

Last Updated 03/26/2020

PERICARDIAL DISEASE

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OBJECTIVES

1. Define pericardial effusion.
2. Define cardiac tamponade - how is it different than #1?
3. List common causes of pericardial effusion in the dog and establish a prognosis for each. List common causes in a cat. List two causes in a horse and one in cattle
4. Describe the technique for pericardiocentesis.
5. List the classical findings for pericardial disease on physical examination, ECG, thoracic radiographs and echocardiography.
6. Outline whether you believe that the following drugs are indicated in the treatment of chronic heart failure due to pericardial effusion and explain your rationale.
 - a. Pimobendan
 - b. Palladia
 - c. Furosemide
 - d. Doxorubicin

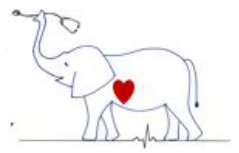
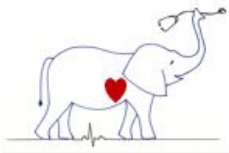
PERICARDIAL DISEASES

I. Introduction

- A. Less common than valvular or myocardial disease in dogs and cats. Approximately 1-5% of dogs with cardiovascular disease have pericardial disease - even less common in cats. Septic pericarditis is one of the key differential diagnoses for heart disease in horses and cattle.
- B. Typically, if in congestive heart failure, animals present with right-sided CHF signs.
- C. Acute pericardial disease (i.e. hemorrhage) leads to sudden collapse and forward heart failure with low output signs.

II. Anatomy and Physiology

- A. The pericardium is thin translucent fibroserous membrane that forms a double envelope around the heart and proximal portions of the great vessels.
 1. Thin serous visceral pericardium = epicardium
 2. Thick serofibrinous parietal pericardium
 3. Potential space containing a small volume (e.g., 1-25 ml - Dog; .5-2cc -Cat) clear lymph-like lubricating fluid



4. Pericardium not essential for life; functions include:
 - a. Ligamentous - maintaining optimal cardiac position and minimized displacement
 - b. Membrane function - lubricating and protecting heart against external friction and inflammation from contiguous structures, esp. lungs.
 - c. Mechanical function - maintaining optimal functional cardiac geometry, transmural pressure and ventricular compliance that balances left and right ventricular output and limits excessive ventricular dilation.

III. Classification of Pericardial Diseases

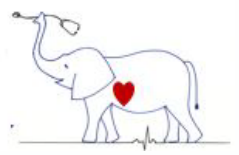
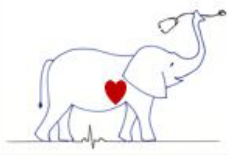
Congenital vs. Acquired

CLASSIFICATION OF PERICARDIAL DISEASES

<u>Congenital Disorders</u>	
Pericardial Defects or Absence of Pericardium	
Peritoneopericardial Diaphragmatic Hernia	
Pericardial Cyst	
<u>Acquired Disorders</u>	
Pericardial Effusion	Constrictive pericardial disease
Transudate (hydropericardium)	Idiopathic
Congestive heart failure	Infectious - bacterial, fungal
Hypoalbuminemia	Pericardial foreign body
Exudate (pericarditis)	Neoplastic
Infectious - bacterial, fungal, viral	
Sterile	Pericardial mass lesions
Idiopathic - viral?	Pericardial cyst (congenital)
Uremia	or abscess
Other infectious diseases	Neoplasm
	Granuloma - actinomycosis,
	coccidioidomycosis
Hemorrhage (hemopericardium)	
Neoplasia - hemangiosarcoma, heart base	
tumors, mesothelioma, other	
Trauma - iatrogenic, external	
Left atrial rupture	
Uremia	
Idiopathic	
Coagulopathy	

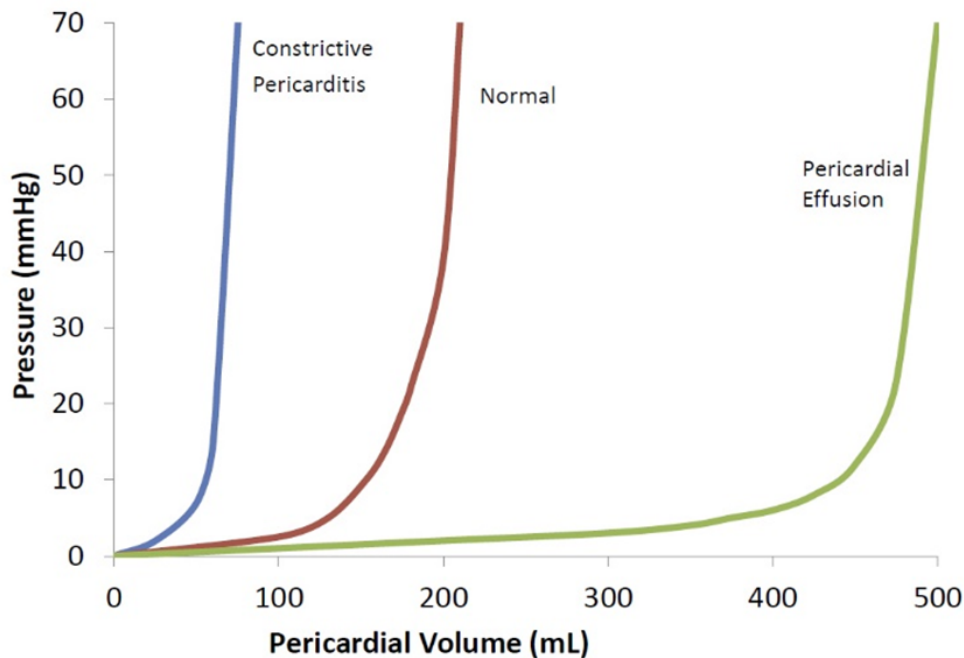
IV. Pathophysiology of Pericardial Disease

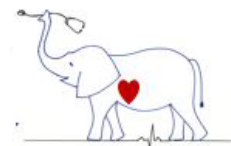
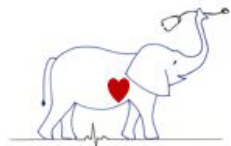
- A. The effects of pericardial disease result from compression (restriction) of ventricular filling, i.e. the effect is on (diastolic) ventricular filling and not primarily on ventricular contractility. Pericardial disease does not typically cause contractile dysfunction, although a reduced volume of blood returning to the heart can lead to low cardiac output.
- B. **Effusion vs. Tamponade - Review**
 1. Pericardial effusion = the development of abnormal volumes of fluid within the pericardial space
 2. Tamponade = sufficient fluid has accumulated the pericardial space that compression of the heart limits cardiac filling. Intrapericardial pressure must be elevated above atrial filling pressures if tamponade is present.



- C. **Pericardial Effusion with Tamponade** - Under normal conditions ventricular filling occurs under a very low (near atmospheric) intrathoracic pressure resulting in low ventricular diastolic, atrial and venous filling pressures. When sufficient pericardial fluid accumulates, pericardial pressure elevates above ventricular filling pressures. This pressure, transferred through the ventricular walls, must be exceeded (via elevations in venous pressures) to allow the ventricles to continue to fill with blood. Cardiac tamponade is present when ventricular filling is compromised. This leads to decreased stroke volume and elevated right atrial filling pressures that can lead to signs of right-sided CHF. Cardiac output is initially maintained by increased heart rate. Because of the equal compression of atria and ventricles, diastolic pressures equilibrate with the intra-pericardial pressure.

The clinical signs of disease are related to underlying cause and rate of fluid accumulation. The pericardium contains both elastic and fibrous tissues. In effusions that develop acutely (i.e. left atrial tear, pericardial hemorrhage), the pericardium is only capable of limited acute stretching until the properties of the elastic tissues are exceeded. Therefore, small amounts of fluid may result in large increases in pericardial pressures (see diagram -normal). Once the elastic limit is reached, even small increases in fluid cause large increases in pericardial and ventricular filling pressures. With acutely developing effusions, hypotension, poor perfusion, and shock (signs of forward heart failure) may predominate. If the effusion develops gradually, the pericardium can stretch to accommodate very large effusions (1000 ml or more). With chronic effusion the neurohumoral systems are activated and fluid is retained, which leads to signs of right-sided CHF.





D. Pericardial Fibrosis with Constriction (constrictive pericarditis)

The pathophysiology is similar to that of cardiac tamponade in that ventricular filling is limited resulting in decreased diastolic ventricular volume and increased venous, atrial, and ventricular diastolic pressures which can ultimately lead to the development of right-sided CHF. The pericardium becomes very thick and fibrinous however it may be only 1-2 mm thick in cases of idiopathic or foreign body pericarditis. Early diastolic filling may be normal, but because of the extreme inelasticity of the pericardium, the rapid filling phase ends abruptly and there may be an accompanying early diastolic heart sound ("pericardial knock"). (In cardiac tamponade, cardiac filling is impeded throughout diastole, therefore no knock). Pericardial knocks are uncommonly ausculted in small animal patients but are noted in some horses and cattle with constrictive pericardial disease.

E. Intrapericardial Mass Lesions

The pathophysiologic events of pericardial mass lesions depend upon the location and size of the lesion and the presence or absence of pericardial effusion and/or pericardial fibrosis. Small masses are often clinically silent. Large masses can cause clinical signs by local invasion or space occupation and displacement of adjacent structures or cardiac compression (especially the atria, pulmonary artery, or aorta). However, the most common cause of clinical signs in animals with intrapericardial masses is concurrent pericardial effusion that results in cardiac tamponade.

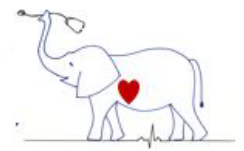
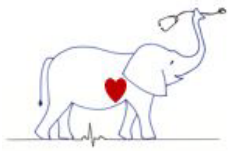
V. Congenital Disorders of the Pericardium - only peritoneopericardial defects are recognized regularly. Minor pericardial defects usually remain subclinical.

A. Pericardial defects

1. Very few clinical cases reported. Most involve a hole or defect on the left side occurring as round or oval opening or hole in the pericardium. Herniation and strangulation of the heart is a potential sequela.
2. Congenital absence of pericardium - no resultant clinical signs have been reported.

B. Peritoneopericardial Diaphragmatic Hernia (PPDH) - Most commonly recognized congenital pericardial defect in dogs and cats.

1. Anatomy - Results from incomplete development of ventral diaphragm and incomplete fusion of the caudal pleuropericardial membrane, this results in a persistent communication between the peritoneal and pericardial spaces. Abdominal contents are herniated into pericardial space, while the pleural space remains intact. Contents of hernia usually include omentum in addition to any of the following: liver, stomach, spleen, small intestine and rarely colon. Frequently causes significant dilation of peri-cardial sac and displacement of heart. Sternal deformities or pectus excavatum may accompany PPDH.
2. Clinical signs - Affected animals may remain asymptomatic or may develop clinical signs of gastrointestinal disease (vomition, anorexia, diarrhea, and weight loss), respiratory disease (dyspnea or cough) or less commonly cardiovascular disease (shock, collapse, or tamponade). PPDH may be discovered in first year of life or go undetected for many years.
3. Physical exam - Heart sounds may be muffled, absent, or displaced. Large hernias may result in a relative absence of abdominal organs on palpation.



4. Thoracic radiographs - the cardiac silhouette is usually dramatically enlarged, the trachea is elevated, and the caudal border of the heart overlies the diaphragm on both views. Abnormal fat or gaseous densities may overlie the heart and cranial abdominal structures may be malpositioned or absent. An upper GI contrast study may help visualize small intestine or stomach within the hernia. ECG may reveal an abnormal QRS axis or small QRS complexes.
5. Additional tests - fluoroscopy, nonselective angiography, positive contrast peritoneography can be performed, however echocardiography and thoracic radiography is less invasive and is usually able to permit identification of organs or adipose tissue in the pericardial space.
6. Surgical correction is curative - prognosis usually good. A number of surgical complications are recognized (necrotic strangulated tissue leads to sepsis or cytokine release, lung re-expansion pulmonary edema, etc.)

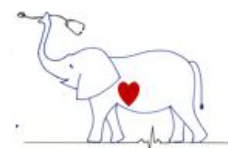
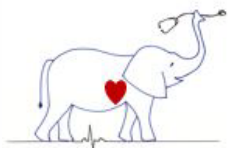
VI. Acquired Disorders of the Pericardium - There are two major pathologic processes which may affect the pericardium; pericardial effusion and constrictive pericarditis. Most animals with pericardial disease have pericardial effusion, while constrictive pericarditis is less frequently recognized.

- A. Pericardial effusion** – Of the domestic species, pericardial effusion is most commonly seen in dogs, and it is one of the most common cardiac emergencies seen at Tufts University. The two conditions most commonly associated with pericardial effusion in the dog are cardiac neoplasia and idiopathic ("benign") pericardial effusion. The cardiac tumors most frequently reported are hemangiosarcoma originating in the right atrial wall or atrial appendage and heart base tumors (chemodectoma, aortic body tumor, thyroid carcinoma). Idiopathic pericardial effusion has also been described as benign pericardial effusion and idiopathic hemorrhagic pericardial effusion. The term benign pericardial effusion is misleading, as life threatening cardiac tamponade is a very real potential sequela, and the effusions are not universally hemorrhagic. Thickening of the parietal pericardium and epicardium with fibrosis and mild inflammation are the predominant histologic features of idiopathic pericardial effusion. Mesothelioma is another cause for pericardial effusion, and it can be very difficult to differentiate idiopathic pericardial effusion from mesothelioma. Lymphoma is an uncommon cause in dogs but a common cause in cattle and one of the 5-6 most common causes of pericardial effusion in cats

Pericardial effusion is reported in association with some viral infections (i.e., African swine fever) and with bacterial infections in horses and cattle. Cattle may develop pericardial disease in association with traumatic reticulitis and peritonitis when the foreign body crosses the diaphragm and enters the pericardial sac.

Pericardial effusion has been reported in cats in association with feline infectious peritonitis, congestive heart failure, renal failure, metastatic neoplasia, coagulopathies, and bacterial pericarditis. Primary cardiac tumors resulting in pericardial effusion are uncommon in the cat and idiopathic pericardial effusion is uncommon in this species.

1. **Clinical signs** - Idiopathic pericardial effusion is most common in male dogs of medium and large breeds with an age range of 1 to 14 years (average 6-8 years). Golden Retrievers, German Shepherds, Great Danes and St. Bernard's are probably predisposed. Large breed dogs of middle to old age are predisposed to neoplastic effusions, with the German shepherd dog and Golden retriever predisposed to both right atrial hemangiosarcoma and idiopathic pericardial effusion. Boxers, bulldogs, and Boston terriers have been reported to be predisposed to heart base tumors (chemodectoma).



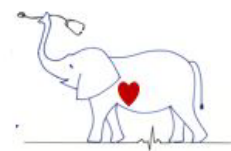
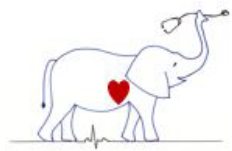
- a. Historical findings - (See table) May include lethargy, weakness, exercise intolerance, weight loss, abdominal distension, syncope, and tachypnea. Dogs presented with torn left atria usually have a history of mitral insufficiency with acute decompensation (weakness, collapse, pallor, or worsening of heart failure). Other acutely developing effusions, likewise, produce acute decompensation with weakness and collapse.
- b. Physical examination - Findings with chronic disease typically include muffled heart sounds, pericardial friction rub (an uncommon finding in small animals), jugular venous distention, weight loss, ascites, hepatosplenomegaly, pleural effusion, pallor, sinus tachycardia, and arrhythmias. In more acutely developing cases, collapse, pallor, and hypotension are recognized. Pulsus paradoxus may be noted as pulse quality increases and decreases with expiration and inspiration.

Clinical Signs Frequently Associated With Pericardial Disease

Historical findings	Physical findings
Lethargy	Tachypnea
Weakness	Dyspnea
Exercise intolerance	Mucous membrane pallor
Abdominal distension	Prolonged capillary refill time
Syncope	Diminished precordial impulse
Tachypnea	Muffled heart sounds
Cough	Pericardial friction rub
	Jugular venous distension
	Tachycardia
	Weak pulse
	Arrhythmias
	Pulsus paradoxus
	Hepatomegaly, splenomegaly
	Positive hepatojugular reflex
	Ascites

B. Diagnostic approach

1. Clinical pathology - Hypoproteinemia, mild anemia, and a neutrophilic leukocytosis are fairly frequently reported. Non-specific changes include elevated hepatic enzymes (secondary to right heart failure) and mild azotemia (pre-renal azotemia). Hemangiosarcoma may cause anemia, circulating nucleated red blood cells, and schistocytes. FIP titers and FELV tests should be performed in cats. High elevations of cardiac troponin I in dogs is associated with hemangiosarcoma.
2. Thoracic radiographs - Longstanding pericardial disease results in stretching of the fibrous component of the pericardial sac and radiographic evidence of severe globoid cardiomegaly with loss of cardiac chamber definition. The edges of the heart often look very well defined due to lack of cardiac motion. Enlargement of the caudal vena cava is variably noted, and pleural effusion may interfere with evaluation of the cardiac silhouette. Dogs with heart base tumors may have an increased soft tissue density at the heart base and/or tracheal displacement. Cats frequently demonstrate moderate cardiomegaly.



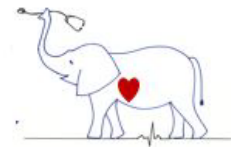
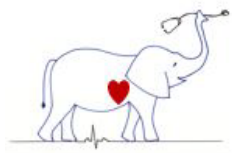
3. Electrocardiography

Diminished QRS amplitude - < 1 mv in all leads in the dog

Electrical alternans - A regular variation in QRS size or morphology (i.e., every second or third complex) that results from swinging of the heart within the fluid filled pericardial cavity. Although electrical alternans is not observed in every case (it is more common with large effusions), its presence is highly suggestive of pericardial effusion.

Abnormalities in the ST segment (usually elevation), may be present, as well as P-mitrale. Normal sinus rhythm or sinus tachycardia are the most common rhythm diagnosis, but ventricular or supraventricular arrhythmias may be recorded. While many dogs have one or more ECG finding indicative of pericardial effusion (low voltage complexes, electrical alternans, ST elevation), no single finding is seen in more than 30-50% of cases.

4. Central venous pressure - less than 5 cm of water in normal animals; patients with right heart failure due to pericardial disease will usually have measurements in excess of 10 to 15 cm of water.
5. Echocardiography - the most sensitive and specific means for detection of pericardial effusion. Echo-free space between the myocardium and the pericardium. This space is observed circumferentially with two-dimensional echocardiography, and the heart may swing to and fro within the pericardial sac. Diastolic right atrial and ventricular collapse suggests cardiac tamponade. In animals with cardiac neoplasia or other mass lesions, the masses can be imaged directly, and the location of the mass (atrium or heart base) can often be identified. Echocardiography is currently the best test to determine whether neoplasia is present or not.
6. Pericardiocentesis - The preferred therapy for cardiac tamponade, providing prompt relief of clinical signs. The decision whether to perform pericardiocentesis is difficult in cases of confirmed or suspected active pericardial hemorrhage. Pericardiocentesis is performed with the patient in lateral or sternal recumbency. The right hemithorax is clipped, blocked, and aseptically prepared between the third and eighth intercostal space, from the sternum to above the costochondral junction. The fourth or fifth intercostal space is selected and a long (5 cm) large bore (18 or 16 gauge) over-the-needle catheter is attached to polyethylene tubing, a three way stopcock, and a large (30 to 60 cc) syringe. Under continuous ECG monitoring, the catheter and needle are cautiously advanced toward the heart and gentle suction is applied to the syringe. Once pericardial fluid is obtained, the catheter is advanced over the needle into the pericardial sac and as much fluid as possible is removed.
 - a. Complications of pericardiocentesis
 - Coronary artery laceration - tap from right side of the thorax to avoid
 - Ventricular arrhythmias - move needle or catheter if observed
 - Exsanguination into the pleural space - cases of active intrapericardial hemorrhage
 - b. Pericardial fluid evaluation - Pericardial effusions can be classified according to their physical characteristics. In addition to fluid analysis and cytology, an aliquot of fluid should be for culture and sensitivity testing.
 - **Transudate (or modified transudate)**
 - Secondary to congestive heart failure, hypoalbuminemia
 - **Exudative** - less common in dogs, cats; more common in horses/cattle.
 - Infectious - bacterial and fungal
 - Traumatic reticulopericarditis in cattle - foreign body penetrates reticulum and works its way through the

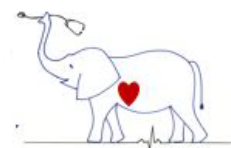
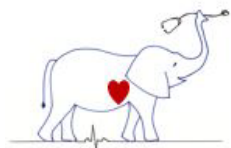


- diaphragm and into the pericardium; results in purulent pericarditis.
- Extension from other structures - pleuritis in horses will sometimes extend to pericardium.
 - Disseminated infection - tuberculosis, coccidiomycosis, actinomycosis, *Pasteurella multocida*, FIP, toxoplasmosis, leptospirosis, canine distemper, etc.
 - Sterile - inflammatory
 - Idiopathic - fluid characteristics indicate inflammation but no cause is found. Immune mediated?
 - Uremia
 - **Hemorrhagic (hemopericardium)** - the great majority of clinically significant pericardial effusions in dogs are hemorrhagic, sterile and non-inflammatory.
 - Neoplastic - intrapericardial neoplasms such as hemangiosarcoma, heart base tumor, mesothelioma, LSA, Thyroid tumors, metastatic neoplasms, and others.
 - Idiopathic ("benign") pericardial effusion
 - Acute hemopericardium - secondary to left atrial rupture
 - Penetrating chest trauma
 - Cytologic evaluation of hemorrhagic pericardial effusates in dogs usually fails to discriminate between hemangiosarcoma, heart base tumors, and idiopathic pericardial effusion. There is significant overlap of the protein content, red cell count, and nucleated cell count for these three diseases. In addition, reactive mesothelial cells, which have many characteristics in common with neoplastic cells, are present in all three diseases.
7. MRI, CT, or angiographic contrast studies can also be used to search for cardiac masses and assess for possible surgical or other interventions. These techniques may allow identification of the mass or they may show filling defect within the heart caused by an intracardiac tumor (typically within the auricular wall), and the vascular blush of a heart base tumor. MRI may be one of the best tests.
8. Cardiac troponin I is elevated more in dogs with hemangiosarcoma than dogs with other causes of pericardial effusion.

C. General Therapy for Pericardial Effusion.

The management of animals with pericardial disease will vary greatly dependent on the underlying disorder and the pathophysiologic consequences. Pericardial effusions associated with systemic or metabolic disease processes (i.e. hypoproteinemia, renal failure, congestive heart failure, peritoneopericardial diaphragmatic hernia) will usually resolve with correction of the underlying disease. The initial therapy for animals with substantial pericardial effusion and tamponade is pericardiocentesis. All animals with cardiac tamponade and without active hemorrhage require pericardiocentesis. There is no medical therapy that takes the place of or provides the immediate and specific therapeutic benefit of pericardiocentesis.

As pericardial effusion is a disease of diastolic dysfunction, other cardiac medications are typically not indicated unless clinically significant supraventricular or ventricular tachyarrhythmias are present. Afterload reducing agents (arteriolar vasodilators) should be avoided as hypotension frequently accompanies cardiac tamponade. Diuretics and vasodilators should be used cautiously (typically avoided) because overzealous preload



reduction will further decrease cardiac output, leading to azotemia, hypotension, and weakness.

D. Therapy for Specific Disease Processes

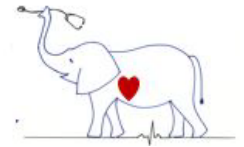
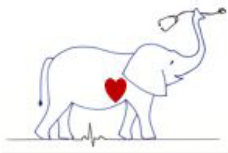
Idiopathic pericardial effusion. Dogs suspected of having idiopathic pericardial effusion are initially managed conservatively with pericardiocentesis. Approximately 50% of dogs will respond to one or two therapeutic pericardiocentesis. The remaining dogs will have recurrence several days to several years after pericardiocentesis. Anti-inflammatory drugs such as antiprostaglandins and corticosteroids may be valuable, although there are no controlled studies to document this in dogs (NSAID better than corticosteroids in people). Dogs that require frequent or repeated pericardiocentesis usually benefit from pericardiectomy. Subtotal peri-cardiectomy below the phrenic nerve is the surgical procedure of choice, and many dogs (approximately 85%) remain asymptomatic afterwards. Thoracoscopy can be used as a minimally invasive surgical method to perform pericardiectomy.

Cardiac mass lesions. Animals who are identified as having mass lesions may undergo surgery or be managed with repeated pericardiocentesis. Pericardial cysts or abscesses may be surgically resectable, while pericardial granulomas are usually fungal in the origin and treatment should be directed at the underlying agent. Primary cardiac neoplasms have variable prognoses based on location, size, presence of metastasis, and tumor type. Aspirin and other drugs that can alter coagulation are best avoided in these cases.

If metastasis is noted at the time of surgery, the prognosis is poor. Small masses may be resectable, but are found in the minority of cases. Hemangiosarcoma is typically incurable, has already metastasized by the time of diagnosis and surgical attempts to remove the mass are associated with short survival times, however survival with surgery plus chemotherapy (doxorubicin) is reportedly better than survival without surgery (3-6 months vs weeks to 1 month). Heart base tumors are slower growing and less likely to metastasize, and though they are difficult or impossible to excise, pericardiectomy is frequently useful to relieve cardiac tamponade and surgery has been shown to prolong survival compared to conservative management. Palladia may also be useful in dogs with chemodectoma. Cats with lymphosarcoma may be placed on chemotherapy. Thoracoscopy can be performed, which allows for removal of the pericardial sac, but does not allow good visualization of the heart base to search for cardiac masses. Some feel that thoracoscopy plus chemotherapy may improve outcome, and trial are underway to examine the role of thoracoscopy in dogs with pericardial effusion due to hemangiosarcoma.

Viral, bacterial or fungal pericarditis. Antibiotic therapy for infectious pericarditis should be dictated by the results of bacterial or fungal culture and sensitivity. Aggressive therapy might include intravenous antibiotics, intrapericardial antibiotics, and placement of an indwelling pericardial catheter for continuous drainage or intermittent lavage and antibiotic instillation. Animals with viral pericarditis often have other organ systems affected. Infectious pericarditis carries a guarded prognosis.

Pericardial hemorrhage. Active pericardial hemorrhage represents the exception to the rule that pericardiocentesis is always indicated with cardiac tamponade. If tamponade is life-threatening, pericardiocentesis is performed with the realization that further pericardial hemorrhage may result in reoccurrence of tamponade and/or exsanguination into the thorax. If hemorrhagic diathesis (e.g. anticoagulant intoxication) produces life-threatening tamponade, pericardiocentesis may be delayed until specific therapy (e.g., Vitamin K₁, plasma) can have effect. When pericardial hemorrhage is associated with less severe compromise in cardiac function, conservative management such as cage rest, judicious fluid



therapy, and careful patient monitoring is advised. Pericardial hemorrhage in stallions may result from aortic rupture.

- E. **Constrictive pericardial disease** - due to pericardial fibrosis with loss of pericardial compliance. The pericardium is usually dramatically thickened, and may be adherent to the epicardium. It is usually seen in combination with a small volume of effusion but can be seen alone.
1. **Causes**
 - a. Infection - actinomycosis, coccidiomycosis
 - b. Metallic foreign body - shotgun pellets, bullets, wires ingested by ruminants
 - c. Neoplasia, diffuse mesothelioma
 - d. Idiopathic - 1o occurrence
 2. **Clinical signs** - similar to patients with pericardial effusion. Right CHF due to previously discussed mechanism. Square root sign on cardiac catheterization.
 3. **Diagnosis and Treatment** - The diagnosis is difficult to establish, although echocardiography, cardiac catheterization, and exploratory thoracotomy are the most commonly used diagnostic tests. Treatment is usually pericardiectomy with epicardial stripping if indicated and should be performed by a surgeon experienced with this technique.

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