo showing systolic and diastolic LV function	• CHF—left sided or biventricular • Arterial thromboembolism • Arrhythmias • Sudden cardiac death	• Prior HCM with progressive myocardial failure or infarction (?) • Myocarditis (?)
Congenital mitral valvular disease	• Mitral valve dysplasia (MV malformation; generally causes MR; rarely MS) • Echo: Mitral valve malformation; LA and LV dilatation	• Systolic heart murmur • Development of CHF	• Congenital • Genetic?
Heartworm disease	• Pulmonary vascular disease • Pulmonary thromboembolism, pneumonitis, and fibrosis • Aberrant infection • Echo: parasites in the PA	• Signs related to pulmonary disease (cough), vomiting • Dyspnea and lung infiltrates due to thromboembolism or spontaneous worm death • CHF—chylothorax (uncommon)	• Dirofilaria immitis—adult parasites found in the pulmonary arteries and heart
Arrhythmias: PACs, PVCs; AV block	Necropsy or Echo may demonstrate cardiac lesions but often there is no overt structural lesion	• Syncope • Sudden cardiac death • CHF	• Cardiomyopathy • Degeneration of conduction system • Metabolic disorders • Hypoxia

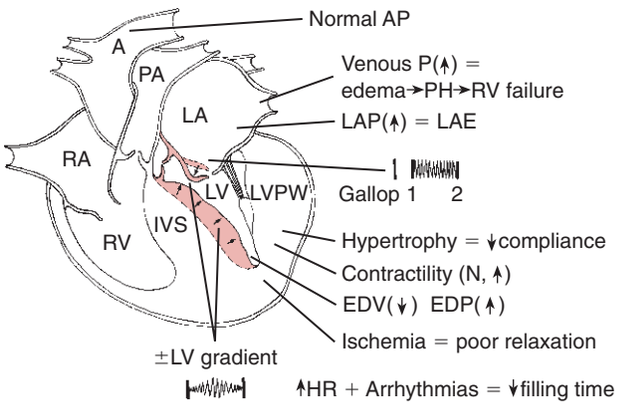

Figure 150-1. Diagrammatic representation of hypertrophic cardiomyopathy. Explanation of abbreviations can be found in text.

LV ventricular distensibility. Tissue injury and fibrosis increase myocardial and chamber stiffness, requiring elevated LA filling pressures. This creates a situation of rapid early diastolic filling that becomes restricted as the stiff ventricle is distended. This correlates to a ventricular (S3) or summation (S3+4) gallop.

- As the left atrium distends, a loss of atrial contractility may develop. This reduces filling effectiveness and also predisposes to stagnant flow, formation of atrial thrombi, and atrial fibrillation.
- The roles of myocardial ischemia, infarction, and neurohormonal activation in the pathogenesis of progressive tissue injury and cardiac dysfunction are possible therapeutic targets because β-blockers and angiotensin system inhibitors blunt these detrimental responses.
- Demand ischemia—the sudden increase in myocardial oxygen demand that outstrips coronary blood supply—may contribute to the sudden development of left-sided CHF (flash pulmonary edema) so often observed in stressed cats with HCM. Ischemia impairs myocardial filling and contraction. For this reason, drugs with anti-ischemic effects (atenolol, diltiazem) are often prescribed in this disease.
- Systolic abnormalities are identified in some cats with HCM. These include subtle abnormalities detected only by tissue Doppler echocardiography; identification of apical or free wall-infarcts; regional wall motion abnormalities; or rarely, a global loss of LV systolic function.
- Dynamic and labile pressure gradients between the LV and aorta are often identified during ejection across the LV outflow tract. In most cases, systolic gradients stem from either septal and papillary muscle hypertrophy (midventricular obstruction) or systolic anterior motion (SAM) of the mitral valve causing mitral septal contact. These abnormalities can be documented on high-quality echocardiographic studies. The presence of significant SAM is invariably associated with an eccentric jet of mitral regurgitation (MR), readily seen by color Doppler examination.
- Some chronic cases of HCM appear to evolve into a restrictive form of cardiomyopathy with either regional wall dysfunction (suggestive of myocardial infarction) or globally reduced LV systolic function (suggesting fibrosis or ischemia). Rarely, a cat will progress to a grossly dilated form of disease.

Clinical Findings in Feline HCM

The clinical presentation and examination findings in feline HCM are variable.

- Male cats are predisposed in some reports, and cats of any age, including young cats, may be affected. As previously noted, certain breeds are at genetic risk for this disease, and it is not uncommon to examine affected cats that are related.
- Most often, the idea of HCM is prompted by auscultation of a murmur or gallop sound in a cat that has no other signs of heart disease. Nonspecific signs such as lethargy or anorexia may be reported.

▼ ***Key Point*** Most cats with HCM are healthy and asymptomatic for the disease.

- When symptomatic for left-sided CHF, a cat will demonstrate tachypnea and dyspnea, signs attributable to pulmonary edema or pleural effusion. Cough can occur but is an inconsistent sign.
  - Stress, fever, moderate-to-severe anemia, thyrotoxicosis, anesthesia, surgical procedures, trauma, or fluid therapy may precipitate CHF in a previously stable cat.
  - Prior therapy with corticosteroids may be another risk factor, though cause and effect are not firmly established.
- Urgent presentation may follow ATE to the terminal aorta, a forelimb, or cerebrum.
- Syncope or sudden cardiac death can occur but are less common than in the human disease. Sudden death may be explained by a coronary embolus, a ventricular arrhythmia, or if signs of CHF are unrecognized and the cat succumbs to hypoxia.
- Typical physical examination features of HCM include various combinations of the following:
  - Gallop rhythm—This is related to ventricular diastolic dysfunction or heart failure.
  - Systolic murmur—Murmurs are commonly due to MR or dynamic LV outflow obstruction. These murmurs can vary, often increasing in intensity with higher heart rates (and higher sympathetic tone). This finding is not specific because functional ejection murmurs also become more intense with increasing sympathetic drive, and functional

murmurs are extremely common in cats of all ages.
  - Clinical signs of ATE—These are discussed below.
  - Auscultatory evidence of pulmonary edema or pleural effusion include increased bronchovesicular sounds, crackles or a fluid line, indicating CHF.
  - Prominent left apical impulse is a sign of possible LV hypertrophy.
  - Arrhythmias may be detected in some cats with HCM.
- ABP is usually normal in cats with HCM; however, some cats demonstrate profound hypotension associated with cardiogenic shock (along with hypothermia and bradycardia).
  - Low ABP also may be detected in the cat receiving diuretic and ACEI therapy for CHF.
  - Systemic hypertension may cause secondary LV hypertrophy; but HCM does not cause systemic hypertension.

Diagnostic Tests in HCM

A number of routine diagnostic tests are helpful in recognizing and staging HCM.

- The *electrocardiogram* may be abnormal, but results are very inconsistent. Increased amplitude R-waves in lead II (exceeding 0.7–1.0 mV.) or a left axis deviation compatible with concentric hypertrophy or left anterior fascicular block may be observed.

▼ ***Key Point*** A normal ECG does not exclude a diagnosis of cardiomyopathy.

- *Thoracic radiographs* can be normal, but in moderate to severe disease will demonstrate abnormalities.
  - Cardiomegaly (elongation), apex shifting (to the right or left), and LA enlargement (most evident as an auricular bulge on the DV view) are common findings.
  - In cats with CHF, the cardiac silhouette may be further enlarged by a small to moderate pericardial effusion caused by CHF. Cardiac silhouette size may be reduced considerably after diuretic therapy.
  - Prominent pulmonary vascular patterns may indicate pulmonary hypertension secondary to elevated LV diastolic pressure or fluid retention.
  - Increased lung densities are compatible with pulmonary edema and may be focal, patchy, diffuse, and often in more dependent areas than is typical for dogs with CHF.
  - Pleural effusion is common in acute CHF and in chronic, longstanding cases of heart failure. Evaluation of the effusion typically reveals a modified transudate and sometimes chylothorax.
- Routine *CBC and clinical chemistries* are unremarkable in most cases unless there is thromboembolism or intercurrent disease. The creatine kinase (CK), AST, and ALT all derived from skeletal muscle origin are markedly elevated in thromboembolism to the limb(s).
  - *Renal function* may become impaired in cats with concurrent renal disease or in those treated for heart failure with diuretics and ACEIs. In many cases of advanced, treated CHF there will be mild to moderate azotemia.
  - Serum *thyroxine* is normal in cats with idiopathic HCM (unless they are manifesting two diseases).
  - A number of recent reports indicate the potential value of measuring serum or plasma cardiac *troponin-I* (cTN-I) since this protein increases in cats with HCM. This may become a useful screening test for identifying cats with HCM.

▼ ***Key Point*** In a large percentage of cats with systolic murmurs, echocardiography demonstrates a normal heart or trivial cardiac pathology. Heart murmurs in these cases are considered functional, likely related to sympathetic stimulation of the heart.

- *Echocardiography*—Definitive diagnosis and staging of HCM relies on echocardiography and Doppler studies interpreted in light of clinical findings.
  - Typical HCM is characterized echocardiographically by papillary muscle thickening, generalized thickening of the LV walls (generally to 6 mm or more in diastole), normal to decreased intraluminal size, and normal or increased systolic shortening fraction.
  - There is a marked heterogeneity to the pattern of hypertrophy, and not all wall segments may be involved.
    There may be generalized involvement with greater involvement of the septal or free wall segments.
    Some cats demonstrate markedly asymmetric hypertrophy mainly affecting the LV free wall. This finding usually portends development of CHF.
    Conversely, focal midventricular hypertrophy, even with midventricular obstruction, is usually benign. In older cats, isolated, focal, dorsal septal hypertrophy is a common finding. Whether this represents true HCM, or a growth response to aortic dilation and altered subaortic blood flow, is uncertain, but the condition is generally benign.
  - Increased left atrial size is a strong indicator of risk for ATE or CHF.
  - Doppler studies may demonstrate MR, dynamic obstruction, or abnormal LV filling patterns. Early diastolic dysfunction is characterized by abnormal myocardial relaxation, shown on Doppler studies as delayed LV relaxation in early diastole with a vigorous LA contraction to support late diastolic filling.
  - Progressive ventricular disease is associated with reduced chamber compliance. Doppler studies

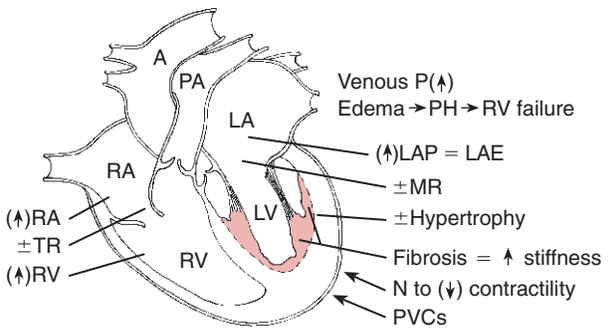

Figure 150-2. Diagrammatic representation of restrictive cardiomyopathy. Explanation of the abbreviations can be found in the text.

often show a prominent early filling (E-) wave with trivial atrial contraction (A-) wave. These findings generally precede development of CHF.

- The differential diagnosis of feline cardiomyopathy is extensive (Table 150-2), including other cardiovascular and noncardiac disorders.

FELINE RESTRICTIVE CARDIOMYOPATHY (RCM)

Feline RCM represents a heterogeneous disorder, and some latitude is used in placing cats within this category. The disorder described below might be interpreted by others as "intermediate cardiomyopathy" or as "unclassified cardiomyopathy."

Overview and Pathophysiology of Feline RCM

- The key pathologic feature is diffuse or multifocal endomyocardial or myocardial fibrosis.
- The pathogenesis of these lesions is undetermined. Antecedent myocarditis seems a likely, though unproven, initiating cause. In other cats, RCM clearly represents a late stage of HCM complicated by myocardial fibrosis or myocardial infarction.
- A variety of necropsy lesions have been observed in cats demonstrating clinical features of RCM.
  - LV endomyocardial fibrosis may be patchy, multifocal, or diffuse in distribution.
  - The left ventricle can exhibit regional hypertrophy, but overall the walls are not thickened. Often there is regional thinning or infarction of the LV free wall or apex interspersed with focal hypertrophy. Prominent papillary muscle hypertrophy or fibrosis is evident in some cats.
  - The LV cavity may be dilated but is usually normal to reduced in size.
  - Extreme endocardial fibrotic scarring can involve the mitral valve apparatus, lead to mid-ventricular stenosis, or obliterate the LV apex.
  - A common feature of RCM is striking biatrial dilation.
  - Systemic thromboemboli are common and LA 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.
- The *pathophysiology* of RCM in the cat is unresolved but in many ways fits the "intermediate" label initially suggested by Harpster (Figure 150-2).
  - Echocardiography generally demonstrates mild systolic dysfunction, regional LV wall dysfunction, mild mitral or tricuspid valvular regurgitation, elevated LA pressures, and impaired LV distensibility with a "restrictive" filling pattern (tall but abbreviated E-wave; small A-wave).
  - Myocardial or endomyocardial fibrosis is the most likely explanation for these abnormalities.
  - Progressive increases of LA pressure develop, and the combination of ventricular dysfunction, atrial stiffness, and renal retention of sodium elevate pulmonary venous pressures and predispose to CHF and to pulmonary hypertension.
  - Pulmonary edema, pleural effusion, jugular venous distention, and hepatic congestion are typical manifestations of CHF in this disease. Clinically a diagnosis of "biventricular" CHF is often made.
  - Stasis of blood and the stretched LA places affected cats at risk for atrial thrombi and systemic thromboembolism.

Clinical Findings in Feline RCM

- The clinical findings and diagnostic studies of RCM are in many ways similar to those of HCM with a few notable differences.
  - Most cats with RCM are middle aged or older and present with signs of CHF or ATE.
  - Some have previously been diagnosed with HCM.
  - The most consistent physical auscultatory finding is a loud gallop sound; murmurs are variable and less common than in HCM.
  - Premature ventricular or atrial beats are common, leading to an irregular rhythm and arterial pulse.
  - Signs of elevated systemic venous pressure, including hepatomegaly, pleural effusion, and elevated jugular venous pressure, are common. This may indicate RV dysfunction from RV involvement, pulmonary hypertension, or simply the generalized response of fluid retention in compensation for chronic left heart failure.
- The *electrocardiogram* is frequently abnormal showing cardiomegaly patterns, axis deviations, or conduction disturbances along with atrial or ventricular ectopy.
- Thoracic *radiography* is often impressive and characterized by LA dilation and cardiac elongation that is typical of LV enlargement.

- The cardiac apex can be pointed or rounded.
- Some cats manifest astounding biatrial enlargement. Pericardial effusion may further enhance cardiac silhouette size.
- Pleural effusion is typical.

- *Echocardiography* demonstrates a number of possible abnormalities. The most characteristic feature of RCM viewed by echocardiography is marked LA or biatrial dilation, mildly reduced shortening fraction, and irregular or hyperechoic ventricular walls, +/− bands spanning the LV. Often there is marked wall thinning typical of myocardial infarction. Infarction or severe myocardial fibrosis often creates a segmental, hypocontractile wall.
- *Clinical laboratory tests* of cats with RCM are not specific and most abnormalities are attributable to CHF, diuretic therapy, or thromboembolism as described above for HCM. A plasma or whole blood taurine should be measured in cats with decreased LV ejection fraction. 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 in response to the irritation.

DILATED CARDIOMYOPATHY IN CATS

As shown by Pion and colleagues, dietary deficiency of taurine accounted for the vast majority of feline cases of dilated cardiomyopathy. Today DCM in cats is a relatively rare occurrence requiring echocardiographic evaluation for diagnosis. Taurine deficiency may still be observed in cats eating mostly "custom" diets or dog food, but most cases of DCM are idiopathic or a consequence of myocarditis.

- The primary post-mortem lesions of primary DCM are left-sided or four-chamber dilatation, accompanied by necropsy findings of CHF. There is no demonstrable congenital, coronary, or valvular heart disease. Histological findings include myocyte loss with prominent interstitial fibrosis and variable degrees of hypertrophy, myocytolysis, and inflammation (which is typically minimal).
- Left-sided or biventricular CHF, often complicated by systemic thromboembolism, are the typical consequences of this disorder. These conditions are readily identified by careful clinical examination and results of thoracic radiography.
- Certain breeds are historically at risk for DCM, notably the Burmese cat.
- Classic physical examination features of DCM include soft heart sounds (from reduced contractility or pleural effusion); gallop rhythm with or without a systolic murmur; hypokinetic arterial pulses; dull left apical impulse; and clinical signs of profound CHF. Exceptional cases are seen prior to onset of CHF.
- Cats with DCM are very likely to present in "cardiogenic shock" with sinus or junctional bradycardia, marked hypothermia, and severe hypotension (systolic ABP <70).
- Ophthalmic examination may indicate hyperreflective lesions of retinal degeneration adjacent to the optic disk (if the cause is taurine deficiency).
- The principle functional disturbance of DCM as shown by *echocardiography* is marked reduction of myocardial contractility as measured by shortening or ejection fractions. Morphologically, a dilated, thin-walled, hypokinetic left ventricle is observed often with dilatation of the other cardiac chambers. Ventricular filling also is impaired related to abnormal relaxation of the muscle and pronounced cardiac dilatation, which reduces diastolic compliance. There is often MR and TR by Doppler studies.

OTHER FELINE MYOCARDIAL DISEASES

A number of other diseases that affect the myocardium of the cat are briefly considered below.

- Myocarditis—Nonsuppurative myocarditis occurs sporadically in cats. The cause is unknown and definitive diagnosis requires microscopic examination of myocardium. Since myocardial biopsy is difficult in cats, and enzyme or plasma troponin-I elevations are nonspecific for inflammation, the diagnosis is usually tentative or reserved for the necropsy table. Some cats with myocarditis are presented for ventricular arrhythmias, while others develop fulminant heart failure, RCM (chronic myocarditis, healing phase), or thromboembolism.
- Right Ventricular Cardiomyopathy—A cardiomyopathy involving the RV has been reported in cats. The clinical findings can be explained by right-sided myocardial failure and severe right ventricular cardiac dilatation. There may be atrial standstill or apparent atrial fibrillation. A murmur of tricuspid regurgitation may be evident. Ventricular ectopic rhythms are common. Pleural effusion and ascites can develop from CHF and sudden death may occur. Diagnosis depends on echocardiography and exclusion of other predominately right-sided diseases such as atrial septal defect, tricuspid valve malformation, and pulmonary hypertension.
- Hyperthyroidism—Clinical findings of hyperthyroid heart disease are common in older cats with functional thyroid tumors. Thyrotoxicosis causes cardiac hypertrophy related to a hypermetabolic state, peripheral vasodilation, and increased demands for cardiac output. In addition, increased sympathetic activity and elevated thyroid hormone concentrations may stimulate myocardial hypertrophy.

- In chronic cases of hyperthyroidism, the left ventricle becomes hypertrophied. Concurrent systemic hypertension may contribute to this hypertrophy.
- Constitutional signs such as weight loss and abnormal behavior are typical. A thyroid "slip" is generally identified during physical examination.
- Cardiovascular findings can include sinus tachycardia (that can approach 300 per minute); premature atrial or ventricular complexes; hyperkinetic (bounding) arterial pulses; gallop sounds; and systolic murmurs (either functional ejection murmurs or murmurs stemming from mitral or tricuspid regurgitation).
- Isolated systolic hypertension or combined systolic/diastolic hypertension may be evident.
- In most situations, it is practical to obtain thoracic radiographs to evaluate cardiopulmonary status. Most examinations show only mild cardiomegaly characterized by cardiac elongation and mild LA prominence. In this group of cats, echocardiography is unlikely to contribute materially to the management of the patient.
  When done, typical echocardiographic findings include LV wall hypertrophy, mild LV dilation, normal to mildly increased left and right atrial dimensions, and hyperdynamic LV.
- ECG recordings often demonstrate sinus tachycardia (>240/min); cardiomegaly (increased QRS voltages); axis deviation (to the left or right); and premature atrial or ventricular complexes.
- In most cases, the cardiovascular complications of hyperthyroidism regress following successful treatment of the underlying condition.
  LV hypertrophy usually decreases *except* in the cat with concurrent diseases of uncontrolled hypertension or with primary (idiopathic) HCM.
  Hypertension may improve or resolve as cardiac output decreases with reduction of thyroid concentration; however, *other* causes of hypertension may endure (especially primary renal disease), requiring medical management with amlodipine.
  Sinus tachycardia and premature beats usually resolve with initiation of anti-thyroid medication (methimazole, Tapazole). Persistent tachycardia may indicate concurrent CHF or a need for low-doses of a beta-blocker (atenolol, $\frac{1}{4}$ of a 25-mg tablet PO, once or twice daily).
- In a small percentage of cats, the cardiac effects of hyperthyroidism are manifested in a more clinically significant manner. Thoracic radiographs will demonstrate that the heart is moderately to severely enlarged, and careful scrutiny may indicate a small (or even a large) pleural effusion. In these patients, a full cardiac workup is indicated.
  Re-examination of the patient may indicate prominent jugular pulses or overt jugular venous distension, compatible with plasma volume expansion and heart disease.
  In advanced hyperthyroidism, there can be sufficient cardiac dysfunction and volume expansion to cause more generalized cardiomegaly. Echocardiography often shows biatrial dilatation with normal or even reduced LV shortening fraction despite thickened LV wall measures.
  Affected cats should be evaluated for concurrent hypertension, anemia, or renal failure.
  Great care must be taken when administering fluid therapy as large pleural effusions may occur. Thoracocentesis may be needed.
  In cats with advanced cardiac disease, anti-thyroid medication should be initiated without delay; beta-blockers avoided to prevent cardiac depression; and an ACEI prescribed for cardiac protection, control of incipient (or overt) CHF, and for antihypertensive effects.
- Therapy of hyperthyroid heart disease is predicated on controlling the underlying disorder and is discussed in Chapter 31. Treatment of CHF as a complication of hyperthyroidism is discussed below.

- Systemic hypertension—Cats with systemic hypertension may develop progressive LV disease with concentric ventricular hypertrophy. The left ventricle and small coronary arteries represent one of the "target organs" of high blood pressure.
  - Most healthy cats have systolic ABP measurements of <150 to 160 mm Hg in the hospital setting. Persistent elevation of ABP, particularly values exceeding 160 to 170 mm Hg in the presence of target organ injury, is highly suggestive of hypertensive disease.
  - While systemic hypertension does increase the LV workload and stimulates myocardial hypertrophy, heart failure is not a common complication of this disease unless hypertension progresses unchecked or is superimposed on another form of heart disease.
  - Initial clinical signs more often are referable to the other target organs, namely the eyes (retinal hemorrhages, detachments), brain (depression, abnormal behavior, stroke), and kidneys (progressive azotemia).
  - Dissection of the aorta is a rare vascular complication of hypertension.
  - The cardiac changes of hypertension most often resemble mild HCM. Often there is a gallop sound or murmur (of uncertain origin), along with mild cardiac enlargement, evident by radiography or echocardiography. As many of these cats are older, there may be degenerative changes of the aorta observed such as aortoannular ectasia (dilatation) or aortic redundancy.
  - The diagnosis of hypertension is usually straightforward and is discussed in detail in the Chapter 153 in this section.

- Assessment of hypertension can be more complicated. For example, hypertension in a hyperthyroid cat may be related to
  High cardiac output from LV hypertrophy and a sympathetically-driven heart.
  Increased aortic impedance or stiffness, related to concurrent aortoannular ectasia.
  Abnormalities of plasma volume or renin-angiotensin regulation from concurrent (often masked) renal disease.
- Causes of systemic hypertension, including intrinsic renal disease, hyperthyroidism, and Conn's syndrome should be sought.
- LV hypertrophy may regress following successful control of blood pressure.
- The treatment of systemic hypertension in cats is discussed fully in Chapter 153.

SYSTEMIC ARTERIAL THROMBOEMBOLISM IN CATS

Acute arterial thromboembolism is most commonly associated with cardiomyopathy, though it may be encountered in multisystemic disorders including hematologic disease, endocarditis, and cancer.

- Thrombi generally arise in the LA/auricle. Many are large and traverse the aortic arch to lodge in the terminal aorta. This creates the classic "saddle thrombus" at the origin of the external and iliac arteries. The saddle thrombus also obstructs the internal iliac branches (serving the tail) and obstructs flow in the femoral arteries (as these extend directly from the external iliac system).
- Smaller clots may be diverted to other vascular beds, causing myocardial infarction (with arrhythmias, sudden death, or acute CHF); thrombotic stroke; forelimb monoparesis; renal infarcts; or rarely, mesenteric ischemia with severe colic.
- The pathogenesis of atrial thrombus formation is likely related to atrial dilation, stagnant blood flow, reduced atrial contractility, exposure of platelets to subendocardial collagen, and other ill-defined hemostatic factors particular to the cat. Impaired collateral blood flow is believed to be pivotal in the genesis of clinical signs of ATE, since simple ligation of the femoral arteries does not reproduce the syndrome in cats.
- Historical signs of ATE typically include the sudden inability to walk (or use a forelimb), severe pain with vocalization and obvious distress, and rapid or deep breathing patterns.
- Physical examination usually reveals a distressed, non-ambulatory patient, often assuming a sitting position with extended, firm, and painful rear limbs.
  - Respiratory rate is increased either from pain or concurrent CHF. Radiography is often needed to delineate the basis for dyspnea. Management of CHF is needed in some cats (see above).
  - Results of cardiac auscultation depend in part on the experience of the examiner, but often a murmur or gallop sound will be detected. In some cats, heart sounds are remarkably normal.
  - Shock-like signs are evident in some cats, probably related to systemic reaction and release of mediators from the thrombus. ABP must be measured in a forelimb.
  - Bradycardia is likely to be associated with hypotension and require additional treatments such as dobutamine.
  - Laboratory tests are variable and probably relate in part to any underlying disease. Stress-related hyperglycemia is typical, and a variety of electrolyte abnormalities may be seen.
- Diagnosis of aortoiliac ATE is straightforward and based on the usual history and results of physical examination demonstrating the triad of peripheral vascular disease, muscle injury, and peripheral neuropathy.
  - Loss of regional *vascular supply* leads to cold, pulseless, pale limbs. Doppler flow signals within the proximal femoral arterial system are absent indicating no flow. With reduced collateral blood flow, the superficial rectal temperature is often reduced, and the thermometer should be lubricated and very carefully advanced to obtain a more representative body temperature.
  - Severe *skeletal muscle injury* with extensive rhabdomyolysis occurs.
    This leads to ischemic contracture with severe muscle pain, as well as release of high levels of CK, AST, and ALT from damaged muscles into the blood.
    The limbs are typically very firm to palpation (especially the semitendinosus and gastrocnemius muscles).
    Since muscle contains very high concentrations of potassium that also leak out from the cell, there may be profound hyperkalemia following reperfusion of the damaged tissues.
    Some cats develop antibiotic-responsive fever within 2 to 7 days of the thrombotic event; we treat affected cats empirically with amoxicillin trihydrate + potassium clavulanate (Clavamox) for 10 days.
    Development of limb edema indicates severe tissue injury and portends a very poor prognosis for limb recovery. In some cases, tissue necrosis and limb contracture may require wound management or even limb amputation.
  - Peripheral (ischemic) *neuropathy* is identified.
    Motor function is absent in the rear limbs (or forelimb in the case of a brachial thrombus). Tail movement is lost in the typical saddle thrombus.

Neurological signs are usually bilateral, but there may be some asymmetry noted between the limbs; this often correlates with presence or return of pulse on the least-affected side.
After 24 to 48 hours, a relatively clear superficial sensory level can be detected in the proximal limb; with time, this descends toward the toes.
With revascularization, tail function returns first, and motor function is restored from proximal to distal.
Residual, distal proprioceptive deficits are common but do not prevent functional limb use.

- Recovery from the thrombus is *common,* and after 72 hours many cats have already begun to revascularize the limbs spontaneously. Mortality in the first 72 hours is generally due to one of three factors: (1) euthanasia; (2) reperfusion hyperkalemia; or (3) uncontrolled CHF, usually present at the time of admission.
  - Most studies report a worst-case scenario of about 35% recovery (release) rate because cats that are euthanatized without treatment or given sufficient time for recovery are included. Obviously, the client's and the veterinarian's perceptions and expectations weigh heavily into these figures. When euthanatized cats are not considered, at least 50% of cats are reported to be released from the hospital in most retrospective studies. More recent surveys, including the largest Minnesota study, demonstrate up to a 75% release rate for cats supported and managed aggressively for their disease.
  - Concurrent CHF worsens the prognosis. In the retrospective study of Smith and colleagues the difference in median survival for cats released from the hospital was 77 days for CHF cats compared to 223 days for those without CHF.
  - Despite the potential for short-term success, the complication of ATE creates difficult decisions for clients. The risk for future ATE is very high (probably exceeding 50% within 6 months); however, subsequent embolic events are often better tolerated, presumably related to development of collateral circulation. Clients also must be advised regarding the severity of the underlying heart disease (which should be evaluated by radiography, echocardiography, and an ECG).
- Management of ATE is discussed below.

THERAPY OF FELINE CARDIOMYOPATHY

A number of CV drugs are used in the management of myocardial and other feline CV disorders. While there some well-conducted studies of antihypertensive therapy in cats, there is little in the way of controlled and sufficiently powered clinical studies that address the treatment of asymptomatic HCM, therapy of heart failure, or management of ATE in cats with primary cardiomyopathies. Accordingly, treatment approaches to myocardial diseases remain largely empiric and are certainly guided by experience and clinical prejudice.

Major therapeutic end-points deal with survival, client observed symptoms, and the need for hospitalization related to clinical signs of disease. More theoretically based treatments (and the rationale for many current recommendations for therapy) consider drug effects on: (1) left ventricular function (diastolic filling; dynamic obstruction during systole); (2) protection of the myocardium from stress, catecholamines, or neurohormones; (3) prevention or control of CHF; (4) prevention or treatment of ATE; and (5) prevention of arrhythmias and sudden cardiac death.

The clinical pharmacology of specific drugs used in treatment of CHF in cats is detailed in "Cardiovascular Drugs" elsewhere in this section. The management of systemic hypertension in cats is discussed in detail in Chapter 153.

Management of the Asymptomatic Cat with HCM

In most practices, asymptomatic HCM is the most common form of idiopathic cardiomyopathy identified in cats. The main benefits of any therapy in this group would relate to: (1) improved ventricular diastolic function; (2) reduction of dynamic outflow tract gradients with decrease in MR; (3) reduced chance of sudden cardiac death; (4) prevention of ATE; or (5) regression of LVH. Currently, no data indicate a substantial benefit of therapy in asymptomatic cats with HCM, and it is well known that many cats live for years without apparent problems.

- Increasingly, cats with asymptomatic or mild HCM and normal LA size are left untreated. Many cats show little progression of disease at follow up. Thus, in the asymptomatic cat, the veterinarian could reasonably consider prescribing no therapy or, empirically, a β-adrenergic blocker or diltiazem. Some clients will indicate that their cat is more active when receiving treatment, but this may simply represent a placebo effect.
- Initially, cats with asymptomatic disease are examined by repeated echocardiography within 1 to 3 months of initiation of any stable therapy regimen and again 6 to 12 months later, depending on the level of concern for impending CHF or ATE. Echocardiography has the advantage of providing objective measures of wall thickness and LA size, and a Doppler study can be used to document a reduction in the dynamic obstruction and associated MR when these flow disturbances are identified at initial examination.
- The stable cat is seen every 6 to 12 months, with the intervals extending if follow up examinations show no disease progression. In many cases, the disease is unchanging, but in others, there is clear progression

and eventually signs of CHF or ATE occur, even years after initial diagnosis.

- Therapy with Atenolol–β-blockers are recommended in the management of HCM with moderate to severe LV outflow tract obstruction. Atenolol is most often prescribed for this purpose as it is a twice daily drug (compared to tid propranolol). The usual starting dose of atenolol is ¼ of a 25-mg tablet PO for 3 days and thereafter ¼ tablet PO q12h. Dosage is adjusted to achieve an examination heart rate of 120 to 160/min. Typically cats receive ½ tablet in the AM and either ¼ or ½ tablet in the PM.
  - Atenolol effectively reduces LVOT gradients and consistently slows the heart during times of stress (for example, a veterinary examination).
  - Cardiac benefits of beta–blockers in cats with HCM include preventing sinus tachycardia, reducing dynamic outflow obstruction, decreasing SAM and attendant mitral regurgitation, and prolonging diastole. Myocardial oxygen demand is reduced through decreases in heart rate, contractility, and blood pressure.
  - Unfortunately, the net effect of beta–blockade on diastolic function in cats with HCM is unknown (see "Cardiovascular Drugs" for a discussion).
  - Beta–blockade is especially helpful for reducing pressure gradients caused by dynamic LV outflow obstruction in cats with HCM. The murmur of mitral regurgitation generally becomes softer following beta-blockade, and the peak outflow tract velocity is substantially reduced in the majority of cats given an adequate dose of atenolol. In a small European study, another beta-blocker (propranolol), was associated with regression of LV hypertrophy, but this finding is inconsistent, and should not be expected.
  - Beta-blockers are contraindicated in cats with overt hypotension, bradycardia, uncontrolled pulmonary edema, AV block, or recent arterial thromboembolism (until collateral circulation has been restored); furthermore, their value in cats with recent-onset CHF appears to be unfavorable, based on a recent multicenter study, and should not be routinely prescribed for short-term management of the CHF patient.
  - Therapy with Diltiazem—When HCM is characterized by moderate to severe LV hypertrophy without obstruction, and especially when there is concurrent LA dilatation, diltiazem may be a therapeutic consideration. Dosing typically involves a long-acting preparation as standard diltiazem dosed at ¼ of a 30-mg tablet PO q8h is simply impractical for most cat owners. Dilacor XR (brand of diltiazem) can be administered at a dosage of 30 mg once or twice daily (open the 240 mg capsule and cut the four 60-mg pills in half). Others have used long-acting diltiazem capsules (Cardizem CD) compounded in a palatable syrup, starting at 30 mg of diltiazem once daily. The bioavailability and dosing regimens of these preparations have been issues. Diltiazem is thought to improve LV relaxation, but the precise mechanism for this benefit has not been elucidated (See "Cardiovascular Drugs" for a discussion).
  - Overall, diltiazem should reduce myocardial oxygen demand by decreasing contractility, blood pressure, and heart rate (though less effectively than atenolol).
  - While diltiazem is a negative inotrope, effects on reducing dynamic outflow tract gradients have been somewhat disappointing at the doses commonly used.
  - While the chronic administration of diltiazem has been reported to decrease LV hypertrophy in cats with very severe HCM, it is very uncommon to observe regression, even with prolonged therapy.
  - Thus, the main reason to choose diltiazem therapy in cats with HCM is for potential improvement of diastolic function and for prevention or treatment of CHF in HCM.
  - Contraindications to administration of diltiazem in cats are uncontrolled CHF, sinus bradycardia, hypotension, and AV block.
  - Bradycardia, hypotension, depression, and skin reactions (erythema/edema) have been observed in some cats receiving this drug. Anorexia is a relatively common client complaint. Adverse effects were reported in just over 20% of cats in one clinical report.
  - As with atenolol, diltiazem does not appear to have a role in the short-term management of CHF in cats.
  - ACEI Therapy—The potential of an angiotensin converting enzyme inhibitor (ACEI) to benefit HCM has not been demonstrated thus far, except in cats with overt CHF. Theoretically ACEI, especially with more 'tissue-sensitive' ACEI (such as ramipril) could prevent progressive myocardial injury or fibrosis in asymptomatic HCM. However, with no firm evidence of benefit, the authors' recommendations are to reserve an ACEI for cases of documented CHF or when moderate to severe LA dilatation is documented by echocardiography (especially in the setting of Doppler evidence of elevated LA pressure).

Hospital Management of the Cat with Acute CHF

Treatment of acute heart failure in cats is a challenge and may require aggressive initial treatment.

- Efforts are directed at improving tissue hypoxia, relieving stress, and reducing the venous and pulmonary capillary pressures.
- Many cats can be managed medically using the F–O–N–S approach (furosemide–oxygen–nitroglycerine–sedation). Thoracocentesis is performed if

there is a moderate or large pleural effusion. Intubation for 2 to 6 hours of artificial ventilation may be needed to manage impending respiratory arrest in cats expectorating edema fluid.

- Initial dosages of furosemide are typically 2 to 4 mg/kg IV/IM, followed by 1 to 2 mg/kg boluses IV or IM every 6 to 8 hours until the cat is stable.
- The cat should be placed at rest, administered oxygen (40–50%) by cage oxygenator, and sedated in most cases to relieve anxiety (butorphanol, 0.25 mg/kg, mixed with acepromazine, 0.05–0.1 mg/kg, with the cocktail administered subcutaneously. If rectal temperature is <99°F, or in the setting of bradycardia, avoid the acepromazine).
- Nitroglycerin (2%) ointment is also administered at a dose of ¼ inch, q12h for moderate to severe pulmonary edema.
- If an IV can be established without stress, a constant rate infusion of furosemide can be substituted for repeated boluses (calculate the daily dose and infuse continually for 24 hours). This treatment is continued for 24 to 48 hours. The CRI of lasix can be supplemented with additional IV boluses as needed.
- The cat with cardiogenic shock (hypothermia, bradycardia, systolic ABP <70 mm Hg) is treated with IV dobutamine infusion (2.5–10 mcg/kg/min titrated to an ABP of 90–100 mm Hg) for 24 to 48 hours. This is an effective therapy for cardiogenic shock regardless of the underlying form of cardiomyopathy.
- Once the cat has been diuresed and ventilation is stable, oxygen is withdrawn, nitrate ointment discontinued, and the dosage of furosemide reduced. The ultimate dose of furosemide should be titrated to the severity of pulmonary edema or pleural effusion.
- Many cats develop hypokalemia and pre-renal azotemia during intensive diuretic therapy. Fresh water and palatable food should be available shortly after diuresis has been initiated.
- Mild cases of renal failure need not be treated, but if the cat refuses to eat and drink after 24 to 36 hours of therapy, judicious fluid therapy of a balanced solution (e.g., 20–30 ml/kg/day) combined with potassium supplementation (IV or oral) will be needed.
- Liquid nutritional support given by an indwelling nasogastric tube may be considered if anorexia persists for more than 60 hours; however, most cats begin to eat following effective resolution of CHF.

Home Management of the Cat with Chronic CHF

- Therapy of chronic CHF in the cat with cardiomyopathy is based on two drugs: furosemide (1–2 mg/kg, PO, once or twice daily) and an ACEI, such as enalapril or benazepril (0.25–0.5 mg/kg, PO, once or twice daily, up-titrating the dose over a number of weeks). Spironolactone (6.25 mg, or ¼ of the 25-mg tablet, once daily) can be given for empiric cardioprotection and potassium-sparing effects.
- Since these cats also have LA dilation, a treatment to prevent thromboembolism is usually considered (see below). However, aspirin therapy when combined with an ACEI and diuretic may predispose to renal failure. When aspirin is prescribed for this purpose, ultra-low doses (5 mg per cat, q24–72h) may be a safer alternative.
- In general, neither atenolol nor diltiazem should be administered to cats with overt CHF, as such therapy has been shown to be either detrimental or not beneficial to short-term outcome.
- After at least 1 month of stable CHF control, atenolol can be considered for the cat with severe LVOT obstruction. Begin at ¼ of a 25-mg tablet once daily and cautiously up-titrate the dosage over several weeks to relieve obstruction. Excessive doses may worsen CHF, leading to pleural effusion or recurrent pulmonary edema.
- The benefits of diltiazem in cats with CHF from HCM have not been proven but might be considered once a cat is very stable on furosemide + ACEI +/− spironolactone.
- Cats with dilated cardiomyopathy are evaluated for taurine deficiency (particularly at-risk breeds including the Burmese, Abyssinian, and Siamese) and treated with taurine (250–500 mg twice daily for 12 weeks) pending results of a whole-blood taurine analysis.
- The bioflavonoid, Rutin (250 mg q12h), is prescribed when there is evidence of recurrent pleural effusion with chylothorax. Rutin improves macrophage function and may reduce reactive pleuritis by decreasing the accumulation of chylomicrons within the pleural space.
- Clinical trials with the inodilator pimobendan are underway in cats and may provide an additional treatment for cats with chronic CHF.
- The overall efficacy of heart failure therapy can be gauged by monitoring respiratory rate and depth at home and by regular re-examinations. Consideration of the affected cat's activity level, appetite, and interaction with family members offers a reasonable gauge of quality of life. Objective measures of CHF control can be obtained by a careful physical and cardiovascular examination and from inspection of serial thoracic radiographs. Morphologic or functional progression of heart disease can be assessed by echocardiography if desired.
- Clinical reevaluation should include a client interview; physical examination; ABP measurement; serum biochemical profile; thoracic radiographs (even one lateral view can provide objective evidence regarding fluid retention); and a focused, recheck echocardiogram.
- The timing of specific examinations depends on clinical circumstances and economic considerations but initially should occur within the first 7 to 10 days from initial diagnosis of CHF and continue every one to two weeks until the CHF is controlled and renal func-

tion stable. Thereafter, the interval may be extended to every one to three months, depending on the patient's progress.

- In general, progressive azotemia indicates the effects of diuretics plus an ACEI. If possible, the doses should be reduced.
- In some cats the heart may stabilize and allow drug diuretic therapy to cease.
- In other cases, there is a clear need to simply tolerate azotemia to prevent pleural effusion or pulmonary edema.
- Treatment of ventricular tachycardia (VT) in cats with CHF is very problematic. Propranolol (2.5–5 mg, PO, q8h), atenolol (6.25 mg, PO, once or twice daily), and procainamide ($^1/_4$ of a 250-mg capsule compounded or mixed in the food q8h) have been used. Sotalol has been used in cats, but it is hard to dose, and in research studies was effective mainly at the beta-blocking dosage. Negative inotropic effects of each of the mentioned drugs; poor client and patient compliance; and lack of efficacy studies limit the application of each of these treatments. In general, therapy of VT is reserved for symptomatic (i.e., syncopal) patients or those with dangerous ventricular arrhythmias documented by ECG.
- Diltiazem is a very effective blocker of AV nodal conduction and represents an excellent choice for heart rate control in cats with atrial fibrillation.
- The long-term prognosis of CHF in cats is guarded and quite variable.
- Although some reports indicate a survival time of six months or less, a 1-year survival is not uncommon following onset of heart failure, provided the client can medicate the cat at home and is willing to obtain consistent veterinary care. Some cats have been successfully managed for CHF for over 2 years.
- Remarkably, some cats with CHF can be weaned from medications (the reason is unknown); whereas, others have a relentless downhill course requiring higher and higher doses of diuretics or regular thoracocentesis.
- Progressive CHF, refractory pleural effusion, or ATE each present formidable obstacles to long-term survival in some cats.

Treatment and Prevention of Systemic Arterial Thromboembolism (ATE)

Management of thromboembolic complications in feline cardiomyopathies remains a serious challenge. Beyond the anticipated spontaneous revascularization of the limbs (once sufficient time elapses), there is no established medical, surgical, or interventional catheter treatment available for resolving acute ATE in cats. Unfortunately, there are no prospective studies demonstrating efficacy of any preventative treatment.

- Acute thromboembolic event—Treatment requires high-quality critical care, good nursing, and "tincture of time." There remains a propensity to euthanize cats with ATE within the veterinary community though published data suggest at least a >50% chance for good functional recovery and a median survival time of over 7 months for cats without CHF. Prognosis has been discussed previously in this chapter.
- For clients requesting care, sufficient time (at least 7 days) should be allowed for improvement. In most cases, a 2 to 3 day hospital stay is needed. Most cats show improvement within 48 to 72 hours with conservative therapy, and pain is markedly diminished within 36 hours of the event.

▼ ***Key Point*** Management of pain is the main therapeutic concern during the first 24 hours of treatment of cats with arterial thromboembolism.

- The initial treatment of cats with ATE involves analgesia with opioids. If the ABP is normal, acepromazine (0.05–0.1 mg/kg) is added to sedate the patient. Opioids for use in cats include:
  - Butorphanol—This drug is both an agonist and antagonist of the mu receptor, and can be dosed at 0.2–0.4 mg/kg IM/SQ q6–8h. While this drug is readily available in veterinary practices, it is a relatively weak analgesic for this magnitude of pain. Butorphanol should be considered only in the "step-down" of analgesic therapy (with potential to reverse some effects of other mu agonists).
  - Buprenorphine (Buprenix)—Dosed at 0.005 to 0.01 mg/kg, IM or SQ, q6h buprenorphine is a longer acting (partial) mu agonist and a better alternative to butorphanol.
  - Hydromorphone or Morphine—These opiates are full mu agonists and can be used in cats at 0.1 mg/kg IM q6–8h. Beware of respiratory depression, CNS excitation, or hyperthermia. If possible, combine with acepromazine.
  - Fentanyl—Fentanyl is a potent mu agonist and can be infused at 2 mcg/kg as an initial slow IV bolus and then maintained at 1 to 5 mcg/kg/hour. It also can be combined with acepromazine.
  - The opiate + acepromazine combination provides effective analgesia/sedation for many cats in moderate distress.
  - Epidural anesthesia is very effective in controlling rear limb pain in cats with ATE, but the injections require expertise in local analgesia and may increase the risk for epidural hemorrhage in cats receiving anticoagulation therapy.
  - Sodium bicarbonate (1 mEq/kg, IV, over 10–20 minutes) is sometimes administered to cats in shock with documented evidence of metabolic acidosis and/or hyperkalemia from muscle necrosis and reperfusion.
- Control of body temperature—Many cats with ATE are hypothermic, especially those with concurrent CHF. While a warm and preferably oxygen enriched

environment should be supplied, it is important to avoid over-heating cats with ATE.
  - Damaged limbs cannot dissipate heat normally and may burn.
  - Opiates used for analgesia may impact the thermoregulatory center. Sometimes cats on opiates will pant and this will abate once the external environmental temperature is lowered, a heating blanket removed, or a dose of acepromazine administered.
  - If elevated temperatures persist, true fever may be evident. Alternative causes of ATE should be considered, including bacterial endocarditis or disseminated neoplasia. However, in most cases the fever is related to the ATE and usually responds to IV cefazolin or oral Clavamox.
- Heparin is administered in ATE to prevent further thrombosis (initial dose is 200–300 U/kg intravenously, then subcutaneously at 100–200 U/kg every 8 hours for 48–72 hours).
- Some clinicians also administer one baby aspirin (81 mg) to cats that present within 2 to 3 hours of an ATE event.
- Beta-blockers, especially propranolol, should be avoided until the cat is walking without difficulty.
- If CHF is not an issue, an IV catheter is placed in a forelimb and *maintenance fluid therapy* is administered to maintain urinary output and reduce hyperkalemia following reperfusion.
- Excitement has waned for IV streptokinase (90,000 IU IV over 30 min followed by 45,000 I.U./hour for 3–6 hours) Streptokinase is no longer available. Excitement has waned for IV tissue plasminogen activator (0.25–1 mg/kg/hour to a total dose of 1–10 mg/kg). This expensive treatment is difficult to control and carries a very high mortality rate probably related to reperfusion hyperkalemia. The clinician must appreciate that limb reperfusion—whether spontaneous or induced by a thrombolytic drug—can lead to fatal hyperkalemia from rapid reperfusion of necrotic muscles.
  - Most cats are released from the hospital in about 3 days, provided there is evidence of revascularization (femoral pulses, improved motor function to the tail and proximal limbs). Clients should be counseled regarding home care, which includes
    Protecting the limbs from trauma or burning; daily inspection for edema.
    Maintaining a written log of progress relative to limb function and ambulation.
    Providing a low stress environment, comfortable bed, and an area for the cat to convalesce. It is likely that the bed will be soiled with urine or stool, so it may be helpful to use easily washable fabrics or apply appropriate protection to the bedding.
    Offering highly palatable food and fresh water that is readily available near the bed and supplemented with hand-feedings to encourage eating and drinking.
    Placing a litter pan relatively near the bed and assisting the cat in using the litter pan if necessary. If constipation becomes a problem, a small amount of soluble fiber ($^1/_4$ teaspoon of guar gum or Benefiber) or canned pumpkin mixed in the food may soften the stool.
    Administering any prescribed medications for CHF.
    Administering a drug to prevent further thrombotic episodes (see the following).
- Prevention of ATE—Drug prevention against thromboemboli is recommended when there is atrial enlargement (>17 mm on 2D echo) or a prior history of ATE. The aggressiveness of treatment is usually proportional to the risk. High risk cats include those with any of the following findings: prior documented thromboembolism; established thrombus in the LA or appendage; evidence of spontaneous LA echocardiographic contrast; a LA dimension exceeding 20 mm, especially with loss of an active auricular contraction (measured by PW Doppler echocardiography); or atrial fibrillation.

Three empirical approaches for prevention have developed:

- Aspirin to interfere with platelet function (81 mg coated, buffered aspirin given every third day or ultra-low dose aspirin given at 5 mg per cat, every 24–72 hours). This is the easiest to administer preventative but has the disadvantage of relatively poor efficacy.
- Daily warfarin to inhibit vitamin-K dependent clotting factors (starting at $^1/_2$ of a 1-mg tablet daily). This approach creates practical problems in terms of dosing and monitoring and creates some risk for iatrogenic hemorrhage.
- Low molecular weight heparin, subcutaneously injected, once or twice daily to inhibit thrombogenesis. Dalteparin or enoxaparin, each dosed at 100 U/kg SQ q12h, have been used (though once-daily dosing with dalteparin also might be successful). There has been empirical success with these drugs, but expense and the requirement for injection have limited widespread use.

These specific approaches, as well as additional details about preventing thromboembolism, are discussed more fully in Chapter 153, along with newer treatment approaches such as clopidogrel bisulfate (Plavix $^1/_2$ of a 75-mg tablet daily).

CANINE CARDIOMYOPATHY

Myocardial diseases are a common cause of heart failure, arrhythmia, and cardiovascular mortality in the dog, following chronic valvular heart disease in preva-

lence and clinical importance. Recognized forms of cardiomyopathy in dogs include the following conditions.

- *Dilated Cardiomyopathy* (DCM)—The most common canine myocardial disease is idiopathic (genetic) dilated cardiomyopathy. DCM is characterized by decreased left ventricular ejection fraction, cardiac remodeling with LV dilatation, and congestive heart failure. Arrhythmias—both atrial and ventricular—are common during all phases of the disease. Sudden cardiac death is relatively common in affected breeds.
- *Arrhythmogenic Right Ventricular Cardiomyopathy* (ARVC)—Aside from DCM, the most often recognized form of cardiomyopathy is arrhythmogenic right ventricular cardiomyopathy (ARVC), best characterized in the boxer dog, and associated with ventricular ectopy, syncope, heart failure, and sudden cardiac death. A less common variant of this disease is right ventricular dysplasia, characterized by severe replacement of myocardium with connective tissue and progressive right-sided CHF.
- *Persistent Atrial Standstill*—This disorder is caused by replacement of atrial myocardium with fibrous connective tissue. Consequences are chronic bradycardia and right-sided CHF, mainly affecting Springer spaniels.
- *Idiopathic Hypertrophic Cardiomyopathy* (HCM)—The condition of true HCM is rare in dogs but included in the differential diagnosis of left-sided CHF and sudden death. Hypertrophic cardiomyopathy must be distinguished from congenital subaortic stenosis, mitral malformation causing dynamic subvalvular aortic stenosis, hypertensive heart disease with secondary hypertrophy, and disease caused by iatrogenic thyrotoxicosis.
- *Secondary Cardiomyopathies*—Causes of canine myocardial disease include profound hypothyroidism, iatrogenic hyperthyroidism, doxorubicin (Adriamycin) administration, catecholamine injury (including pheochromocytoma), head trauma (brain-heart syndrome), systemic carnitine deficiency, severe taurine deficiency, protracted myocardial ischemia, and Duchenne's myopathy.
- *Cardiomyopathy of Overload*—Chronic volume or pressure overload (caused by congenital shunts, valvular diseases, and hypertension) can progress to the "cardiomyopathy of overload," wherein the ventricle is hypertrophied and systolic myocardial function impaired.
- *Tachycardia-induced Cardiomyopathy*—Relentless supraventricular or ventricular tachycardias are causes of reversible myocardial failure.
- *Inherited Arrhythmogenic Cardiomyopathy in German Shepherds*—This is a malignant ventricular tachycardia of young German shepherds that has been described in detail by Moise and colleagues.
- *Myocarditis*—Cardiac inflammation in dogs can be due to Chagas' disease (in endemic areas), septicemia, Lyme disease, and in newborn puppies by parvovirus.

Overview and Pathophysiology of Canine DCM

- Dilated cardiomyopathy is an idiopathic, genetic, or familial myocardial disease characterized by left ventricular or biventricular dilation, reduced myocardial contractility, and histologic abnormalities within the ventricle.
  - Necropsy studies and 2D echocardiography often demonstrate four-chamber dilatation with profound enlargement of the left ventricle and left atrium.
  - CHF is often identified in canine patients and at post-mortem examination.
  - Microscopic lesions include absence of inflammation, attenuated wavy fibers, or fibro-fatty replacement of myocytes; interstitial fibrosis; and other alterations in the cytoskeletal matrix.
  - Extramural coronary arteries are normal and the valves unremarkable, except in older dogs with concurrent mitral or tricuspid valve endocardiosis.
- The disease in most dogs is believed to be familial, and in Doberman pinschers is probably a dominant trait. The time-course of progression of DCM is reportedly great; however, some patients clearly develop LV dysfunction within a very short time interval.
- A deficiency of a myocardial metabolic substrate (such as L-carnitine or taurine) is identified in a very small percentage of affected dogs, often related to familial disease or gross dietary deficiencies. While supplementation with these micronutrients or other nutriceuticals (such as coenzyme Q_{10}) may be beneficial to the energetics of a failing cardiac muscle, such treatment does not reverse canine DCM except in rare cases of systemic substrate depletion.
- As systolic dysfunction progresses, there is a limited cardiac output which is compensated for by activation of neurohormones and cytokines released to support arterial blood pressure.
  - Neurohormonal assault causes further myocardial damage.
  - As the left ventricular ejection fraction continues to decrease, the heart dilates, and ventricular diastolic dysfunction can be recognized by detailed echocardiographic studies.
  - Secondary atrioventricular valvular regurgitation often develops leading to murmurs of mitral or tricuspid regurgitation.
  - Exercise capacity is reduced as an early sign of heart failure.
  - Arterial under-filling promotes renal sodium retention, which expands the plasma volume. Combined

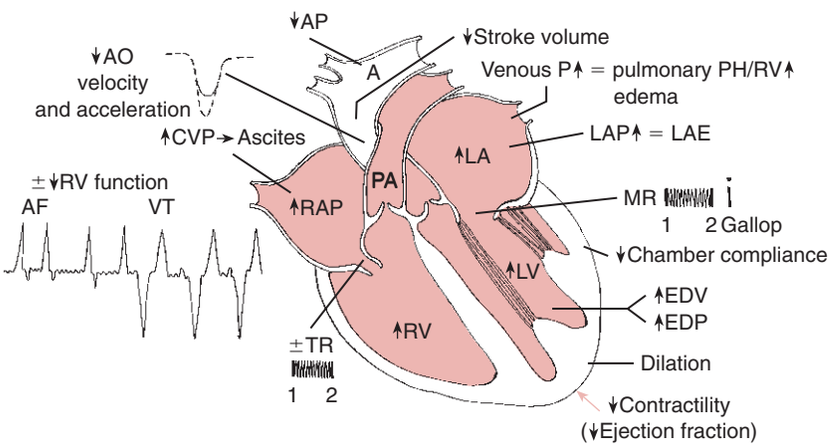

Figure 150-3. Diagrammatic representation of dilated cardiomyopathy. Explanation of the abbreviations can be found in the text.

with reduced left ventricular performance, venous pressures increase and CHF ensues.

- Arrhythmias can occur at any time during the course of DCM. Syncope, sudden cardiac death, or the onset of CHF are potential consequences of rhythm disturbances. Sudden death is especially common in Doberman pinschers with DCM. Frequently, biventricular CHF is precipitated by development of AF in a dog with previously "compensated" DCM (See Figure 150-3).
- Dilated cardiomyopathy occurs most often in middle-aged and older large and giant breed dogs, such as the Doberman pinscher, Great Dane, Irish wolfhound, Newfoundland, and boxer, but DCM can affect dogs of any age and many other breeds.
  - Often male dogs are predisposed or more likely to be affected at a young age. In breeds at risk, older dogs often tend to be females.
  - In addition to a high prevalence in the larger breeds, DCM is recognized regularly in a variety of spaniel and retriever breeds, in Dalmatians, and Portuguese water dogs. DCM occurs sporadically in small canine breeds.
  - The genetic and familial basis for DCM is obvious in many breeds, but the specific mutations or alleles responsible have not yet been demonstrated.
- The four most common clinical presentations of DCM are: (1) occult DCM; (2) CHF; (3) cardiac arrhythmia; and (4) sudden cardiac death. The first three of these conditions will be reviewed. The reader is also directed to the Chapter "Heart Failure in the Dog" for detailed descriptions of treatment plans for canine heart failure; "Cardiovascular Drugs" for discussions of the clinical pharmacology and use of drugs for heart failure and arrhythmias; and "Cardiac Rhythm Disturbances" for a review of electrocardiographic features of arrhythmias.

Occult Dilated Cardiomyopathy

- Occult DCM refers to the overtly *healthy* dog with evidence of *systolic dysfunction* by echocardiography. Some also consider the diagnosis of occult DCM viable when a breed-at-risk for DCM, such as a Doberman pinscher or Irish wolfhound, develops persistent or recurrent atrial or ventricular *arrhythmias* that can not be attributed to another recognized cause.
  - In this regard, there is some cross-over and reasonable debate between the designation of occult DCM with arrhythmia and a normal echocardiogram and that of *arrhythmogenic cardiomyopathy*, in which the principle disturbance is electrical and the echocardiogram is normal (see below). Myocardial dysfunction certainly develops in many, but not all dogs with persistent cardiac arrhythmias. But there is little doubt that many dogs with DCM spend time as "arrhythmogenic cardiomyopathy" before progressing to a more typical dilated form.
  - For the purpose of this discussion, we classify dogs with persistent arrhythmias and a normal echocardiogram as "arrhythmogenic cardiomyopathy" and those with LV dysfunction—with or without arrhythmias—as "occult DCM". While this distinction may seem academic, there is a clear trend to use cardioprotective drugs such as beta-blockers and ACEIs in dogs with occult DCM. Thus, one's perspective on the requirement to demonstrate systolic dysfunction before labeling a patient "occult" DCM may influence whether or not early intervention is prescribed.
  - Most diagnoses of occult DCM are made after a breeder requests that a cardiologist screen an important dog or following a veterinary examination that uncovers a murmur or arrhythmia.
- *Echocardiography*—The *diagnosis* of occult DCM is traditionally based on echocardiographic examina-

tion, with the minor axis estimate of LV systolic function (the shortening fraction) as the diagnostic criterion.
- LV shortening fraction = LV diastolic dimension minus the LV systolic dimension, divided by the LV diastolic dimension).
- Values below 25% are considered suspicious for occult DCM, but there is no unanimity about one specific figure that indicates myocardial failure. Some healthy dogs live for many years with shortening fractions <20%. A single linear approach to diagnosis also can be questioned because larger dogs shorten relatively more in the apical to basilar direction, and this motion is not assessed by shortening fraction.
- However, some data in Doberman pinschers indicate that specific ventricular measurements, such as an end-diastolic dimensions of >49 mm or end-systolic dimensions >42 mm, are highly predictive of DCM.
- Before accepting a diagnosis of occult DCM, the clinician should request more detailed echocardiographic measures of systolic function including LV short-axis shortening area (normally >48%), apical-to-basilar mitral annular motion, and volumetric estimates of LV ejection fraction (normally >45–50% in single plane models). Advanced Doppler methods of assessment are also available but require further definition.
- Serial echocardiographic examinations are very helpful in establishing a downward trend in LV function. One should accept however that a 5% to 8% day-to-day variation is not uncommon in measured or calculated echocardiographic variables, so that large differences and trends are more meaningful than tiny up or down movements.

- *Holter ECG*—The 24-hour ambulatory ECG is a useful adjunct in the diagnosis of occult DCM or arrhythmogenic cardiomyopathy. The Holter recording may help establish the diagnosis in breeds highly prone to DCM with cardiac arrhythmias, such as Doberman pinschers. Most cardiologists consider >50 VPCs per day clearly abnormal. Some consider even lower numbers of VPCs abnormal. In dogs in which ventricular ectopy is evident from auscultation and routine ECG, a Holter recording provides more objective information about the severity of the rhythm disturbance.
- *Other diagnostics*—Future directions are likely to lead to more dependence on *biomarkers* (troponins, natriuretic peptides) for identification of myocardial disease in breeds at risk or when screening echocardiograms return ambiguous results.
  - Breeders are always hoping for tests that will provide the earliest recognition of disease, but it is unrealistic to expect phenotype testing, no matter how sophisticated, to identify all genetically affected animals within a breeding line.
  - Many dogs that develop DCM do not demonstrate any signs until their later years, long after breeding has ceased.
  - In this regard, genetic testing will be a better answer for this particular group of clients and dogs.
- *Management* of occult DCM involves protection of the myocardium and management of serious arrhythmias.
  - An ACEI is prescribed for dogs with documented occult DCM based on echocardiography. Enalapril or benazepril at 0.5 mg/kg PO once or twice daily is appropriate. If LV function is very poor, b.i.d. dosing should be attained over a 2-week time. In the report of O'Grady and colleagues, in Doberman pinschers, treatment with enalapril roughly doubled the time duration between diagnosis of occult DCM and onset of overt signs of heart failure.
  - Beta-blockade with carvedilol or metoprolol also is cardioprotective and should be considered in dogs with occult DCM.
    In large breed dogs, long-acting metoprolol is usually well tolerated ($^1/_2$ of a 25-mg tablet, q12h).
    Carvedilol (Coreg) is relatively expensive, but dogs with occult DCM are more likely to tolerate it than dogs with overt CHF. Optimal target dosages are unknown, but initial dosing of 0.1 mg/kg PO q12h can be increased every 2 to 4 weeks to a target of 0.4 to 0.5 mg/kg q12h. If lethargy or exercise intolerance develops, insure that CHF has not been precipitated.
  - Blood pressure and renal function tests should be followed with these medications.
  - If cardiac arrhythmias are also present, a 24-hour Holter ECG should be done to assess arrhythmia severity (unless a routine ECG already shows that it is severe) and antiarrhythmic therapy considered. This is discussed more fully below under arrhythmogenic cardiomyopathy.
- *Prognosis*—Prediction of survival in occult DCM is difficult
  - One of the problems relates to that of precisely establishing a diagnosis of occult DCM.
  - Once unambiguous evidence of LV systolic dysfunction is identified (LVSF typically 15% or less in a dog with sinus rhythm and normal ventricular conduction), the development of CHF is likely within 6 to 12 months, even in the setting of cardioprotective drugs.
  - When less stringent criteria are set for diagnosis of occult DCM, many dogs will still be alive 2 to 4 years later.

DCM with Congestive Heart Failure

Advanced cases of DCM usually present with a history of exercise intolerance and clinical signs of CHF.

- Syncope related to ventricular arrhythmia or neural mediated syncope (inappropriate bradycardia and vasodilation) may be reported by the owner.
- Physical examination reveals signs typical of CHF:
  - There can be marked weight loss and cachexia.
  - The arterial blood pressure usually is normal owing to vasoconstriction and neurohormonal activation, but it will be decreased in profound DCM with cardiogenic shock.
  - Auscultation may reveal atrial and ventricular gallops, systolic murmurs, or arrhythmias.
  - The intensity of the first heart sound and strength of the arterial pulse is often diminished, indicating reduced LV contractility and stroke volume.
  - Crackles of pulmonary edema or a pleural fluid line may be evident.
  - Clinical signs of left-sided CHF include tachypnea, respiratory distress, abnormal breath sounds, and coughing related to pulmonary edema.
  - Right-sided CHF is characterized by jugular pulses and jugular venous distension, hepatomegaly, and ascites.
  - Pleural effusion is common in biventricular failure.
- Diagnostic studies in advanced cases of DCM.
  - The standard 6-lead ECG may demonstrate a number of abnormalities:
    Cardiomegaly (wide or tall P-waves; wide or increased amplitude QRS complexes).
    Myocardial disease (wide QRS, slurred R-wave descent with ST-segment coving, small complexes in boxers and English bulldogs; left bundle branch block).
    Atrial or ventricular premature complexes; atrial fibrillation; or ventricular tachycardia.
  - The signal averaged ECG may demonstrate late potentials indicating increased risk for ventricular fibrillation.
  - Thoracic radiography reveals cardiomegaly and typical vascular and pulmonary parenchymal features of heart failure. Pleural effusion is common.
  - The echocardiogram shows left ventricular dilation with reduced LV shortening fraction. Other common findings include:
    Increased mitral E-point to septal separation.
    Decreased LV or septal wall excursions.
    LA dilation.
    Variable right-sided cardiomegaly.
    Doppler evidence of mitral regurgitation and tricuspid regurgitation.
    Possible evidence for pulmonary hypertension.
    Diastolic ventricular dysfunction with a restrictive filling pattern.
- Routine chemistry laboratory tests are usually normal or reflect intercurrent disease, consequences of CHF, or complications of CHF therapy.
  - Specialized blood tests for taurine may be performed in selected cases (mainly in American cocker spaniels, golden retrievers, Newfoundlands, breeds atypical for DCM, and in dogs receiving all lamb and rice diets).
  - Cardiac troponin-I is usually elevated along with increased plasma ANP and BNP.
- Therapy of CHF associated with DCM is discussed in detail in Chapter 147.
- *Principles of Hospital Management of CHF include*
  - Administer *furosemide* (2–5 mg/kg IV); follow this with repeated IV or IM injections. Alternatively begin a constant rate infusion of furosemide.
  - Provide supplemental *oxygen* by nasal prongs or other method appropriate for the size of the dog. If oxygen is unavailable, direct a fan to the facial region to minimize dyspnea.
  - Administer *nitroglycerin* ointment topically (1–1.5 inches for a large breed dog q12h).
  - Treat life-threatening pulmonary edema with afterload reduction using an infusion of sodium *nitroprusside* (0.5–2.5 mcg/kg/min is the typical dosage range) with careful attention paid to arterial blood pressure. Titrate the infusion to a systolic value of 90 to 100 mm Hg. A less effective alternative for load reduction is enalapril at 0.25 to 0.5 mg/kg PO q12h.
  - Perform *thoracocentesis* if there is a moderate to large pleural effusion.
  - For CHF with systemic hypotension begin an infusion of *dobutamine* (2.5–10 mcg/kg/min) for 24 to 48 hours. Dobutamine can have benefits beyond the period of infusion.
- In the setting of hypotension, arterial vasodilators such as nitroprusside or an ACEI should be avoided until the pressure is stabilized by dobutamine.
- In dogs with AF, digoxin (0.01mg/kg PO q12h for the first two doses; 0.005 mg/kg PO q12h thereafter) is prescribed to control the ventricular rate response.
- Principles of long-term home management of CHF include
  - Furosemide (2–4 mg/kg PO q8-12h)
  - Spironolactone (1–2 mg/kg PO once or twice daily)
  - Enalapril or benazepril (0.25 mg/kg PO q12h; increase to 0.5 mg/kg PO q12h after the first reevaluation)
  - Digoxin (0.003–0.005 mg/kg PO q12h) unless there are contraindications for therapy such as ventricular ectopy or renal failure.
  - Pimobendan (Vetmedin, 0.2–0.3 mg/kg PO q12h) if available, generally supplants digoxin except in AF when both drugs are administered.
  - A sodium-restricted diet.
  - A β-blocker may be considered to blunt the cardiotoxic effects of the sympathetic nervous system; however, heart failure must be well controlled first. Consider carvedilol (Coreg), starting at 0.05 to 0.1 mg/kg PO q12h; up-titrate the dose every 2 to 4 weeks to a target of 0.2 to 0.4 mg/kg PO q12h.

Having pimobendan on-board facilitates up-titration of the beta-blocker.
Unfortunately, the prescription drug (Coreg) is expensive.
Dosing can be difficult in that dogs may not tolerate the negative inotropy of any β–blocker.

- When AF complicates CHF, diltiazem (up-titrate from 0.5–2.0 mg/kg PO q8h) is prescribed to control ventricular rate (see details in next section). Once heart rate is controlled, a long-acting form of diltiazem can be substituted (using the same total daily dose, but administered once or twice daily).
- Fish oil supplements containing omega-3 fatty acids may improve appetite and reduce cardiac cachexia (EPA—30–40 mg/kg PO daily; DHA—20–25 mg/kg PO daily).
- In dogs with a diagnosis of hypothyroidism, ensure that the plasma level is checked to prevent iatrogenic hyperthyroidism, a condition that increases the demand for cardiac output and is arrhythmogenic. In general, even a giant breed dog with hypothyroidism should not receive more than 0.6 to 0.8 mg of L-thyroxin daily.
- For serious ventricular arrhythmias in the setting of CHF: mexiletine (5–8 mg/kg tid) plus a low dose beta-blocker. Amiodarone or procainamide are alternatives, but results have not always been favorable. Optimally, a Holter ECG should be used to assess therapy.

Arrhythmogenic Cardiomyopathy

The term "arrhythmogenic cardiomyopathy" is a useful expression that refers to recurrent or persistent ventricular or atrial arrhythmias in the setting of a normal echocardiogram. The most commonly observed rhythm disturbances are PVCs and ventricular tachycardia (VT). However, atrial rhythm disturbances may be recognized including atrial fibrillation, paroxysmal or sustained atrial tachycardia, and atrial flutter.

- As discussed above, some dogs affected with arrhythmogenic cardiomyopathy clearly progress to classic DCM; however, many others do not. Thus, in some dogs, the key to clinical management of cardiomyopathy is control of the cardiac arrhythmia.
- ARVC—Arrhythmogenic cardiomyopathy with ventricular arrhythmias is particularly common in the boxer dog (and also in English bulldogs), where the term *arrhythmogenic right ventricular cardiomyopathy* (ARVC) is used to indicate the putative origin of arrhythmia. This term has largely replaced the "boxer cardiomyopathy" designation, but Harpster's original classification is still useful.
  - Many boxers demonstrate only isolated PVCs (upright or with a left bundle branch block morphology in leads I and II). Many boxers carry this Type I designation for years without incident.
  - Boxers often collapse or faint due to sustained VT; these were classified as Type II.
  - Some boxers will progress to develop more "classic" DCM as well, often with marked biventricular CHF. Ventricular and atrial arrhythmias are common in these Type III dogs.
- *Doberman Pinschers*—The Doberman pinscher is another breed that often manifests ventricular ectopics prior to the development of overt myocardial failure (DCM). Many of these dogs die suddenly, without premonitory bouts of syncope and before the onset of heart failure. Others progress to classic DCM with left-sided or biventricular CHF.
- *Lone AF*—The Irish wolfhound, Great Dane, and Newfoundland are giant breeds prone to AF without obvious impairment of LV contractility. Frequently, onset of AF is preceded by atrial premature complexes or paroxysmal atrial tachycardia or flutter.
  - This can be considered another form of arrhythmogenic cardiomyopathy, though it is more often designated as lone AF or occult DCM.
  - In one report, the average time interval between recognition of AF and CHF in Irish wolfhounds was about 2 years, but progressive DCM was a common feature of many dogs.
  - The results of other reports indicate that a relationship between AF and DCM is less clear.
- *Clinical Assessment*—A data base should be obtained from dogs with suspected arrhythmogenic cardiomyopathy, including
  - Careful review of clinical signs relevant to the arrhythmia.
  - Medication history.
  - Complete physical examination.
  - CBC and serum biochemical profile (including electrolytes).
  - Serum troponin-I (cTn-I).
  - Routine ECG with a long rhythm strip.
  - Ambulatory (Holter) ECG, especially when the rhythm is characterized by only isolated atrial or ventricular premature complexes and there are no related clinical signs. The Holter ECG is particularly important in the asymptomatic patient with a rhythm strip that does not indicate a clear need for therapy.
  - Echocardiogram.
  - Thoracic radiograph (optional).

From this information, the clinician should determine the most likely *etiology* of the rhythm disturbance and also attempt to judge the *overall clinical significance* of the arrhythmia. This assessment is pivotal to any therapeutic decisions.

- *Differential Diagnosis*—Arrhythmogenic cardiomyopathy must be distinguished from other causes of cardiac arrhythmias with normal left ventricular function.

- Other recognized disorders associated with cardiac arrhythmias should be excluded, for example:
  Cardiac tumors (hemangiosarcoma)
  Electrolyte imbalance (hypokalemia, calcium disturbances)
  Systemic hypertension
  Splenic tumor
  Postoperative or traumatic ventricular arrhythmia (caused by ischemia and reperfusion injury).
- A drug history should be obtained to ensure the arrhythmia is not caused by drugs or hormones that increase sympathetic tone (including excessive supplementation of L-thyroxin).
- In those cases where LV systolic function is reduced, a revised diagnosis of DCM with arrhythmia is appropriate, so long as a tachycardia-induced cardiomyopathy is eliminated.
  Sustained tachyarrhythmias can cause a reversible tachycardia-induced dilated cardiomyopathy; this is most likely when the tachycardia is relentless, with few intervals of sinus rhythm.
  In such cases, it is valuable to assess LV function before and 3 to 4 weeks after control of the tachyarrhythmia. Once the rhythm or heart rate response has been controlled, a more objective assessment of ventricular function can be obtained.

- *Management Approach*—Successful management of isolated arrhythmias in dogs is similar to that associated with treatment of arrhythmias in CHF, but with the advantage that normal ventricular function allows a wider selection and higher dosages of anti-arrhythmic drugs to be used. Most of the drugs used to control heart rhythm also depress cardiac function. This effect limits anti-arrhythmic drug use in heart failure. In this regard, the clinician should be vigilant, since an arrhythmia may be the first sign of progressive myocardial disease, and DCM and CHF may develop in the future.
  - The first question to address is whether the arrhythmias should even be treated. For example, isolated PVCs or atrial premature complexes probably should not be treated with potent anti-arrhythmic drugs unless there have been signs related to collapse or syncope.
  - The goals of therapy are three: prevent sudden death; prevent or reduce clinical signs; and protect the ventricle from tachycardia-induced cardiomyopathy.
  - When anti-arrhythmic therapy is prescribed, discuss the adverse drug effects with the owner, the importance of follow up ECGs (including Holter recordings), and discuss the potential for pro-arrhythmia (worsening of the rhythm).
  - Remember that the duration of therapy depends on the likely etiology of disease. In many cases of arrhythmogenic cardiomyopathy, treatment will be lifelong.
  - Have the client record any symptoms that might be related to the arrhythmias or possible adverse effects of the drugs.
  - Follow up with the patient at regular intervals. Begin with a client interview and routine auscultation. Follow with a standard ECG (if an arrhythmia is detected). Consider the use of a Holter ECG.
  - When a patient is stable on routine ECGs and is receiving a consistent dose of medication, perform another Holter ECG.

▼ ***Key Point*** Evaluate the response to therapy with both a routine ECG and a Holter ECG.

- *Lone Atrial Fibrillation*—In dogs with lone AF, Holter data provide insight about the daily heart rate and the exercise heart rate. Average daily heart rates that exceed 90 to 95/min or moderate-level exercise heart rates that exceed 200/min are reasonable grounds for slowing the heart rate response to AF or referring for cardioversion.
  - *Beta-blocker therapy* for heart rate control—Control of the ventricular rate response can be achieved with atenolol (0.5–1 mg/kg PO q12h) or metoprolol (12.5 mg PO twice daily in giant breeds). These drugs are also potentially cardioprotective if the AF is a premonitory sign of future DCM.
    For the first three days, the initial dose of the beta-blocker should be 50% of the prescribed dose, to prevent undue lethargy.
    Thereafter, the drug dose can be titrated up over 2 to 4 weeks to achieve an appropriate average daily heart rate (generally in the range of 70–80/min).
  - *Diltiazem therapy* for heart rate control—The use of this calcium channel blocker (dosed at 1–2.0 mg/kg PO q8h) is effective in controlling heart rate but does not confer the "cardioprotection" of beta-blockers should the arrhythmia represent early DCM. An initial dose of 0.6 mg/kg PO q8h for the first day is recommended before increasing the dose. Diltiazem can be used in combination with a beta-blocker. A long-acting preparation of diltiazem can also be used if q8h dosing is difficult (using the same total daily dosage, divided q12h).
  - *Digoxin therapy*—While digoxin can be prescribed for lone AF, cardiac glycosides are less effective for controlling excessive exercise-related rates and are not recommended by us when there is no evidence of heart failure.
  - *Cardioversion*—The conversion of AF back to sinus rhythm is definitely possible in dogs with lone AF. The use of procainamide, sotalol, or amiodarone for this purpose has met with mixed, and generally unfavorable, results. However, electrical DC biphasic cardioversion is highly successful in the setting of lone AF, especially in giant breeds, provided low-dose amiodarone is administered following the

procedure to maintain normal rhythm. This procedure requires referral to a cardiologist.

- *Ventricular arrhythmias and ventricular tachycardia*—Grading the severity of ventricular arrhythmias in terms of relative risk for sudden death is difficult but highly pertinent to management of these dogs. Once this had been done, and if a decision is made to treat the arrhythmia, a long-term plan for management should be established.
  - Relative Risk—Clearly the presence of clinical signs (collapse, syncope) is an indication to control ventricular tachycardia if the clinician is certain that a tachyarrhythmia is the basis for the episodes. In most cases, the situation is less clear cut, and the clinician must "grade" the arrhythmia in terms of severity.

    Isolated PVCs or runs of monomorphic, "slow" VT (usually <160/min) frequently are not treated. Couplets are not necessarily more dangerous than single PVCs, but closely timed couplets may indicate a higher "grade" of arrhythmia.

    Polymorphic VT (including torsade de pointe); non-sustained but flutter-like runs of VT; long runs of monomorphic, fast VT (exceeding 200/min); frequent multiform PVCs; and PVCs falling on the prior T-waves (R on T) suggest a higher grade or complexity of the arrhythmia. Anti-arrhythmic therapy is usually recommended.

    When serious arrhythmias are evident on a routine ECG, there is probably no need to perform a Holter ECG until after therapy has begun, especially in the dog with clinical signs. When a routine ECG shows "low-grade" arrhythmias such as isolated PVCs or runs of "slow" VT, it is reassuring to know if the results of a 24-hour Holter ECG support a low grade of complexity before deciding not to treat.

    When doubt remains, obtain consultation if possible.

▼ ***Key Point*** Decisions about initiating anti-arrhythmic therapy are imperfect, and dogs with recurrent PVCs or VT—whether on or off therapy—always carry a risk for sudden cardiac death. No anti-arrhythmic drug has been proven to prevent sudden death in dogs.

  - *Isolated PVCs*—Generally, it is better not to treat isolated PVCs. However, when they are frequent (such as >10,000 per day or about 7 PVCs per minute) they may be difficult to ignore. One well tolerated approach is to prescribe a beta-blocker such as atenolol (0.5–1 mg/kg PO q12h), which will likely reduce the total number of ectopics but not create a pro-arrhythmic situation.
  - *Ventricular Tachycardia*—When treatment is elected, the choice of drug depends largely on personal preference, but some recommendations can be advanced. The Chapter "Cardiovascular Drugs" describes the clinical pharmacology, use, and adverse effects of these drugs.

    Sotalol (1–2 mg/kg PO q12h) is generally well tolerated in dogs and clearly improves Holter ECG recordings in some breeds (such as boxers). This drug should not be used in German shepherds with inherited ventricular ectopy.

    Mexiletine—An oral drug related to lidocaine, mexiletine (Mexitil) is an effective ventricular anti-arrhythmic in many dogs (5–8 mg/kg PO q8h). We combine it with a β-blocker such as propranolol (0.5–1 mg/kg PO q8h) or atenolol (0.5–1 mg/kg PO q12h). Anorexia, tremors, and vomiting are adverse effects. For unresponsive patients, sotalol (1 mg/kg PO q12h) can be substituted for the other beta-blocker.

    Amiodarone (Cordarone) is an effective drug for VT, but may be more pro-arrhythmic and carries a higher incidence of adverse effects than sotalol. With a long elimination half-life, a loading dose is used initially (5–10 mg/kg PO q12h) followed by a lower maintenance dose (4–6 mg/kg PO once daily).

    Procainamide—The use of a long-acting procainamide preparation (15–20 mg/kg PO q8h) is recommended as procainamide HCl has a very short elimination half-life in dogs. As with mexiletine, it may be more effective when combined with a beta-blocker.

SUPPLEMENTAL READING

Basso C, Fox PR, Meurs KM, Towbin JA, Spier AW, Calabrese F, Maron BJ, Thiene G: Arrhythmogenic right ventricular cardiomyopathy causing sudden cardiac death in boxer dogs: A new animal model of human disease. Circulation 109(9):1180–5, 2004.

Ferasin L, Sturgess CP, Cannon MJ, Caney SM, Gruffydd-Jones TJ, Wotton PR: Feline idiopathic cardiomyopathy: A retrospective study of 106 cats (1994–2001). J Feline Med Surg 5:151–9, 2003.

Meurs KM: Boxer dog cardiomyopathy: An update. Vet Clin North Am Small Anim Pract 34:1235–44, 2004.

O'Grady MR, O'Sullivan ML: Dilated cardiomyopathy: An update. Vet Clin North Am Small Anim Pract 34:1187–207, 2004.

Smith SA, Tobias AH: Feline arterial thromboembolism: An update. Vet Clin North Am Small Anim Pract 34(5):1245–71, 2004.