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CHAPTER 10

Cardiovascular System and Lymphatic Vessels[1]

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Key Readings Index

Structure

Development of the Heart and Great Vessels

The heart is a conical, muscular organ that in mammals has evolved into a four-chambered pump with four valves. During early fetal development, it is converted from an elongated muscular tube into a C-shaped structure by a process termed *looping* (E-Fig. 10-1). Subsequently, septation occurs to produce the right and left atrial and ventricular chambers and separation of the common truncus arteriosus into the aorta and pulmonary artery, respectively. The heart is interposed as a pump into the vascular system, with the right side supplying the pulmonary circulation and the left side the systemic circulation (E-Fig. 10-2; also see Chapter 2). The vascular system is subdivided into arterial, capillary, venous, and lymphatic segments. The arteries are classified into three types: elastic arteries, muscular arteries, and arterioles. The venous vessels are termed *venules* and *veins*. The lymphatic vasculature includes lymphatic capillaries and lymphatic vessels. Interposed between the arterial and venous segments are the capillary beds. A vascular segment termed the *microcirculation* (systemic capillary beds) includes arterioles, capillaries, and venules and is the major area of exchange between the circulating blood and the peripheral tissue (see E-Fig. 10-2; also see Chapter 2).

Macroscopic Structure

The heart lies within a fibroelastic sac called the *pericardium*, and the wall of the heart is composed of three layers: the epicardium, the myocardium, and the endocardium (Fig. 10-1). Structurally, the heart contains in order of blood flow four major blood vessels (vena cava, pulmonary artery, pulmonary vein, and aorta), four chambers (right atrium/auricle, right ventricle, left atrium/auricle, and left ventricle), and four valves (tricuspid, pulmonic semilunar, mitral, and aortic semilunar) (Fig. 10-2).

Myocardium

The myocardium is the muscular layer of the heart. It consists of cardiac muscle cells (cardiac myocytes [also known as *cardiac rhabdomyocytes*] or cardiomyocytes) arranged in overlapping spiral patterns. These sheets of cells are anchored to the fibrous skeleton of the heart, which surrounds the atrioventricular valves and the origins of the aorta and pulmonary artery. The myocardial thickness is related to the pressure present in each chamber; thus the atria are thin walled and the ventricles are thicker. In adult animals, the thickness of the left ventricular free wall is approximately threefold that of the right ventricle, measured in a transverse section across the middle of the ventricles, because the pressure is greater in the systemic circulation than in the pulmonary circuit.

The arterial supply to the heart is the left and right coronary arteries, which arise from the aorta at the sinus of Valsalva behind the left and right cusps of the aortic valves. The arteries course over the heart in the subepicardium and give off perforating intramyocardial arteries that supply a rich capillary bed throughout the myocardium. Extensive anastomoses occur between the capillaries that tend to run parallel to the elongated cardiac muscle cells. The ratio of the area of capillaries to that of muscle cells is approximately 1:1, a fact evident when the myocardium is viewed histologically in cross section. Cardiac myocytes are dependent on oxidative phosphorylation for energy requirements. This requires a constant supply of oxygen delivered by coronary arteries.

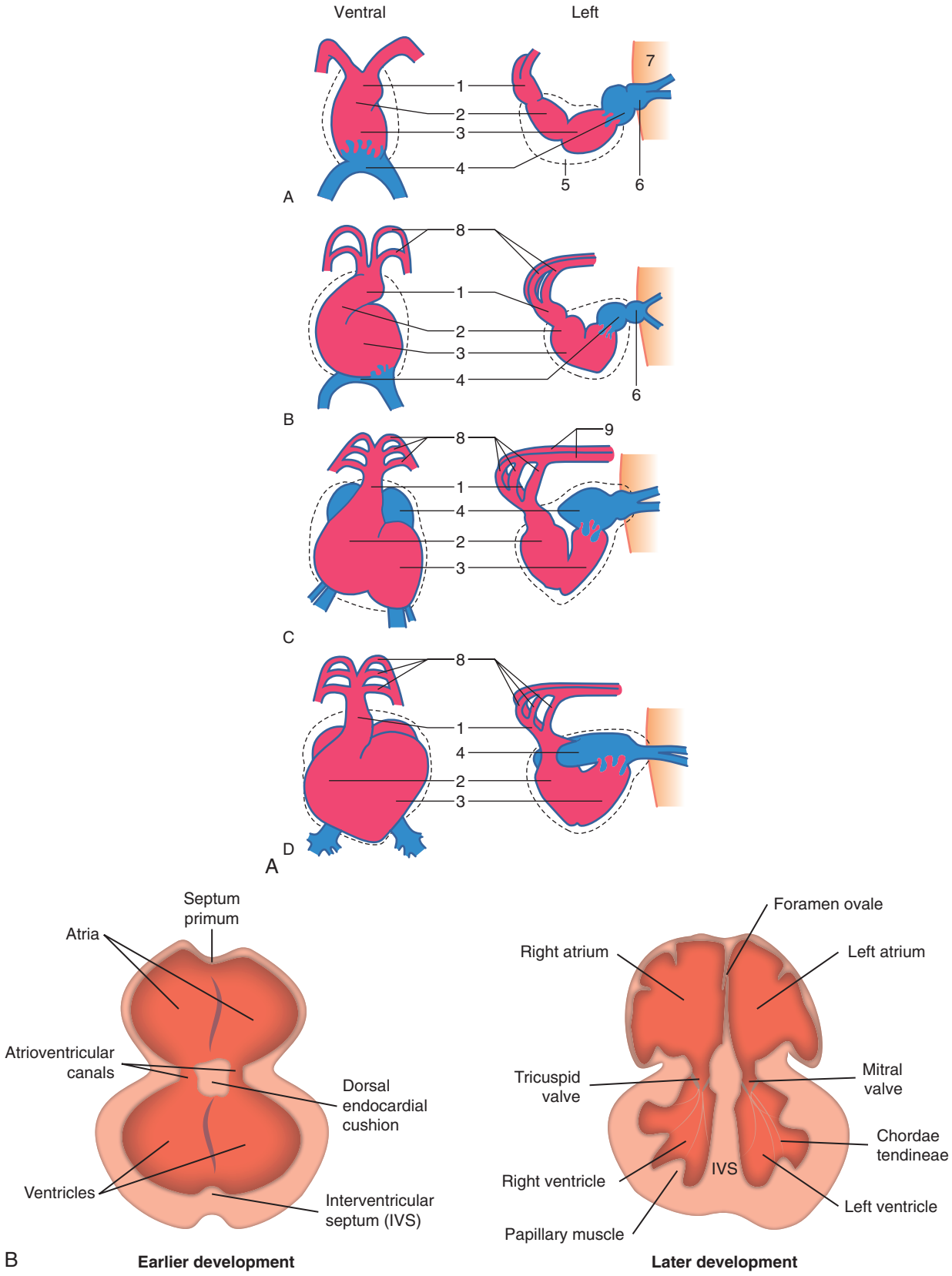
Cardiac Conduction System

The heart is a muscular four-chamber pump that simultaneously supplies blood to the pulmonary and systemic circulatory beds (see E-Fig. 10-2). Mechanical pumping is composed of sequential contraction (systole) and relaxation (diastole) that must be preceded by an electrophysiologic process that triggers a coordinated chronologic sequence of electrical events that result in muscle contractions. This electrophysiologic process is made possible by a network of

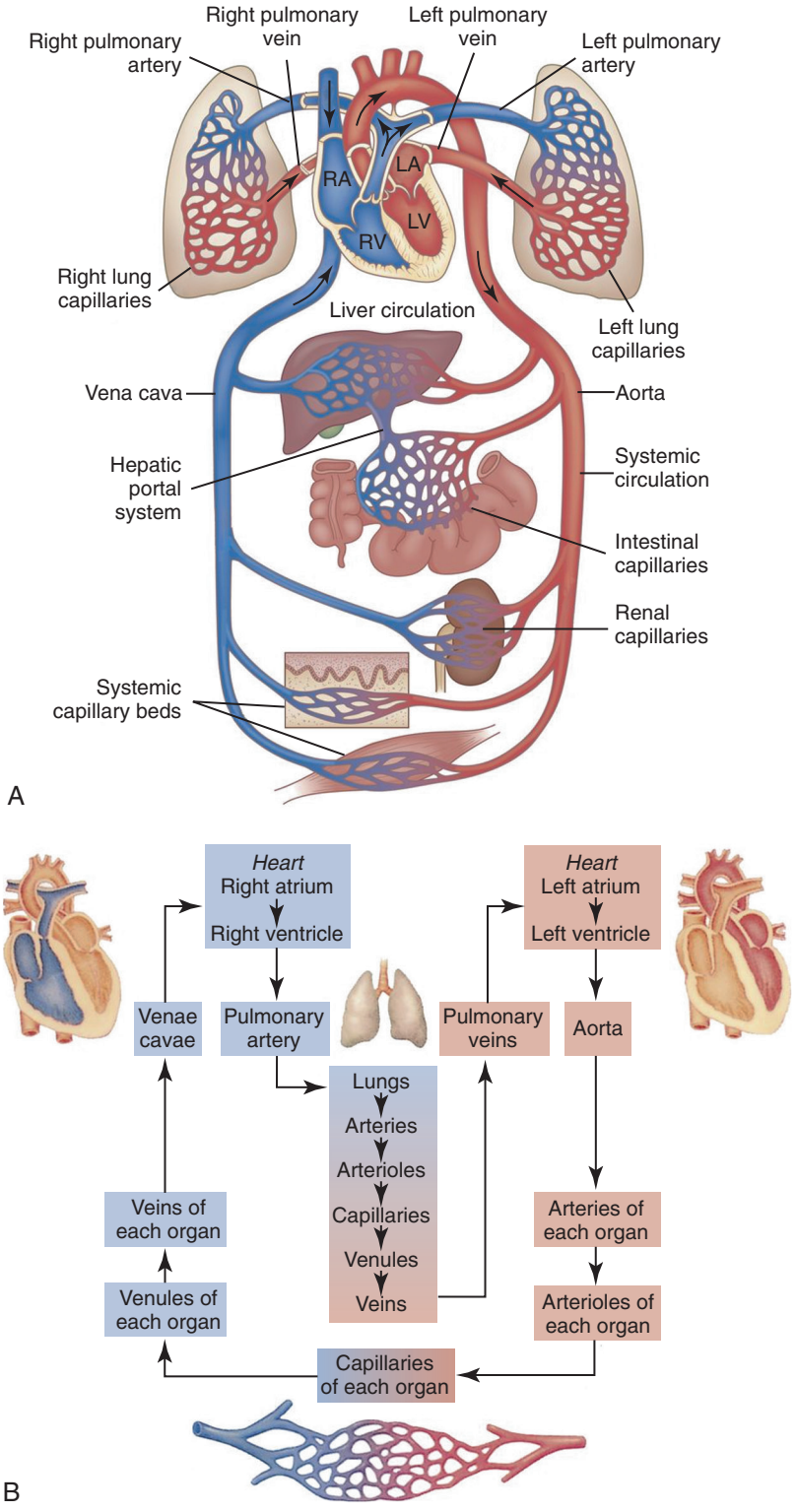
[1]For a glossary of abbreviations and terms used in this chapter, see E-Glossary 10-1.

E-Glossary 10-1 Glossary of Abbreviations and Terms

ABP–Arterial blood pressure
ADH–Antidiuretic hormone
AGII–Angiotensin-2
ANP–Atrial natriuretic peptide
ARVC–Arrhythmogenic right ventricular cardiomyopathy
AS–Aortic stenosis
ASD–Atrial Septal Defect
AST–Aspartate aminotransferase
ATE–Arterial thromboembolus
AV–Atrioventricular
AVN–Atrioventricular node
AVVs–Atrioventricular valves
BB–Bundle branch
BH–Bundle of His
BNP–Brain natriuretic peptide
CFB–Central fibrous body
CHF–Congestive heart failure
CK–Creatine kinase
CNP–C-type natriuretic peptide
CO–Cardiac output
CTD–Cor triatriatum dexter
DCM–Dilated cardiomyopathy
DIC–Disseminated intravascular coagulation
DNP–Dendraspis natriuretic peptides
ESR–Erythrocyte sedimentation rate
EDV–End diastolic volume
HCM–Hypertrophic cardiomyopathy
HR–Heart rate
HSA–Hemangiosarcoma
LDH–Lactate dehydrogenase
LV–Left ventricle
LVOT–Left ventricular outflow tract
MiVD–Mitral valve dysplasia
MVO_2–Myocardial oxygen consumption
MVD–Myxomatous valvular degeneration
MYBPC–Myosin-binding protein
NE–Norepinephrine
NO–Nitric oxide
PPDH–Peritoneopericardial diaphragmatic hernias
PDA–Persistent ductus arteriosus
PRAA–Persistent right aortic arch
RAAS–Renin-angiotensin-aldosterone system
RCM–Restrictive cardiomyopathy
RV–Right ventricle
SAM–Systolic anterior motion
SAN–Sinoatrial node
SV–Stroke volume
TnT–Troponin T
TnT1–Troponin 1
TOF–Tetralogy of Fallot
TVD–Tricuspid valve dysplasia
UCM–Unclassified cardiomyopathy
VSD–Ventricular septal defect



E-Figure 10-1 Development of the Heart. A, Ventral and left aspects of the segmentation and loop formation of the heart at progressive stages of development (**A** to **D**). Truncus arteriosus *(1)*, bulbus cordis *(2)*, ventricle *(3)*, atrium *(4)*, pericardial cavity *(5)*, sinus venosus *(6)*, septum transversus *(7)*, aortic arches *(8)*, and dorsal aortae *(9)*. **B,** Partitioning of the mammalian heart into chambers. (A from Hyttel P: *Essentials of domestic animal embryology*, St. Louis, 2010, Saunders. **B** courtesy Dr. L. Miller, Atlantic Veterinary College; and Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)



E-Figure 10-2 Pulmonary and Systemic Circulatory Systems. Schematic diagram showing serially connected pulmonary and systemic circulatory systems and how to trace the flow of blood. **A,** Right heart chambers propel unoxygenated blood through the pulmonary circulation, and the left heart propels oxygenated blood through the systemic circulation. **B,** The direction of blood flow begins at the left ventricle of the heart; flows to the arteries, arterioles, capillaries of each body organ, venules, veins, right atrium, right ventricle, pulmonary artery, lung capillaries, pulmonary veins, and left atrium; and then goes back to the left ventricle. *RA,* Right atrium; *RV,* right ventricle; *LA,* left atrium, *LV,* left ventricle. (From McCance, K: *Pathophysiology: The biologic basis for disease in adults and children,* ed 6, St. Louis, 2009, Mosby.)

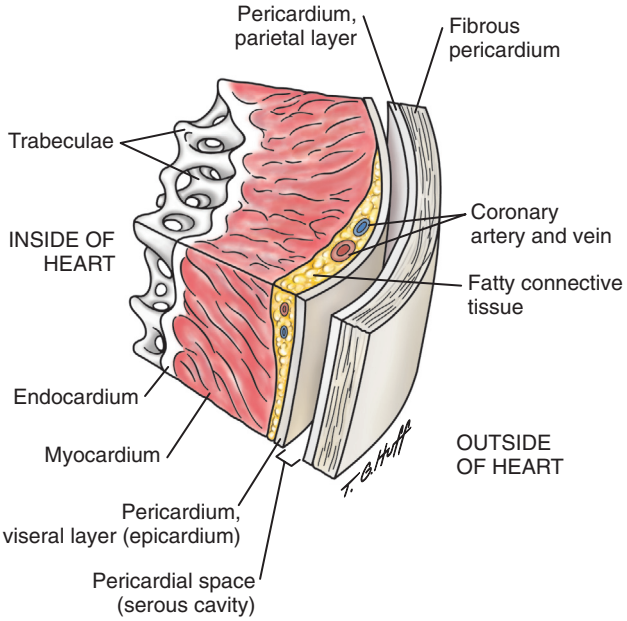


Figure 10-1 Structure of the Wall of the Heart.

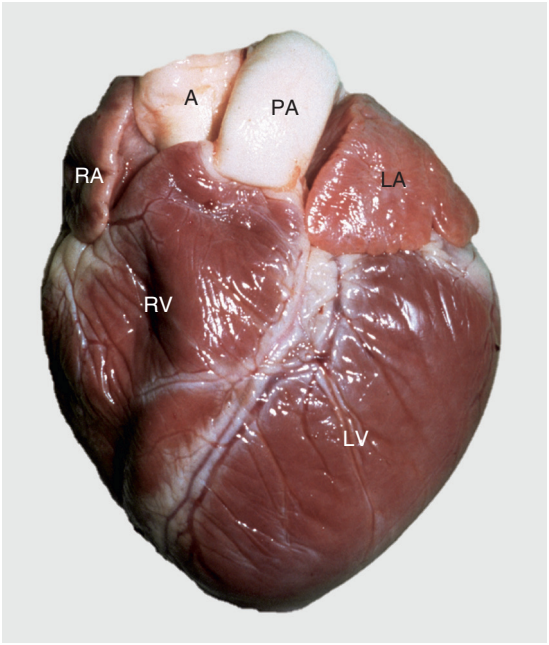


Figure 10-2 Normal Heart, Pig. *A*, Aorta; *LA*, left atrium; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RV*, right ventricle. (Courtesy School of Veterinary Medicine, Purdue University.)

special conducting fibers that are collectively referred to as the *cardiac conduction system*.

The cardiac conduction system is infrequently examined in animals because it is a labor-intensive process. Exceptions are cases with documented electrocardiographic alterations of undetermined origin. Components include (1) the sinoatrial node (SAN) at the junction of the cranial vena cava and the right atrium, (2) the atrioventricular node (AVN) located above the septal leaflet of the tricuspid valve and the atrioventricular (AV) bundle traversing the lower atrial septum onto the dorsal portion of the muscular interventricular septum, and (3) the right and left bundle branches that descend on each side of the muscular interventricular septum and eventually ramify in the ventricular myocardium as the Purkinje fiber network.

The major pacemaker of the cardiac conduction system is the SAN. This disk-shaped structure lies between the wall of the cranial vena cava and the external wall of the right auricular appendage. Four internodal pathways connect the SAN with the AVN. The AVN is present in the wall of the right atrium dorsal to the septal cusp of the tricuspid valve. For the atria to be electrically insulated from the ventricles so that an unwarranted ectopic conduction wave will not activate the ventricles (or vice versa) and disrupt the synchronous events of the cardiac cycle, a fibrous cardiac skeleton composed of a layer of dense collagen (central fibrous body [CFB]), as well as occasional plates of chondroid and osseous metaplasia, separates the atrial from the ventricular myocardium. This skeleton forms two fibrous rings around the AV orifices and the aortic and pulmonic orifices. Conduction fibers arising from the AVN, known as the *bundle of His* or *AV bundle*, pierce through the CFB into the ventricles and continue along the subendocardium of the interventricular septum. The AV bundle then splits into the right and left bundle branches, which further split and ramify into many other smaller branches that blend into the ventricular myocardium. Purkinje fibers constitute the AV bundle and downstream conduction pathways.

Endocardium and Heart Valves

The endocardium is the innermost layer of the heart and lines the chambers and extends over projecting structures such as the valves, chordae tendineae, and papillary muscles. The endocardium of the atria is thicker than that of the ventricles and thus normally appears white to gray on gross examination. The surface of the endocardium is endothelium that lies on a thin layer of vascularized connective tissue; the subendocardial layer contains blood vessels, nerves, and connective tissue. Purkinje fibers are distributed in the subendocardium throughout both ventricles. The heart valves (tricuspid valve [right AV valve], mitral valve [left AV valve], aortic valve, and pulmonary valve) are attached to fibrous rings and have thin avascular cusps. The valves open and close to regulate blood flow through the heart. During embryogenesis, endocardial cushions (mesenchymal tissue covered by endothelium) are precursors of the valve cusps. By remodeling, growth, and elongation, the cushions become thin mature cusps composed of connective tissue with an endothelial covering.

Pericardium and Epicardium

The pericardium, which normally contains a small amount of clear, serous fluid, is composed of an outer fibrous component and an inner serous layer, which form the sac surrounding the heart. The outer component is continuous with the mediastinal pleura. The base of the fibrous pericardium surrounds and blends with the adventitia of the greater arteries and veins exiting and entering the heart. The serous pericardium forms a closed sac surrounding the heart and the roots of the great vessels.

The epicardium (also known as *visceral pericardium*), the outermost layer of the heart, is continuous at the cardiac base with the parietal pericardium. The parietal pericardium is fused with the fibrous pericardium. The entire inner surface of the pericardial cavity is covered by mesothelium. The subepicardial layer is attached to the myocardium and consists of a thin layer of fibrous connective tissue, variable but generally abundant amounts (in well-nourished animals) of adipose tissue, and numerous blood vessels, lymphatic vessels, and nerves.

Blood and Lymphatic Vascular Systems

Blood Vessels. The aorta originates from the left ventricle and provides oxygenated blood to the entire body via arteries. In a tree-like manner, arteries branch and become smaller arterioles as they approach capillary beds (see E-Fig. 10-2; also see Chapter 2). These beds and postcapillary venules provide the site for exchange of oxygen, carbon dioxide, nutrients, and waste. Small venules return the exchanged fluid and blood to larger veins, and eventually the postcava and precava drain into the right atrium. The poorly oxygenated blood enters the pulmonary artery from the right ventricle. Oxygen exchange occurs in the capillaries of the lung, and oxygenated blood is returned to the heart via the pulmonary veins into the left atrium.

Lymphatic Vessels. Lymphatic vessels are thin-walled, endothelial-lined channels that originate near the capillary beds and serve as a drainage system for returning interstitial tissue fluid and inflammatory cells to the blood. Afferent lymphatic vessels drain lymph into regional lymph nodes, which then filter and provide immunologic surveillance of the lymph, its cells, and the foreign matter it contains. The filtered lymph continues into larger efferent lymphatic vessels, which eventually drain into the caval blood via the thoracic duct. Both lymphatic vessels and veins have valves to prevent backflow of fluid. A more complete description can be found in Chapter 2.

Microscopic Structure

Myocardium

The myocardium consists of cardiac muscle cells surrounded by interstitial components that include blood and lymphatic vessels, nerves, and connective tissue cells, such as fibroblasts, histiocytes, mast cells, pericytes, primitive mesenchymal stem cells, and extracellular matrix elements of connective tissue, including collagen fibrils, elastic fibers, and acid mucopolysaccharides. Cardiac muscle cells can be divided into two populations: the contracting myocytes and the specialized fibers of the conduction system. The contracting myocyte is a cross-striated branching fiber of an irregular cylindric shape that measures 60 to 100 µm in length and 10 to 20 µm in diameter, with centrally located, elongated nuclei. Myocytes in young animals are smaller and have less sarcoplasm. Atrial myocytes are smaller than ventricular myocytes. Adjacent myocytes are joined end-to-end by specialized junctions known as *intercalated disks* and less frequently by side-to-side connections termed *lateral junctions*. Multinucleated fibers with nuclei arranged in central rows are frequently seen in hearts of young pigs (Fig. 10-3). The myocytes of old animals commonly have large polyploid nuclei. The cytoplasm (sarcoplasm) of myocytes is largely occupied by the contractile proteins that are highly organized into sarcomeres, the repeating contractile units of the myofibril (see Figs. 15-3 and 15-8). Myofibrils are formed by end-to-end attachment of many sarcomeres. The cross-striated or banded appearance of myocytes is the result of sarcomere organization into A bands composed of myosin in the form of "thick" filaments (12 to 16 nm in diameter), I bands composed of actin in the form of "thin" filaments (5 to 8 nm in diameter), and dense Z bands at the end of each sarcomere. Thick and thin filaments interdigitate and provide the basis for the sliding mechanism of muscle contraction. Myocytes are enclosed by the sarcolemma, which consists of the plasma membrane and the covering basal lamina (external lamina). Other important components of cardiac muscle cells are generally only apparent in electron micrographs and include abundant mitochondria, a highly organized network of intracellular tubules termed the *sarcoplasmic reticulum*, cylindric invaginations of the plasma membrane called *T tubules*,

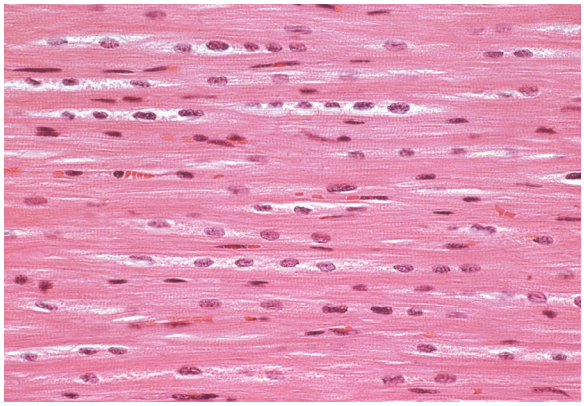


Figure 10-3 Normal Cardiac Muscle. Left ventricular myocardium, longitudinal section, normal young pig. The multiple nuclei in a myocyte are readily seen and evaluated in a longitudinal section. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

ribosomes, cytoskeletal filaments, glycogen particles, lipid droplets, Golgi complexes, atrial granules (contain atrial natriuretic factor), lysosomes, and residual bodies (E-Fig. 10-3).

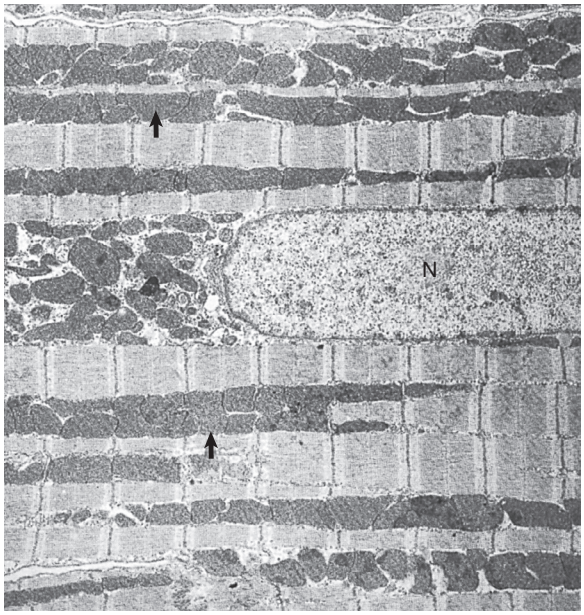
Cardiac Conduction System

The morphologic features of the cardiac muscle cells that form specialized conduction tissues, including the SAN, AVN, AV bundle (bundle of His), and bundle branches, vary greatly at different sites and among animal species but generally are thin, branching nodal muscle cells with scarce myofibrils separated by highly vascularized connective tissue (Fig. 10-4; E-Fig. 10-4). Autonomic nerve fibers are contained within the SAN. The Purkinje fibers (cardiac conduction fibers) are distinguished by their large diameters (in horse and ox) and abundant pale eosinophilic sarcoplasm rich in glycogen and poor in myofibrils.

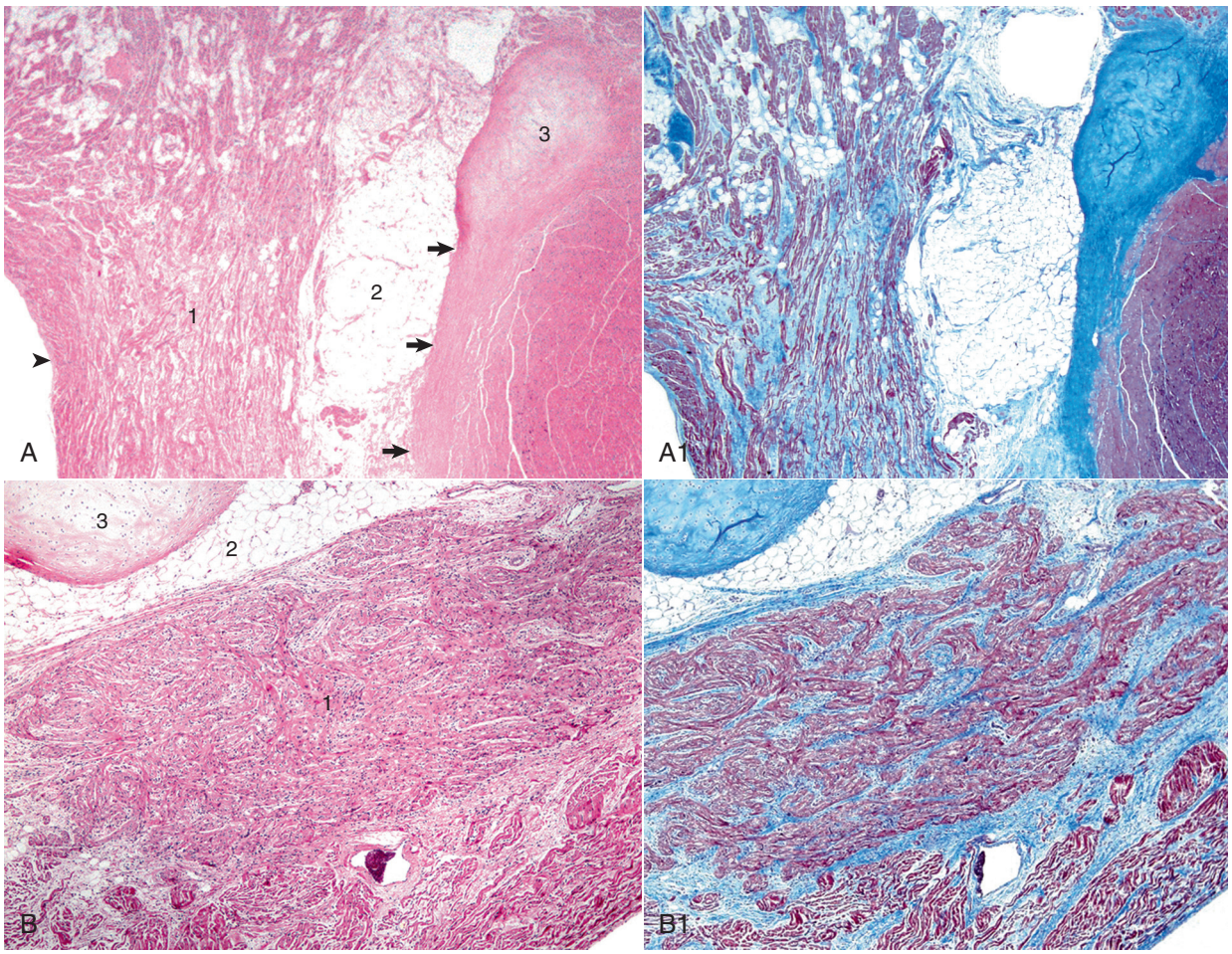
Sinoatrial Node. The SAN is positioned adjacent to the epicardial adipose tissue and is often centered around a branch of the right coronary artery (Fig. 10-4, *A*). Several large autonomic nervous system ganglions can occasionally be seen clustering in the epicardium adjacent to the node. The SAN lacks discrete structure, and its ill-defined borders merge with the adjacent atrial wall. It structurally consists of a collection of haphazardly oriented myofibers that appear as a pseudosyncytium and are embedded within abundant loose collagenous and elastic connective tissue, with rare cores of epicardially oriented dense collagen fibers (Fig. 10-4, *A1*). The nodal myofibers have discrete cell borders, a moderate amount of wavy sarcoplasm with sparse myofibrils, and an elongated nucleus that contains clumps of coarse chromatin (Fig. 10-4, *A2*).

Atrioventricular Node, Atrioventricular Bundle, and Bundle Branches. The AVN lies within the right atrial subendocardium and consists of a discrete, compact to loose mass of interconnecting myofibers that are often embedded within adipose tissue. A small nodal artery, parasympathetic ganglia, and large myelinated autonomic nerves are often present adjacent to the AVN. The nodal myofibers that have characteristic pale eosinophilic and thin sarcoplasm generally run parallel to each other but occasionally have an interweaving pattern with intervening loose collagen fibers. These myofibers contain a moderate amount of sarcoplasm with abundance of distinct striations and a short oval to elongated nucleus with dispersed chromatin.

The AV bundle (Fig. 10-4, *B*) emerges from the cranial pole of the AVN (Fig. 10-4, *B1*) and pierces through the CFB,



E-Figure 10-3 Normal Cardiac Muscle. Heart, left ventricular myocytes, longitudinal section, normal rat. Numerous dense mitochondria *(arrows)* lie between myofibrils, which have prominent bands. *N*, Nucleus. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-4 Heart, Fibrous Stroma of the Cardiac Conduction System, Goat. A, Atrioventricular *(AV)* node. The AV node *(1)* is composed of interconnecting nodal myofibers that are supported by loose collagenous and elastic fibrous stroma. The node is embedded in adipose tissue *(2)* that is adjacent to the cardiac fibrous skeleton *(arrows)* that has undergone focal chondroid metaplasia *(3)*. Endocardium *(arrowhead)*. H&E stain. **A1,** AV node, goat. Serial section of **A**. Note the overall deposition of collagen fibers *(blue)* in the structures labeled 1 and 3 in **A.** Masson's trichrome stain. **B,** AV bundle. In this illustration, the AV bundle *(1)* travels diagonally through the center of the image from the lower left to the upper right margins. It is supported by a loose to dense intervening interstitial collagenous stroma and is surrounded by adipose tissue *(2)*. Cardiac cartilaginous skeleton *(3)*. H&E stain. **B1,** AV bundle, goat. Serial section of **B**. Note the overall deposition of collagen fibers *(blue)* in the structures labeled in **B.** Masson's trichrome stain. (Courtesy Dr. A. Gal and Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)

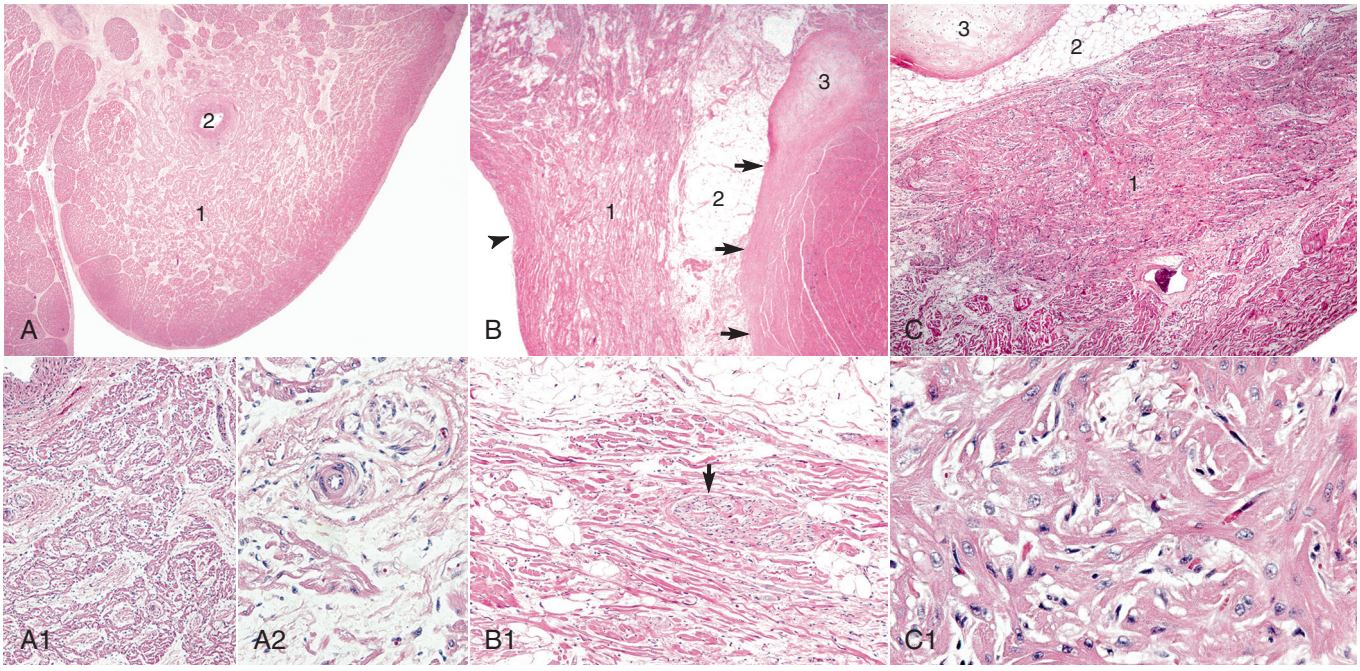


Figure 10-4 Cardiac Conduction System. A, Sinoatrial *(SA)* node, foal. The center of the SA node *(1)* contains a nodal artery *(2)*. H&E stain. **A1,** Higher magnification. Haphazardly oriented myofibers are embedded within abundant loose collagenous and elastic connective tissue. H&E stain. **A2,** Higher magnification. Nodal myofibers have discrete cell borders, a moderate amount of wavy sarcoplasm, and an elongated nucleus. H&E stain. **B,** Atrioventricular *(AV)* node, goat. The AV node *(1)* is composed of interconnecting nodal myofibers that are supported by loose collagenous and elastic fibrous stroma. The node is embedded in adipose tissue *(2)*. Note that in this illustration the AV node (1) is a poorly demarcated region (see *B1* for greater detail) that is elongated *(flattened)* from top to bottom and that it and its surrounding adipose tissue are positioned adjacent to the cardiac fibrous skeleton *(arrows)* that has undergone focal chondroid metaplasia *(3)*. The position and overall shape of the AV node in a histologic section is dependent on the plane of section. Endocardium *(arrowhead)*. H&E stain. **B1,** AV node, goat. In this higher magnification of *B*, AV nodal myofibers have a characteristic pale eosinophilic and thin sarcoplasm, with abundance of distinct striations and a short oval to elongated nucleus with dispersed chromatin. An autonomic myelinated nerve is present in the AV node *(arrow)*. H&E stain. **C,** AV bundle, goat. The AV bundle *(1)* travels diagonally through the center of the figure from the lower left to the upper right margins. It is formed by an interweaving pseudosyncytium of cardiac myofibers supported by a loose to dense intervening collagenous stroma (see *C1* for greater detail) and may be surrounded by adipose tissue *(2)*. Cardiac cartilaginous skeleton *(3)*. H&E stain. **C1,** Higher magnification. The AV bundle myofibers of the pseudosyncytium have moderate to large, pale eosinophilic sarcoplasm with prominent striations and large nuclei with fine stippled chromatin. H&E stain. (Courtesy Dr. A. Gal, Institute of Veterinary, Animal and Biomedical Sciences, Massey University; and Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)

approximately at the level of the annuli of the aortic and mitral valves (Fig. 10-4, *B2*), to become the left and right bundle branches. The size of an AV bundle myofiber progressively enlarges, and its cytomorphology transitions from a pale eosinophilic, small and thin (AVN-like morphology) myofiber to a pale eosinophilic, foamy to waxy, large, and somewhat rectangular myofiber that lacks cross-striations (a Purkinje-like cellular morphology) (Fig. 10-4, *C*).

Autonomic Nervous System. The nerve supply to the heart is autonomic and includes sympathetic, parasympathetic, and non-adrenergic noncholinergic innervation. Histologically, large nerves can be seen in the epicardium and adjacent to the coronary blood vessels, whereas special staining techniques are required for demonstration of neural tissue elsewhere. Electron microscopy and immunohistochemistry allow differentiation between sympathetic and parasympathetic nerves that are otherwise indistinguishable with H&E stain. Preganglionic parasympathetic fibers pass to the heart through the cardiac branch of the vagal nerve and synapse with parasympathetic ganglionic neurons. Postganglionic neurons are distributed to the SAN and AVN, as well as to atrial and, to a much lesser extent, ventricular myocardium (however, the ventricular conduction system is well supplied by cholinergic innervation). Postganglionic sympathetic fibers arising from the cervicothoracic and middle cervical ganglia intensely innervate the SAN and AVN and, to a lesser extent, the AV bundle. The atrial endocardium, myocardium, and epicardium are evenly innervated, whereas the ventricles are considerably less innervated, with epicardium more densely populated by neural tissue than the endocardium.

Endocardium and Heart Valves

The endocardium, lining the atrium and ventricles, consists of a continuous endothelium, subendothelium, and subendocardium. The subendothelial layer contains dense irregular fibroblasts intermixed with collagen and elastic fibers and occasional smooth muscle cells. Elastic fibers are abundant within the subendocardium of the atria. The subendocardial layer contains vascular structures, elastic and collagen bands, and fibroblasts and is continuous with the myocardium. Purkinje fibers are located in the subendocardium. The heart valves are poorly vascularized, endocardial folds covered by endothelium. The subendothelial layer is composed of fibroblasts with abundant elastic and collagen fibers. The AV valves (AVVs) consist of a layer of stratum spongiosum and stratum fibrosum. The stratum spongiosum consists of loosely arranged fibroblasts with moderate amounts of collagen and elastin fibers and vascular structures. The stratum fibrosis contains fibroblasts and collagen, which are continuous with the annulus fibrosis and chordae tendineae.

Pericardium and Epicardium

The pericardial sac is composed of parietal and visceral pericardium, both of which are covered by mesothelium. Beneath the visceral

mesothelium is a thin layer of fibrous connective tissue, adipocytes, and vascular structures. This organization forms the subepicardium and interdigitates with the myocardium. The parietal pericardium is composed of an inner layer of mesothelium that interdigitates with the dense connective tissue forming the outer pericardial sac.

Blood and Lymphatic Vascular Systems

The overall design of the blood and lymphatic vessels is similar, except that luminal diameter, wall thickness, and the presence of other anatomic features, such as valves, vary between the different segments. The luminal surface of all vessels is lined by longitudinally aligned endothelial cells covering a basal lamina. Vessel walls are divided into three layers or tunics: intima, media, and adventitia. However, some of the layers can be absent or all of the layers can be thinned in some segments of the vascular system, depending on the intravascular pressures. The large elastic arteries such as the aorta have (1) an intima composed of endothelium and subendothelial connective tissue; (2) a very thick tunica media composed of fenestrated elastic laminae with interposed smooth muscle cells and ground substance and bordered internally by the internal elastic lamina and externally by the external elastic lamina; and (3) an outer tunica adventitia layer composed of collagen and elastic fibers and connective tissue cells with penetrating blood vessels, termed the *vasa vasorum*, supplying nutrients to the adventitia and the outer half of the media. In muscular arteries and arterioles, the tunica media is largely composed of smooth muscle cells arranged in a circumferential pattern. Arterioles are the smallest arterial channels and are generally less than 100 μm in diameter and with one to three layers of smooth muscle cells in the tunica media.

Capillaries are 5 to 10 μm in diameter, and their endothelium is one of three types: (1) continuous, (2) fenestrated (as in the endocrine glands), or (3) porous (as in renal glomeruli). The endothelium rests on an external lamina surrounded by pericytes. Pericytes are located abluminally to capillaries and postcapillary venules and because of their location, contractility, and cytoskeletal proteins may play a role in regulating capillary and venular blood flow. Lesions of the endothelium might not be evident by light microscopy, and electron microscopy is required for characterization.

Veins have thin walls in relation to their luminal size compared with those of arteries, in which blood pressure is greater. The adventitia is the thickest layer. Valves are present to prevent retrograde blood flow (i.e., away from the heart).

Lymphatic capillaries lack a basal lamina. Large lymphatic vessels are similar in structure to veins and generally have large lumina, thin walls, and a greater number of intimal valves but contain lymph.

The morphology of large arteries, veins, microvasculature, and lymphatic vessels is described in Chapter 2 and is not discussed further in this chapter.

Necropsy Assessment of Heart and Vascular Structures

For information on this topic, see E-Appendix 10-1 and E-Figs. 10-5 and 10-6 at www.expertconsult.com.

Examination of the Cardiovascular System and Lymphatic Vessels at Necropsy and Tissue Sampling for Histopathologic Evaluation

For information on this topic, see E-Appendix 10-2 and E-Fig. 10-7 at www.expertconsult.com.

Function

The primary function of the cardiovascular and lymphatic systems is to maintain an adequate and steady supply of nutrients to and facilitate the removal of waste products from all organs and tissues of the body. Cardiac myocytes provide the force of contraction; the conduction system and the nervous system control the flow and volume.

Myocardium

The results of normal cardiac function include the maintenance of adequate blood flow, called cardiac output, to peripheral tissues that provide delivery of oxygen and nutrients, the removal of carbon dioxide and other metabolic waste products, the distribution of hormones and other cellular regulators, and the maintenance of adequate thermoregulation and glomerular filtration pressure (urine output). The normal heart has a threefold to fivefold functional reserve capacity, but this capacity can eventually be lost in cardiac disease and the result is impaired function.

Cardiac Conduction System

Cells of the cardiac conduction system are modified cardiac myofibers that are able to spontaneously depolarize, which is also called *autoexcitation*, and function to (1) coordinate the sequence of events required for efficient ventricular filling during diastole and ejection during systole and (2) maintain the pressure in the pulmonary and systemic circuits (see E-Fig. 10-2).

Depolarization of the membrane of these pacemaker cells is due to a transiently increased rapid permeability to sodium ions and a slightly longer lasting increase in permeability to calcium ions that results in their influx into the myofiber sarcoplasm, thus changing the membrane potential (see Chapter 14). As this transient permeability is lost, membranal potassium channels open, and rapid outward potassium flux results in myofiber membranal hyperpolarization (along with sodium and calcium efflux), ultimately bringing the membrane potential back to a "normal" steady state (resting potential). During this period of time (refractory period), the myocyte cannot depolarize again because of a special conformation of membrane sodium channels that is transiently lost with depolarization and regained only with hyperpolarization. Intrinsically, the resting membrane potential of pacemaker cells is more positive than that of contracting cardiomyocytes and slightly more negative than the membrane threshold potential. This difference is due to leakiness of the pacemaker cell membrane to sodium and calcium ions and a steady low-grade influx of these ions.

Once one pacemaker cell depolarizes, a wave of depolarization propagates through the surrounding myocytes because these cells are connected to each other by special membranal pores (gap junctions), which allow for ionic exchange between adjacent cells. The number of gap junctions between cells of the conduction system is therefore a property that affects conduction velocity. Because the heart cycle must be strictly coordinated so that both atria and both ventricles contract and relax at the same time, and atrial contraction occurs simultaneous to the late ventricular relaxation, the depolarization wave has to be conducted fast at certain points along the conduction pathway and slower at others. Therefore, at different anatomic regions along the conduction pathway, the degree of cell-to-cell interaction dictates a slightly different cellular morphology.

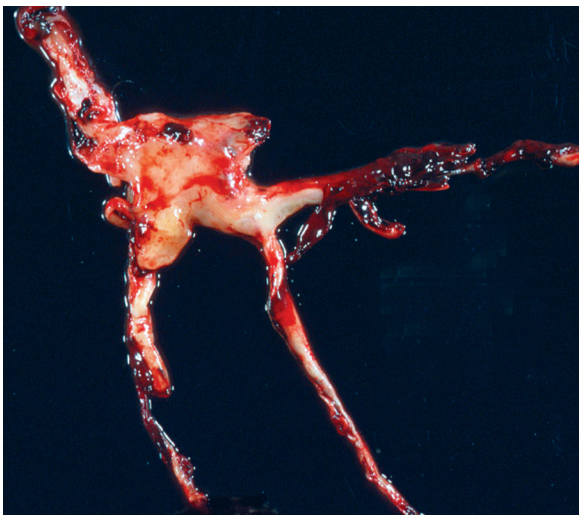
When an electric signal (a propagating depolarization front) is generated in the sinoatrial node (SAN) and spreads throughout the atria from cell to cell and eventually reaches the atrioventricular node (AVN), it is also conveyed through the specialized internodal conducting fibers. The conduction in these fibers is approximately

E-Appendix 10-1 Necropsy Assessment of Heart and Vascular Structures

Occasionally, normal features in animal hearts can be misinterpreted as lesions. The epicardial lymphatic vessels, especially in cattle, can appear as prominent white streaks that could be interpreted as areas of necrosis. The septal cusp of the tricuspid valve in dogs is normally rather tightly attached to the ventricular septum. In young ruminants up to 2 to 3 weeks of age, the ductus arteriosus and foramen ovale can be probed patent, but unless the openings are large, no significant shunting of blood is likely to occur during life. The overall shape of normal hearts can vary from the elongated conical profile in the horse to the somewhat rounded shape in the dog. Cardiac weights vary greatly among species and breeds; pigs have relatively small hearts (approximately 0.3% of body weight), and dogs have relatively large hearts (from 0.75% of body weight in nonathletic breeds to 1.25% in athletic breeds).

Postmortem alterations in hearts and vascular structures must be recognized and correctly interpreted. Rigor mortis occurs in myocardium much as in skeletal muscles and produces contracted, rigid ventricular walls, which empties the more muscular left ventricle. After rigor passes, the ventricular walls relax.

Postmortem blood clotting produces red ("currant jelly") clots in the atria, right ventricle, and large vessels at the base of the heart. Postmortem blood clots are found in these anatomic structures because they lack contractile elements (large vessels) or have less muscle mass (atria, right ventricle) to undergo contraction during rigor mortis. In postmortem evaluations of the heart, it is important to note the presence (or absence) of blood clots in the ventricles and their appearance ("currant jelly" vs. "chicken fat") (E-Fig. 10-5).



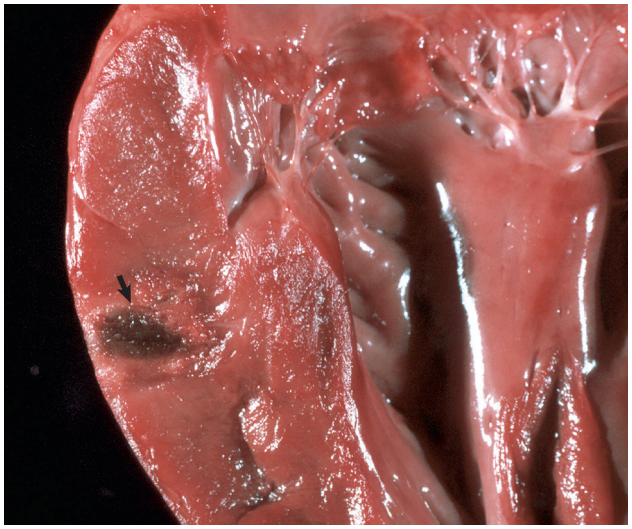
E-Figure 10-5 **Postmortem "Chicken Fat" Arterial Cast, Dog.** Note how the clot conforms to the shape of the lumens of the vessels from which it was removed. Chicken fat clots consist primarily of clotted plasma and fibrin and other proteins of the coagulation cascade. They are often indicative of anemia; however, in all animals their formation by the separation of the red blood cells from the rest of the components of blood depends on the erythrocyte sedimentation rate (ESR). Separation can occur in all animals in response to systemic inflammation, which increases the ESR, but the horse normally has a high ESR because equine erythrocytes clump together in rouleau formation, which increases the ESR. Thus, depending on the ESR, postmortem clots may be pale white to yellow ("chicken fat" clot) or shiny red ("currant jelly" clot) or sometimes a mixture. (Courtesy Dr. R.K. Myers, College of Veterinary Medicine, Iowa State University.)

Under normal conditions, because of its larger chamber volume and thinner walls, a blood clot will be found in the right ventricle, whereas little or no blood clot will be found in the left ventricle because of its smaller chamber volume and thicker walls. Animals with prolonged heart disease may lack adequate glycogen reserves in cardiac myocytes. As a result, the ventricular chambers may fail to contract during rigor mortis, allowing a blood clot to form in the left ventricle.

Occasionally, pale "chicken fat" clots that contain reduced numbers of erythrocytes form in animals with severe anemia, systemic inflammatory disease, leukemia, or after prolonged agonal periods. Horses more often have pale clots because of a rapid erythrocyte sedimentation rate termed rouleaux formation. Postmortem lysis of erythrocytes followed by imbibition of hemoglobin produces diffuse red staining of the endocardium and epicardium and simulates the appearance of hemorrhage.

Usually 12 to 24 hours after death, erythrocytes lyse, and the resultant imbibition of hemoglobin produces red discoloration of the normally white intima of blood vessels. Postmortem clotting must be differentiated from thrombosis. Postmortem clots, found in veins and large elastic arteries as red "currant jelly" type or occasionally as pale "chicken fat" type, are readily removed by traction or gentle flushing at necropsy, in contrast to thrombi, which are adherent. Postmortem contraction of muscular arteries because of rigor mortis extrudes blood. Microscopically, these muscular arteries are devoid of blood, and their internal elastic lamina is wavy in cross sections of the contacted vessel.

Other potentially misleading findings at necropsy of young dogs and horses include diffuse or patchy myocardial pallor that subsequently fails to correlate with any detectable microscopic alterations. Also, the intracardiac injection of euthanasia solution and other substances can cause hemopericardium and myocardial pallor from tissue dissolution and from crystalline deposits at the site of solution deposition (E-Fig. 10-6).



E-Figure 10-6 **Focal Hemorrhage and Discoloration, Intracardiac Injection, Euthanasia Solution, Left Ventricle, Dog.** Euthanasia solution is often injected into the left ventricle. In this case, solution was injected into the myocardium and caused a localized area of hemorrhage and discoloration. A mixture of euthanasia solution and blood often form a brownish sludge in the ventricle. (Courtesy College of Veterinary Medicine, University of Illinois.)

E-Appendix 10-2 Examination of the Cardiovascular and Lymphatic Systems at Necropsy and Tissue Sampling for Histopathologic Evaluation

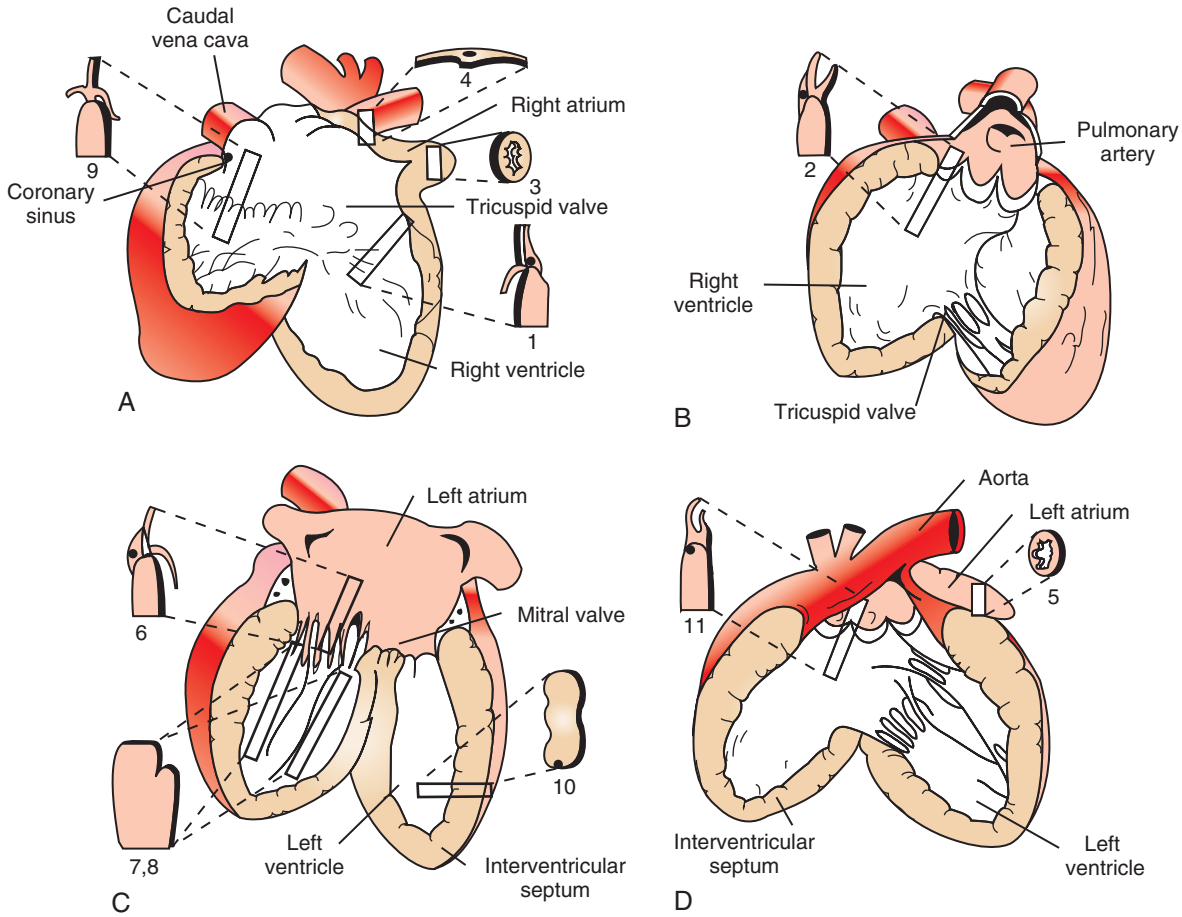
It has been stated that there are as many ways to open and evaluate the heart as there are pathologists! Your goal is to use a consistent method, which allows examination of the entire heart and its associated vascular structures.

1. First evaluate the pluck—both in situ and then after removal. If possible, carefully open the pericardial sac and observe the quantity and quality of the pericardial fluid. If the fluid appears abnormal, now is the time to take samples for bacterial isolation.
2. Remove the heart from the lungs and place the heart so that the auricles are facing you. This is an excellent time to look at the pulmonary arteries for thrombi. Once the heart and lungs are separated, it can be difficult to locate a thrombus. Note: The more vascular structures you leave attached to the heart, the easier you will find dissection.
3. Open the right atrium and remove any clotted blood using a transverse incision.
4. Assess the tricuspid valve by looking down into the lumen of the right ventricle.
5. Open the right ventricle. Start by cutting through the atrioventricular valve nearest the septum. Then with either scissors or a knife, using the ventricular septum as your guide, follow the septal wall to the pulmonary artery.
6. Evaluate the tricuspid and pulmonic valves, thickness of the right ventricle, and endocardium.
7. Open the left auricle in the same manner as the right auricle. Remove blood clots and examine the mitral valve. Now is the time to evaluate the functionality of the mitral valve. By using water (from the tap), you can evaluate whether or not the mitral valve closes completely. This is also the perfect time to look for a ruptured chordae tendineae.
8. By starting midway between the left ventricle, insert your knife and cut to the apex. Remove blood, and examine the mitral valve. Then make a "window" and exit out the aortic outflow. Note: This is the time when people usually stop—that is, before they examine the aortic valves and outflow. Do not make this mistake. This is an important area that needs to be carefully examined.
9. Examine the aortic valves, papillary muscles, endocardium, and mitral valve.
10. Measurements can be made at this time. By using string, you can measure the diameter of the aortic valve and pulmonic valves. They should be roughly similar in length. Measure the left and right ventricular free wall. Be sure to consistently measure at the same place and not include the thickness of the papillary muscles. Remember that the normal measurement should be roughly 3 : 1 for left to right measurement.

Whatever technique you decide to use, *be consistent*. Always remember to examine the following: pericardial sac and contents, epicardial surface, and myocardium—left, right, and papillary muscles, valves (all four), endocardium, pulmonary and aortic outflow, and intimal surfaces. If you do this, you will be a successful cardiac pathologist. Now all you have to do is know what abnormalities are significant.

After fixation for at least 24 hours, tissue samples should be removed from standard heart sites for histopathologic evaluation (see E-Fig. 10-7). If gross lesions are apparent, representative samples should be taken of those lesions. In small-sized hearts, the fixed specimen is bisected perpendicular to the long axis of the septum to provide a sample for histopathologic study that includes sections of all four chambers and interventricular and interatrial septa.

Special sampling procedures are available for comprehensive evaluation of the cardiac conduction tissue.



E-Figure 10-7 Gross and Microscopic Examination of the Heart. Diagrams **A** to **D** illustrate the heart opened. The numbers indicate the area and the shape of the blocks of tissue removed for histopathology. **A,** Right ventricle and right atrium. **B,** Right ventricular cavity and pulmonary outflow tract. **C,** Left ventricle and left atrium. **D,** Left ventricle and aortic outflow tract. *1,* Right ventricular free wall, atrioventricular valve, and atrium. *2,* Pulmonic valve, right ventricular outflow tract, and pulmonary artery. *3,* Right auricular appendage. *4,* Sinoatrial node. *5,* Left auricular appendage. *6,* Left atrioventricular valve, ventricle, and atrium. *7* and *8,* Left ventricular free wall and papillary muscles. *9,* Atrioventricular node, right atrioventricular valve, and atrium. *10,* Interventricular septum. *11,* Aortic valve, left aortic outflow tract, and aorta. (From Bishop SP: Necropsy techniques for the heart and great vessels. In Fox P, Sisson D, Moise N, editors: *Textbook of canine and feline cardiology*, ed 2, Philadelphia, 1999, Saunders.)

three times faster than that of the atrial myofibers. By conveying the signal through these fibers, both atria can contract simultaneously and in a coordinated manner that allows the process of pushing of blood into the ventricles. Correlating with their special fast conducting function, these cells have a Purkinje-like morphology. The conduction velocity is then slowed down when propagating through the AVN. The time it takes to conduct the signal through the AVN and penetrating AV bundles is approximately four times longer than the time it takes for it to be conducted from the SAN to the AVN. This delay in conduction serves to empty the atria from blood before the ventricles start to contract. It also contributes to the unidirectional blood flow between the atria and the ventricles, above and beyond the similar role played by the atrioventricular valves (AVVs).

Finally, the signal is delivered through the AV bundle, bundle branches, and Purkinje fibers in a velocity approximately 150 times faster than that of the AVN. The bundle branches run along the subendocardium of the interventricular septum and free ventricular walls and give rise to Purkinje fibers that supply the myocardium in a subendocardial-to-epicardial direction. This organization allows for a rapid and synchronous contraction of both ventricles at an order that ultimately enables blood to be "squeezed" from apex to base, toward both outflow tracts.

Cardiac myofibers have a unique property of intrinsic coupling of the electrical stimulation with mechanical contraction, which is fundamental for cardiac function. Diastole starts immediately at the end of ventricular contraction, as the cardiac muscle (myocardium) starts to relax. For a brief moment, relaxation leads to a rapid fall in ventricular pressure, without change in ventricular volume as the AVVs are still sealed off (isovolumetric relaxation). Because of the fall in ventricular pressure, the blood that has pooled in the atria during systole, along with incoming blood that constantly flows from systemic and pulmonary veins through the atria, pushes the AVV open and rapidly and passively fills the ventricles (rapid-filling phase). Next, because of the resultant pressure rise in the ventricles, the flow of blood that continues to enter the ventricles through the atria abruptly ends (diastasis phase). The last phase of diastole is active contraction of the atria, which pushes blood into the (now somewhat less compliant) ventricles and further raises their pressure ("atrial kick").

In systole, the myocardium contracts, leading to a rapid increase in intraventricular pressure. Because the aortic and pulmonary valves are shut during diastole, the sudden rise in pressure leads to closure of the AVVs. In this brief period, which is termed *isovolumetric contraction*, the change in ventricular pressure has not led to a change in ventricular volume because the blood had not yet been ejected into the aorta and pulmonary arteries. When the pressure in the ventricles exceeds the pressure in the great arteries, the aortic and pulmonary valves (semilunar valves) open and the ejection of the blood through the right and left side outflow tracts ensues (ejection phase). Simultaneously with the ejection phase, the atria relax, atrial pressure falls, and blood enters the atria and pools within it passively.

An additional level of complexity is brought about by the innervation of the autonomous nervous system (ANS). In general, the ANS influences heart rate (chronotropy), alters the rate of conduction (dromotropy), and controls myocardial contractility (inotropy) and the rate of mechanical relaxation (lusitropy). Parasympathetic postganglionic nerve terminals secrete acetylcholine that affects muscarinic (M2) receptors, whereas sympathetic postganglionic nerve terminals secrete norepinephrine that predominantly acts on the β_1-adrenergic receptors. The latter, when stimulated by catecholamines, lead to a chain of intracellular events that increases calcium influx, increases the magnitude of potassium and chloride repolarization, and shortens the refractory period. Therefore adrenergic agonists are said to be positive chronotropes, inotropes, dromotropes, and lusitropes, whereas parasympathetic agonists have the opposite effects. Heart rate is primarily regulated by opposing effects of adrenergic and cholinergic nerve terminals on the SAN and at the same time by modulation of conduction velocity of the AVN and AV bundle. Physiologically, the force of contraction represents the sum of interactions between myocardial contractility, which is positively modulated by adrenergic nerve terminals that act on β_1 receptors on ventricular myocardial myofibers (positive inotropic effect), and by the volume of blood that is present in the ventricles just before contraction (preload), as well as by the resistance in front of which contraction actually takes place (afterload).

Endocardium and Heart Valves

The endocardium lines the myocardium and contains Purkinje nerve fibers, which transmit a rhythmic action potential throughout the myocardium leading to contraction. The endocardium is lined by endothelial cells, which modulate many aspects of normal hemostasis. In normal states, the endothelial cells are antithrombotic, preventing circulating cells from attaching and thus allowing normal flow of blood through the heart and blood vessels. The endocardium is continuous with the endothelium of blood and lymphatic vessels. Normal flow of blood through the heart depends on functional valves (see Chapter 2). Properly functioning valves serve as one-way valves, allowing blood either to flow from one chamber to another (through AVVs) or to exit from the heart and enter either the pulmonary circulation (pulmonic valve) or the systemic circulation (aortic valve).

Pericardium and Epicardium

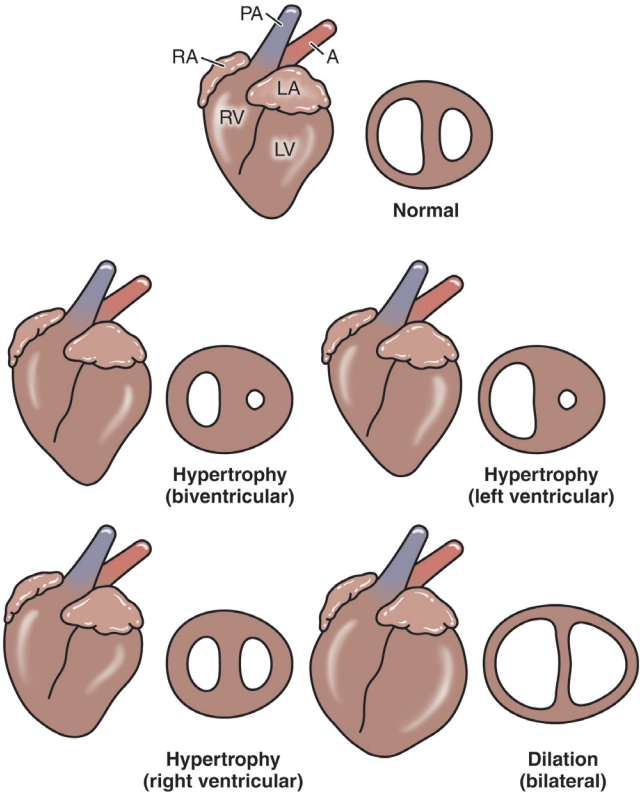
The pericardium contains a small amount of serous fluid, which allows frictionless cardiac movement of the mesothelial surfaces of the pericardium and epicardium on each other. The pericardial sac can adapt to changes in the heart size provided adequate time. The pericardium functions to provide a protective environment for cardiac function. Rapid, abnormal filling with blood (hemopericardium), fluid (hydropericardium), or exudate (suppurative pericarditis) can result in compression of the heart (cardiac tamponade), particularly the large veins, right atrium, and right ventricle. Animals can survive without a pericardial sac.

Blood and Lymphatic Vascular Systems

Blood and lymphatic vessels have several important functions. Blood vessels regulate the differential distribution of blood flow to tissues. Blood vessels actively synthesize and secrete vasoactive substances that regulate vascular tone and antithrombotic substances, which maintain the fluidity of the blood. Blood and lymphatic vessels play an important role in transporting and controlling inflammation and thrombosis. Blood and lymphatic vessels also constitute an important pathway for disease dissemination through transport of bacteria and tumor cells to distant sites.

Dysfunction/Responses to Injury

Common pathophysiologic responses of the cardiovascular system to injury are listed in Box 10-1 and shown in E-Fig. 10-8. The key characteristics of these responses are summarized here. The specific diseases that result from these responses are discussed in greater detail in the sections covering diseases that occur in all domestic animal species or that are unique to one species.



E-Figure 10-8 Types of Myocardial Hypertrophy and Dilation. Left lateral view and midventricular cross section *(not drawn to same scale)*. *A*, Aorta; *LA*, left atrium; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RV*, right ventricle. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

Box 10-1 Pathophysiologic Mechanisms of Cardiovascular Dysfunction

- Pump failure: Weak contractility and emptying of chambers, impaired filling of chambers
- Obstruction to forward blood flow: Valvular stenosis, vascular narrowing, systemic or pulmonary hypertension
- Regurgitant blood flow: Volume overload of chamber behind failing affected valve
- Shunted blood flows from congenital defects: Septal defects in heart, shunts between blood vessels
- Rupture of the heart or a major vessel: Cardiac tamponade, massive internal hemorrhage
- Cardiac conduction disorders (arrhythmias): Failure of synchronized cardiac contraction

Dysfunction: Heart Failure

Pathophysiology of Heart Failure

Heart failure is a progressive clinical syndrome in which impaired pumping decreases ventricular ejection and impedes venous return. The heart fails either by decreased blood pumping into the aorta and/or pulmonary artery to maintain arterial pressure (low-output heart failure) or by an inability to adequately empty the venous reservoirs (congestive heart failure) (see Box 10-1). Anamnestic signs of low cardiac output include depression, lethargy, syncope, and hypotension, and those of congestion include ascites, pleural effusion, and pulmonary edema.

Syndromes of Cardiac Failure or Decompensation: Congestive Heart Failure

Congestive heart failure can be right-sided, left-sided, or bilateral and can occur with cardiac dilation and/or hypertrophy (Fig. 10-5). Right-sided congestive heart failure is associated with signs of congestion in the systemic circulation (i.e., ascites and peripheral edema [Figs. 10-6 and 10-7]), whereas left-sided congestive heart failure causes signs of congestion in the pulmonary circulation (i.e., pulmonary edema and dyspnea). In small animals, *pleural effusion* is usually associated with bilateral congestive heart failure.

Heart failure may result from an inability of the heart to eject blood adequately (systolic failure), from inadequate ventricular filling (diastolic failure), or both. The resultant reduction in stroke volume (SV) leads to a decrease in cardiac output (CO) and a decrease in arterial blood pressure.

Indices of Cardiac Function

Arterial blood pressure (ABP) ~ CO × Z (where Z is the *aortic input impedance*) and CO = SV × heart rate (HR). Increases in HR increase CO linearly until a plateau is reached, at which point further increases in HR will decrease CO because of decreased diastolic filling (the Frank-Starling law of the heart). Contractility and the two coupling factors, preload and afterload, primarily determine SV. The latter increases with increases in preload and contractility and decreases in afterload. *Preload* reflects the degree of ventricular filling just before contraction. End diastolic volume (EDV) can estimate preload. The force opposing ventricular ejection is termed *afterload*. *Aortic input impedance* best describes the opposition that the ventricle encounters at the time of ejection. An increase in afterload communicates itself to the ventricles during systole by increasing wall stress. *Contractility* is a change in the heart's ability to do work when the preload, afterload, and HR are kept constant. Diastolic ventricular filling, ventricular wall motion abnormalities, space-occupying lesions, and arrhythmias also affect SV.

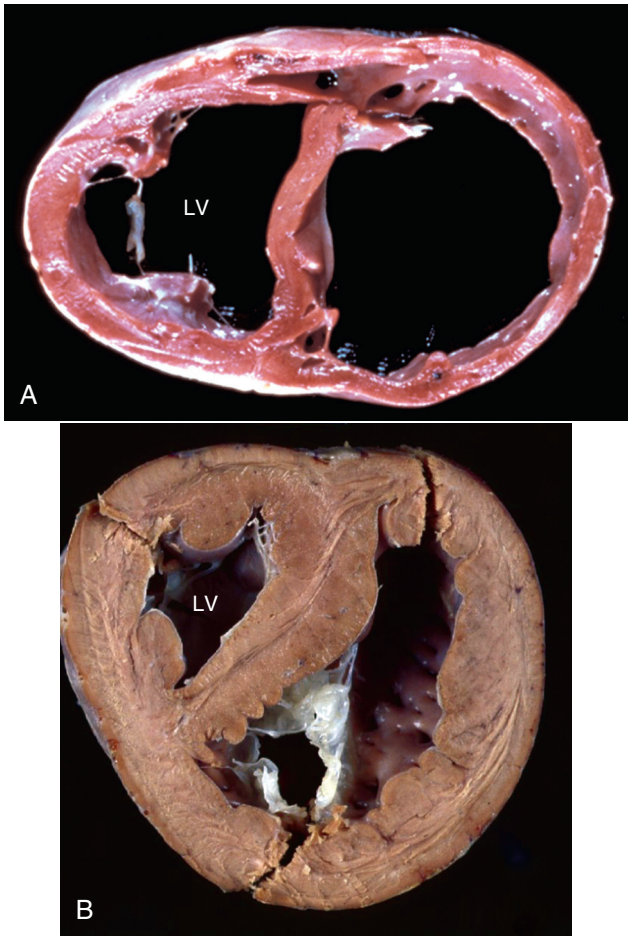


Figure 10-5 Cardiac Dilation and Hypertrophy, Heart, Transected Ventricles, Dog. A, Cardiac dilation. Note the thin walls of both dilated ventricles. *LV,* Left ventricle. **B,** Cardiac hypertrophy *(fixed tissue)*. Note that the right ventricular and left ventricular *(LV)* walls are approximately the same thickness, indicating that there is right ventricular hypertrophy. (**A** courtesy Dr. Y. Niyo, College of Veterinary Medicine, Iowa State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia. **B** courtesy College of Veterinary Medicine, University of Florida; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

The properties of the arterial system can be described by the total arterial compliance, the peripheral resistance, and the characteristic impedance. *Total arterial compliance* corresponds to the elastic properties of arteries (i.e., aorta) and reflects change in volume from a given change in pressure. *Peripheral resistance* is largely determined by small arteries and arterioles and involves steady (nonpulsatile) flow. *Characteristic impedance* is the opposition to pulsatile flow.

Left ventricular (LV) afterload is increased by an increase in peripheral resistance and characteristic impedance and a decrease in total arterial compliance. Subsequently, the left ventricle ejects into a stiff vasculature, increasing both the energetic cost to maintain blood flow and myocardial oxygen consumption (MVO_2). Characteristic impedance, a property of the proximal aorta, increases whenever the stiffness of the aorta increases or its radius becomes smaller. Peripheral resistance has a greater effect on ventricular performance than does characteristic impedance or compliance.

Systolic and Diastolic Heart Failure

Systolic heart failure is characterized by normal filling of the ventricle and a decrease in the forward stroke volume (SV). The decrease in

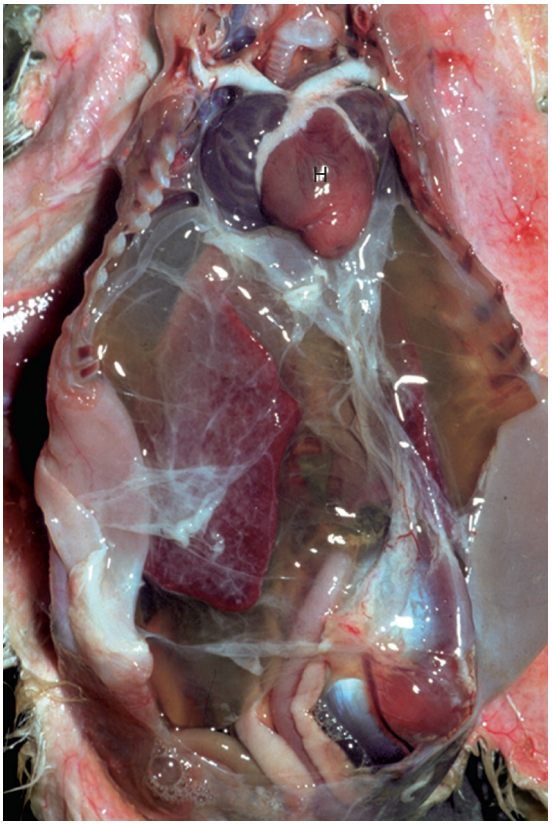


Figure 10-6 Ascites, Congestive Heart Failure, Furazolidone Cardiotoxicity, Heart and Liver, Duckling. Note prominent accumulations of serous fluid in the coelomic cavity and fibrin deposits over the surface of the liver. The heart *(H)* is dilated. (Courtesy School of Veterinary Medicine, Purdue University.)

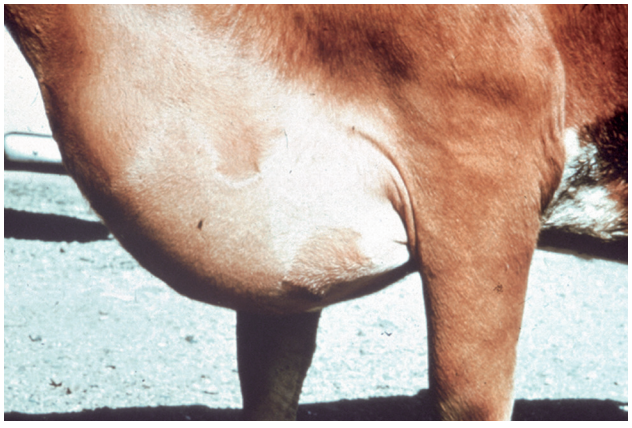


Figure 10-7 Subcutaneous Edema, High-Altitude Disease with Congestive Heart Failure ("Brisket Disease"), Presternal, Sternal, and Caudal Sternocephalic Regions (Brisket), Cow. The extensive subcutaneous edema is the result of chronic congestive heart failure. (Courtesy School of Veterinary Medicine, Purdue University.)

Box 10-2 Mechanisms Leading to Systolic Heart Failure

MYOCARDIAL FAILURE
- Dilated cardiomyopathy
- Infectious myocarditis
- Doxorubicin toxicity
- Cardiomyopathy of overload (pressure/volume)
- Myocardial infarcts
- Right ventricular cardiomyopathy

VOLUME OVERLOAD
- Valvular diseases
  - Myxomatous endocardial degeneration
  - Endocarditis
  - Rupture of mitral chordae tendineae
  - Valvular dysplasia
- PDA/VSD/ASD
- Thyrotoxicosis
- Chronic anemia
- Peripheral arteriovenous fistula

PRESSURE OVERLOAD
- Subaortic stenosis
- Pulmonic stenosis
- Systemic hypertension
- Pulmonary hypertension
  - Primary
  - Pulmonary embolism
  - Heartworm disease

ASD, Atrial septal defect; *PDA,* patent ductus arteriosus; *VSD,* ventricular septal defect.

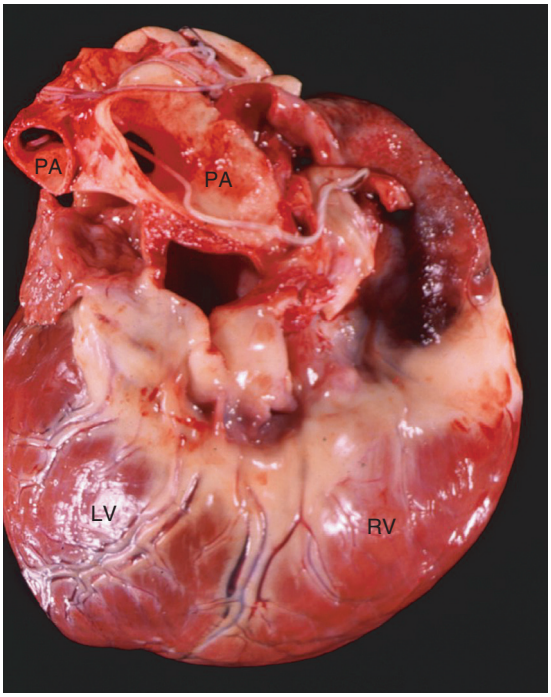
SV may result from a decreased contractility (*myocardial failure*), from a primary increase in ventricular pressure (*pressure overload*), or or from an increase in ventricular volume (*volume overload*) (Box 10-2). Myocardial failure may be primary (e.g., dilated cardiomyopathy) or may occur secondary to chronic volume or pressure overload. The most common causes for pressure overload in domestic animals are subaortic stenosis and hypertension (left-sided congestive heart failure) and heartworm disease (E-Fig. 10-9), pulmonic stenosis (see Fig. 10-32), "brisket disease" ("high-altitude disease") in cattle (see Fig. 10-7), and chronic alveolar emphysema ("heaves") in horses (see Fig. 9-13) (right-sided congestive heart failure). Leaking valves, an abnormal communication between the systemic and pulmonary circulations, or high-output states (e.g., hyperthyroidism) usually result in increased ventricular volume (increased preload). Decrease in contractility lowers the SV, CO, and ABP and negates the heart's ability to compensate for the decrease in CO. *Diastolic heart failure* is characterized by improper filling of ventricles. This dysfunction may be caused by an impaired energy ventricular relaxation, myocardial dysfunction, obstruction to ventricular filling, or pericardial abnormalities (Box 10-3).

Concentric Hypertrophy

In pressure overload states, the increase in resistance to ejected blood leads to compensatory dilation (*concentric hypertrophy*). Chamber dilation in turn helps to overcome the increased resistance and to maintain SV at the expense of MVO_2, which eventually will lead to myocardial failure.

$$\text{LV wall stress} = \text{LV pressure}\frac{\text{LV radius}}{2 \times \text{LV wall thickness}}$$

From the previous equation, it can be depicted that decreased wall stress can be achieved by decreasing LV *radius* and/or by increasing LV *wall thickness*. With a sustained pressure overload, the ventricular muscle adapts by undergoing concentric hypertrophy, which leads to an increase in wall thickness at the expense of a decrease in chamber size (decrease in ventricular radius), thus returning ventricular wall stress toward normal and increasing contractility. The



E-Figure 10-9 Dirofilariasis, Heart, Dog. Note the hypertrophy of the right ventricle *(RV)* and adult *Dirofilaria immitis* in the pulmonary artery and its branches *(PA)*. *LV,* Left ventricle. (Courtesy Dr. K. Read, College of Veterinary Medicine, Texas A&M University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

Box 10-3 Mechanisms Leading to Diastolic Heart Failure

IMPAIRED ENERGY-DEPENDENT VENTRICULAR RELAXATION OR ABNORMAL VENTRICULAR CHAMBER OR MUSCLE PROPERTIES

- Ventricular hypertrophy
  - Hypertrophic cardiomyopathy
  - Subaortic stenosis
  - Pulmonic stenosis
  - Heartworm disease
  - Systemic hypertension
- Dilated cardiomyopathy
- Myocardial infarct
- Restrictive cardiomyopathy

OBSTRUCTION TO VENTRICULAR FILLING AT VEINS, ATRIA, AND ATRIOVENTRICULAR VALVES

- Mitral stenosis
- Tricuspid stenosis
- Intracardiac obstruction by neoplasia
- Cor triatriatum

PERICARDIAL ABNORMALITIES

- Constrictive disease
- Cardiac tamponade

hypertrophied ventricle is prone to ischemia, which leads to fibrosis and an increase in collagen content that interferes with diastolic filling, decreasing preload and SV. Therefore, in the end both systolic and diastolic dysfunction occur.

Eccentric Hypertrophy

In volume overload, the increase in chamber size occurs as a result of the need to accommodate a large ventricular EDV. Dilation of the ventricle by increasing the EDV leads to a lesser increase in wall stress than in pressure overload, and it subsequently results in ventricular *eccentric hypertrophy* in order to normalize wall stress. Volume overload is marked by an eccentric hypertrophy with a mild increase in wall thickness in the face of a large increase in LV radius.

Diastole can be divided into four phases: (1) isovolumic relaxation (aortic valve closure to mitral valve opening), (2) rapid early mitral inflow (rapid filling phase during which most of ventricular filling occurs), (3) diastasis (slow filling phase during which little change occurs in ventricular volume and pressure), and (4) atrial contraction (atrial systole that actively pumps blood to the ventricle). Diastolic ventricular filling takes place during the second through fourth phases. *Relaxation* (phase 1) is a dynamic, *energy-dependent* process. β-Adrenergic stimulation improves relaxation, whereas ischemia, asynchrony of relaxation, an increase in afterload, ventricular hypertrophy, and abnormal calcium fluxes in the myocardial cells *delay relaxation*. Ventricular *compliance* (phases 2 through 4) is the ability of the heart to fill passively. Ventricular compliance is determined by volume, geometry, and the tissue characteristics of the ventricular wall. Ventricular compliance decreases with an increase in filling pressure and intrinsic myocardial stiffness (e.g., infiltrative diseases, fibrosis, and ischemia), with hypertrophy and cardiac tamponade. *Lusitropy* comprises the relaxation and filling phases. Ventricular filling may be affected by several factors, including isovolumic relaxation rate, synchrony between atrial kick and ventricular relaxation, compliance, and atrioventricular pressure gradient. The latter is the driving force for ventricular filling (which is mostly affected by intravascular volume and the degree of vasodilatation). The isovolumic relaxation rate is also an important determinant of early ventricular filling; *adrenergic stimulation* increases the rate of relaxation, improving relaxation to a greater extent than it improves contractility. Tachycardia shortens the duration of the diastasis. Loss of atrial contraction is one reason why dogs with dilated cardiomyopathy or myxomatous valvular degeneration develop heart failure when the atria start to fibrillate.

Asynchronous relaxation (decrease in the uniformity of relaxation) of the left ventricle may be observed in cats with restrictive cardiomyopathy. LV hypertrophy decreases LV compliance and leads to poor diastolic function because of an increase in cardiomyocyte size, collagen formation, and wall thickening. Constrictive pericardial disease or cardiac tamponade impose their mechanical properties on those of the ventricle during the final phases of diastole. Hence, *diastolic dysfunction* results from abnormal relaxation (early diastole), abnormal compliance (early to late diastole), or external constraint by the pericardium (tamponade).

Neuroendocrine Compensatory Mechanisms in Heart Failure

Heart failure results in chronic activation of neuroendocrine compensatory mechanisms to restore and maintain ABP. High-pressure baroreceptors in the aortic arch and carotid sinus, mechanoreceptors in the ventricular myocardium, volume receptors in the atria and great veins, and the juxtaglomerular apparatus in the kidneys can sense alteration in ABP that results from a diminished CO. A reactive neuroendocrine activation decreases parasympathetic drive (immediate and short-lived) and increases sympathetic drive (slow but long-lasting), causing vasoconstriction (increasing arterial impedance) and tachycardia. A decrease in renal blood flow leads to renin-angiotensin-aldosterone system (RAAS) activation, contributing to vasoconstriction and sodium and water retention (increases the circulating volume). To maintain ABP, the cardiovascular system allows the venous pressure to increase and redistributes CO, maintaining blood flow mostly to essential organs. The cardiomyocytes also undergo changes to adapt to ventricular dysfunction, initially by performing extra work (stable hyperfunction) but over a long period these cardiomyocytes die (exhaustion and progressive cardiosclerosis phase). The net effect of neuroendocrine activation is vasoconstriction, sodium and water retention, LV hypertrophy, and coronary and peripheral vessel remodeling.

Role of Catecholamines in the Progression of Heart Failure

Dogs with congestive heart failure have increased norepinephrine (NE) concentrations secondary to NE "spillover" into plasma, and they have decreased uptake by adrenergic nerve endings. Despite the increase in the plasma concentration of NE, there is depletion of NE from the atria and ventricles (secondary to β-adrenoreceptor downregulation), which blunts the response to sympathetic activation. In normal hearts, the ratio of β_1 to β_2 receptors is approximately 80:20, whereas in failing hearts, it approaches 60:40. The decrease in NE stores and the changes in adrenoreceptors lead to a decrease in the contractile response of the myocardial cells and in a positive chronotropic response (increased HR). Chronic adrenergic stimulation also leads to an increase in afterload and MVO_2, development of ventricular arrhythmias, and progression to left ventricular dysfunction.

Role of Baroreceptors in the Progression of Heart Failure

Baroreflex control is altered during congestive heart failure. Normally, an increase in atrial pressure (volume overload) stimulates atrial stretch receptors, inhibits the release of antidiuretic hormone (ADH), decreases sympathetic activity, and increases renal blood

flow and the glomerular filtration rate. During congestive heart failure, atrial and arterial receptors have a decreased response to stimulation, and baroreceptor function is impaired. The overall effect is a decrease in parasympathetic activity and subsequent impaired restraint on the SAN, which results in a higher HR and decreased HR variability.

Role of Renin-Angiotensin-Aldosterone System in the Progression of Heart Failure

In congestive heart failure, renin is continuously released in the juxtaglomerular apparatus of the kidneys secondary to the low CO. Consequently, perpetuation of angiotensin II (AGII) effects leads to a vicious cycle that contributes to further declines in ventricular function. These include AGII-mediated increase in afterload, increase in MVO_2, and increase in preload (through a decrease in venous capacity). AGII also stimulates the release of ADH and aldosterone (both contribute to total body water retention); the latter contributes to baroreceptor dysfunction, increased stiffness and decreased compliance of the arterial system, and increased Mg and K excretion. Increases in plasma aldosterone are associated with an inflammatory response that is thought to lead to intramural coronary artery remodeling and fibrosis. AGII stimulates growth factors, promoting remodeling in the vessels and myocardium (reduced NO synthesis or by increasing local angiotensin-converting enzyme breakdown of bradykinin). Consequently, vascular remodeling (i.e., smooth muscle hyperplasia, hypertrophy, and apoptosis) results in structural changes that further decrease the compliance of the arterial system. AGII has a key role in the development of pathologic hypertrophy, exerting cytotoxic effects on the myocardium, causing myocyte necrosis, and contributing to myocardial loss.

Role of Natriuretic Peptides and Nitric Oxide in the Progression of Heart Failure

The natriuretic peptides are counterregulatory hormones involved in volume homeostasis and cardiovascular remodeling, and they promote natriuresis, diuresis, peripheral vasodilatation, and inhibition of the RAAS. They consist of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), C-type natriuretic peptide (CNP), dendraspis natriuretic peptides (DNP), and urodilatin. Despite the natriuretic peptides' beneficial effects during congestive heart failure, their release is overridden by the release of agents that cause vasoconstriction and sodium and water retention. NO regulates cardiac function through both vascular-dependent (coronary vessel tone, thrombogenicity, proliferative and inflammatory properties, and cellular cross-talk that supports angiogenesis) and vascular-independent (effects on several aspects of cardiomyocyte contractility, from the fine regulation of excitation-contraction coupling to modulation of autonomic signaling and mitochondrial respiration) effects. Overall, NO may play an important compensatory role in congestive heart failure during resting conditions by antagonizing neuroendocrine vasoconstrictive forces.

Summary of Pathophysiology of Heart Failure

In summary, long-term overload-induced cardiac hypertrophy is accompanied by myocardial cell death and cardiac fibrosis (i.e., cardiomyopathy of overload). The hypertrophied ventricle outstrips its blood supply. The relative decrease in oxygen delivery worsens the increased MVO_2 demand. The ischemia resulting from hypertrophy and stretching beyond certain limits decreases contractile strength and eventually leads to loss of contractile proteins within these cells or loss of these cells. These processes result in atrophy of the affected myocardium and lead to the development of multifocal myocardial fibrosis and atrophy, which consequently interferes with diastolic function. When early interstitial fibrosis progresses to individuation of cardiac myocytes (with progression of hypertrophy), both systolic and diastolic functions are impaired. Therefore congestive heart failure is a progressive and irreversible disease with myocardial cell death and functional myocardial failure that ultimately leads to death. The cycles resulting in progressive left heart failure are detailed in Fig. 10-8.

Cardiac Syncope

Cardiac syncope, an acute expression of cardiac disease, is characterized clinically by collapse, loss of consciousness, and extreme changes in heart rate and blood pressure, and with or without demonstrable lesions. Syncope can be caused by massive myocardial necrosis, ventricular fibrillation, heart block, arrhythmias, and reflex cardiac inhibition (e.g., that associated with high intestinal blockage).

Types of Heart Failure

A wide variety of experimental animal models of heart failure exist (E-Table 10-1). The models have been used to develop an understanding of human cardiac disease.

Clinical Diagnostic Procedures

For information on this topic, see E-Appendix 10-3 at www.expertconsult.com.

Responses to Injury: Myocardium

Common responses of the myocardium to injury are listed in Box 10-4.

Disturbances of Circulation

Hemorrhage: Trauma (Physical Injury). See section on Disorders of Domestic Animals: Myocardium, Disturbances of Circulation, Hemorrhage: Trauma (Physical Injury).

Disturbances of Growth

Myocardial Hypertrophy. See the discussion on hypertrophy in Chapter 1.

Hypertrophy of the myocardium represents an increase in muscle mass, which is the result of an increase in the size of cardiac muscle cells (Fig. 10-9; also see Fig. 10-5, *B* and E-Fig. 10-9). Two anatomic forms of hypertrophy are recognized. Eccentric hypertrophy results in a heart with enlarged ventricular chambers and walls of normal to somewhat decreased thickness. Volume-overload hypertrophy is characterized by new sarcomeres being assembled in series within sarcomeres resulting in increased length of myofibers. In concentric hypertrophy, the heart is characterized by small ventricular chambers and thick walls. Pressure-overload hypertrophy is the result of the formation of new sarcomeres assembled predominantly in parallel to the long axes of cells resulting in an increase in thickness of the myofiber. Some cats with hyperthyroidism have a cardiac hypertrophy that is mediated by enhanced production of myocardial contractile proteins under the influence of increased concentration of circulating thyroid hormones (Fig. 10-10). The hypertrophy is reversible on return to euthyroidism.

Three stages of myocardial hypertrophy are recognizable: (1) initiation, (2) stable hyperfunction, and (3) deterioration of function associated with degeneration of hypertrophied myocytes. Microscopically, in myocardial hypertrophy, the myocytes are enlarged and have large nuclei (Fig. 10-11).

Physiologic Atrophy. Physiologic atrophy of heart muscle may occur in confined animals and also occurs as a result of

E-Table 10-1 Experimental Models of Heart Failure

Experimental Model	Experimental Method	Species
Pressure loading	Pulmonary artery banding	Rat, dog, pig, sheep, pony
	Aortic constriction	Rat, rabbit, dog, sheep
	Supravalvular aortic constriction	Dog
	Aortic valve stenosis	Rabbit, dog
	Pulmonary valve stenosis	Dog
	Experimental hypertension	Rat, dog
Volume loading	Fluid overload	Baboon
	Aorta-to-vena cava fistula	Rat, dog
	Aortic valve incompetence	Rat, rabbit
	Atrial septal defect	Cat
Myocardial infarction	Sustained atrial pacing	Dog
	Coronary ligation	Dog, pig
	Controlled occlusion–subclavian-to-carotid shunt	Dog
	Coronary embolism	Dog, calf, pig
	Thrombus generation	Dog
	Chronic hypoxia	Rat
Cardiomyopathy and other conditions	Left ventricular Dacron patch	Dog
	Spontaneous cardiomyopathy	Hamster, mouse, cattle, rat, turkey, cat, dog
	Barbiturate overdose	Dog
	Furazolidone cardiomyopathy	Turkey, duckling
	Adriamycin cardiomyopathy	Rat, dog, mouse, pig
	Isoprenaline	Rat
	Noradrenaline	Dog
	Amphetamine	Rat
	Cobalt chloride	Rat, pig
	Vitamin E deficiency	Rat, mouse, calf, lamb
	Alcohol intoxication	Rat
	Coxsackie viral myocarditis	Mouse
	Viral encephalomyocarditis	Mouse
	Altered cardiac development and/or function	Transgenic mice

Modified from Smith HJ, Nuttall A: *Cardiovasc Res* 19:181-186, 1985.

E-Appendix 10-3 Clinical Diagnostic Procedures

The array of diagnostic tools available to the veterinarian to detect and evaluate changes in cases of cardiac disease has increased dramatically in the past several decades as many procedures have been adapted from use in human medicine. Procedures include physical examination, radiography, electrocardiography, echocardiography, angiocardiography, and cardiac catheterization. Cardiac myocardial damage can be detected by increased activity of serum enzymes and isoenzymes, such as creatine kinase (CK), lactate dehydrogenase (LDH), troponin T (TnT), troponin I (TnI), and aspartate aminotransferase (AST), which are specifically leaked from injured cardiac muscle cells. Also, increased plasma concentrations of plasma natriuretic peptides (A type [atrial] ANP and B type [brain BNP) may indicate cardiac disease. These hormones are synthesized and released by cardiac muscle cells in increased amounts during cardiac dysfunction. In research studies of cardiac diseases in animals, endomyocardial biopsies have been used to assess the light microscopic and ultrastructural alterations during the course of the disease.

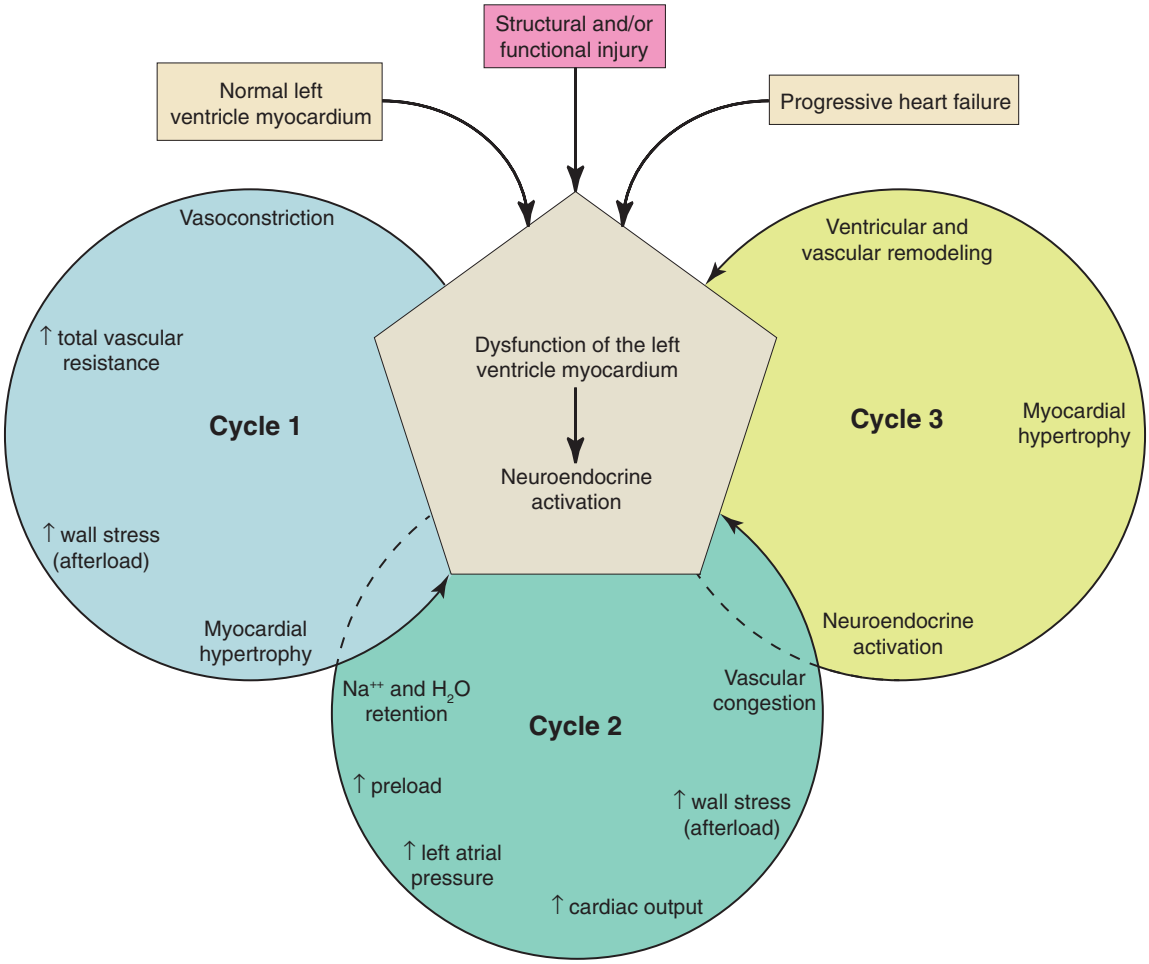


Figure 10-8 Pathophysiology of Left Heart Failure. Pathophysiologic cycles that lead to progressive left heart failure. *Cycle 1:* Increased total vascular resistance increases myocardial wall stress that induces myocardial hypertrophy. *Cycle 2:* Water and sodium retention leads to increased preload and vascular congestion. *Cycle 3:* Neuroendocrine activation leads to myocardial and vascular remodeling. All cycles contribute to further myocardial dysfunction and neuroendocrine activation. (Adapted from Ettinger SJ, Feldman EC: *Textbook of veterinary internal medicine*, ed 6, St. Louis, 2005, Saunders.)

Box 10-4 Responses of the Myocardium to Injury

DISTURBANCES OF CIRCULATION
Hemorrhage
Effusions
Thrombosis and embolism

DISTURBANCES OF GROWTH
Atrophy (dilation)
Hypertrophy
Agenesis (aplasia), hypoplasia, dysplasia (dysgenesis)
Developmental errors, congenital anomalies
Neoplasia (neoplastic transformation)

CELL DEGENERATION AND DEATH
Cell and metabolic dysfunction
Oncotic necrosis
Apoptosis

INFLAMMATION

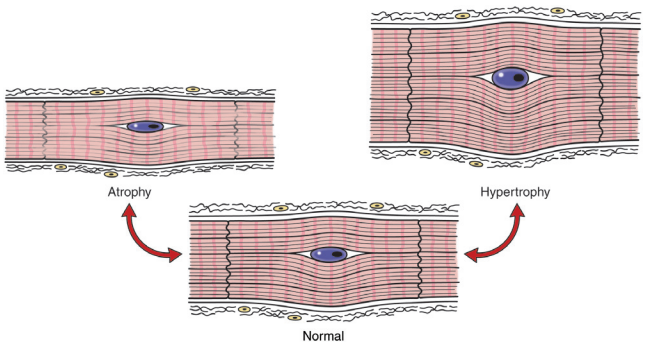


Figure 10-9 Cardiac Muscle Cells. Growth disturbances of atrophy and hypertrophy. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

decompensation of cardiac myocytes in chronic congestive heart failure (see Fig. 10-5, *A*). Initially, these myocytes respond through hypertrophy with increased contractile force according to the Frank-Starling phenomenon. However, stretching beyond certain limits decreases contractile strength and eventually leads to loss of contractile proteins within these cells or loss of these cells resulting in atrophy of the affected myocardium (see Fig. 10-9).

Neoplastic Transformation. See Chapter 6 for a discussion of the mechanisms involved in neoplastic transformation. Rhabdomyomas and rhabdomyosarcomas are primary tumors that originate from the myocardium in domestic animals. Fibrosarcomas also occur rarely. Numerous types of secondary tumors, such as

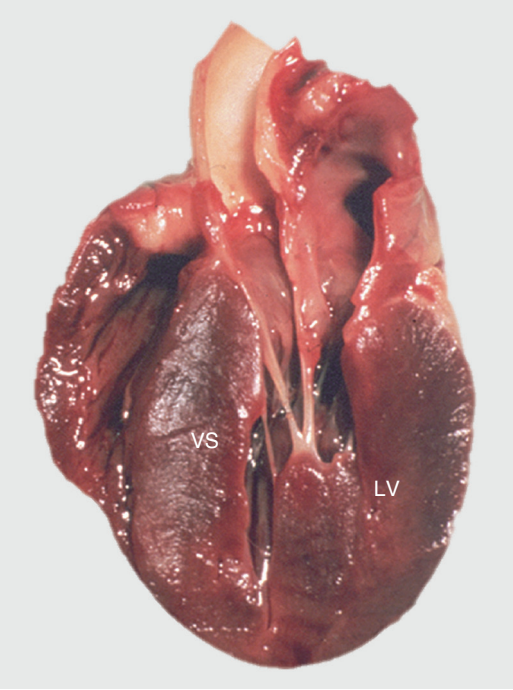


Figure 10-10 Left Ventricular Hypertrophy, Hyperthyroidism, Heart, Bisected, Cat. Note prominent thickening of the left ventricular *(LV)* free wall. The ventricular septum *(VS)* is also thickened. (Courtesy School of Veterinary Medicine, Purdue University.)

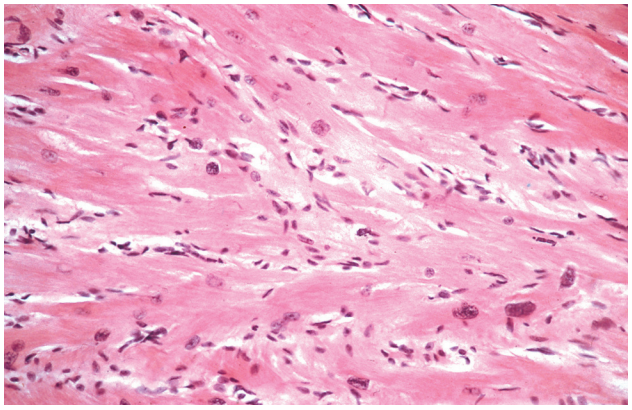


Figure 10-11 Hypertrophic Cardiomyopathy, Myocyte Hypertrophy, Heart, Myocardium, Cat. Cardiac myocytes are hypertrophied, and there is an increase in interstitial fibroblasts. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

lymphosarcomas, metastasize to the myocardium and are discussed in this chapter and other chapters of this book. Hemangiosarcomas are tumors of blood vessels of the myocardium of the right atrium and are discussed later.

Cell Degeneration and Death

Sublethal cardiac muscle cell injuries include lipofuscinosis, fatty degeneration, myocytolysis, and vacuolar degeneration (Fig. 10-12; see Chapter 1). Histopathologic study of sections of the myocardium is substantially limited with respect to specific diagnoses and only rarely can an etiologic diagnosis be made from the morphologic alterations. This inadequacy exists because the spectrum of pathologic reactions is limited, and many agents that damage the heart produce similar lesions. Myocardial necrosis can be confused with

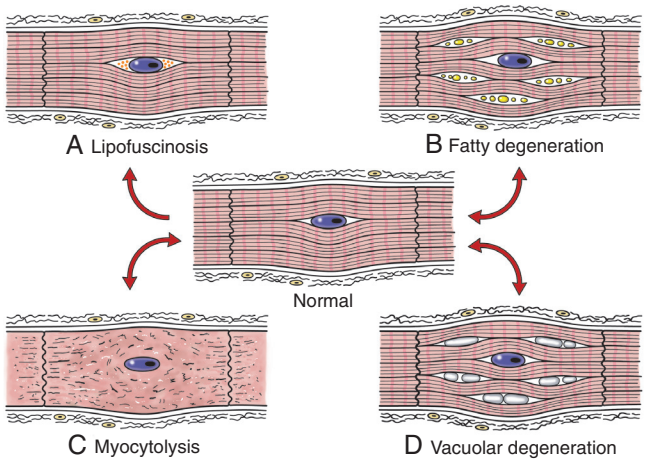


Figure 10-12 Various Sublethal Cardiac Muscle Cell Injuries. A, Lipofuscinosis. **B,** Fatty degeneration. **C,** Myocytolysis. **D,** Vacuolar degeneration. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

myocardial inflammation with secondary necrosis because both lesions have substantial leukocytic infiltration. Some animals that die peracutely from cardiac failure lack detectable microscopic alterations and are presumed to have suffered from an arrhythmic episode resulting in syncope. Hearts with long-standing myocardial damage have foci of fibrosis, regardless of the cause of the loss of myocytes. Correlation between the severity of clinical cardiac disease and the severity of myocardial injury can be poor: A small lesion at a critical site, such as a portion of the conduction system, can be fatal, whereas a widespread myocardial lesion, such as myocarditis, can be asymptomatic.

Cardiac myofibers can respond to toxins in a variety of ways—apoptosis, myofibrillar lysis, and coagulation necrosis are but a few mechanisms that may result from toxic exposure. A long list of toxins are responsible for causing myocardial injury; some of the most frequently observed current examples are ionophore toxicity in horses and ruminants, vitamin E–selenium deficiency in the young of many species, "heart-brain syndrome" of dogs (see Fig. 10-82), anthracycline toxicity in dogs, and gossypol toxicosis in pigs (Box 10-5). In various localized areas throughout the world, numerous deaths in ruminants have resulted from consumption of poisonous plants such as *Acacia georginae* and *Dichapetalum cymosum*.

Cardiotoxicity has emerged as a significant clinical entity in veterinary medicine in recent years with the growing use of antineoplastic drugs in small animal practice and the widespread use of growth promotants in ruminants (see Fig. 10-49). The mechanisms of cardiotoxicities include (1) exaggerated pharmacologic action of drugs acting on cardiovascular tissues, (2) exposure to substances that depress myocardial function, (3) direct injury of cardiac muscle cells by chemicals, and (4) hypersensitivity reactions.

Oncotic Necrosis. Necrosis of cardiac muscle cells is generally followed by leukocytic invasion and phagocytosis of sarcoplasmic debris (Fig. 10-13; also see Figs. 15-13 and 15-14). The end result is persistence of collapsed sarcolemmal "tubes" of basal lamina surrounded by condensed interstitial stroma and vessels. Lesions with severe disruption of the myocardium have residual changes of fibroblastic proliferation and collagen deposition to form scar tissue. Regeneration of cardiac muscle cells generally does not occur, except in less evolved animals, such as amphibians and fish, and in certain inbred mouse strains. The continual contraction of intact cardiac muscle cells impairs the mechanisms for regeneration. Also,

Box 10-5 Causes of Myocardial Necrosis in Animals

NUTRITIONAL DEFICIENCIES

Vitamin E–selenium, potassium, copper, thiamine, magnesium

TOXICITIES

Cobalt, catecholamines, vasodilator antihypertensive drugs, methylxanthines (theobromine, theophylline, caffeine), ionophores (monensin, lasalocid, salinomycin, maduramicin, narasin), vitamin D and calcinogenic plants (*Cestrum diurnum*, *Trisetum flavescens*, *Solanum malacoxylon*, *Solanum torvum*), other poisonous plants (*Acacia georginae*, *Gastrolobium* spp., *Oxylobium* spp., *Dichapetalum cymosum*, *Persea americana*, *Cassia occidentalis*, *Cassia obtusifolia*, *Karwinskia humboldtiana*, *Ateleia glazioviana*, *Eupatorium rugosum*, *Adonis aestivalis*, *Pachystigma pygmaeum*, *Fadogia homblei*, *Pavetta harborii*, *Tetrapterys multiglandulosa*), blister beetles (*Epicauta*), high-erucic-acid rapeseed oil, brominated vegetable oils, gossypol, T-2 mycotoxin, sodium fluoracetate (compound 1080), selenium, uremia

PHYSICAL INJURIES AND SHOCK

Central nervous system lesions and trauma ("heart-brain syndrome"), gastric dilation and volvulus, stress, overexertion, electrical defibrillation, hemorrhagic shock

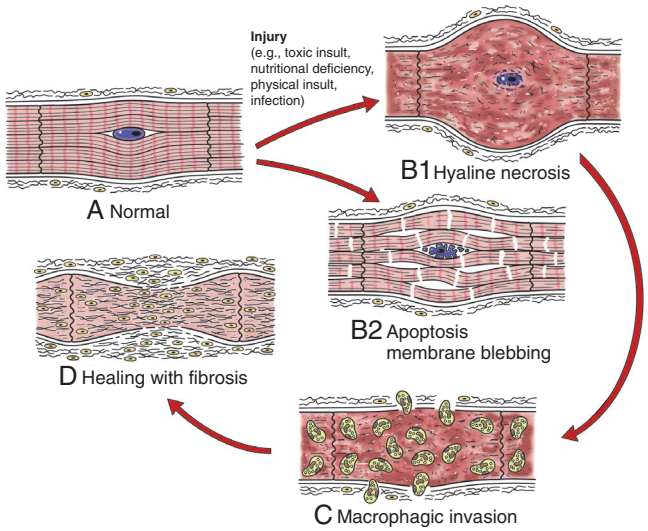


Figure 10-13 Sequential Events in Myocardial Necrosis. A, Various injuries lead to **(B1)** hyaline necrosis or **(B2)** apoptosis membrane blebbing. **C,** Healing with phagocytosis of cellular debris by macrophages, and **(D)** subsequent healing with fibrosis, rather than by regeneration. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

in hearts of neonatal animals and more often in avian hearts, a limited amount of myocyte regeneration has been reported. Hyperplasia of myocytes is a normal component of cardiac growth in fetal development and during the first few weeks of life. Thereafter, proliferation ceases and "normal growth" is the result of hypertrophy until cell size normal for each species is reached. Recent studies indicate that stem cells exist in adult animal and human hearts, and with myocardial injury, these cells may differentiate into cardiac muscle cells. However, the extent of myocyte regeneration is probably minimal.

Apoptosis. Apoptosis (programmed cell death of cardiac myocytes) is increasingly recognized for its role in the development of various myocardial lesions and cardiac diseases (see Chapter 1). These conditions include cardiac development, ischemic injury, several types of experimentally induced heart failure (ischemia-reperfusion, hypoxia, and pressure-overload hypertrophy), and cardiotoxicity. In some cell systems, apoptosis can be triggered by the presence of excessive amounts of oxygen free radicals. Cells dying by apoptosis shrink and form apoptotic bodies. In contrast to cell death by necrosis, apoptosis is not accompanied by an inflammatory reaction and fibrosis.

Fatty Infiltration. Fatty infiltration is the presence of increased numbers of lipocytes interposed between myocardial fibers. The lesion is associated with obesity and age and appears as abundant epicardial and myocardial deposits of adipose tissue. Grossly, the myocardium has irregular layers of adipose tissue infiltrating normal myocardium. The atria and right ventricle are most often affected.

Fatty Degeneration. Fatty degeneration (fatty change) is the accumulation of abundant lipid droplets in the sarcoplasm of myocytes. Microscopically, affected myocytes have numerous variably sized spherical droplets that appear as empty vacuoles in paraffin sections but stain positively for lipids with lipid-soluble stains in frozen sections. This lesion occurs with systemic disorders, such as severe anemia, toxemia, and copper deficiency, but is seen much less often in the heart than in the liver and kidneys (also see Chapter 1).

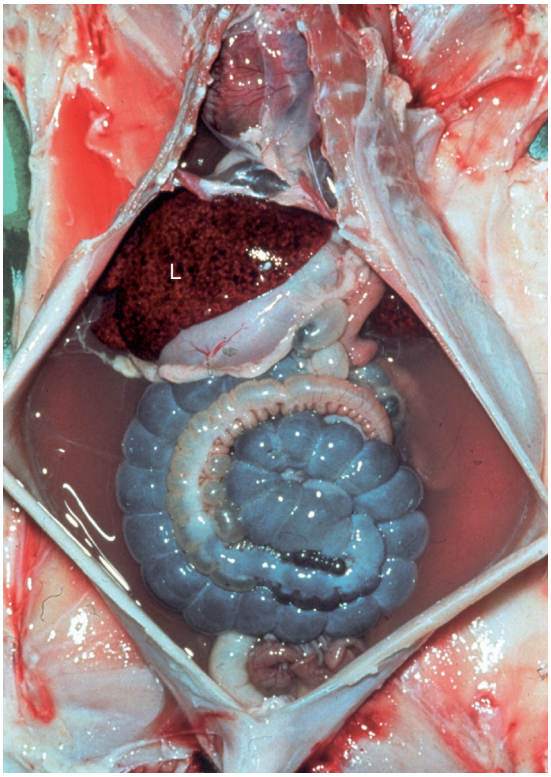
Hydropic Degeneration. Hydropic degeneration, a distinctive microscopic alteration in cardiac muscle cells, is associated with chronic administration of anthracyclines, a group of antineoplastic drugs. Chronic passive congestion with ascites and cardiac dilation may result (E-Figs. 10-10 and 10-11); see Figs. 10-5, *A* and 10-6). Affected fibers have extensive vacuolization of sarcoplasm that is initiated by distention of elements of sarcoplasmic reticulum and eventually ends in lysis of contractile material (E-Figs. 10-12 and 10-13).

Hydropic degeneration of cardiac muscle cells may also result from drug-induced injury to mitochondria. Antiretroviral drugs, such as nucleoside reverse transcriptase inhibitors (zidovudine or AZT), are linked to this distinctive lesion. Scattered cardiac muscle cells appear swollen with pale sarcoplasm by light microscopy. Electron microscopy reveals extensive mitochondrial swelling and disruption of cristae with subsequent formation of myelin figures from the membrane debris of damaged mitochondria.

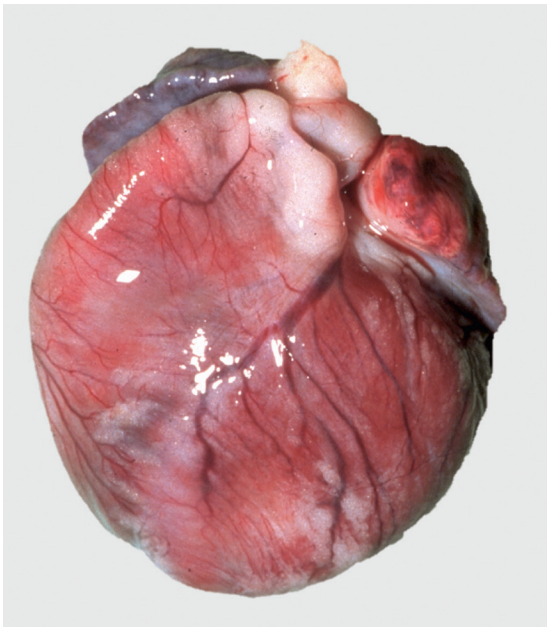
Myofibrillar Degeneration. Myofibrillar degeneration (myocytolysis) represents a distinctive sublethal injury of cardiac muscle cells. Affected fibers have pale eosinophilic sarcoplasm and lack cross-striations. Ultrastructurally, myofibrils have a variable extent of dissolution (myofibrillar lysis). This lesion has been described in furazolidone cardiotoxicity in birds (Fig. 10-14; E-Fig. 10-14) and potassium deficiency in rats.

Lipofuscinosis. Lipofuscinosis (brown atrophy) of the myocardium occurs in aged animals and in animals with severe cachexia, but it also has been described as a hereditary lesion in healthy Ayrshire cattle. Severely affected hearts appear brown and microscopically have clusters of yellow-brown granules at the nuclear poles of myocytes. These granules represent intralysosomal accumulation of membranous and amorphous debris (residual bodies).

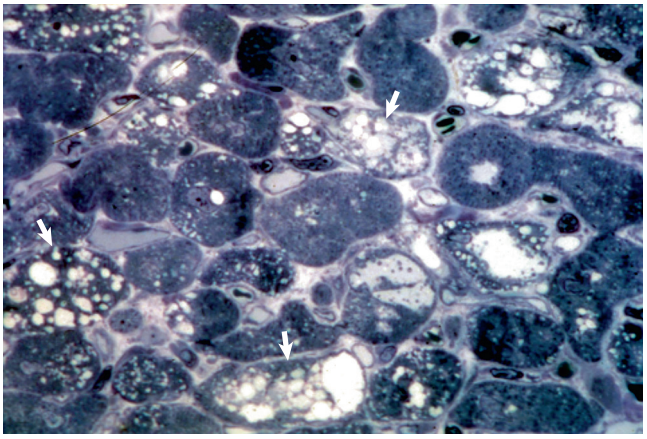
Mineralization. Myocardial mineralization (calcium) is a prominent feature in several diseases, such as hereditary calcinosis in mice, cardiomyopathy in hamsters, vitamin E–selenium



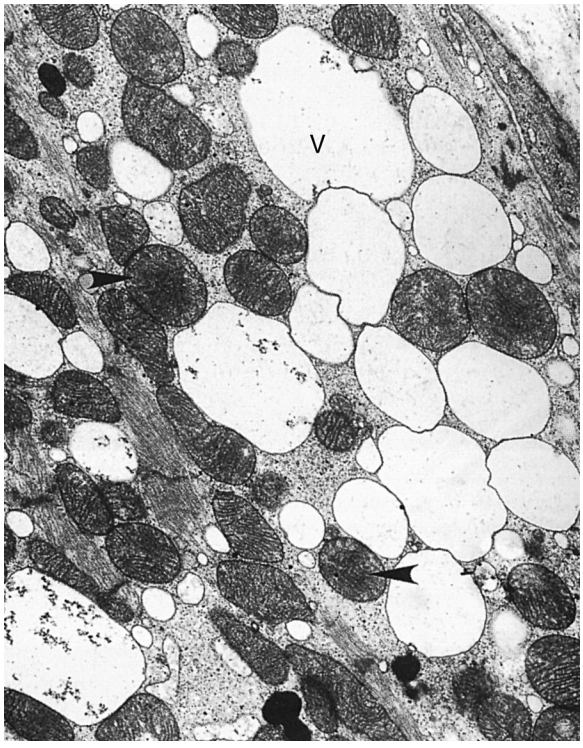
E-Figure 10-10 Chronic Passive Congestion, Doxorubicin Cardiotoxicity, Congestive Heart Failure, Liver, Ascites, Rabbit. Note the light-red-stained transparent fluid in the peritoneal cavity (ascites) and the mottled liver *(L)* characteristic of chronic passive congestion. (Courtesy School of Veterinary Medicine, Purdue University.)



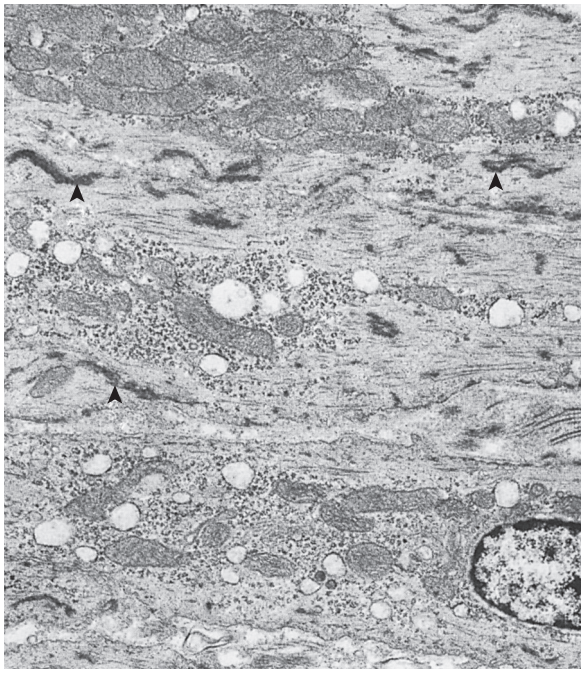
E-Figure 10-11 Cardiac Dilation, Doxorubicin Cardiotoxicity, Heart, Rabbit. All cardiac chambers are dilated. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-12 Myocardial Vacuolar Degeneration, Chronic Doxorubicin Cardiotoxicity, Heart, Section of Myocardium, Dog. The affected myocytes have prominent sarcoplasmic vacuolation *(arrows)*. Plastic-embedded, toluidine blue–stained section. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-13 Sarcoplasmic Vacuolation, Chronic Doxorubicin Cardiotoxicity, Heart, Section of Myocardium, Dog. The prominent sarcoplasmic vacuolation *(V)* is produced by distention of elements of sarcoplasmic reticulum. Even though the myofibrils have extensive lysis, mitochondria *(arrowheads)* are intact. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-14 **Myofibrillar Lysis, Furazolidone Cardiotoxicity, Heart, Ventricular Myocardium, Duckling.** Affected myocytes have extensive dissolution of myofibrils with scattered free myofilaments and dense clumps of Z-band material *(arrowheads)*. Other organelles appear normal. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)

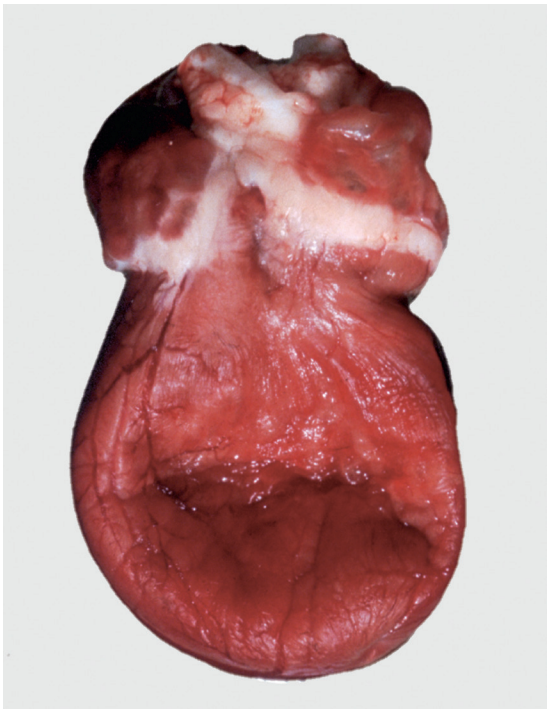


Figure 10-14 **Ventricular Dilation, Furazolidone Cardiotoxicity, Heart, Duckling.** Note that the dilated ventricles have collapsed once the blood was removed. (Courtesy School of Veterinary Medicine, Purdue University.)

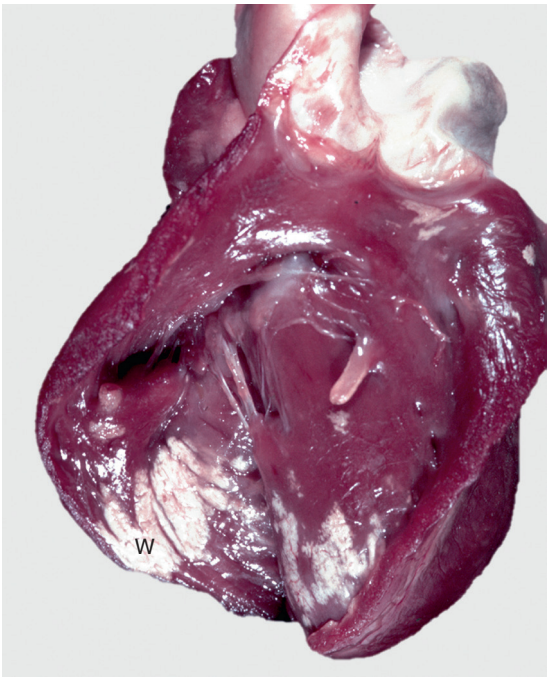


Figure 10-15 **Calcification, Vitamin E–Selenium Deficiency, Myocardial Necrosis, Heart, Right Ventricle, Lamb.** The multiple white (*W*) subendocardial lesions are areas of calcified necrotic cardiac myocytes. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

deficiency in sheep and cattle (Fig. 10-15), vitamin D toxicity in several species, calcinogenic plant toxicosis in cattle ("Manchester wasting disease"), and spontaneous myocardial calcification in aged rats and guinea pigs.

Myocardial Necrosis. Myocardial necrosis can result from a number of causes, including nutritional deficiencies, chemical and plant toxins, ischemia, metabolic disorders, heritable diseases, and physical injuries (see Box 10-5). Grossly, affected areas appear pale initially, and some progress to prominent yellow to white (see Fig. 10-49), dry areas made gritty by dystrophic mineralization. The lesions are focal, multifocal, or diffuse. The most frequent sites of focal lesions are the left ventricular papillary muscles and the subendocardial myocardium, especially when such lesions are related to transient reduction of vascular perfusion. These lesions can be overlooked at necropsy unless multiple incisions are made in the ventricular myocardium. In diseases with diffuse cardiac necrosis, such as white muscle disease of calves and lambs due to vitamin E–selenium deficiency, the discrete white lesions can be readily observed beneath the epicardial and endocardial surfaces (Fig. 10-16).

Microscopically, the appearance depends on the age of the lesions. Fibers in areas of recent necrosis often appear swollen and hypereosinophilic (hyaline necrosis). Striations are indistinct, and nuclei are pyknotic. Necrotic fibers often have scattered basophilic granules (Fig. 10-17) that represent calcified mitochondria and can be confirmed by electron microscopy (E-Fig. 10-15). In a second pattern of necrosis, affected myocytes have a "shredded" appearance because of hypercontraction and the formation of multiple transversely oriented bars of disrupted contractile material (often termed *contraction band necrosis*) (E-Fig. 10-16). A third pattern is seen in necrotic myocytes in large areas of ischemic necrosis (infarcts). These myocytes have features of coagulation necrosis and have relaxed rather than hypercontracted contractile elements.

Within 24 to 48 hours after injury, necrotic areas are infiltrated by inflammatory cells, mainly macrophages and a few neutrophils; these phagocytose and lyse the necrotic cellular debris (E-Fig. 10-17). In early stages of healing of necrosis, it is often difficult to distinguish the lesions from those found in some types of myocarditis (see later discussion). Later, when necrosis has progressed somewhat, lesions consist of persistent stromal tissue (interstitial fibroblasts, collagen, and capillaries) and empty "tubes" of basal laminae formerly occupied by necrotic myocytes (see Chapter 15). The healing phase is characterized by proliferation of connective tissue cells (fibroblasts) (Fig. 10-18) and by deposition of connective tissue products (collagen and elastic tissue and acid mucopolysaccharides). Grossly, these areas with healing of myocardial necrosis appear as white, firm, contracted scars.

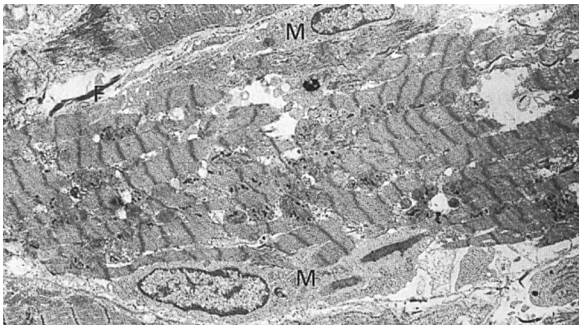
The outcome of myocardial necrosis varies, depending on the extent of the damage:

- Many animals die unexpectedly of acute cardiac failure if the myocardial damage is extensive.
- Early deaths from necrosis-related arrhythmias also occur when cardiac conduction is disrupted.
- Some cases eventually develop cardiac decompensation and die with cardiac dilation, scarring, and lesions of chronic congestive failure.

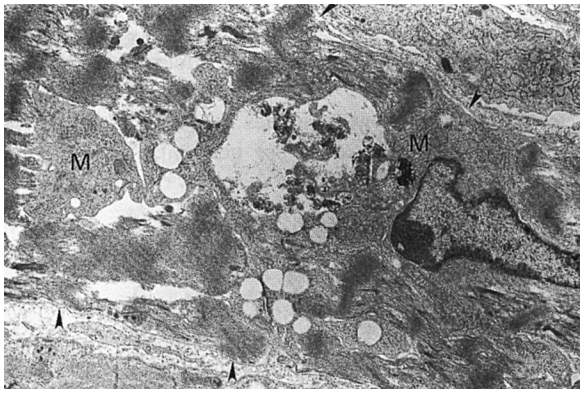
Hearts with minimal damage have only microscopically detectable myocardial fibrosis when death eventually occurs from other diseases.

Inflammation

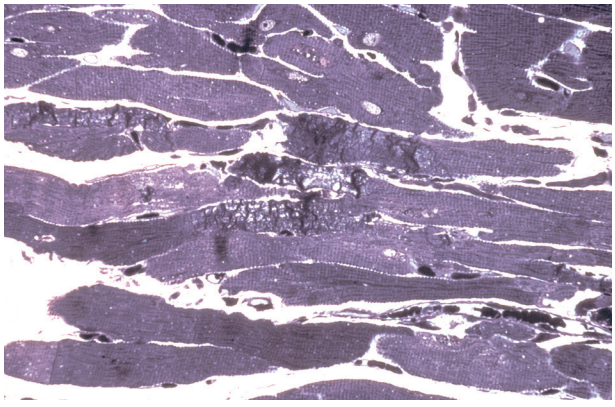
Myocarditis. The various infectious diseases that cause myocarditis in animals are summarized in Box 10-6. Myocarditis generally



E-Figure 10-15 Myocardial Necrosis, Monensin Toxicosis, Necrotic Myocyte, Heart, Longitudinal Section, Calf. The necrotic myocyte *(center)* has disrupted myofibrils, damaged mitochondria with matrical densities, and several invading macrophages *(M)*. *F,* Fibrin. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-17 Myocardial Necrosis, Monensin Toxicosis, Heart, Section of Myocardium, Calf. Necrotic myocyte has disrupted contractile material invaded by a macrophage *(M)*. The basal lamina of the necrotic myocyte is noted by *arrowheads*. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-16 Myocardial Necrosis, Electric Shock Overdose by Defibrillator, Heart, Dog. The dark shredded segments of myocytes are due to acute contraction band necrosis. The time interval between defibrillation and the fixation of the heart was 24 hours. Plastic-embedded, toluidine blue–stained section. (Courtesy School of Veterinary Medicine, Purdue University.)

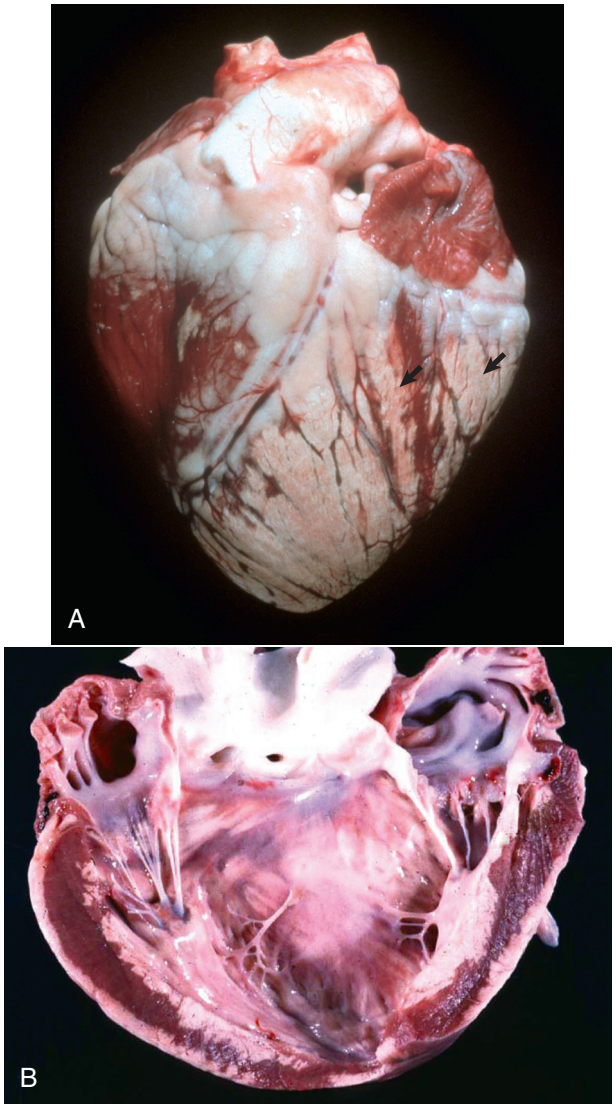


Figure 10-16 Myocardial Necrosis, Vitamin E–Selenium Deficiency, Heart, Left Ventricular Myocardium, Calf. A, Note the prominent white chalky areas of necrosis with mineralization *(arrows)* of the myocardium. **B,** Similar necrosis is subepicardially and subendocardially in the sectioned free walls of the left ventricle and subendocardially in the myocardium of the ventricular septum *(center)*. (**A** courtesy School of Veterinary Medicine, Purdue University. **B** courtesy Dr. P.N. Nation, Animal Pathology Services; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

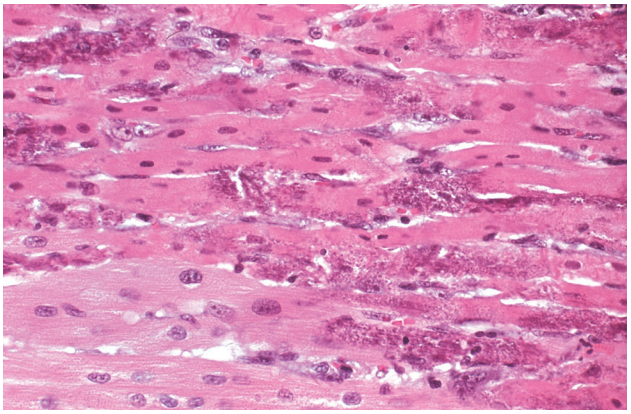


Figure 10-17 Acute Myocardial Necrosis with Mineralization, Minoxidil Cardiotoxicity, Heart, Ventricular Myocardium, Pig. The darker red myocytes are necrotic, and some are mineralized *(purplish areas)*. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

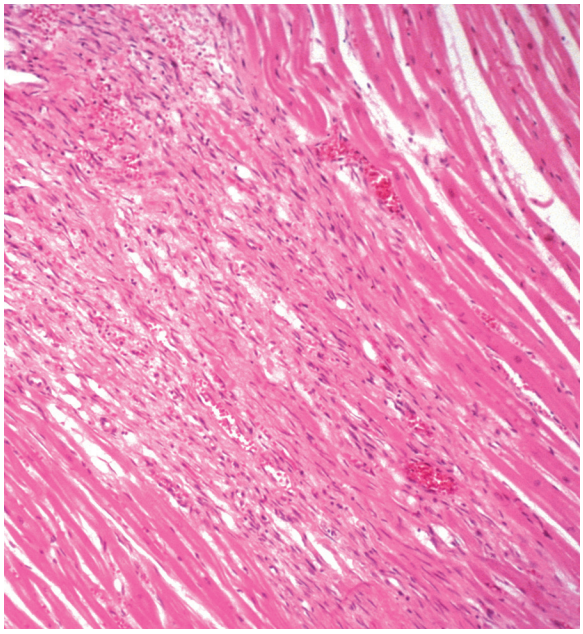


Figure 10-18 Healing, Postmyocardial Necrosis, Heart, Ventricle, Dog. The necrotic myocytes have been removed by phagocytosis by macrophages *(not seen here)*, and the area is now undergoing fibrosis. H&E stain. (Courtesy Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)

is the result of infections spread hematogenously to the myocardium and occurs in various systemic diseases. Infrequently, the heart is the primary location in affected animals and responsible for death. Types of inflammation provoked by infectious agents that produce myocarditis include suppurative, necrotizing, hemorrhagic, lymphocytic, and eosinophilic. Suppurative myocarditis results from localization of pyogenic bacteria in the myocardium (Fig. 10-19) that are trapped in thromboemboli most commonly originating from vegetative valvular endocarditis on the mitral and aortic valves. Septic infarcts with pale, disseminated lesions may be grossly evident in the myocardium. These foci consist of neutrophils and necrotic myocytes that form abscesses.

The pathogenesis and expected outcome of cases of myocarditis remain an important area of research because of the severity of this lesion in cardiac failure in human beings. The sequelae to myocarditis include (1) complete resolution of lesions, (2) scattered residual myocardial scars, or (3) progressive myocardial damage with acute or, in some cases, chronic cardiac failure as secondary dilated (congestive) cardiomyopathy. In experimental studies of myocarditis induced in mice by coxsackie B virus, the severity of myocarditis was influenced by the virulence of the virus and mouse strain and was enhanced by host factors such as young age, male sex, pregnancy, poor nutrition, whole-body ionizing radiation, cold environmental temperatures, alcohol ingestion, exercise, and cortisone administration. Much of the myocardial damage in coxsackie B virus infection is induced by immunologic reactions (with T lymphocyte involvement) rather than by direct viral injury.

Responses to Injury: Cardiac Conduction System

In domestic animals, injury of the cardiac conduction system involves forms of cell degeneration and death, inflammation, and

fibrosis. The response to injury of the conduction system is poorly documented because histopathology of the conduction system is labor-intensive and rarely performed. In rare cases in which histopathology and electrocardiographic studies were available, atrial and/or ventricular origin of arrhythmia was associated with inflammation, degeneration, and fibrosis along the cardiac conduction system (Fig. 10-20).

Box 10-6 Diseases that Cause Myocarditis in Animals

VIRAL

Canine parvovirus, encephalomyocarditis, foot-and-mouth disease, pseudorabies, canine distemper, cytomegalovirus, Newcastle disease, avian encephalomyelitis, eastern and western equine encephalomyelitis, West Nile virus

BACTERIAL

Blackleg (*Clostridium chauvoei*), listeriosis (*Listeria monocytogenes*), Tyzzer's disease (*Clostridium piliforme*, formerly *Bacillus piliformis*), necrobacillosis (*Fusobacterium necrophorum*), tuberculosis (*Mycobacterium* spp.), caseous lymphadenitis (*Corynebacterium pseudotuberculosis*), Lyme disease (*Borrelia burgdorferi*), disseminated infections by *Actinobacillus equuli*, *Staphylococcus* sp., *Corynebacterium kutscheri*, *Trueperella* (*Arcanobacter*) *pyogenes*, *Histophilus somni*, *Pseudomonas aeruginosa*, *Streptococcus equi*, and *Streptococcus pneumoniae*

PROTOZOAN

Toxoplasmosis (*Toxoplasma gondii*), sarcocystosis (*Sarcocystis* sp.), neosporosis (*Neospora caninum*), encephalitozoonosis (*Encephalitozoon cuniculi*), trypanosomiasis (Chagas' disease [*Trypanosoma cruzi*]), East Coast fever (*Theileria parva*)

PARASITIC

Cysticercosis (*Cysticercus cellulosae*), trichinosis (*Trichinella spiralis*)

IDIOPATHIC

Eosinophilic myocarditis

Responses to Injury: Endocardium and Heart Valves

Disturbances of Circulation

Hemorrhage. Endocardial hemorrhages are commonly seen and may be the result of trauma or septicemias, especially those with endotoxins, or can occur agonally at death (Fig. 10-21). See the previous sections on the Pericardium and Epicardium and the Myocardium and Box 10-4 and also Chapter 2.

Disturbances of Growth

Valvular Anomalies and Dysplasia. See the discussion on valvular anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves.

Cellular Degeneration and Death

See Chapter 1 for discussion of the causes of cell injury, irreversible cell injury and cell death, and chronic cell injury and cell adaptations.

Myxomatous Valvular Degeneration (Endocardiosis). See the discussion on myxomatous valvular degeneration (endocardiosis) in the section on Disorders of Dogs and Fig. 10-83.

Mineralization. Mineralization of the endocardium is seen with vitamin D toxicity, calcinogenic plant toxicosis in cattle, and calcium phosphorus imbalance, as well as in Johne's disease (Fig. 10-22; see Chapter 7). The endocardium and large elastic arteries are prone to mineralization because of their abundant elastic fibers.

Inflammation

See Chapters 3 and 5 for discussion of the processes and mechanisms of acute and chronic inflammation.

Responses to Injury: Pericardium and Epicardium

Disturbances of Circulation

Hemorrhage. See section on Disorders of Domestic Animals, Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Hemorrhage.

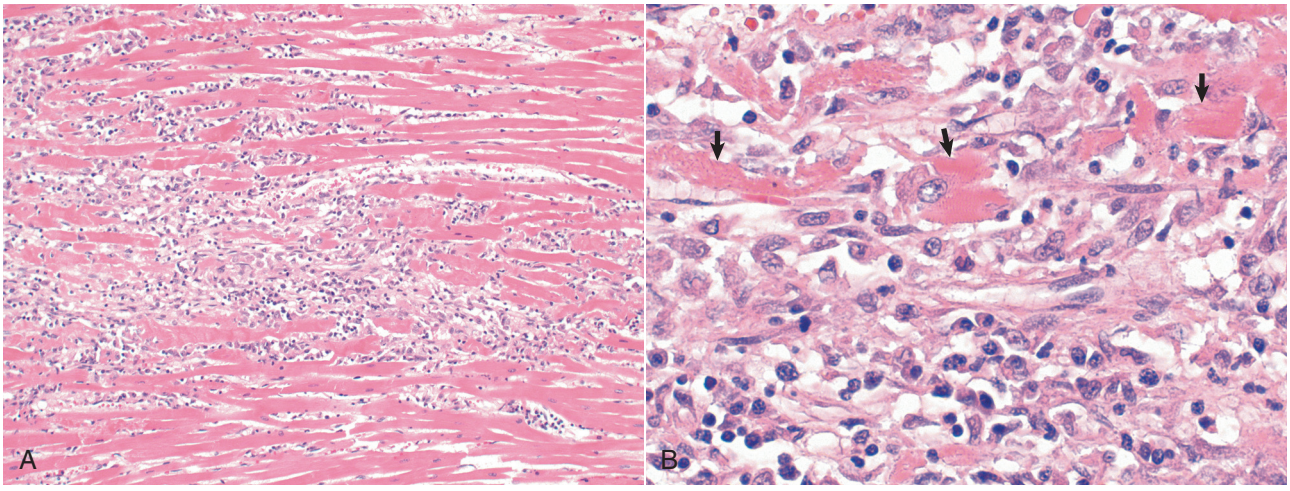


Figure 10-19 **Acute Myocarditis, Horse. A,** The parallel arrays of myofibers are disrupted by acute inflammatory cells, edema fluid, and fibrin. **B,** Higher magnification of **A.** Note the myocardial fiber degeneration and necrosis with loss of cross striations (*arrows*); fragmentation of cardiac rhabdomyocytes (cardiomyocytes); and hypereosinophilia, coagulation, and clumping of the sarcoplasm. Neutrophils are the predominant inflammatory cell in the exudate. H&E stain. (Courtesy Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)

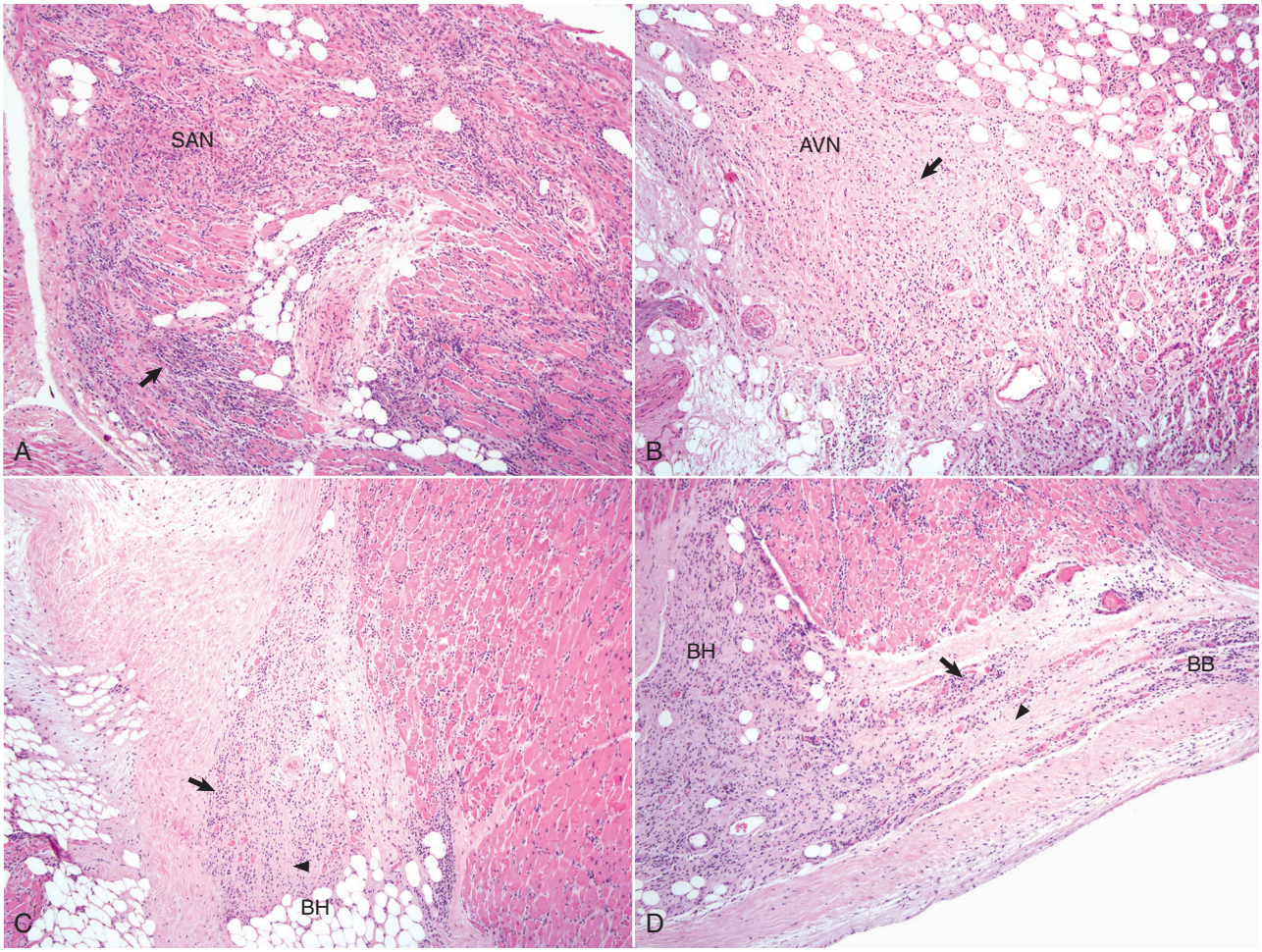


Figure 10-20 Inflammation in the Conduction System From a Dog. A, Sinoatrial node *(SAN)*. Moderate numbers of lymphocytes and plasma cells *(arrow)* multifocally infiltrate the interstitial spaces between cardiomyocytes. H&E stain. **B,** Atrioventricular node *(AVN)*. Small numbers of lymphocytes and plasma cells *(arrow)* multifocally infiltrate the interstitial spaces between cardiomyocytes. H&E stain. **C,** Bundle of His *(BH)*. Small numbers of lymphocytes and plasma cells *(arrow)* multifocally infiltrate the interstitial spaces between cardiomyocytes; fibrous connective tissue *(arrowhead)* multifocally replaces lost cardiomyocytes. H&E stain. **D,** Bundle of His *(BH)* and bundle branch *(BB)*. Small numbers of lymphocytes and plasma cells *(arrow)* multifocally infiltrate the interstitial spaces between cardiomyocytes; fibrous connective tissue *(arrowhead)* multifocally replaces lost cardiomyocytes. H&E stain. (Courtesy Dr. A. Gal, Institute of Veterinary, Animal and Biomedical Sciences, Massey University and Drs. M. Bates and P. Roady, College of Veterinary Medicine, University of Illinois.)

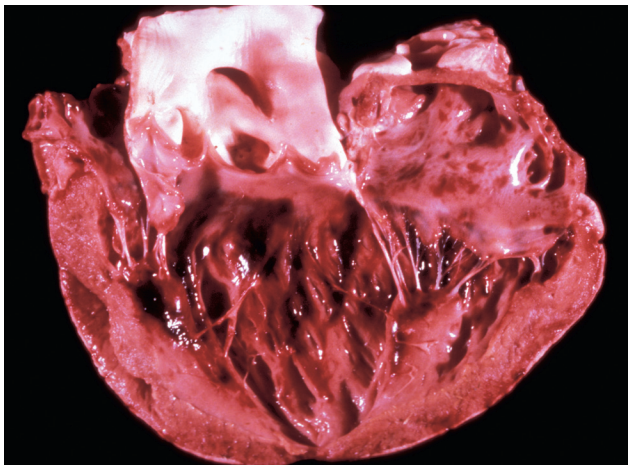


Figure 10-21 Endocardial Suffusive Hemorrhage, Heart, Left Ventricle, Calf. A red to dark-red sheet of suffusive hemorrhage is present in the endocardium of the left ventricle and left atrium. Suffusive hemorrhage is often attributed to severe septicemia, endotoxemia, anoxia, or electrocution. (Courtesy College of Veterinary Medicine, University of Illinois.)

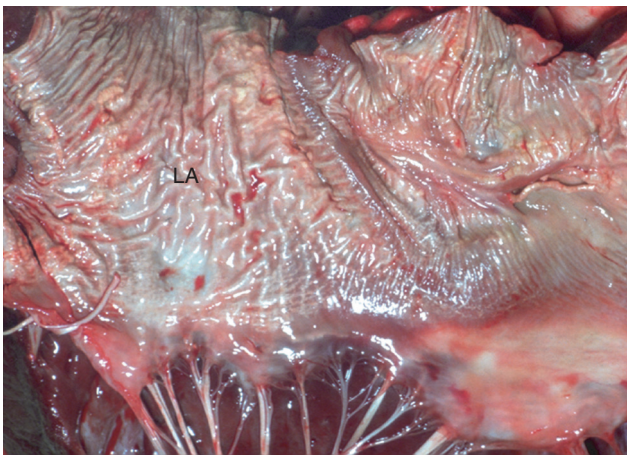


Figure 10-22 Endocardial Mineralization, Johne's Disease, Heart, Left Atrial Endocardium, Cow. The left atrial *(LA)* endocardium is white, thick, and wrinkled from mineralization. (Courtesy School of Veterinary Medicine, Purdue University.)

Effusions. See section on Disorders of Domestic Animals, Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Hemopericardium and Hydropericardium.

Disturbances of Growth

Anomalies and Dysplasia. See section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies.

Serous Atrophy. See section on Disorders of Domestic Animals, Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Growth, Serous Atrophy.

Inflammation

Pericarditis. See section on Disorders of Domestic Animals: Pericardium and Epicardium, Inflammation, Pericarditis.

Responses to Injury: Blood and Lymphatic Vascular Systems

The responses of blood and lymphatic vessels to injury involve a complex interaction among the cellular and noncellular elements of the vessel wall and the cellular and noncellular elements of the blood. The key cells of vessels in these reactions are endothelial cells and smooth muscle cells. Endothelial cells are metabolically active and provide a thromboresistant monolayer at the interface of blood and the vessel wall unless damaged. Endothelial cells play an important role in fluid distribution, inflammation, angiogenesis, and hemostasis (see Chapters 2 and 3). Responses of blood vessels to a variety of toxins are listed in E-Box 10-1.

Key functions of endothelial cells include prostacyclin production, macromolecular transport, and recruitment of inflammatory cells. Injury of endothelial cells is followed by separation from the underlying basement membrane and increased permeability to movement of plasma proteins into the subendothelium. Necrosis of endothelium exposes subendothelial collagen and elicits thrombus formation. Endothelial cells at the margin of denuded areas proliferate and re-endothelialize the damaged area. The arterial intima has regional differences in the uptake of macromolecules, as well as other unique structural and functional features that result in lesion-prone areas of the vasculature. Bilirubin staining of the intima results in yellow discoloration in jaundiced animals (Fig. 10-23).

The other major cellular component of vessels involved in reaction to injury is the smooth muscle cell. These cells have important functions, including production of extracellular components, such as collagen, elastin, and proteoglycans; maintenance of vascular tone; monocyte recruitment; lipoprotein metabolism; production of bioactive lipids, such as prostaglandins; and formation of oxygen-free radicals. These functions are regulated by a wide variety of biochemical mediators, such as various growth factors, cytokines, and inflammatory mediators.

Blood Vessels

Disturbances of Circulation

Hemorrhage. Hemorrhage resulting from vascular injury is a frequent lesion of the epicardium, endocardium, and myocardium. Hemorrhages vary in size from petechiae (1- to 2-mm diameter) to ecchymoses (2- to 10-mm diameter) to suffusive (diffuse). Animals dying from septicemia, endotoxemia, anoxia, or electrocution often have prominent epicardial (Fig. 10-24; E-Fig. 10-18 and endocardial (see Fig. 10-21) hemorrhages. Horses dying of any cause usually have agonal hemorrhages on the epicardial and endocardial surfaces. A distinctive example of a specific disease with cardiac hemorrhage is mulberry heart disease, associated with vitamin E–selenium deficiency in growing pigs. In these pigs, hydropericardium accompanies severe myocardial hemorrhage that results in a red, mottled (mulberry-like) appearance of the heart. Also see the previous discussions on disturbances of circulation in the sections on the Pericardium and Epicardium and the Myocardium in the Responses to Injury section.

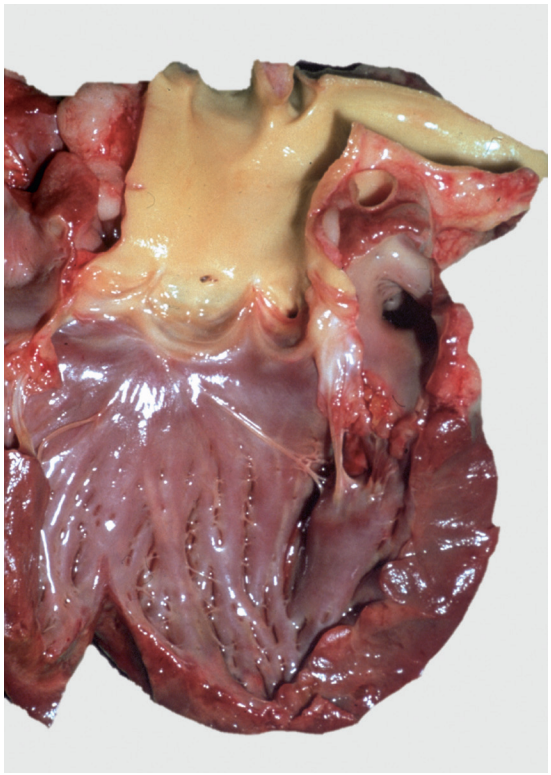


Figure 10-23 Jaundice, Heart, Aorta, Dog. Note yellow discoloration of the aortic intima. (Courtesy School of Veterinary Medicine, Purdue University.)

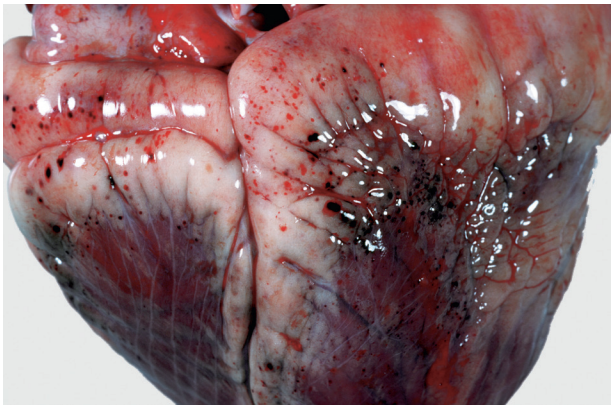


Figure 10-24 Epicardial Hemorrhage, Petechiae and Ecchymoses, Endotoxemia, Heart, Cow. Note the epicardial and subepicardial hemorrhages in the fat of the coronary groove (a common site). Petechiae and ecchymoses are often attributable to severe septicemia, endotoxemia, anoxia, or electrocution. In this case, the hemorrhage resulted from injury to the endothelium from endotoxin (component of the cell wall of Gram-negative bacteria). The smaller, pinpoint hemorrhages (1 to 2 mm) are petechiae. The larger hemorrhages (3 to 5 mm) are ecchymoses. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

Effusions. See section on Disorders of Domestic Animals, Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Hemopericardium and Hydropericardium.

Disturbances of Growth. See Chapter 1 for discussion of the causes of disturbances of cell growth (see cell adaptations).

E-Box 10-1 Toxicants Affecting Blood Vessels

ARTERIES

Toxicants that produce arterial medial smooth muscle proliferation
- Ergot (*Claviceps purpurea*), ergotamine
- Fescue (*Festuca arundinacea*) parasitized by endophytic fungi (*Epichloe typhina*, *Acremonium coenophialum*)

Toxicants that induce arterial medial calcification
- Vitamin D (dietary excess or cholecalciferol-containing rodenticides)
- Calcinogenic plants (*Cestrum diurnum*, *Trisetum flavescens*, *Solanum malacoxylon*, *Solanum torvum*)

Toxicants that induce necrosis of arterial medial smooth muscle and medial hemorrhage
- Epinephrine, norepinephrine, digoxin, theobromine, minoxidil, hydralazine, fenoldopam mesylate, phosphodiesterase inhibitors, endothelin receptor antagonists, dopamine receptor agonists, others

Toxicants that alter arterial connective tissue to produce aneurysms
- β-Aminopropionitrile (*Lathyrus* sp. product)
- Penicillamine, aminoacetonitrile

Toxicants that induce arterial intimal proliferation
- Ergotamine, methylsergide, estrogen and/or progesterone-containing oral contraceptives, others

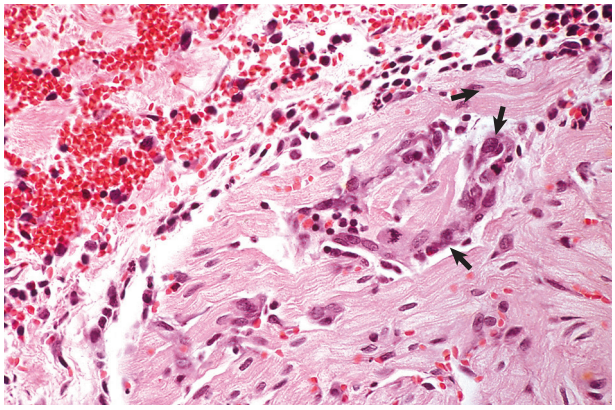
Toxicants that induce arterial fibrinoid necrosis
- Organic mercury, lead

VEINS

Toxicants that induce venous hyaline degeneration
- Phenylbutazone

CAPILLARIES

Toxicants that incite microangiopathy
- Cadmium, cyclophosphamide



E-Figure 10-18 Epicardial Hemorrhage, Minoxidil Cardiotoxicity, Heart, Left Atrium, Pig. Note epicardial hemorrhage *(upper left)* and prominent small blood vessels with swollen endothelial cells *(arrows)*. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Anomalies and Dysplasia. See section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies.

Hypertrophy. Arterial hypertrophy is a response to sustained increases in pressure or volume loads. Affected vessels are generally muscular arteries, and the increase in wall thickness is predominantly caused by hypertrophy (and, to some degree, hyperplasia) of smooth muscle cells of the tunica media. Muscular pulmonary arteries of cats are frequently affected, and the lesion has been associated with infection by several parasites, including *Aelurostrongylus abstrusus* (the lungworm of cats), *Toxocara* sp., and *Dirofilaria immitis* (Fig. 10-25). However, the lesions often occur in the absence of parasitic infections (Fig. 10-26). Often, no clinical disease is associated with the lesion in cats, but asthmatic signs have been seen in cats with these parasitic infections. Similar hypertrophy of muscular pulmonary arteries occurs in cattle with hypoxia-induced pulmonary arterial vasoconstriction and subsequent pulmonary hypertension associated with right-sided heart failure from exposure to high altitudes (so-called high-altitude disease or "brisket disease") (see section on the stages of myocardial hypertrophy). Also, cardiovascular anomalies that shunt blood left to right in animals result in pulmonary hypertension; these animals may have hypertrophy of the muscular pulmonary arteries, which can result in plexogenic pulmonary arteriopathy. Uterine arteries in pregnant animals are hypertrophic.

Inflammation. See Chapters 3 and 5 for discussion of the processes and mechanisms of acute and chronic inflammation.

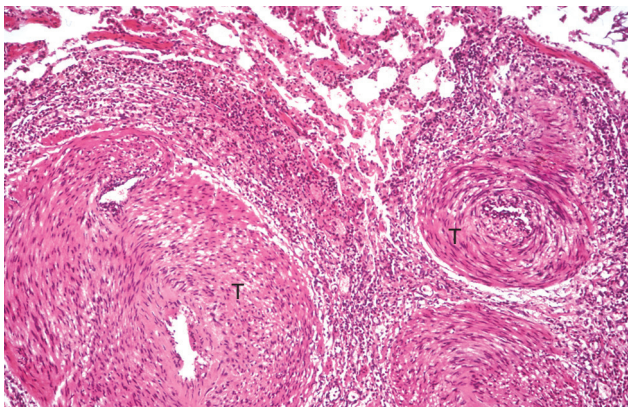


Figure 10-25 Medial Hypertrophy, Periarteritis, Dirofilariasis, Lung, Small Pulmonary Arteries, Cat. Note the massively thickened tunica media *(T)* of the small branches of the pulmonary arteries and their periarterial cuff of chronic inflammatory cells and some eosinophils. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

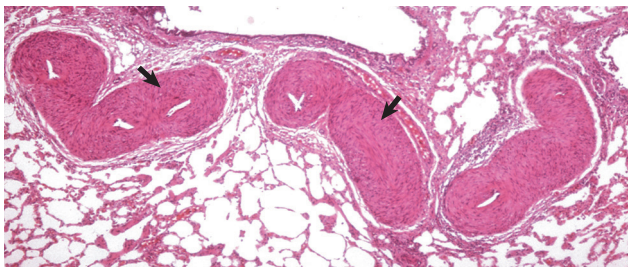


Figure 10-26 Medial Hypertrophy, Lung, Small Pulmonary Arteries, Cat. Proliferation of smooth muscle cells *(arrows)* has resulted in marked thickening of the tunica media. Note luminal narrowing. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Arteritis and Vasculitis. Arteritis occurs as a feature of many infectious and immune-mediated diseases (Box 10-7). Often, all types of vessels are affected rather than only arteries, and then *vasculitis* or *angiitis* (a term that includes blood and lymphatic vessels) is the term applied to the lesions. The vascular system serves as the major mechanisms for transport of organisms—for example, *Bacillus anthracis*. In inflamed vessels, leukocytes are present within and surrounding the walls, and damage to the vessel wall is evident as fibrin deposits or necrotic endothelial and smooth muscle cells. As a result of endothelial damage, thrombosis, which can result in ischemic injury or infarction in the circulatory field, may be present. Arteritis and vasculitis can develop from endothelial injury caused by either infectious agents or immune-mediated mechanisms or may be caused by local extension of suppurative and necrotizing inflammatory processes in adjacent tissues. Arteritis is a prominent feature of several parasitic diseases.

Systemic infections with phlebitis as a lesion include salmonellosis in several species and feline infectious peritonitis. In pigs with various septicemias, such as salmonellosis and colibacillosis, the gastric fundic mucosa is often severely congested and hemorrhagic because of venous endothelial damage and thrombosis. In severe local infections, such as in metritis or hepatic abscesses, inflammation extends into the walls of adjacent veins and produces phlebitis, with or without thrombosis. Intravenous injections of irritant solutions, injecting solutions into the vascular wall, or intimal trauma produced by indwelling venous catheters result in vascular damage and create an opportunity for localization and proliferation of infectious agents and development of phlebitis and thrombosis (Fig. 10-27). Animals with phlebitis complicated by thrombosis have the additional risk of septic embolism, which can cause endocarditis and pulmonary abscesses or pulmonary infarcts.

Many reportable foreign animal diseases are viral diseases, which are endotheliotropic and result in vasculitis; examples include

Box 10-7 Diseases that Cause Arteritis in Animals

VIRAL

Equine viral arteritis, African horse sickness, equine infectious anemia, equine morbillivirus, malignant catarrhal fever, bovine virus diarrhea, bovine ephemeral fever, bluetongue, hog cholera, African swine fever, feline infectious peritonitis, Aleutian mink disease

BACTERIAL

Bartonella henselae, leptospirosis, Salmonellosis, erysipelas (*Erysipelothrix rhusiopathiae*), *Haemophilus* spp. infections (*Haemophilus suis*, *Haemophilus somnus*, *Haemophilus parasuis*), heartwater (*Ehrlichia ruminantium*), Rocky Mountain spotted fever (*Rickettsia rickettsii*), Lyme disease (*Borrelia burgdorferi*)

MYCOTIC

Phycomycosis, aspergillosis

PARASITIC

Equine strongylosis (*Strongylus vulgaris*), dirofilariasis (*Dirofilaria immitis*), French heartworm (*Angiostrongylus vasorum*), spirocercosis (*Spirocerca lupi*), onchocerciasis, elaeophoriasis (*Elaeophora* sp.), filariasis in primates, aelurostrongylosis

IMMUNE-MEDIATED

Canine systemic lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa, lymphocytic choriomeningitis, drug-induced hypersensitivity

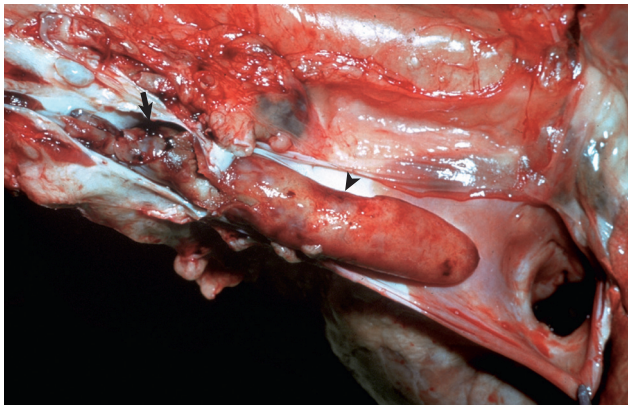


Figure 10-27 Thrombus (Mural), Jugular Vein (Opened), Dog. Note the nodular mural thrombus *(left [arrow])* in the jugular vein. This thrombus likely occurred at a site of venipuncture and a subsequent phlebitis. The smooth-surfaced red-tan thrombus *(right [arrowhead])* extending toward the heart is a trailing thrombus, a continuation of the mural thrombus. (Courtesy School of Veterinary Medicine, Purdue University.)

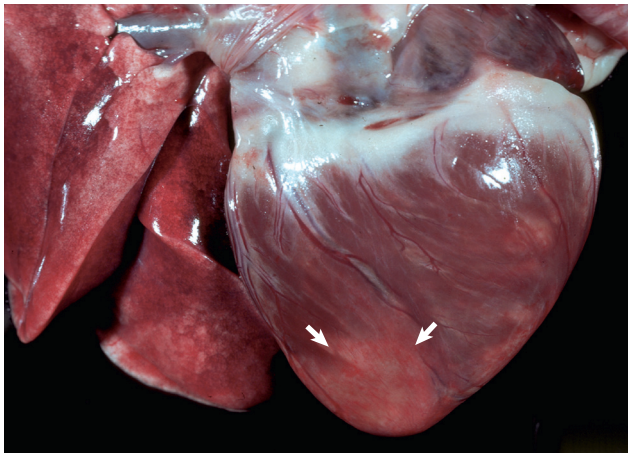


Figure 10-28 Myocardial Infarction, Heart, Left and Right Ventricles, Dog. Pale, necrotic, circumscribed areas *(arrows)* are present in the ventricular walls and are most prominent at the apex. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

classic swine fever (hog cholera), African horse sickness, and African swine fever (see the sections on disorders of specific animal species).

Thrombosis and Embolism

Coronary and Other Arteries. Thrombosis or embolism of the coronary arteries can result in myocardial infarction (Fig. 10-28) and cardiac failure. These lesions are much less common in animals than in human beings. Affected animals generally have one of several types of coronary arterial disease, including atherosclerosis, arteriosclerosis, or periarteritis. In atherosclerosis associated with hypothyroidism or diabetes mellitus (discussed previously), severe lesions are present in the extramural (epicardial) coronary arteries of dogs, but this only rarely leads to thrombosis and myocardial infarction. In contrast, severe arteriosclerosis of intramural cardiac arteries in aged dogs can cause small multifocal myocardial infarcts (see Fig. 10-28). Affected dogs often also have myxomatous valvular degeneration (valvular endocardiosis), which is also an age-related disease. Thrombosis of or embolism to other large arteries, such as the interlobular artery of the kidney, can lead to infarction of the tissue supplied by the artery (E-Fig. 10-19; also see Chapter 2).

Box 10-8 Diseases that Cause Lymphangitis in Animals

BACTERIAL

Porcine anthrax (*Bacillus anthracis*), Johne's disease (*Mycobacterium paratuberculosis*), tuberculosis (*Mycobacterium* spp.), actinobacillosis (*Actinobacillus lignieresii*), glanders (farcy) (*Burkholderia mallei*), cutaneous streptothricosis (*Dermatophilus congolensis*), bovine farcy, ulcerative lymphangitis of horses, sporadic lymphangitis of horses, ulcerative lymphangitis (*Corynebacterium pseudotuberculosis*, *Pseudomonas aeruginosa*)

MYCOTIC

Epizootic lymphangitis of horses (*Histoplasma farciminosum*), sporotrichosis (*Sporothrix schenckii*)

PARASITIC

Brugia spp. infection of dogs and cats

Lymphatic Vessels

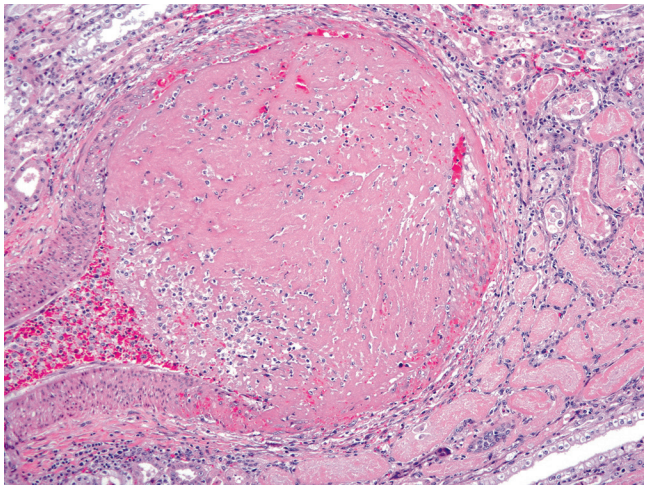
Inflammation. The endothelial cells lining the lymphatic vessels are subject to the same reactions to injury and inflammation as the vascular system. Inflammation of the lymphatic vessels is called *lymphangitis* and may be seen with specific diseases such as septicemias caused by bacteria like *Salmonella* spp. (Box 10-8). Lymphangitis may be acute, subacute, granulomatous, or chronic resulting in lymphedema. See Chapters 3 and 5, and also see the discussion on Glanders disease and other cutaneous lymphangitides in the section on Disorders of Horses.

Aging

Aging changes are evident in the cardiovascular system. Lipofuscin granules, primarily perinuclear, increase in number with age of cardiac myocytes (see sections on Lipofuscinosis, Cell Degeneration and Death, Disturbances of Growth, and Responses to Injury: Myocardium). Fatty infiltration of the pericardium and myocardium increases with the age of the animal. Hearts from aged sheep often have abundant amounts of adipose tissue, particularly within the right ventricle (see sections on Fatty Degeneration, Cell Degeneration and Death, Disturbances of Growth, and Responses to Injury: Myocardium). Myxomatous valvular disease increases in incidence with age in small breed dogs (see section on Disorders of Dogs; also see Fig. 10-83). Degenerative vascular disease associated with aging includes arteriosclerosis, amyloidosis, and hyaline degeneration of cardiac arteries (see section on Hyaline Degeneration, Fibrinoid Necrosis, and Amyloidosis and section on Disorders of Domestic Animals: Blood and Lymphatic Vascular System). The incidence of neoplastic disease increases with age in the cardiovascular and lymphatic system.

Portals of Entry/Pathways of Spread

Routes used to enter the cardiovascular system and lymphatic vessels are numerous and listed in Box 10-9. Toxic chemicals and pathogenic organisms can enter via ingestion, inhalation, cutaneous contact, trauma, or iatrogenic injection and gain access to the cardiovascular system. Microorganisms and toxins penetrate and enter deeper tissues, dermis, lamina propria, subcutis, or submucosa, triggering an acute inflammatory reaction. All three of the major components of acute inflammation may be responsible for entry of the toxin or organism into the vascular or lymphatic system. The increase in the vascular caliber increasing blood flow increases the number of capillary beds exposed to the agent. Changes in the



E-Figure 10-19 **Arterial Thrombosis, Subacute, Interlobular Artery, Kidney, Dog.** An interlobular artery contains a thromboembolus, which has firmly attached to the vessel wall. Note the large size of the thromboembolus compared to the luminal diameter (see bottom left corner) of the artery. This finding suggests that it is "growing" in size via the mechanisms of Virchow's triad and the adherence of platelets and fibrin to the initial embolus. (Courtesy College of Veterinary Medicine, University of Illinois.)

microvasculature that allow the exit of plasma proteins and leukocytes also increase the entry of an agent. Finally, the increase in leukocytes can result in vascular injury and phagocytosis of material. Organisms that are not diluted, but are denatured by molecules from lysosomes of neutrophils, or restricted in movement by being trapped in fibrin at the site of inflammation can gain entry into the lymphatic vessels, thin-walled capillaries, or venules. Entry into lymphatic vessels allows invading microorganisms to be carried in lymph to draining regional and systemic lymph nodes and eventually via the thoracic duct to the circulatory system. Microorganisms that gain access to veins spread with the circulation and can localize in the lungs. In occurrences in which severe pulmonary inflammation leads to the formation of AV fistulas, microorganisms can gain access to pulmonary veins, be pumped through the left heart, and enter the systemic arterial circulation. The circulatory system can distribute organisms and materials to other organs and tissues (see E-Fig. 10-2; also see Chapter 2).

Myocardium

Pathogens gain entry to the myocardium through the vascular system from the coronary arteries, which provide blood flow to the myocardium. Coronary arteries originate in the sinus of Valsalva at the origin of the aorta and travel in the coronary grooves to the apex of the heart supplying blood to both ventricles. Branches of the coronary arteries bifurcate and send smaller arteries on the outer surface of the heart within the visceral pericardium. These smaller arteries then penetrate the myocardium, becoming arterioles and finally a rich network of capillaries in which there is nearly one vessel adjacent to each cardiac muscle cell. This rich network of capillaries provides an opportunity for bacteria or virus to gain entrance into the myocardium once they have entered the circulatory system. As a result, many bacterial and viral infections may result in myocarditis. Bacteria within fibrin and inflammatory debris loosely attached to affected valves (bacterial valvular endocarditis) may detach and lodge in coronary arteries. This septic emboli damages endothelial cells and initiates acute inflammation resulting in myocarditis. Toxins or toxic by-products can directly damage endothelial cells or diffuse through the endothelium to affect myocardial fibers. In addition, the myocardium is susceptible to direct extension of pathogens located within the endocardium or pericardium.

Box 10-9 Portals of Entry for the Cardiovascular System

PERICARDIUM
Hematogenous dissemination
Foreign body penetration most commonly from reticulum (cattle)
Direct extension from pleural cavity or mediastinum

ENDOCARDIUM
Hematogenous dissemination
Parasitic migration (direct or hematogenous)
Intravenous and intracardiac catheters (long-term placement)
Uremia-induced vascular damage and secondary endocardial ulceration (dog, left atrium)

MYOCARDIUM
Hematogenous dissemination
Embolic dissemination of infective material fragments from vegetative endocarditis lesions into coronary arterial tree
Direct extension from endocardium or pericardium

ARTERIES
Hematogenous dissemination
Local extension of suppurative and necrotizing inflammatory processes
Immune-mediated arterial injury
Parasitic migration

VEINS
Hematogenous dissemination
Local extension of severe inflammatory processes
Intravenous injections and indwelling catheters
Parasitic migration
Immune-mediated venous injury

LYMPHATIC VESSELS
Hematogenous dissemination
Local extension of severe inflammatory processes
Parasitic migration

Endocardium and Heart Valves

The endocardium and the cardiac valves are in direct contact with any pathogen that enters the circulatory system, including parasites, bacterial and viral pathogens, and toxins. The endocardium, especially the left atrial endocardium, is particularly susceptible to toxins resulting from renal failure in the dog.

Epicardium and Pericardium

Bacteria and viruses can enter the pericardial sac via endothelial damage to capillaries on visceral (epicardium) and parietal (pericardium) surfaces. Bacteria can enter by direct penetration. In cattle, foreign bodies exiting the reticulum and penetrating the diaphragm carry bacterial pathogens into the pericardial cavity. Direct entry from bacterial or viral infections in the pleural cavity or mediastinum can also occur.

Blood and Lymphatic Vascular Systems

The circulatory systems are intrinsically susceptible to microbial organisms and toxins because of the primary role of providing oxygen and nutrients to and removing waste from tissues. Hematogenous and lymphogenous dissemination of microbial pathogens and toxins directly exposes the corresponding vasculature to these hazards. Parasitic migration and local extension of an inflammatory process can directly result in entry into the circulatory or lymphatic system and directly damage these tissues.

Defense Mechanisms/Barrier Systems

Defense mechanisms used by the cardiovascular system and lymphatic vessels are listed in Box 10-10. These structures are fortunate

Box 10-10 Defense Mechanisms

CONSTANT BLOOD FLOW
Endocardium, blood and lymphatic vascular components
Endothelium-facilitated barrier systems (see Chapters 2 and 4)

INNATE RESPONSES
Inflammation
Complement
Chemical mediators of inflammation

PHAGOCYTOSIS
Monocyte-macrophage system
Intravascular macrophages
Adaptive immune system

HUMORAL RESPONSES

CELL-MEDIATED RESPONSES

in that most of the components of the innate and humoral immunity are present within the lumen. A review of inflammation (see Chapter 3), immune function (see Chapter 5), and circulatory disturbances (see Chapter 2) is invaluable in understanding the defense mechanisms of the cardiovascular and lymphatic systems. The constant flow of blood and lymph through intact circulatory and lymphatic systems, respectively, provides the surface endothelium of the chambers and vessels with constant exposure to nutrients, plasma proteins such as immunoglobulins, preformed chemical mediators, and circulating leukocytes.

Disorders of Domestic Animals

Developmental Errors/Congenital Anomalies[2]

The complex events involved in the embryologic development of the heart and great vessels allow substantial opportunities for congenital anomalies to develop (see E-Fig. 10-1). The functional significance of these anomalies varies widely. Animals with the most extreme defects are unable to survive in utero, and those with the mildest lesions could have no clinical signs of disease during life. However, animals with defects of intermediate severity are most likely to be presented to a veterinarian because of gradually developing signs of cardiac failure, including poor exercise tolerance, cyanosis, and stunted body growth. Ectopia cordis is a congenital development of the heart at an abnormal site outside of the thoracic cavity. In cattle, cases in healthy adult animals have been described in which the heart was located subcutaneously in the caudoventral neck area. The most frequently observed cardiovascular anomalies in domestic animals are listed in Box 10-11.

The causes of congenital cardiovascular anomalies are varied. Most animal species have a low background frequency of spontaneous cardiac malformations. In many species, especially in dogs, these defects are heritable and can be attributed to either single or multiple gene effects. Under experimental conditions, cardiovascular congenital defects can be elicited by exposure of pregnant dams to various chemicals and drugs, physical agents, toxins, or nutritional deficiencies. Chemical compounds implicated include thalidomide, ethanol, salicylates, griseofulvin, and cortisone. Prenatal exposure to x-irradiation or fetal hypoxia can induce defects. Maternal nutritional deficiencies of vitamin A, pantothenic acid, riboflavin, or zinc and excess intake of vitamin A, retinoic acid, or copper can result in cardiovascular anomalies in newborn animals. Infectious diseases have been incriminated, but not confirmed, in cardiovascular defects; they include bluetongue infections in sheep, bovine virus diarrhea in cattle, and parvoviral infections in dogs and cats.

Congenital cardiac malformations may be grouped into four large categories according to their pathophysiology: (1) defects that cause volume overload (with subcategories of systemic to pulmonary shunting [left to right shunt] and valvular regurgitation), (2) defects that cause pressure overload, (3) defects that cause cyanosis, and (4) miscellaneous cardiac and vascular defects.

Anomalies in the first category that lead to left to right shunting include patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrial septal defect (ASD), and endocardial cushion defects. In this category, a defect between the right and left cardiac compartments leads to flow of cardiac blood according to a pressure gradient from the left side (systemic circulation, high pressure) to the right side (pulmonic circulation, low pressure). The consequence of blood shunting is overloading of the low-pressured pulmonary circulation, which results in increased volume of blood that enters the left cardiac compartment after returning from the lungs. This in turn leads to eccentric hypertrophy of the left ventricle and atrium to accommodate the increased volume of blood. Anomalies in the first category that lead to valvular regurgitation include mitral and tricuspid dysplasia and aortic and pulmonic insufficiency. The regurgitated blood from the ventricles to the atria leads to progressive atrial dilation and eccentric ventricular dilation.

Anomalies in the second category that cause pressure overload include pulmonic and aortic stenosis and coarctation and interruption of the aorta. In these anomalies, ventricular outflow obstructions result in progressive and chronic increase in intraventricular pressure. The increased intraventricular pressure induces concentric ventricular hypertrophy that eventually results in a diastolic failure.

Anomalies in the third category that cause cyanotic heart disease include tetralogy of Fallot, pulmonary to systemic (right to left) blood shunting (some VSD and PDA), tricuspid atresia/right ventricular hypoplasia, double-outlet right ventricle, transposition of the great vessels, truncus arteriosus, and aorticopulmonary window (see Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies). In these anomalies, nonoxygenated blood from the right cardiac compartment flows to the left compartment or bypasses the left compartment and flows directly into the systemic circulation. This portion of nonoxygenated blood mixes and dilutes the oxygenated blood in the systemic circulation and induces cyanosis in multiple tissues.

Anomalies in the fourth category include peritoneopericardial diaphragmatic hernias (PPDHs), persistent right aortic arch (PRAA), endocardial fibroelastosis, anomalous pulmonary venous return, double aortic arch, retroesophageal left subclavian artery, valvular hematomas, and situs inversus.

Box 10-11 Most Common Cardiovascular Anomalies in Domestic Animal Species

HORSES
Ventricular septal defect
Patent ductus arteriosus
Persistent truncus arteriosus

RUMINANTS (CATTLE, SHEEP, AND GOATS)
Valvular hematomas
Patent foramen ovale
Ventricular septal defect
Transposition of aorta and pulmonary artery

PIGS
Endocardial cushion defects
Dysplasia of the tricuspid valve
Subaortic stenosis

DOGS
Patent ductus arteriosus
Pulmonic stenosis
Subaortic stenosis
Persistent right aortic arch
Ventricular septal defect

CATS
Endocardial cushion defects
Mitral malformation
Ventricular septal defect
Endocardial fibroelastosis
Patent ductus arteriosus

[2]See E-Box 10-2 for a list of inherited cardiovascular diseases of animals; E-Box 10-3 for a list of canine breed predilections for congenital cardiac anomalies; and E-Box 1-1 for a list of potential, suspected, or known genetic disorders.

Sites of the major cardiovascular anomalies in the dog are shown in Fig. 10-29.

Developmental Errors/Congenital Anomalies: Myocardium

See the following section on Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves.

Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves

Failure of Closure of Fetal Cardiovascular Shunts

Interventricular Septal Defect. A ventricular septal defect indicates failure of complete development of the interventricular septum and allows the shunting of blood between the ventricles (Fig. 10-30). The defect occurs in many species and more commonly in the upper interventricular septum—below the aortic valves (on the left), proximal to the crista supraventricularis (near the septal tricuspid valve leaflet), or distal to the crista supraventricularis (below the pulmonic valve).

Among breeds of dogs, the greatest frequency has been observed in the English bulldog, English springer spaniel, and West Highland white terrier.

Atrial Septal Defect. An atrial septal defect could represent the failure of closure of the foramen ovale, which is an interatrial septal shunt that allows blood to bypass the lungs of the fetus, or it can be the result of true septal defects at another site because of faulty development of the interatrial septum. Although this defect occurs in all domestic animal species, dog breeds with greatest frequency of this defect are the boxer, Doberman pinscher, and Samoyed.

Tetralogy of Fallot. Tetralogy of Fallot is a complicated cardiac anomaly seen in all animal species with four lesions (Fig. 10-31). The three primary defects are a ventricular septal defect located high in the septum, pulmonic stenosis (see later discussion), and dextroposition of the aorta (see later discussion). The fourth defect, which develops secondarily, is hypertrophy of the right ventricular myocardium. The major pathophysiologic significance in this condition is the increased pressure in the right side that shunts unoxygenated blood from the hypertrophic right side to the underdeveloped left side (systemic circulation) and results in systemic hypoxemia and secondary polycythemia. Cyanosis is often an associated clinical sign. The anomaly is one of the most common cardiac abnormalities seen in hearts of human beings (so-called blue babies). This complex anomaly is inherited in keeshond dogs and is frequent in English bulldogs. In genetic and pathologic studies of keeshond dogs, the basic defect has been determined to be hypoplasia and malpositioning of the conotruncal septum. Wide variability in the severity of the lesions has been observed. The inheritance pattern in keeshonds is a simple autosomal locus with partial penetration in heterozygotes and complete penetrance in homozygotes.

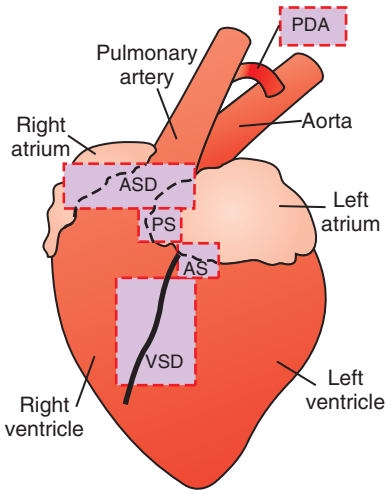


Figure 10-29 Sites of the Major Cardiovascular Anomalies of the Dog. *AS*, Aortic stenosis; *ASD*, atrial septal defect; *PDA*, patent ductus arteriosus; *PS*, pulmonic stenosis; *VSD*, ventricular septal defect. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

Failure of Normal Valvular Development

Pulmonic Stenosis. Pulmonic stenosis has been recognized as a frequently occurring anomaly in dogs and is inherited in the beagle (Fig. 10-32). Other breeds in which this lesion is frequent are basset hound, boxer, Chihuahua, Chow Chow, cocker spaniel, English bulldog, Labrador retriever, mastiff, Newfoundland, Samoyed, schnauzer, and terrier. Several types of valvular lesions have been described and include formation of a circumferential band of fibrous

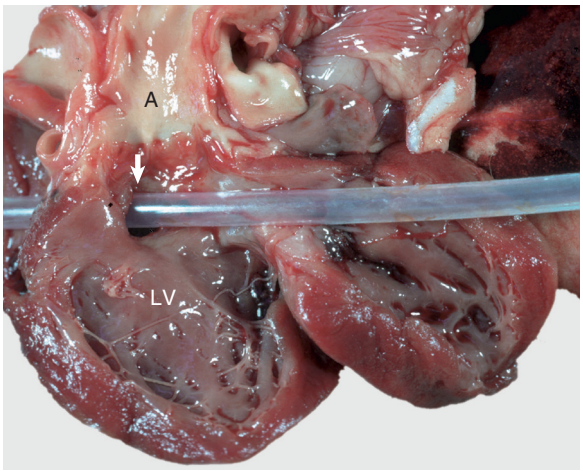


Figure 10-30 Ventricular Septal Defect (High Defect), Heart, Opened Left Side, Calf. Note the large opening in the basal portion of the ventricular septum *(arrow)* immediately below the aortic valve through which the tube has been passed. *A*, Aorta; *LV*, left ventricle. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

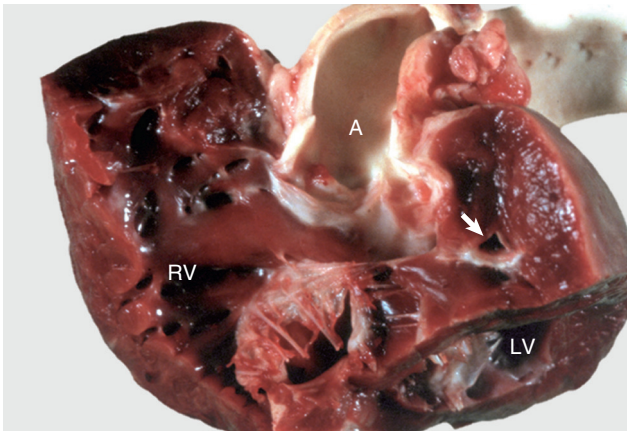


Figure 10-31 Tetralogy of Fallot, Heart, Dissected, Dog. Above the large membranous ventricular septal defect is an overlying, straddling aorta *(A)*. There is also severe pulmonic stenosis *(arrow)* with massive right ventricular hypertrophy. *LV*, Left ventricle; *RV*, right ventricle. (Courtesy School of Veterinary Medicine, Purdue University.)

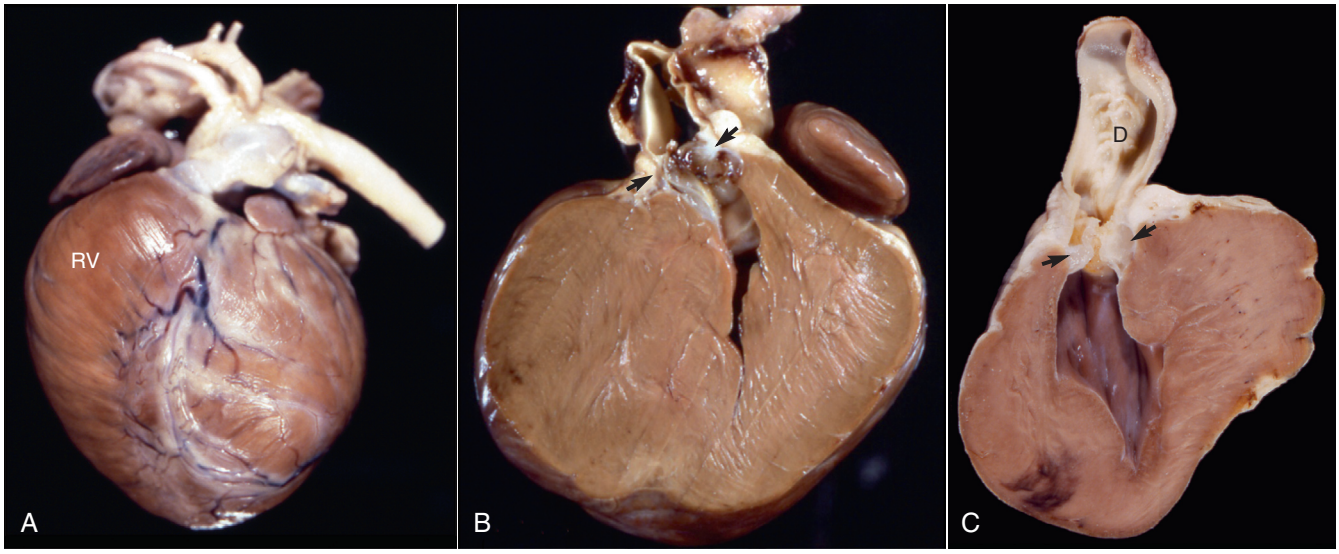


Figure 10-32 Pulmonic Stenosis, Heart, Pulmonary Artery, Dog. A, Closed heart, and **B,** sectioned heart. Note the prominent concentric right ventricular *(RV)* hypertrophy resulting from pressure overload. The orifice of the pulmonic valve *(arrows)* is markedly narrowed. **C,** Sectioned heart, there is poststenotic dilation *(D)* of the pulmonary artery with irregular intimal thickenings (jet lesions). (Courtesy Atlantic Veterinary College, University of Prince Edward Island.)

or muscular tissue beneath the valve (subvalvular stenosis) or malformation of the valve (valvular stenosis), with a small central orifice in a dome of thickened valvular tissue. A unique form of subvalvular pulmonic stenosis has been described in English bulldogs and boxers in which an anomalous development of a coronary artery obstructs the right ventricular outflow tract. Notable concentric hypertrophy (see the discussion on hypertrophy in the section on Responses to Injury: Myocardium, Disturbances of Growth) of the right ventricle develops from the resulting pressure overload.

Aortic and Subaortic Stenoses. True stenoses of the aortic valve are uncommon. Subaortic stenosis is a cardiac anomaly frequently observed in pigs and dogs. Subvalvular aortic stenosis is the most common congenital cardiac anomaly of large-breed dogs. Bull terriers and boxers are predisposed, and a genetic basis is present in the Newfoundland dog, in which subvalvular aortic stenosis is inherited in an autosomal dominant pattern. Obstruction of the left ventricular outflow tract (LVOT) results from a raised, partial or complete fibrous ring that arises from the endocardium below the aortic valve and may extend to involve the cranioventral leaflet of the mitral valve and the base of the aortic valve (Fig. 10-33). The lesion is also observed in the German shorthair pointer, golden retriever, Great Dane, Rottweiler, Samoyed, and bull terrier breeds. In clinical cases, the stenosis is produced by the presence of a thick zone of endocardial fibrous tissue that encircles the LVOT below the valve. In mild cases, often subclinical, the lesion is limited to white nodules on the ventricular septum immediately below the valve. Microscopically, the altered endocardial tissue contains loosely arranged elastic fibers, mucopolysaccharide ground substance, and collagen fibers admixed with fibroblasts and chondrocyte-like cells. Other cardiac lesions develop as a result of the altered left ventricular outflow; these include left ventricular concentric hypertrophy, disseminated foci of myocardial necrosis, fibrosis in the inner left ventricular wall, and thickening of the walls of intramyocardial arteries.

Valvular Dysplasias: Endocardial Cushion Defects. Other valvular developmental anomalies include endocardial cushion defects (persistent AV canal and atrioventricular canal defect) in pigs, sheep, and cats; mitral dysplasia in cats and dogs; and tricuspid dysplasia in cats and dogs (Fig. 10-34). Endocardial cushion defects are the most common congenital cardiac anomaly seen in cats.

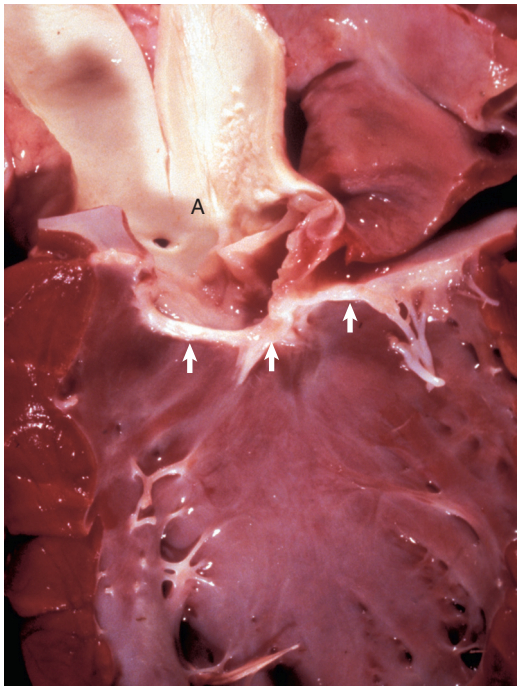


Figure 10-33 Subaortic Stenosis, Heart, Opened Left Side, Dog. A thick, white, broad band of fibrous connective tissue *(arrows)* encircles the left ventricular outflow tract below the aortic valve. The force of the blood ejected through the stenotic lesion is responsible for the "jet lesions" in the overlying aorta (A). (Courtesy College of Veterinary Medicine, University of Illinois.)

Tricuspid Valve Dysplasia. Tricuspid valve dysplasia has a genetic basis in the Labrador retriever dog, in which it is an autosomal dominant trait with reduced penetrance that is mapped to chromosome 9. There is a wide spectrum of morphologic abnormalities that may include (1) shortening, rolling, notching, and thickening of

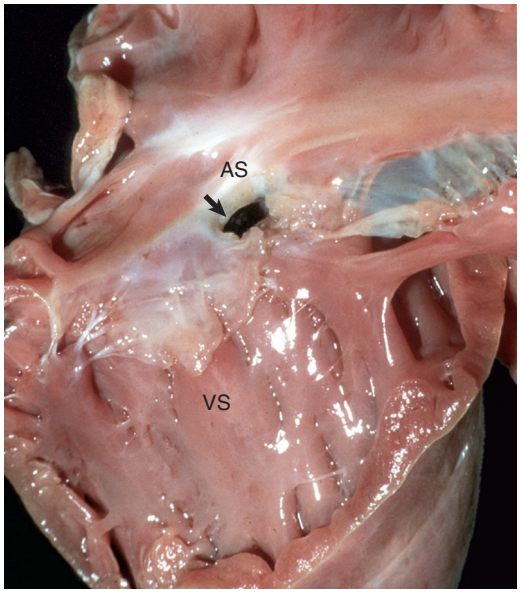


Figure 10-34 Endocardial Cushion Defect and Tricuspid Dysplasia, Heart, Opened Right Side, Pig. The endocardial cushion defect (prominent opening *[arrow]*) can be mistaken as an atrial septal defect but not the location and presence of abnormal valves incorporated in the defect. *AS,* Atrial septum; *VS,* ventricular septum. (Courtesy School of Veterinary Medicine, Purdue University.)

leaflets; (2) incomplete separation of valvular components from the ventricular wall; (3) elongation, shortening, fusion, and thickening of chordae tendineae; (4) direct insertion of the valve edges into a papillary muscle; or (5) atrophy, fusion, and malpositioning of the papillary muscles and chordae tendineae.

Mitral Valve Dysplasia. Mitral valve dysplasia is often associated with other anomalies, such as ASD/VSD and tricuspid valve dysplasia. A similar spectrum of morphological valvular abnormalities is present in mitral valve dysplasia as described previously for tricuspid valve dysplasia. Dysplastic malformations in the atrioventricular valves that result in valvular insufficiency lead to volume overload with resultant atrial dilation and to eccentric ventricular hypertrophy. Dysplastic malformations in the atrioventricular valves that result in valvular stenosis lead to reduced ventricular filling with subsequent low cardiac output (history of syncope, collapse, and hypotension) and increased atrial pressure; in the case of mitral stenosis, increased atrial pressure can lead to pulmonary edema initially and dilation of the right ventricle (right-sided heart failure) from prolonged pulmonary hypertension.

Developmental Errors/Congenital Anomalies: Pericardium and Epicardium

Peritoneopericardial Diaphragmatic Hernias. Peritoneopericardial diaphragmatic hernias (PPDHs) occur in cats and dogs with incomplete development of the diaphragm. PPDHs are rare, but they are the most common congenital pericardial anomaly in cats; Persian and domestic longhair cats were overrepresented in two studies. PPDHs result from defective separation of the developing liver and septum transversum during embryogenesis that allows the peritoneal and pericardial cavities to communicate. Hence, abdominal organs including omental fat may fill the pericardial sac and compress the heart. Parts of the liver are often incarcerated in the pericardial sac and may develop intrahepatic myelolipomas.

Partial/Complete Absence (Agenesis) of the Pericardial Sac. Partial or complete absence of the pericardial sac is an incidental lesion that is rarely found during necropsy and has not been reported to have clinical significance during life. However, there is one report of a dog with a partial tear in the pericardium that was associated with episodes of syncope.

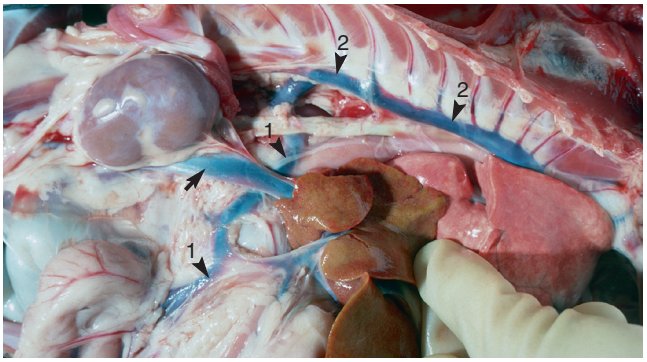


Figure 10-35 Portacaval Shunt, Dog. Note that the branch of the portal vein *(arrowhead 1)* passes under the caudal vena cava *(arrow)* and anastomoses with the azygous vein *(arrowhead 2)*. The azygous vein returns the blood to the caudal vena cava near the heart and thus this blood and its ammoniacal and protein metabolites are shunted away from processing to blood urea nitrogen (BUN) in the liver. The liver is normal color but extremely small, which is typical of these types of shunts (see Chapter 8). (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

Intrapericardial Cysts. Benign intrapericardial cysts are rare, large fluid-filled masses within the pericardial space that originate from the pericardium and consist of encapsulated and hemorrhagic adipose tissue that possibly originated from congenital entrapment of the omentum or falciform ligament. In other cases, these rare lesions are associated with PPDH.

Developmental Errors/Congenital Anomalies: Blood and Lymphatic Vascular Systems

Blood Vessels

Failure of Closure of Fetal Cardiovascular Shunts

Portacaval Shunts. Portacaval shunts occur in animals, particularly in the dog. The normal flow from the portal vein is diverted, either partially or completely, to the systemic circulation, thus bypassing the liver (Fig. 10-35). Normal hepatic detoxification of portal flow is incomplete and may result in neurologic signs and elevated circulating bile acids. The resulting nervous system syndrome is termed *hepatic encephalopathy*. Specifically, the shunts represent retained fetal vascular structures, as in persistent ductus venosus, or arise from prominent dilation of various portosystemic shunts that normally are quite small vessels. See Chapter 8 on diseases of the liver for further details.

Tetralogy of Fallot. See Disorders of Domestic Animals; Developmental Errors/Congenital Anomalies; Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves, Failure of Closure of Fetal Cardiovascular Shunts, Tetralogy of Fallot.

Patent Ductus Arteriosus. Patent ductus arteriosus is a frequent anomaly in poodle, collie, Pomeranian, Chihuahua, cocker spaniel, English springer spaniel, German shepherd, keeshond, Maltese, Yorkshire terrier, bichon frise, and Shetland sheepdog breeds (Fig. 10-36). In poodles, it is an inherited polygenic trait. Female dogs have a greater incidence. The ductus arteriosus is a fetal communication between the aorta and pulmonary artery that serves to divert blood from the right cardiac chamber to the fetal circulation in order to bypass the collapsed fetal lungs. Following parturition, the smooth

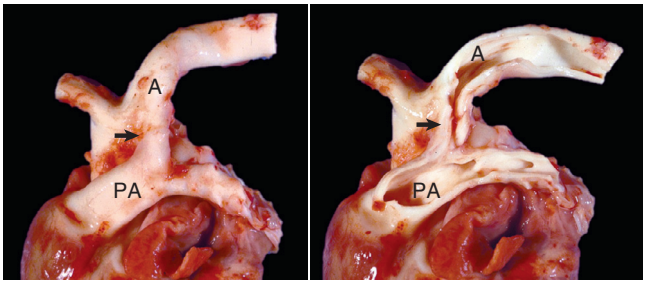


Figure 10-36 Patent Ductus Arteriosus, Heart, Young Dog. Note the prominent ductus arteriosus *(arrow)* between the pulmonary artery *(PA)* and the aorta *(A)* in the undissected *(left)* and dissected vessels *(right)*. (Courtesy Dr. D.D. Harrington, School of Veterinary Medicine, Purdue University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

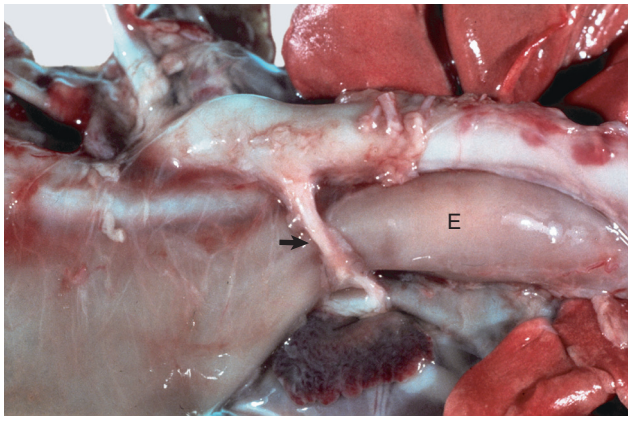


Figure 10-37 Persistent Right Aortic Arch, Ligamentum Arteriosum, Megaesophagus, Calf. During embryogenesis, the aorta was formed from the right aortic arch instead of the left one; thus the aorta is now on the right. For the ligamentum arteriosum *(arrow)* to connect the aorta with the pulmonary artery, it has to pass dorsally over the esophagus and trachea. The ligamentum, together with the aorta and pulmonary artery, form a vascular ring that constricts the esophagus *(E)*, which is dilated cranial to the constriction. (Courtesy Dr. S. Snyder, College of Veterinary Medicine, Colorado State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

muscle in the ductus arteriosus contracts, which results in its occlusion within 7 to 10 days after birth in the dog. When this mechanism fails, the ductus arteriosus remains patent and allows for a portion of the blood from the left cardiac chamber to flow from the aorta into the pulmonary artery and results in overcirculation to the lungs, leading to pulmonary hypertension and increased preload to the left ventricle. Grossly, patent ductus arteriosus is a dilated funnel-shaped communication between the descending aorta and the main pulmonary artery. This vascular channel between the pulmonary artery and aorta allows blood to bypass the lungs during fetal life. Normally, the ductus arteriosus is converted to the solid ligamentum arteriosum postnatally.

Malpositioning of Great Vessels

Persistent Right Aortic Arch. Persistent right aortic arch occurs in dogs; German shepherd, Irish setter, and Great Dane dogs are predisposed (Fig. 10-37). This defect arises because the right fourth aortic arch, rather than the normal left fourth aortic arch, develops and ascends on the right side of the midline so that the ligamentum arteriosum forms a vascular ring over the esophagus and trachea. This arrangement eventually results in esophageal obstruction and proximal dilation (megaesophagus), which often results in aspiration pneumonia as the animal matures and consumes solid feed.

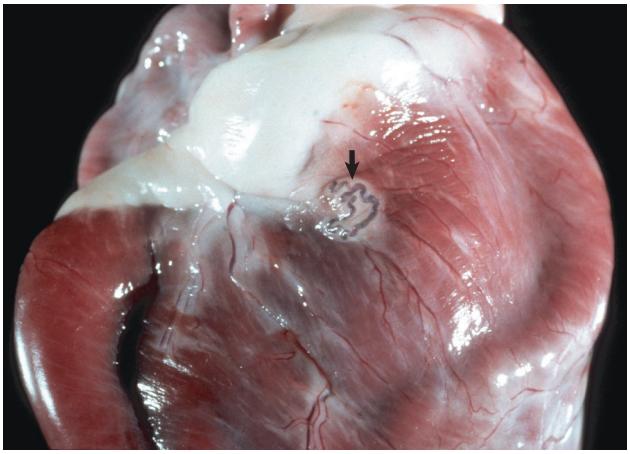


Figure 10-38 Congenital Lymphangiectasia, Epicardium, Young Horse. Note the tortuous appearance of the epicardial lymphatic vessel *(arrow)*. In congenital lymphangiectasia, lymphatic vessels fail to make connections with other vessels or are obstructed because of anomalous development. (Courtesy College of Veterinary Medicine, University of Illinois.)

Transposition of the Aorta and Pulmonary Artery. Transposition of the aorta and pulmonary artery are severe anomalies, of which there are several types. In complete transposition, the aorta serves as the outflow from the right ventricle and the pulmonary artery is the left ventricle primary outflow. Other congenital anomalies, including ventricular septal defect, often accompany this anomaly.

Truncus Arteriosus. In this lesion, there is a large VSD that allows blood flow between the ventricles and a single large vessel that originates above the VSD. Hypoxemia and cyanosis develop, depending on the amount of mixture of nonoxygenated and oxygenated blood.

Lymphatic Vessels

Lymphangiectasia. Lymphangiectasia is dilation of lymphatic vessels. The cause may be a congenital anomaly (Fig. 10-38) or obstruction of lymph drainage by invading masses of malignant neoplasms or inflammation (Fig. 10-39).

Hereditary Lymphedema. Hereditary lymphedema has been described in dogs, Ayrshire and Angus calves, and pigs. Affected animals have prominent subcutaneous edema that, in calves, often causes severe swelling of the tips of the ears. Interference with lymph drainage results from defective development of the lymphatic vessels that are aplastic or hypoplastic.

Disorders of Domestic Animals: Myocardium

The most common cardiac diseases in horses, ruminants, pigs, dogs, and cats are summarized in Boxes 10-12 and 10-13. The most common locations of major neoplastic diseases in the heart are illustrated in Fig. 10-40. Cardiovascular diseases with known or suspected heritability are listed in E-Boxes 10-2 and 10-3.

Disturbances of Circulation

Hemorrhage: Trauma (Physical Injury). Blunt chest trauma may result in myocardial hemorrhage, which can lead to serious clinical consequences. Tears and rupture of tissue resulting from loss of structural integrity attributable to invasive and destructive properties of neoplasms may result in myocardial hemorrhage. See discussion on hemorrhage in Chapter 2.

E-Box 10-2 Inherited Cardiovascular Diseases of Animals (Also See E-Box 1-1)

HYPERTROPHIC CARDIOMYOPATHY: CATS
Maine coon cats: Autosomal dominant
Ragdoll cat: Autosomal dominant (?)
British shorthair cat: Autosomal dominant (?)

DILATED CARDIOMYOPATHY: DOGS
Portuguese water dog: Autosomal recessive
Doberman pinscher dog: Autosomal dominant
Irish wolfhound dog: Autosomal dominant (recessive?)
Newfoundland dog: Autosomal dominant
Great Dane dog: X-linked recessive (?)

CARDIOMYOPATHY WITH X-LINKED MUSCULAR DYSTROPHY: DOGS
Irish terrier, golden retriever, Dalmatian, Shetland sheepdog, Samoyed, Pembroke Welsh corgi, Japanese spitz, Alaskan malamute dog: X-linked recessive

ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY: DOG
Boxer dog: Autosomal dominant

CARDIOMYOPATHY WITH CURLY HAIRCOAT: COW
Poll Hereford cow: Autosomal recessive

DILATED CARDIOMYOPATHY: COW
Holstein-Friesian cow: Autosomal recessive with X-linked muscular dystrophy

CARDIOMYOPATHY WITH MUSCULAR DYSTROPHY: HAMSTER
Syrian golden hamster: Autosomal recessive

MYXOMATOUS VALVULAR DEGENERATION (VALVULAR ENDOCARDIOSIS)
Cavalier King Charles spaniel: Polygenic trait
Dachshund: Polygenic trait

AORTIC STENOSIS (SUBVALVULAR)
Newfoundland: Polygenic trait

TETRALOGY OF FALLOT: CONOTRUNCAL DEFECTS
Keeshond: Simple autosomal locus with partial penetration in heterozygous and complete penetrance in homozygotes

PATENT DUCTUS ARTERIOSUS
Poodle: Polygenic trait

PULMONIC STENOSIS
Beagle: Polygenic trait

TRICUSPID DYSPLASIA
Labrador retriever: Autosomal dominant with reduced penetrance

E-Box 10-3 Canine Breed Predilections for Congenital Cardiac Anomalies

Breed	Defect
Basset hound	PS
Beagle	PS
Bichon frise	PDA
Boxer	SAS, PS, ASD
Boykin spaniel	PS
Bull terrier	MiVD, AS
Chihuahua	PDA, PS
Chow Chow	PS, CTD
Cocker spaniel	PDA, PS
Collie	PDA
Doberman pinscher	ASD
English bulldog	PS, VSD, TOF
English springer spaniel	PDA, VSD
German shepherd	SAS, PDA, TVD, MiVD
German shorthaired pointer	SAS
Golden retriever	SAS, TVD, MiVD
Great Dane	TVD, MiVD, SAS
Keeshond	TOF, PDA
Labrador retriever	TVD, PDA, PS
Maltese	PDA
Mastiff	PS, MiVD
Newfoundland	SAS, MiVD, PS
Pomeranian	PDA
Poodle	PDA
Rottweiler	SAS
Samoyed	PS, SAS, ASD
Schnauzer	PS
Shetland sheepdog	PDA
Terrier breeds	PS
Weimaraner	TVD, PPDH
Welsh corgi	PDA
West Highland white terrier	PS, VSD
Yorkshire terrier	PDA

AS, aortic stenosis; *ASD,* atrial septal defect; *CTD,* cor triatriatum dexter; *MiVD,* mitral valve dysplasia; *PDA,* patent ductus arteriosus; *PPDH,* peritoneopericardial diaphragmatic hernia; *PS,* pulmonic stenosis; *SAS,* subaortic stenosis; *TOF,* tetralogy of Fallot; *TVD,* tricuspid valve dysplasia; *VSD,* ventral septal defect.

Adapted from Oyama MA, Sisson DD, Thomas WP, et al: Congenital heart disease. In Ettinger SJ, Feldman EC, editors: *Textbook of veterinary internal medicine*, ed 7, St. Louis, 2010, Saunders; 1250-1298.

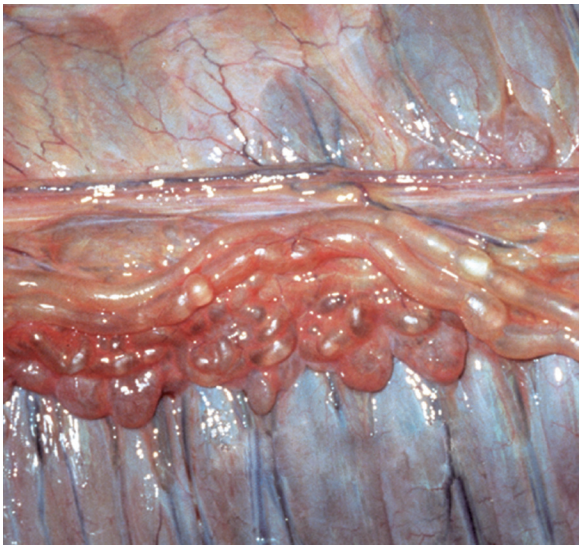


Figure 10-39 Acquired Lymphangiectasia, Lymphoma (Lymphosarcoma), Mesocolon, Horse. Note the distended lymphatic vessels on the serosal surface of the large colon, the result of impeded lymph flow through the colic lymph nodes, caused by compression of their cortical and medullary sinuses by proliferating neoplastic lymphocytes. (Courtesy College of Veterinary Medicine, University of Illinois.)

Box 10-12 Most Common Cardiac Diseases of Horses and Production Animals

HORSES
Fibrinous pericarditis
Toxic cardiomyopathy (ionophores, white snakeroot)
Endocardial fibrosis and calcification
Endocarditis

RUMINANTS (CATTLE, SHEEP, AND GOATS)
White muscle disease (vitamin E–selenium deficiency)
Cardiotoxicity (ionophores, gossypol, *Cassia occidentalis*, *Karwinskia humboldtiana*)
Brisket disease (high-altitude disease)
Pericarditis
Endocarditis
Malignant lymphoma

PIGS
Mulberry heart disease (vitamin E–selenium deficiency)
Pericarditis
Endocarditis

Disturbances of Growth

See the discussion on anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves.

Hypertrophy and Atrophy

Cardiomyopathies. Categorization and causes of primary and secondary cardiomyopathies are listed in Box 10-14. These diseases are divided into five morphologic types: hypertrophic, dilated (congestive), restrictive, arrhythmogenic right ventricular, and unclassified cardiomyopathies. Secondary cardiomyopathies (also termed *specific heart muscle diseases*) are generalized myocardial diseases of known cause.

Hypertrophic Cardiomyopathy. Hypertrophic cardiomyopathy (HCM) occurs frequently in cats, especially in young adult to middle-aged males (1 to 3 years old), and is seen infrequently in dogs, usually affecting males of large breeds.

Hypertrophic cardiomyopathy is the most common feline primary myocardial disease, and it occurs frequently in cats (58% to 68% of all cardiomyopathy cases). There is familial heritability in Maine coon, ragdoll, and American shorthaired cats (in which it is transmitted in an autosomal dominant pattern) and breed predisposition in British shorthair, Norwegian forest, Turkish Van, Scottish fold, Bengal, Siberian, and Rex cats. Young adult to middle-aged males (1 to 3 years old) are often affected. Hypertrophic cardiomyopathy is caused by sarcomeric defects in cardiomyocytes, of which two mutations in cardiac myosin-binding protein C (MYBPC) have been identified in Maine coon and ragdoll cats. Altered sarcomeric function ultimately results in myocytes hypertrophy, collagen synthesis, and myocytes disarray (defined as cellular disorientation of cardiomyocytes in which cardiomyocytes are oriented perpendicular or obliquely to each other forming tangled patterns and/or pinwheel configurations). The left ventricle wall progressively thickens (Fig. 10-41), and its lumen narrows (nondilated concentric hypertrophy) (heart weight to body weight ratio of 7.0 ± 0.3 g/kg compared to normal cats' heart weight to body weight ratio of 3.83 ± 0.2 g/kg). In addition, mild right ventricular enlargement is occasionally present. Left ventricular concentric enlargement results in impairment of the left ventricle's ability to relax during diastole (diastolic failure). Increased left ventricular diastolic filling pressure leads to enlargement of the left atrium with subsequent blood backing up to the lungs, resulting in congestive heart failure with pulmonary edema and/or pleural effusion. In a subset of cases, in addition to concentric hypertrophy of the left ventricle, the interventricular septum contains hypertrophied, anteriorly displaced papillary muscles that pull the chordae tendineae and the anterior leaflet of the mitral valve into the left ventricular outflow tract (LVOT), resulting in a dynamic LVOT obstruction during systole (systolic anterior motion [SAM] of the mitral valve). Therefore a unique kissing lesion forms in the LVOT, which has a diagnostic significance

Box 10-13 Most Common Cardiac Diseases in Dogs and Cats

DOGS
Myxomatous valvular degeneration (valvular endocardiosis)
Congenital heart disease
Dilated cardiomyopathy
Hemorrhagic pericardial effusion
Cardiac neoplasia
Dirofilariasis

CATS
Hypertrophic cardiomyopathy
Dilated cardiomyopathy
Hyperthyroidism-associated hypertrophy
Congenital heart disease

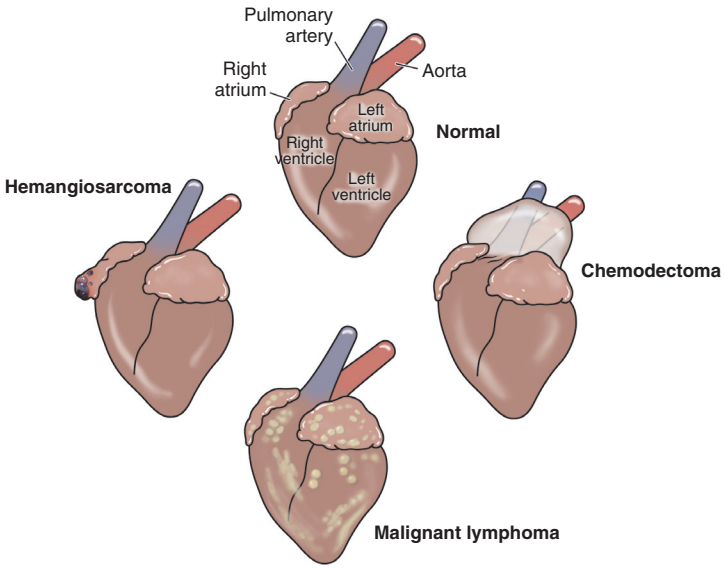


Figure 10-40 Locations of the Major Cardiac Neoplasms. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

Box 10-14 Cardiomyopathies in Animals

PRIMARY CARDIOMYOPATHIES (IDIOPATHIC)

Hypertrophic: Cat, dog, rat, pig
Dilated (congestive): Cat, dog, hamster, turkey, pig, cow, sea otters, sea lions, cynomolgus monkeys
Restrictive: Cat
Arrhythmogenic right ventricular cardiomyopathy: Dog, cat

SECONDARY CARDIOMYOPATHIES (SPECIFIC HEART MUSCLE DISEASES)

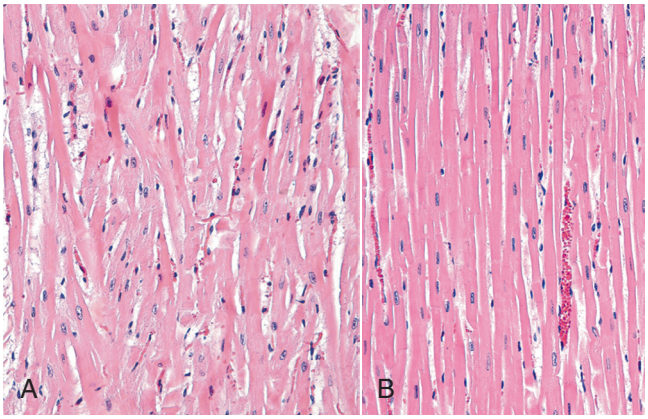
Heritable (known or suspected): Hereditary cardiomyopathy of hamsters, mice, rats, turkeys, and cattle; Duchenne's type, X-linked muscular dystrophy of golden retriever dogs with dystrophin deficiency; glycogenoses
Nutritional deficiencies: See list in Box 10-5; other examples include taurine deficiency in cats and foxes
Toxic: See list in Box 10-5; other examples include anthracycline toxicity, furazolidone toxicity, NaCl toxicity
Physical injuries and shock: See list in Box 10-5
Endocrine disorders: Hyperthyroidism, acromegaly (hypersomatotropism), hypothyroidism, glucocorticoid excess, functional pheochromocytoma, diabetes mellitus
Infections: See lists in Boxes 10-6, 10-7, and 10-8
Neoplastic infiltration: Malignant lymphoma
Systemic hypertension in cats and dogs: Spontaneous or associated with chronic renal disease, hyperthyroidism, diabetes mellitus, acromegaly, primary aldosteronism

because it is seen only in this subset of cats with hypertrophic cardiomyopathy. In addition, the systolic obstruction in the LVOT causes further increase in the left ventricular pressure that worsens its hypertrophy. Approximately 10% to 20% of cats with hypertrophic cardiomyopathy have a state of increased coagulability and develop posterior paresis from concurrent thromboembolism of the caudal abdominal aorta ("saddle thrombosis") (see Fig. 10-91). The aortic thrombus is first formed in the stagnant blood flow of the enlarged left atrium and is subsequently launched into the aorta. Some cats with hypertrophic cardiomyopathy die unexpectedly without premonitory clinical signs. Microscopically, the lesions of the myocardium are prominent disarray or disorganizations of myocytes, with interweaving rather than parallel arrangement of fibers (Fig. 10-42). Myocyte hypertrophy, various degenerative alterations in myocytes, and interstitial fibrosis are present. A second common histologic lesion includes remodeling of the coronary microcirculation associated with arteriosclerosis ("small vessel disease"). The lumen of small coronary vessels is severely narrowed due to smooth muscle proliferation and increased connective tissue elements. Replacement fibrosis due to myocardial infarction/necrosis is occasionally found in regions of remodeled coronary arterioles, implying a probable causal relationship (see Figs. 10-41 and 10-42; E-Fig. 10-20).

Idiopathic hypertrophic cardiomyopathy in dogs is an infrequent pathology, unlike in cats. It is defined as inappropriate concentric myocardial hypertrophy of a nondilated left ventricle in the absence of an identifiable stimulus for the hypertrophy. Most reported cases have been in young males (<3 years old), and an inherited basis has been proposed in the pointer dog breed. Hypertrophy of the left ventricle has been reported to be symmetrical (i.e., both left ventricular free wall and interventricular septum) in most dogs. In addition, most dogs had an antemortem diagnosis of dynamic LVOT obstruction. In these dogs, a thickened opaque plaque of connective tissue was present opposite to the anterior mitral valve. These dogs had an abnormally opposing thickened mitral valve leaflet and/or malpositioned papillary muscles, suggesting that hypertrophic cardiomyopathy in these dogs may not be just simply a disease of myocardium. However, at least in one report, myofibers disarray and asymmetrical hypertrophy of the septum has been reported. Secondary changes in medium-sized coronary arteries that have been reported in cats with hypertrophic cardiomyopathy are also present in dogs with hypertrophic cardiomyopathy, and they include tunica intima hyperplasia with hypertrophy and hyaline degeneration of smooth muscle cells in the tunica media.

Dilated (Congestive) Cardiomyopathy. Dilated or congestive cardiomyopathy (DCM) is an important cause of congestive heart failure in cats, dogs, and cattle.

Affected dogs often are males of large breed, such as Doberman pinschers, Portuguese water dogs, Dalmatians, Scottish deerhounds, Irish wolfhounds, Saint Bernards, Afghan hounds, Newfoundland dogs, Old English sheepdogs, Great Danes, and boxers. However, smaller breeds, such as English cocker spaniels and Manchester



E-Figure 10-20 Hypertrophic Cardiomyopathy, Heart, Ventricular Myocardium, Cat. A, Note the pattern of interwoven cardiac myocytes, indicating myofiber disarray, and the hypertrophic myocytes (compare with Figs. 10-20 and 10-42). The number of fibroblasts is increased in the interstitium. H&E stain. **B,** Normal cardiac myocytes arranged in parallel bundles. (Courtesy Dr. L. Borst, College of Veterinary Medicine, University of Illinois.)

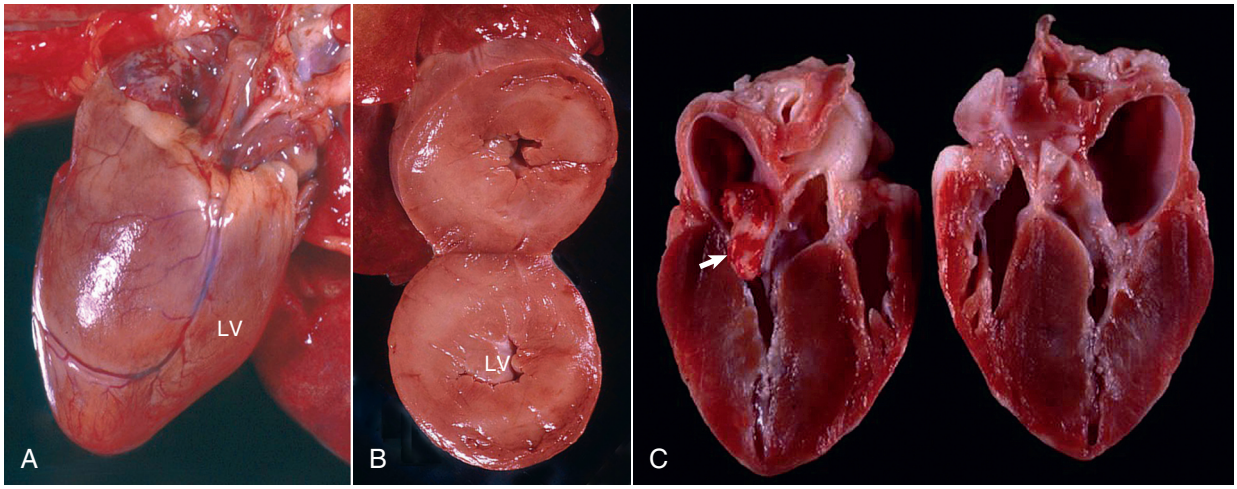


Figure 10-41 Hypertrophic Cardiomyopathy, Heart, Cats. A, Note the thickened left ventricular wall *(LV)*. **B,** The thickened left ventricular free wall and septum have markedly reduced the lumen of the left ventricle *(LV)*. **C,** There is severe diffuse concentric hypertrophy of the left ventricular free wall, interventricular septum, and papillary muscles. Left atrial dilation is present and a large thrombus *(arrow)* arises from and extends through the left atrioventricular valve. (**A** and **B** courtesy Dr. W. Crowell, College of Veterinary Medicine, The University of Georgia; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia. **C** courtesy Ettinger SJ, Feldman EC (editors): *Textbook of veterinary internal medicine. Diseases of the dog and cat*, vol 2, ed 7, Philadelphia, 2010, Saunders.)

terriers, may be affected. The disease often has a familial pattern in the affected breeds, and it appears to be inherited as an autosomal recessive mode in the Portuguese water dog breed; as an autosomal dominant mode in the Irish wolfhound, Newfoundland, and Doberman pinscher dog breeds; and likely as an X-linked recessive mode in boxer dogs. At autopsy (syn: necropsy), lesions of congestive heart failure are present and the hearts are rounded because of biventricular dilation (Figs. 10-43 and 10-44), whereas in some cases dilation of the left atrium and ventricle predominates. The ratio between the ventricular wall and chamber diameter is decreased (i.e., eccentric hypertrophy). The circumference of the annulus of the mitral and tricuspid valves is often increased, and the papillary muscles are often flattened and atrophic. Atrioventricular valvular leaflets are occasionally mildly to moderately thickened, and chordae tendineae are thickened and elongated. The dilated cardiac chambers often have a diffusely white, thickened endocardium. Myocardial hypertrophy is best demonstrated by calculating heart weight to body weight ratio. The term hypertrophy implies a pathologic process in which the weight of the organ is increased because of an increase in cell size rather than number. In myocardial eccentric hypertrophy, the sarcomeres are increased in numbers in series (rather than parallel as in concentric hypertrophy). Two histological patterns have been described in dogs with dilated cardiomyopathy. The attenuated wavy fiber type is seen in many giant, large and medium-sized dogs and the fatty infiltration-degenerative type of dilated cardiomyopathy is seen in mainly boxers and Doberman pinschers. Occasionally, there are additional nonspecific findings, such as necrosis, infarcts, fibrosis, vacuolization of myocytes, and hyperplasia of coronary arteries. In the attenuated wavy fiber type, the cardiomyocytes are less than 6 μm in diameter (normal myofiber diameter ranges from 10 to 20 μm) and have a wavy appearance. The myocytes are separated by clear spaces (i.e., edema fluid), and there is minimal to absent cellular infiltrates. The abnormal attenuated wavy fibers are most abundant in the lateral wall of the left ventricle and therefore this site should be sampled when dilated cardiomyopathy is suspected. The sensitivity and specificity of attenuated wavy fibers of the myocardium of dogs for the diagnosis of dilated cardiomyopathy have been shown to be 98% and 100%, respectively. The attenuated wavy fibers form may represent an early pathologic change in the myocardium of dogs with dilated cardiomyopathy because it has been documented in dogs preceding clinical signs of dilated cardiomyopathy. In the fatty infiltration-degenerative type of dilated cardiomyopathy, histopathology consists of myocytolysis, myofiber degeneration, vacuolization, and atrophy along with extensive fibrosis and fatty infiltration that replaces the myofibers. It is proposed that the two histologically distinct forms of idiopathic canine dilated cardiomyopathy reflect different disease processes. Cardiotoxicity leading to chamber dilation similar to DCM (i.e., secondary dilated cardiomyopathy) has been reported secondary to toxic/environmental (e.g., doxorubicin, irradiation, ethanol, cobalt, lead, catecholamines, histamine, and methylxanthines), infectious (e.g., canine parvovirus), and nutritional (taurine and carnitine deficiency) causes.

Idiopathic dilated cardiomyopathy is a rare feline primary myocardial disease with a suggested complex genetic inheritance that results in a systolic heart failure rather than a diastolic heart failure as seen in cats with hypertrophic cardiomyopathy. Most cats develop secondary dilated cardiomyopathy because of nutritional deficiency (taurine), toxicity (doxorubicin), or severe volume overload (severe mitral insufficiency or congenital defects leading to severe left to right shunting) or, rarely, infection with feline panleukopenia virus. The heart globally enlarges through dilation of all chambers (eccentric hypertrophy), and the heart to body weight ratio is increased (5.4 ± 0.3 g/kg vs. 3.83 ± 0.2 g/kg in normal control cats), although the walls of the ventricles are thinned. This is due to addition of sarcomeres in series, rather than in parallel, which leads to a proportional increase in ventricular wall thickness and internal chamber diameter. Hydrothorax, pulmonary congestion, and edema often accompany dilated cardiomyopathy when congestive heart failure ensues. Similar to cats with hypertrophic cardiomyopathy, arterial thromboembolism occasionally accompanies feline dilated cardiomyopathy, unlike in dogs with dilated cardiomyopathy. Cardiac histopathology consists of mild multifocal to severe and diffuse interstitial edema and fibrosis. Myocardiocytes are thinner, attenuated, and wavier than normal, and they often exhibit myocytolysis.

Three forms of bovine dilated cardiomyopathy are dilated cardiomyopathy in cattle of Canadian Holstein origin, cardiomyopathy

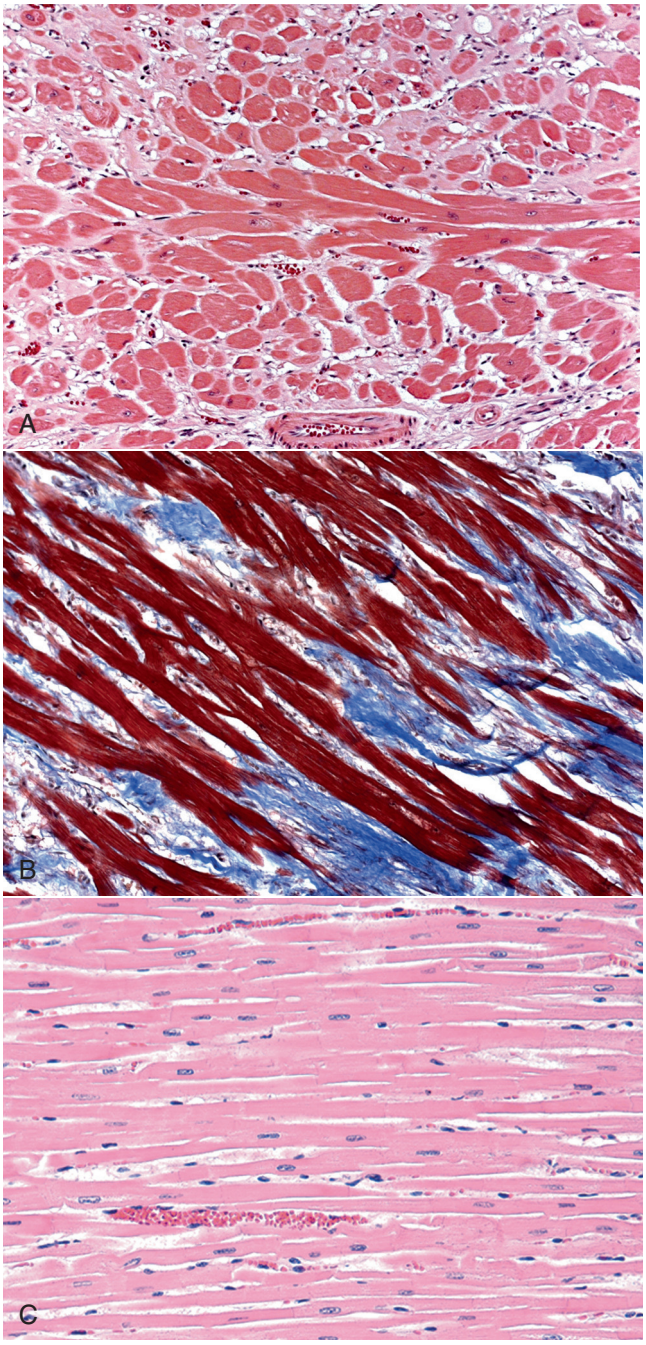


Figure 10-42 Hypertrophic Cardiomyopathy, Heart, Ventricular Myocardium, Cat. A, Cardiac myocytes are hypertrophied and in disarray. H&E stain. **B,** Masson's trichrome stain demonstrates abundant amounts of interstitial collagen *(blue)* produced by fibroblasts. **C,** Normal cardiac myocytes arranged in parallel bundles. H&E stain. (**A** and **B** courtesy Atlantic Veterinary College, University of Prince Edward Island. **C** courtesy Dr. L. Borst, College of Veterinary Medicine.)

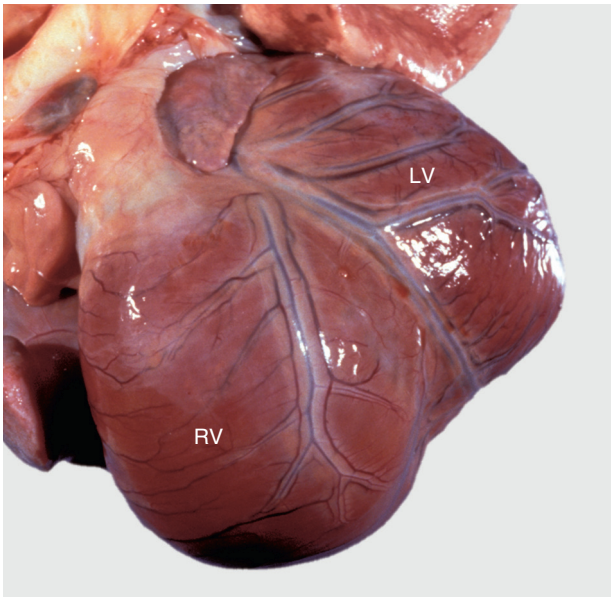


Figure 10-43 Dilated (Congestive) Cardiomyopathy, Heart, Left Ventricle *(LV)* and Right Ventricle *(RV)*, Dog. Biventricular dilation has resulted in the heart having a double apex. (Courtesy Dr. T. Boosinger, College of Veterinary Medicine, Auburn University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

in Japanese black cattle, and congenital cardiomyopathy in Hereford cattle. Cardiomyopathy in cattle of Canadian Holstein origin has been reported in Holsteins, Red Holstein-Friesian, and Red Danish dairy breed; it was first reported in Switzerland for Simmental-Red Holsteins, but is now reported from multiple countries. Breeding studies have indicated an autosomal recessive mode of inheritance. Affected cattle develop congestive heart failure with cardiac dilation. Histopathologic findings are loss of cardiac muscle cells and replacement fibrosis. Japanese black cattle cardiomyopathy occurs in newborn and infant calves. Microscopically, myocardial degeneration and necrosis is marked. A lethal, autosomal recessive gene is suspected. Congenital cardiomyopathy occurs in Poll Hereford cattle in association with wooly haircoat syndrome. Inherited as a lethal autosomal recessive trait, affected calves usually die from congestive heart failure by 12 weeks of age.

Restrictive Cardiomyopathy. Restrictive cardiomyopathy occurs infrequently. Restrictive cardiomyopathy is a functional term rather than disease entity and consists of a spectrum of pathologic phenotype and pathophysiology. The hallmark of restrictive cardiomyopathy is increased stiffness of the myocardium that leads to diastolic heart failure. Stiffness is due to increased myocardial fibrosis and variable infiltration with leukocytes. Sometimes the endocardium is also involved (endomyocardial fibrosis), and it is thought to be a specific subtype of restrictive cardiomyopathy. When the endocardium is involved, there is extreme endocardial thickening secondary to fibrosis and granulation tissue. Restrictive cardiomyopathy in cats can have two types of endocardial changes resultant in impaired vascular filling. In one type, the left ventricular endocardium has diffuse notable fibrosis. Evidence suggests that the fibrotic lesion is preceded by endomyocarditis. The second type results from excessive moderator bands that traverse the left ventricular cavity. Other examples of restrictive cardiomyopathy in animals include endocardial fibrosis in certain strains of aged rats and congenital endocardial fibroelastosis in Burmese cats (Fig. 10-45).

Arrhythmogenic Right Ventricular Cardiomyopathy. Arrhythmogenic right ventricular cardiomyopathy is an important cardiac disease of middle-aged boxer dogs, and rare cases have been reported in cats. Other names for the disease include boxer cardiomyopathy and familial ventricular arrhythmias of boxers. It is inherited as an autosomal dominant trait in boxers, and it is associated with an 8–base pair deletion in the 3′ untranslated region of the Striatin gene on chromosome 17, inhibition of trafficking of Wnt pathway proteins from the endoplasmic reticulum to their proper location within the cell, and potentially with Calstabin2 deficiency. Affected dogs have a high incidence of ventricular arrhythmias with

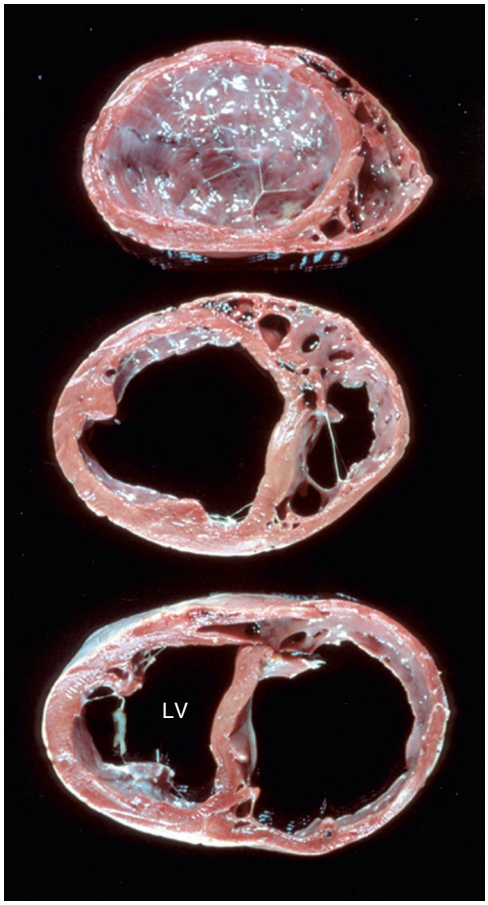


Figure 10-44 Dilated (Congestive) Cardiomyopathy, Heart, Ventricles, Cross Section, Dog. The left ventricle *(LV)* and right ventricle have thin walls, dilated chambers, and white fibrotic endocardium. (Courtesy Dr. Y. Niyo, College of Veterinary Medicine, Iowa State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

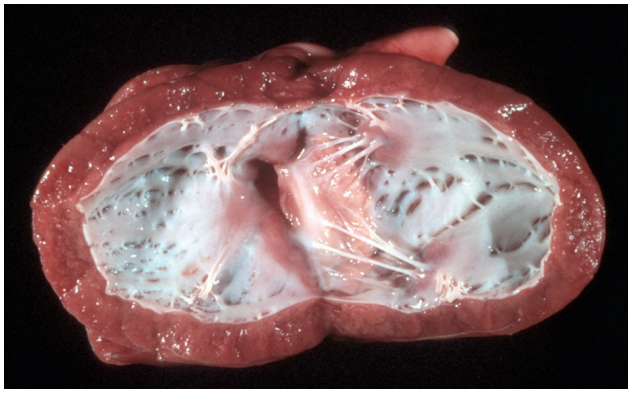


Figure 10-45 Subendocardial Fibroelastosis, Heart, Left Ventricle, Dog. The endocardium is opaque because increased amounts of collagen and elastic fibers were deposited in the subendocardium secondary to turbulence of blood flow within the ventricles. This dog had a persistent ductus arteriosus. This lesion may have a hereditary basis in Burmese cats and is often a sequela to turbulence within ventricles in cardiac disease. (Courtesy College of Veterinary Medicine, University of Illinois.)

predominantly left bundle branch block morphology that originate from the right ventricle, and they often have enlargement of the right ventricular chamber; however, some dogs have normal-sized cardiac chambers, and because of the intermittent nature of the arrhythmia in arrhythmogenic right ventricular cardiomyopathy, they may not have a documented history of ventricular premature complexes on electrocardiogram. Therefore lack of documented arrhythmia and/or enlargement of the right cardiac chamber does not rule out this disease. The distinctive histopathologic findings are similar to those of the disease in human beings and include substantial replacement of right ventricular (RV) cardiac myocytes by adipose or fibrous tissue in a fatty or a fibro-fatty pattern.

It is a rare myocardial disease of cats. Cats have moderate to severe RV eccentric hypertrophy and severe right atrial enlargement with segmental to diffuse wall thinning, and they develop atrial and ventricular arrhythmias from macroreentrant circuits that develop in regions of fibrofatty infiltration.

Unclassified Cardiomyopathy. This is a nebulous category that includes cases with left or bilateral atrial dilation, normal to near normal LV wall thickness, normal systolic function, and diastolic dysfunction. Grossly and histologically, the distinction between restrictive cardiomyopathy and unclassified cardiomyopathy is not apparent unless endomyocardial fibrosis is present. The separation between these two entities can sometimes be made antemortem via echocardiographic evaluation of a restrictive filling pattern on mitral inflow (E and A waves).

Molecular Mechanisms of Hereditary Cardiomyopathies. Our understanding of the molecular mechanisms of the hereditary cardiomyopathies is developing rapidly. In human beings with familial hypertrophic cardiomyopathy inherited in an autosomal dominant manner, a variety of single-gene mutations have been documented. The mutations affect genes that encode sarcomere proteins of cardiac myocytes. Hypertrophic cardiomyopathy-associated altered cardiac proteins include cardiac β-myosin heavy chain, cardiac troponin T and tropomyosin, and myosin-binding protein C. Dilated cardiomyopathy-associated mutated proteins include desmin, mitochondrial proteins, dystropin, titin (titin spans the sarcomere and connects the Z and M restricting the range of sarcomere stretching motion), and a subunit of the surface protein–dystropin-associated glycoproteins. It remains unclear how these mutant proteins result in functional and structural alterations of cardiac muscle cells. However, recent studies suggest hypertrophic cardiomyopathy may arise from defective energy transfer from the mitochondria to the sarcomere. Dilated cardiomyopathy is believed to be associated with abnormalities in the cytoskeletal proteins resulting in abnormal force generation, force transmission, or myocyte signaling. Similar gene mutations and altered proteins were recently discovered in the various heritable cardiomyopathies of animals.

Neoplastic Transformation. Various primary and secondary neoplasms develop either in or near the heart. Primary neoplasms include rhabdomyoma, rhabdomyosarcoma, schwannoma, and hemangiosarcoma. Rhabdomyomas and rhabdomyosarcomas are rare in animals and form white to gray nodules in the myocardium that often project into the cardiac chambers. Congenital rhabdomyomatosis in pigs and guinea pigs is a presumed nonneoplastic hamartoma (i.e., malformation often resembling a neoplasm that is composed of an overgrowth of mature cells and tissues that normally occur in the affected organ). Cardiac rhabdomyomatosis has been reported in cattle, sheep, and dogs. Single or multiple, pale, poorly circumscribed areas are scattered in the myocardium and are composed of large glycogen-laden cells with morphologic features of cardiomyocytes and Purkinje cells.

Malignant lymphoma (lymphosarcoma) is the most common secondary neoplasm occurring in the heart and often causes lesions in the hearts of cattle, which can be severe enough to cause death from cardiac failure. Cardiac lesions may be present in dogs and cats with malignant lymphoma. The neoplastic cell infiltration can be

diffuse or nodular and involve the myocardium, endocardium, and pericardium. Lymphomatous tissue appears as white masses that may resemble deposits of fat (Fig. 10-46). Microscopically, extensive infiltrations of neoplastic lymphocytes are present between myocytes (Fig. 10-47). Other neoplasms, such as malignant melanomas, occasionally have metastatic lesions in the heart.

Heart-based tumors are primary neoplasms of extracardiac tissues in dogs and rarely cats. They arise at the base of the heart and can produce vascular obstruction and cardiac failure. The most common neoplasm arising at this location is the aortic body tumor or paraganglioma (chemodectoma), but occasionally ectopic thyroid or parathyroid tissue gives origin to neoplasms in this area. The aortic body is a chemoreceptor organ. In some cases, aortic body tumors become large, white, firm masses that surround and compress the great vessels and atria (Fig. 10-48). Brachycephalic dog breeds are most frequently affected. Microscopically, the neoplastic cells are polyhedral with vacuolated cytoplasm and are supported by a fine connective tissue stroma (see Fig. 12-47).

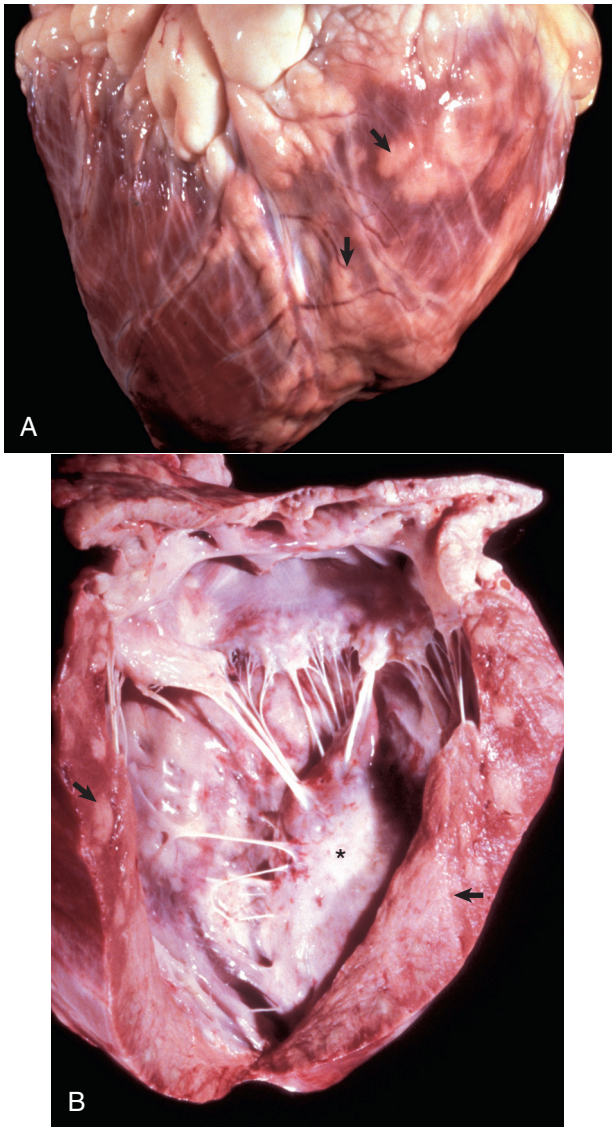


Figure 10-46 Lymphoma (Lymphosarcoma), Heart, Myocardium, Cow. A, Sites of infiltrating neoplastic lymphocytes in the ventricular myocardium are evident as numerous white areas and nodules *(arrows)*. **B,** Similar white areas of tumor are visible in the section of the left ventricular wall *(arrows)* and subendocardially *(*)* in the ventricular septum. (Courtesy College of Veterinary Medicine, University of Illinois.)

Cell Degeneration and Death

Myocardial Necrosis and Mineralization. Myocardial necrosis and mineralization can result from a number of causes, including nutritional deficiencies, chemical and plant toxins, ischemia, metabolic disorders, heritable diseases, and physical injuries (see Box 10-5). From this large list of causes of myocardial injury, some of the most frequently observed current examples are ionophore toxicity in horses and ruminants, vitamin E–selenium deficiency in the young of all species, "heart-brain syndrome" of dogs (see Fig. 10-82), anthracycline toxicity in dogs, and gossypol toxicosis in pigs. In various localized areas throughout the world, numerous deaths in ruminants have resulted from consumption of poisonous plants such as *Acacia georginae* and *Dichapetalum cymosum*. The macroscopic lesions are similar regardless of the specific toxin and include pale white to tan areas and linear streaks throughout the myocardium. Microscopic lesions include multifocal myocardial degeneration and necrosis characterized by vacuolation of myocardial cytoplasm; loss of cross-striations; fragmentation of rhabdomyocytes;

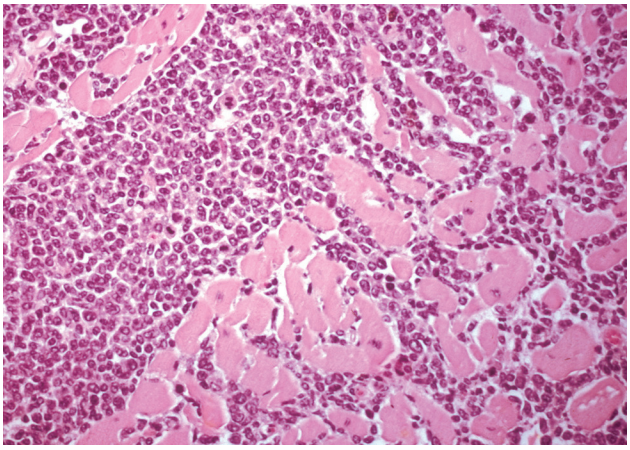


Figure 10-47 Lymphoma (Lymphosarcoma), Heart, Section of Myocardium, Cow. Neoplastic lymphocytes have extensively infiltrated between the cardiomyocytes. Extensive infiltration can result in myocyte atrophy and loss. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

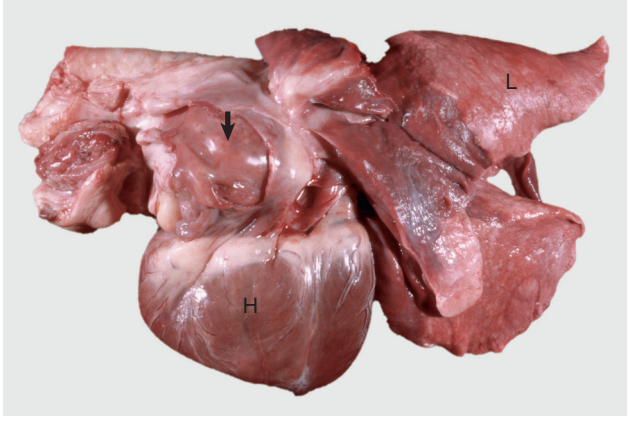


Figure 10-48 Chemodectoma (Heart Base Tumor), Aortic Body, Dog. Note the large mass *(arrow)* at the base of the heart *(H)*. *L,* Lungs. (Courtesy College of Veterinary Medicine, University of Illinois.)

hypereosinophilia, coagulation, and clumping of the sarcoplasm; and nuclear pyknosis and karyolysis (Fig. 10-49).

Toxicoses

Ionophore-Induced Myocardial Degeneration. Ionophores (polyether antibiotics), such as monensin, lasalocid, salinomycin, and narasin, are toxic to horses and dogs at extremely low concentrations. They are used as feed additives to increase feed efficiency and weight gain of beef and dairy cattle and to control coccidiosis in poultry. Horses gain access to ionophores when they consume (1) ruminant feed containing ionophores; (2) horse feed accidentally mixed with ionophores; and (3) horse and dog food accidentally contaminated in a mill producing poultry, cattle, horse, and dog feeds. Ionophores cause acute cardiac rhabdomyocyte degeneration and necrosis; this type of injury is discussed in detail in the section on Responses to Injury: Myocardium, Myocardial Necrosis. Ionophores are lipophilic chelating agents that transport cations across phospholipid bilayer membranes and complexes with monovalent cations, such as Na^+ and Ca^+, and cross cell membranes and enter the cell via ion transport systems in exchange for H^+ and K^+ ions. Increases in the concentrations of intracellular Ca^+ and possibly Na^+ are thought to cause cell membrane injury and dysfunction, resulting in mitochondrial swelling and decreased adenosine triphosphate production. In addition, they cause lipid peroxidation of cell membranes leading to loss of cell membrane integrity, fluid and ion shifts, and oncotic necrosis.

Gossypol-Induced Myocardial Degeneration. Gossypol-induced myocardial degeneration can follow the ingestion of cottonseed or cottonseed products that contain excess free gossypol. Gossypol is a potentially toxic pigment in the cotton plant; however, it is toxic only when in a free form (not bound to protein). Gossypol causes myocardial degeneration and necrosis and cardiac conduction failure (see later discussion). The macroscopic and microscopic characteristics of the lesions are in many ways similar to those caused by ionophore-induced and white snakeroot–induced myocardial degeneration in horses. In addition, acute rhabdomyocytic degeneration and necrosis are discussed in detail in the section on Responses to Injury: Myocardium, Myocardial Necrosis and also in Chapter 15. Monogastric animals, particularly pigs and horses, are more sensitive to gossypol-induced myocardial degeneration and necrosis than ruminants. In summary, macroscopic lesions include pale white to tan areas throughout a "flabby" myocardium; microscopic lesions include multifocal myocardial degeneration and necrosis.

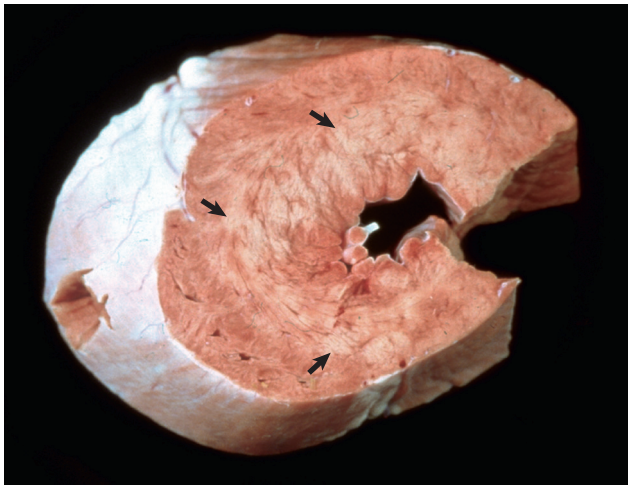


Figure 10-49 **Myocardial Necrosis, Acute Monensin Toxicosis, Heart, Cross Section, Left Ventricular Myocardium, Calf.** Note the pale, mottled, necrotic areas *(arrows)* distributed throughout the ventricular myocardium. (Courtesy School of Veterinary Medicine, Purdue University.)

Chemotherapeutic Agent-Induced Myocardial Degeneration. Cardiotoxicity has emerged as a significant clinical entity in veterinary medicine in recent years with the growing use of antineoplastic drugs in small animal practice and the widespread use of growth promotants in ruminants (see Fig. 10-49; also see E-Figs. 10-12 and 10-13).

Disorders of Domestic Animals: Cardiac Conduction System

Disturbances of Growth

Neoplastic Transformation

Schwannomas. Schwannomas involve cardiac nerves in cattle and appear as single or multiple white nodules detected as incidental findings at slaughter (see Fig. 14-115).

Cell Degeneration and Death

Conduction system diseases have been described mainly in dogs and horses, probably because clinical cardiac evaluations are done most frequently in these species. Secondary conduction system disorders result from myocardial disease (inflammation, neoplasia, or degeneration) near the conduction system. Specific presumably inherited diseases in dogs include (1) syncope in pug dogs with lesions of the bundle of His; (2) intermittent sinus arrest in deaf Dalmatian dogs, presumably associated with lesions in the sinus node; (3) sinoatrial syncope (sick sinus dysfunction) in female miniature schnauzers, West Highland white terriers, cocker spaniels, and dachshunds; (4) inherited ventricular arrhythmia and sudden unexpected death in German shepherds, and (5) widespread conduction pathology in Alaskan sled dogs that died suddenly and unexpectedly in a race. Other arrhythmias in dogs and horses are atrial fibrillation and heart block. Dogs with atrial fibrillation often have concurrent congestive heart failure and have atrial dilation with AV valve insufficiency, but most horses live a normal or near-normal life span, may respond to cardioversion, and at necropsy have atrial myocardial fibrosis. Heart block of the first degree (delay of impulse through the AV node), second degree (intermittent failure to conduct through the AV node with dropped beats), and third degree (complete) has been associated with myocardial lesions, such as areas of scarring, in horses and dogs. Second-degree heart block is considered to be a normal phenomenon in horses.

Persistent atrial standstill (silent atria, AV myopathy) is a progressive cardiac disease of English springer spaniels and cats characterized by notable atrial dilation and fibrosis.

Atrial fibrillation occurs in cattle in association with right atrial dilation and fibrosis and alterations in the SA mode. Also, sudden (unexpected) cardiac death is described in racehorses with right atrial myocardial fibrosis, fibrosis of the upper ventricular septum, and arteriosclerosis of intramyocardial arteries.

Also see the discussion on the cardiac conduction system in the section on Dysfunction/Responses to Injury; Responses: Cardiac Conduction System.

Inflammation

See the previous section on Cell Degeneration and Death.

Disorders of Domestic Animals: Endocardium and Heart Valves

See the discussion of the endocardium and heart valves in the section on Responses to Injury: Endocardium and Heart Valves. The major types of AV valvular diseases are shown in Fig. 10-50.

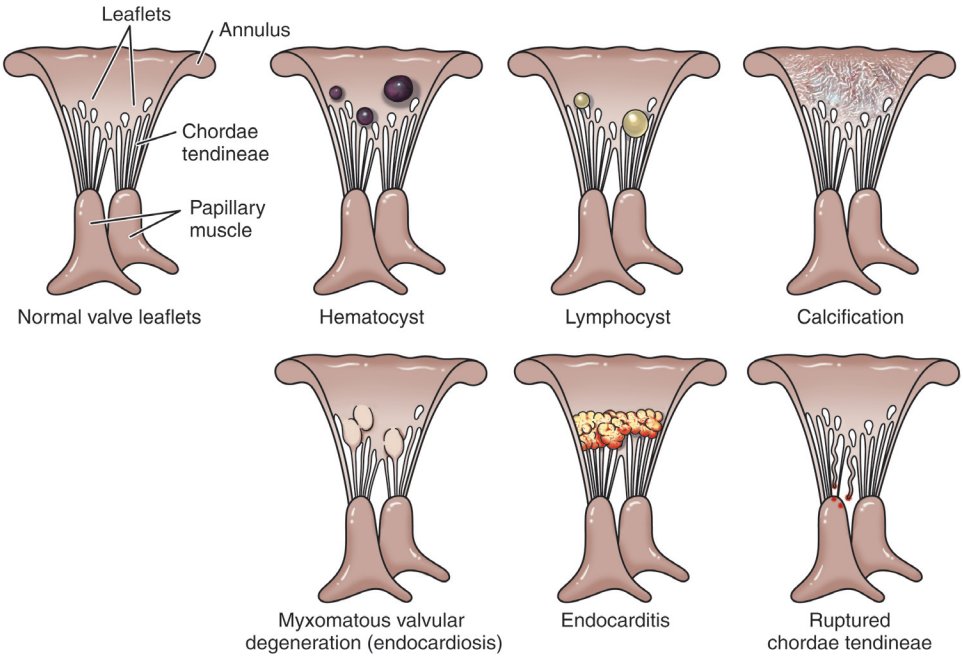


Figure 10-50 Major Types of Cardiac Atrioventricular Valvular Disease. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

Disturbances of Growth

Endocardial Fibroelastosis. Endocardial fibroelastosis in animals was historically recognized as a primary cardiac defect in Burmese and Siamese cats. Affected animals had prominent, white, thickened endocardium, especially of the left ventricle, because of the proliferation of fibroelastic tissue (see Fig. 10-45). Endocardial fibroelastosis is a reaction of the endocardium to hypoxia and often associated with heart disease, which results in dilated cardiac chambers. It is unclear whether this is a true congenital anomaly or a response to left atrial dilation.

Miscellaneous Valvular Anomalies

Valvular Hematomas. Valvular hematomas (hematocysts, valvular telangiectasia) frequently are observed on the AV valves of many species but are common in postnatal ruminants (Fig. 10-51, *A*). These lesions may regress and do not produce any functional abnormalities. Lesions are bulging, blood-filled cysts, several millimeters in diameter, on the AV valves.

Valvular Lymphocysts. Valvular lymphocysts may also occur and appear as yellow serum-filled cysts on the AV valve cusps (Fig. 10-51, *B*).

Cell Degeneration and Death

Ulcerative Endocarditis (Uremic Endocarditis). Uremic endocarditis is most commonly a disorder in dogs that follows acute or repeated episodes of uremia. These episodes cause ulcerative endocarditis (injury of the endothelium) of the left atrium that is resolved via healing characterized by fibrosis, with or without mineralization and chronically dilated atria (Fig. 10-52).

Myxomatous Valvular Degeneration (Valvular Endocardiosis). Degenerative changes in the valves are frequently seen in older dogs, and the process that leads to this lesion is termed *myxomatous valvular degeneration* (valvular endocardiosis). Also see the section on Disorders of Dogs (also see Fig. 10-83).

Endocardial Mineralization. Endocardial mineralization occurs from intake of excessive amounts of vitamin D and from intoxication by calcinogenic plants (*Cestrum diurnum*, *Trisetum flavescens*, *Solanum malacoxylon*, and *Solanum torvum*) that contain vitamin D analogs. These plant-induced syndromes of cattle have been called by different names in various areas of the world, such as "Manchester wasting disease" in Jamaica, "enzootic calcinosis" in Europe, "Naalehu disease" in Hawaii, "enteque seco" in Argentina, and "espichamento" in Brazil. Multiple, large, white, rough, firm plaques of mineralized fibroelastic tissue are present in the endocardium and intima of large elastic arteries. Fibrosis, with or without mineralization, occurs in chronically dilated hearts, in hearts of debilitated cattle with Johne's disease (Fig. 10-53; also see Fig. 10-22), in dogs with healed lesions of left atrial ulcerative endocarditis associated with a prior uremic episode (see Fig. 10-52), and in the so-called jet lesions produced by the trauma of refluxed blood in valvular insufficiencies.

Inflammation

Vegetative Valvular and Mural Endocarditis. Endocarditis is usually the result of bacterial infections, except for lesions produced by migrating *Strongylus vulgaris* larvae in horses and rarely in mycotic infections. The lesions are often very large by the time of death and are present on the valves (valvular endocarditis), although some lesions originate from the underlying myocardium or extend from the affected valve to the adjacent wall (mural endocarditis). Grossly, the affected valves have large, adhering, friable, yellow-to-gray masses of fibrin termed *vegetations*, which can occlude the valvular orifice (Figs. 10-54, *A*, and 10-55). In chronic lesions, the fibrin deposits are organized by fibrous connective tissue to produce irregular nodular masses termed *verrucae* (wartlike lesions). Microscopically, the lesion consists of accumulated layers of fibrin and numerous embedded bacterial colonies underlain by a zone of infiltrated leukocytes and granulation tissue (see Fig. 10-54, *B*). The relative frequency of valvular involvement with endocarditis in animals is mitral > aortic > tricuspid > pulmonary.

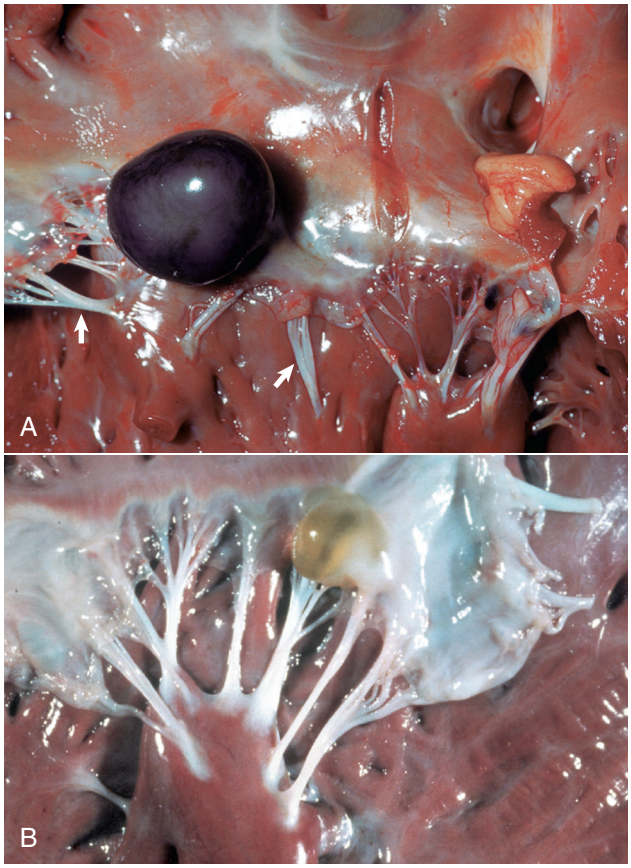


Figure 10-51 Hematocysts and Lymphocysts, Calf. A, Valvular hematocyst, heart, opened left side, mitral valve, postnatal calf. A dark, blood-filled cyst protrudes from a cusp of the mitral valve. *Arrows* indicate chordae tendineae. Hematocysts usually occur in ruminants, do not cause any functional abnormality, and usually regress within a few months of birth. **B,** Valvular lymphocyst, heart. A lymph-filled cyst is on a cusp of the atrioventricular valve. Like hematocysts, lymphocysts usually occur in ruminants, do not cause any functional abnormality, and usually regress within a few months of birth. (**A** courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee. **B** courtesy College of Veterinary Medicine, University of Illinois.)

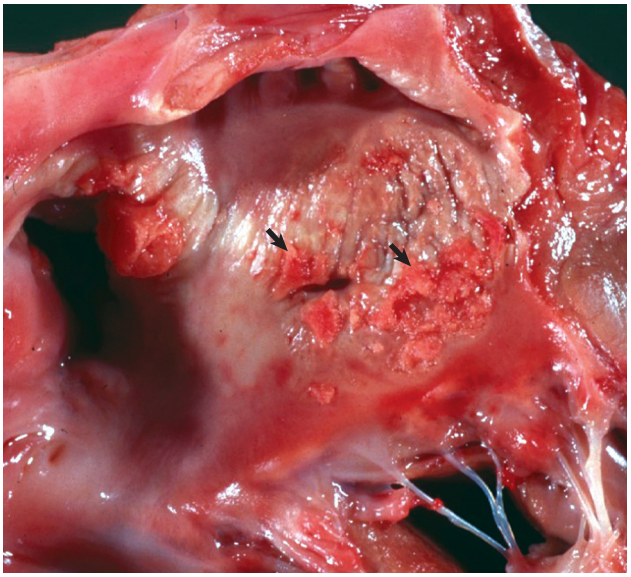


Figure 10-52 Ulcerative Endocarditis (Uremia), Heart, Endocardium of Left Atrium, Dog. Note the white-red, thick, wrinkled area *(arrows)* of endocarditis, mineralization, and fibrous tissue *(scar)* formation caused by uremia in this dog with chronic renal failure. (Courtesy Dr. K. Read, College of Veterinary Medicine, Texas A&M University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

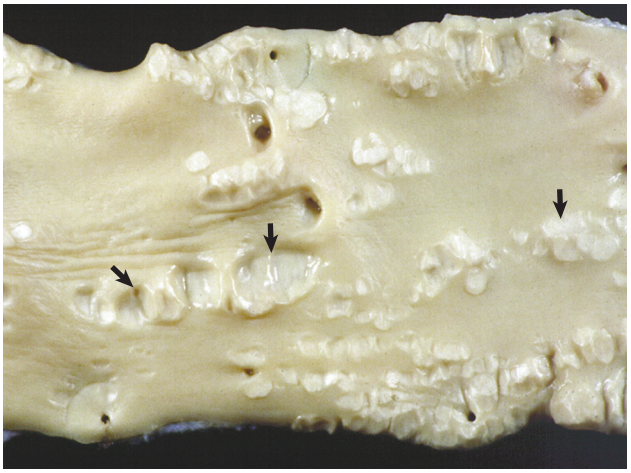


Figure 10-53 Johne's Disease, Arteriosclerosis, Aorta, Cow. Multiple prominent, white, mineralized foci are in the tunica intima and media *(arrows)*. (Courtesy College of Veterinary Medicine, University of Illinois.)

The pathogenesis of endocarditis is complicated and incompletely understood, but the components of Virchow's triad in thrombogenesis—endothelial injury, turbulence, and hypercoagulability—are involved. Affected animals often have preexisting extracardiac infections, such as gingivitis, mastitis, hepatic abscesses, or dermatitis, resulting in one or more bouts of bacteremia. Turbulent intracardiac blood flow associated with congenital anomalies or the presence of intracardiac and vasculature devices, such as catheters, may contribute to initiation of the lesion. Focal trauma–induced endothelial disruption on the surface of the normally avascular valves allows bacteria to adhere, proliferate, and initiate an inflammatory reaction that results in subsequent deposition of masses of fibrin. Death is the result of cardiac failure from valvular dysfunction or the effects of bacteremia. In some animals, septic emboli lodge in organs such as the heart, synovium, bone, liver, kidneys, and meninges, leading to infarction and/or localized inflammation or abscess formation. See the discussion on vegetative valvular and mural endocarditis in the section on Disorders of Domestic Animals: Endocardium and Heart Valves, Inflammation and also Chapter 3.

Atrial Thrombosis. Atrial thrombi may occur with valvular or myocardial disease and are the result of hemostatic abnormalities resulting from stasis or turbulence. Endothelial injury, turbulence, and hypercoagulability are involved in the pathogenesis of atrial thrombi.

Disorders of Domestic Animals: Pericardium and Epicardium

Disturbances of Circulation

Hemorrhage. Hemorrhage involving the pericardium and epicardium (see Fig. 10-24; see E-Fig. 10-18) results from stretching, tearing, lacerating, or crushing blood vessels in these structures and may be caused by penetrating wounds (foreign objects, bullets, or

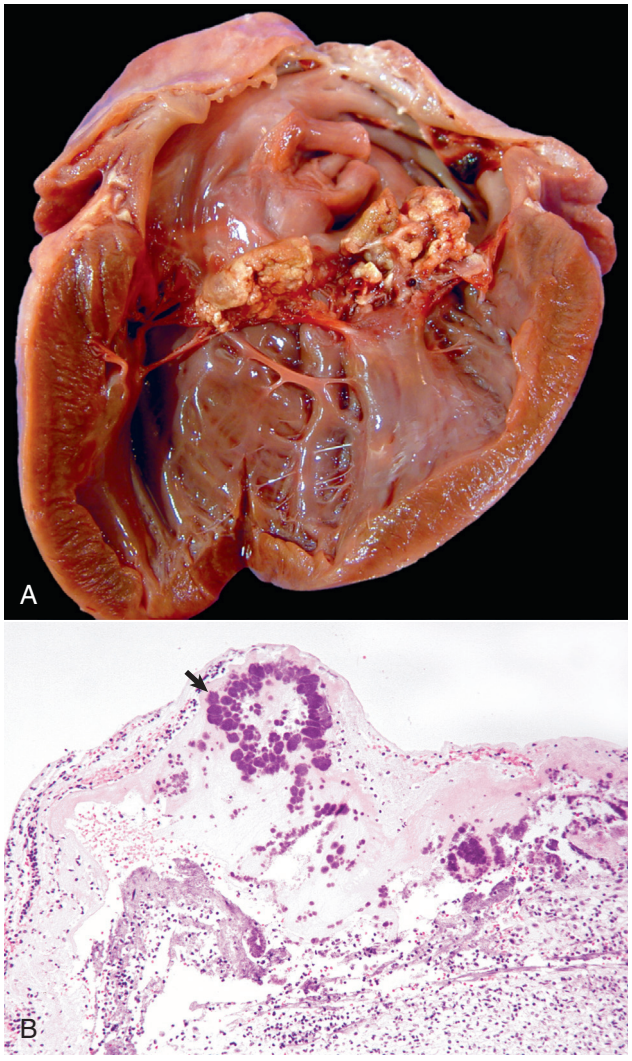


Figure 10-54 Vegetative Valvular Endocarditis. A, Mitral valve, heart, calf. Multiple, large, raised, friable, yellow-red thrombotic masses are attached to cusps of the mitral valve. The roughened and granular surface of the valve leaflets is attributable to fibrin, platelets, and trapped bacteria and erythrocytes. **B,** Bacterial infection, heart, tricuspid valve, cow. Note abundant masses of fibrin and bacterial colonies *(arrow)*. H&E stain. (**A** courtesy Atlantic Veterinary College, University of Prince Edward Island. **B** courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

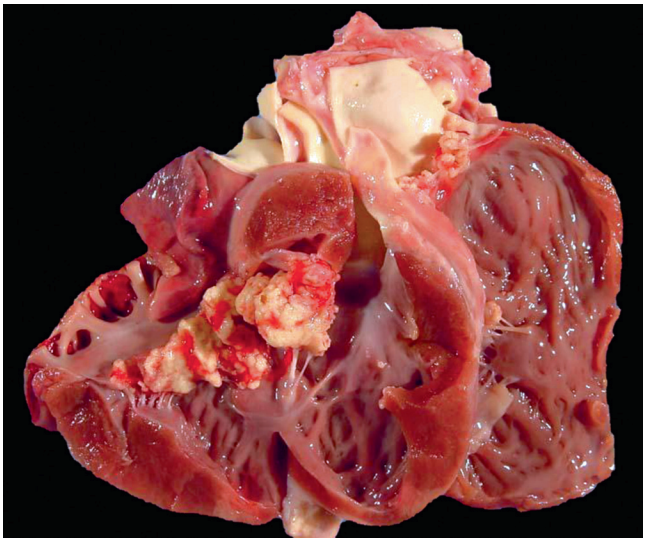


Figure 10-55 Valvular Endocarditis, *Streptococcus Suis*, Heart Mitral and Pulmonic Valves, Pig. Note the friable, yellow material adhering to and replacing some of the normal left atrioventricular valve. The left ventricular chamber is dilated due to failure of normal function of the valve (eccentric hypertrophy). (Courtesy Atlantic Veterinary College, University of Prince Edward Island.)

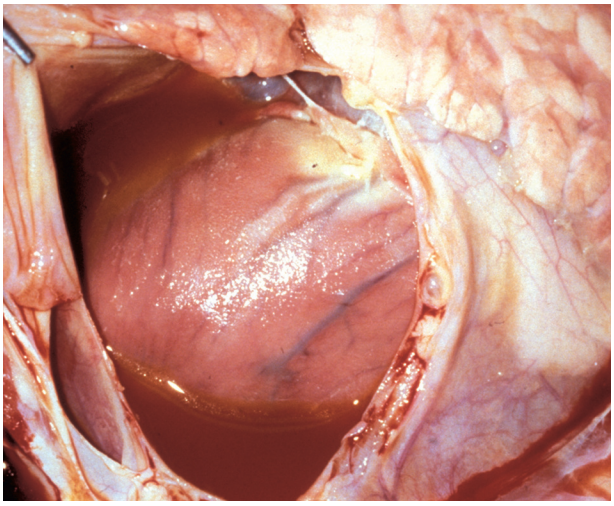


Figure 10-56 Hydropericardium, Pericardial Sac, Pig. The thin-walled dilated pericardial sac contains serous fluid that has accumulated secondary to alterations in hydrostatic pressure between the pericardial cavity, circulatory system, and lymphatic system. (Courtesy College of Veterinary Medicine, University of Illinois.)

knives), lacerations from fractured bone, shear forces that stretch and ultimately tear vessels in tissues (blunt force trauma), and tears and rupture of tissue resulting from loss of structural integrity attributable to invasive and destructive properties of neoplasms such as hemangiosarcomas (see Chapters 2 and 6).

Effusions. See the discussions on the mechanisms of edema formation and Figs. 2-6 through 2-10 in Chapter 2 and on the formation of transudates and exudates and Fig. 3-3 in Chapter 3.

Pericardial Dilatation. The pericardium responds to excess fluid in the pericardial space by dilation. However, this outcome requires adequate time to allow adjustments in size. In hemopericardium, blood rapidly fills the pericardial cavity and death often occurs unexpectedly from cardiac tamponade, a condition with compression of the heart caused by blood accumulation leading to reduced cardiac output. Hydropericardium is the accumulation of clear, light yellow, watery, serous fluid (i.e., transudate) in the pericardial sac (Fig. 10-56). In cases associated with vascular injury, a few fibrin strands are present, and the fluid could clot after exposure to air.

Hydropericardium. Hydropericardium occurs in those diseases that have generalized edema (see Fig. 10-56). Thus ascites and hydrothorax often occur concurrently with hydropericardium. Congestive heart failure is an important mechanism of hydropericardium and is usually the result of primary myocardial, valvular, congenital, or neoplastic diseases. Common specific diseases include dilated cardiomyopathy of dogs and cats and "ascites syndrome" of poultry. Hydropericardium can also accompany pulmonary hypertension (e.g., "brisket disease" or "high-altitude disease" of cattle), renal failure, and hypoproteinemia from various chronic debilitating

diseases. Hydropericardium can also occur in various systemic diseases with vascular injury, such as septicemia in pigs, "heartwater" (*Cowdria ruminantium* infection) in small ruminants, African horse sickness, and bovine ephemeral fever.

Hydropericardium is the accumulation of clear, light yellow, watery, serous fluid (i.e., transudate) in the pericardial sac (E-Fig. 10-21; also see Fig. 10-56; also see section on Disorders of Domestic Animals). As examples, hydropericardium can occur in animals with (1) hypoproteinemia (decreased colloid osmotic pressure) caused by liver disease or protein-losing nephropathy/enteropathy; (2) heart failure (increased hydrostatic pressure) where there is poor venous return to the heart; and (3) vascular injury, where damage to the barrier function of the vascular wall can result in leakage of small quantities of plasma proteins. In this latter example, a few fibrin strands can be present and the fluid could clot after exposure to air. The pericardial surfaces are smooth and glistening in acute cases, but in chronic cases, the epicardium becomes opaque because of mild fibrous thickening and can appear roughened and granular when there is villous proliferation of fibrous tissue, especially over the atria. The mechanisms involved in these fluid shifts are discussed in Chapters 2 and 3.

Hemopericardium. Hemopericardium is an accumulation of whole blood in the pericardial sac (Figs. 10-57 and 10-58; also see section on Disorders of Domestic Animals). Death often occurs unexpectedly from cardiac tamponade, a condition in which the compression of the heart caused by the accumulation of blood in the pericardial sac leads to reduced cardiac output and poor perfusion of vascular beds in all organ systems. As examples, hemopericardium may be caused by blunt force trauma (impact with an automobile) or from rupture of the wall of the right atrium after invasion by a hemangiosarcoma.

Bleeding into the pericardial sac can result from spontaneous atrial rupture in dogs, atrial rupture in dogs with hemangiosarcoma, rupture of the intrapericardial aorta or pulmonary artery in horses, or as a complication of intracardiac injections (see Figs. 10-57 and 10-58).

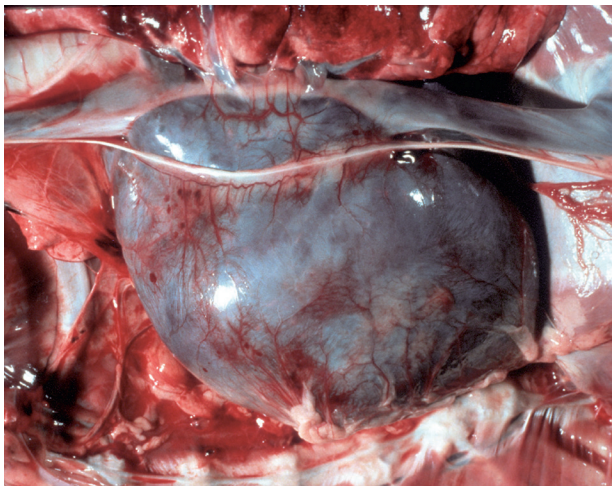


Figure 10-57 Hemopericardium (Cardiac Tamponade), Right Atrium, Hemangiosarcoma, Heart, Dog. The pericardium is distended and dark blue because it contains whole blood secondary to rupture of an atrial hemangiosarcoma. Hemopericardium can cause death if it is sudden and is of sufficient volume to compress the heart and thus reduce cardiac output, a condition known as cardiac tamponade. On clinical examination, heart sounds are muffled. (Courtesy College of Veterinary Medicine, University of Illinois.)

Disturbances of Growth

Serous Atrophy. Serous atrophy of fat is readily identified by the gray gelatinous appearance of epicardial fat deposits (Fig. 10-59). Healthy animals normally have abundant white or yellow epicardial fat deposits, especially along the AV junction. Microscopically, lipocytes are atrophic, and edema is present in the interstitial tissue. Serous atrophy of epicardial fat occurs rapidly during anorexia, starvation, or cachexia because fat is catabolized to maintain energy balance.

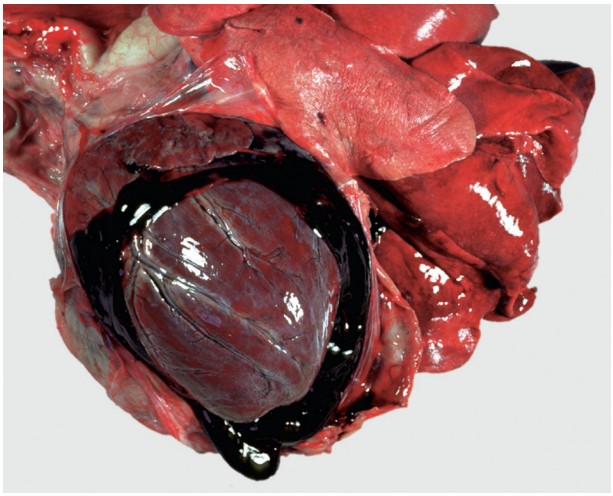


Figure 10-58 Hemopericardium, Pericardial Sac (Opened), Dog. The pericardial sac is filled with clotted blood. Hemorrhage into a body cavity results in pooling of coagulated or uncoagulated blood within that cavity. (Courtesy Dr. D.A. Mosier, College of Veterinary Medicine, Kansas State University.)

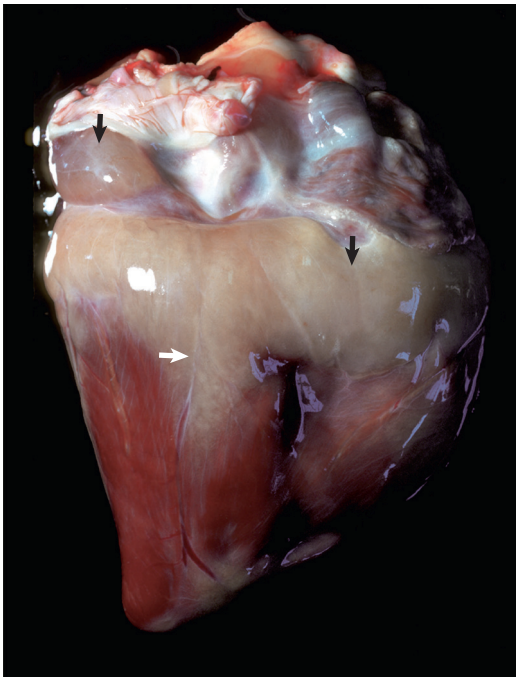
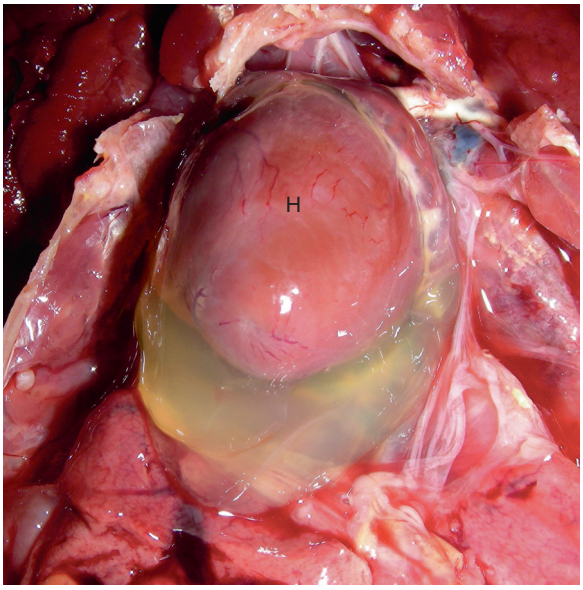


Figure 10-59 Serous Atrophy of Fat, Heart, Epicardium, Cow. The epicardial fat deposits are gray and gelatinous (*arrows*), indicating that fat has been catabolized, for example, as in the early stages of starvation. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)



E-Figure 10-21 Hydropericardium, Chicken. Note the accumulation of clear yellow fluid (transudate) in the pericardial cavity. This fluid may occur as a result of hypoproteinemia, heart failure, and vascular injury. If this accumulation is rapid, it compresses the heart *(H)* and great vessels, leading to a condition known as "cardiac tamponade," which restricts venous return to the heart and reduces the end diastolic pumping volume of the heart. (Courtesy College of Veterinary Medicine, University of Illinois.)

Cell Degeneration and Death

Epicardial Calcification. Epicardial calcification is a feature in hereditary calcinosis in mice and cardiomyopathy in hamsters (E-Fig. 10-22). Myocardial mineralization (discussed later) may be visible on the epicardial surface in vitamin E–selenium deficiency in sheep and cattle, vitamin D toxicity in several species, calcinogenic plant toxicosis in cattle ("Manchester wasting disease"), and spontaneous myocardial calcification in aged rats and guinea pigs.

Gout. Visceral gout has not been reported in domestic animals but does occur in birds and reptiles (E-Fig. 10-23; see Chapter 1).

Inflammation

Pericarditis. Inflammation of the pericardium is frequently seen with bacterial septicemias and typically results in fibrinous pericarditis. Grossly, both the visceral and parietal pericardial surfaces are covered by variable amounts of yellow fibrin deposits, which can result in adherence between the parietal and visceral layers. When the pericardial sac is opened, the attachments are torn away (so-called bread-and-butter heart) (Fig. 10-60). Microscopically, an eosinophilic layer of fibrin with admixed neutrophils lies over a congested epicardium (Fig. 10-61).

The outcome of fibrinous pericarditis varies. Early death is frequent because many of these lesions result from infection by highly virulent bacteria and concurrent septicemia. When survival is prolonged, adhesions form between the pericardial surfaces after fibrous organization of the exudate.

Suppurative pericarditis is seen mainly in cattle as a complication of traumatic reticuloperitonitis ("hardware disease"). Foreign bodies, such as nails or pieces of wire that accumulate in the reticulum, occasionally penetrate the reticular wall and diaphragm, enter the adjacent pericardial sac, and introduce infection. Some affected cattle survive for weeks to months until death ensues from congestive heart failure or septicemia. Grossly, the pericardial surfaces are notably thickened by white, often rough, shaggy-appearing masses of fibrous connective tissue that enclose an accumulation of white to gray, thick, foul-smelling, purulent exudate (Fig. 10-62).

Constrictive pericarditis is a chronic inflammatory lesion of the pericardium accompanied by extensive fibrous proliferation and eventual formation of fibrous adhesions between the surfaces of the visceral and parietal pericardium. The condition is seen in some cases of suppurative pericarditis in cattle and pigs with chronic fibrinous pericarditis. Severe lesions obliterate the pericardial sac and constrict the heart with fibrous tissue and can interfere with cardiac filling and thus cardiac output. Compensatory myocardial hypertrophy can result in diminished ventricular chamber volumes and contribute to the eventual development of heart failure.

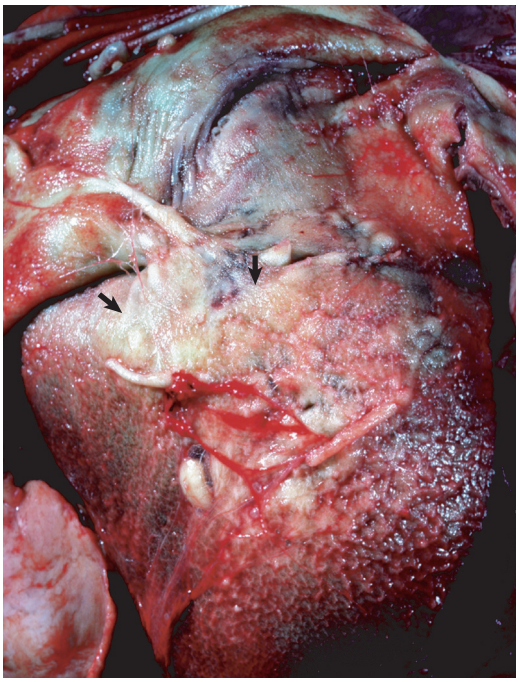


Figure 10-60 Fibrinous Pericarditis, Heart, Epicardium, Horse. The epicardium is covered dorsally by a thick, yellow layer of fibrin *(arrows)* and ventrally by granulation tissue *(finely granular surface)*, thus indicating the chronicity of the inflammatory process. The apposing parietal pericardium (not shown) was also covered with fibrin. This lesion commonly occurs in horses with *Streptococcus equi* subsp. *zooepidemicus* septicemia causing vasculitis. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

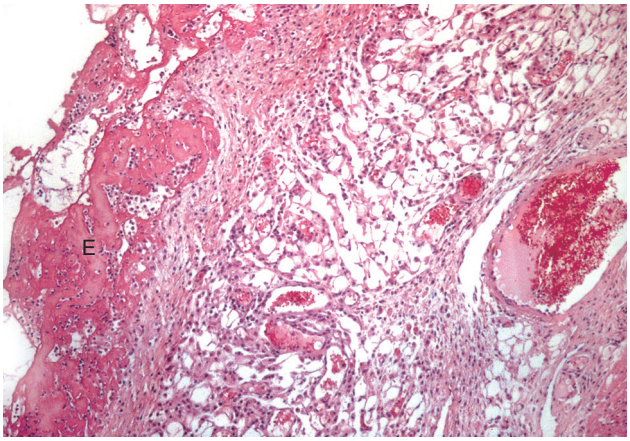


Figure 10-61 Fibrinous Pericarditis, Heart, Epicardium, Pig. Note eosinophilic fibrin deposits *(E) (left)* on the epicardial surface. This lesion commonly occurs with septicemias by bacteria that cause vasculitis. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

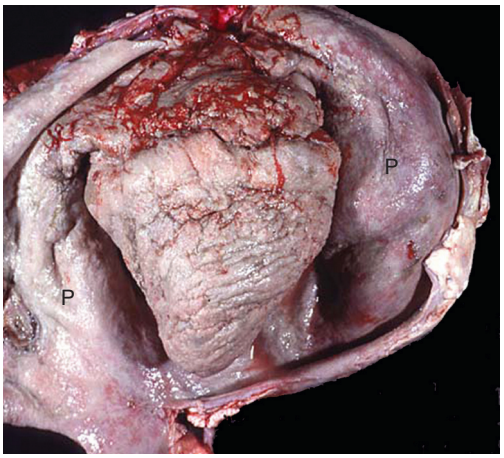
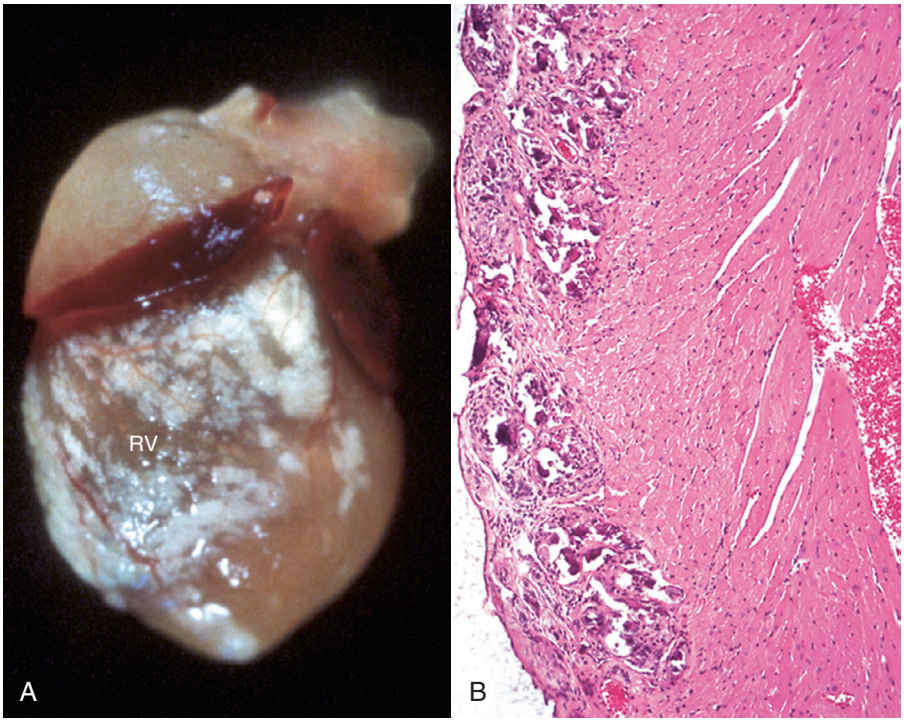
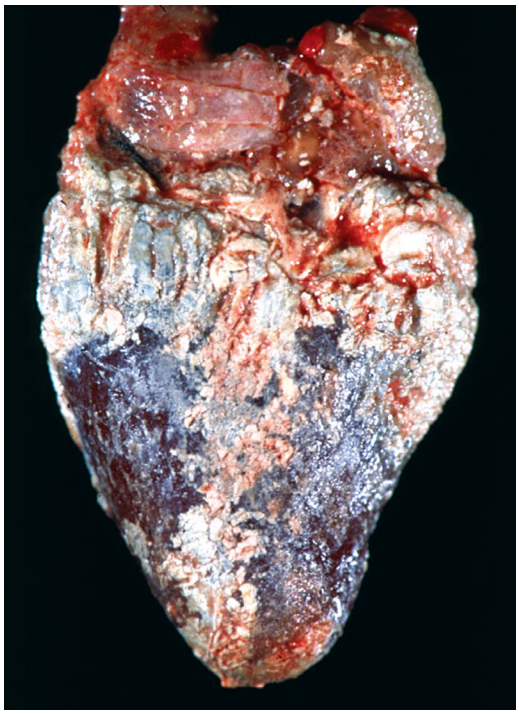


Figure 10-62 Chronic Suppurative (Active) Pericarditis, Traumatic Reticuloperitonitis ("Hardware Disease"), Heart, Pericardial Sac (Opened), Cow. The exposed epicardial and parietal surfaces are notably thickened by fibrous connective tissue and covered by a fibrinopurulent exudate. On clinical examination, heart sounds are muffled. *P,* Reflected parietal pericardium. (Courtesy Dr. J. King, College of Veterinary Medicine, Cornell University.)



E-Figure 10-22 **Epicardial Calcification, Heart, Right Ventricle, Mouse. A,** Note the prominent white mineral deposits over the right ventricle *(RV)*. **B,** The basophilic mineral deposits are present epicardially and in the outer myocardium *(left)*. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-23 **Visceral Gout, Heart, Pericardium, Chicken.** White urate deposits are present on the epicardial surface. (Courtesy College of Veterinary Medicine, The Ohio State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

Fibrinous Pericarditis. Hematogenous spread of specific organisms may result in fibrinous pericarditis. Mannheimiosis, blackleg, coliform septicemias, contagious bovine pleuropneumonia, sporadic bovine encephalomyelitis, and in utero *Brucella* spp. and *Arcanobacter pyogenesis* fetal septicemias may all produce fibrinous pericarditis. In sheep, Mannheimiosis and streptococcal infections most commonly result in fibrinous pericarditis. Sterile swabs of the pericardial exudates are recommended to identify the causative organism.

Disorders of Domestic Animals: Blood and Lymphatic Vascular Systems

See the discussion on blood and lymphatic vascular systems in the section on Responses to Injury: Blood and Lymphatic Vascular Systems. The major arterial diseases are shown in Fig. 10-63.

Blood Vessels

Disturbances of Circulation

Effusions. See the previous discussion on disturbances of circulation in the sections on Pericardium and Epicardium.

Hemopericardium. See the later discussion on the hemopericardium under Effusions in the section on Disorders of Domestic Animals: Pericardium and Epicardium; Disturbances of Circulation.

Hemothorax and Hemoabdomen. Hemothorax and hemoabdomen arise from spontaneous or traumatic rupture of large arteries or veins or from rupture of aneurysms located in the thoracic or abdominal cavity, respectively. An aneurysm is a localized dilation or outpouching of a thinned and weakened portion of a vessel. Usually, arteries are affected, especially large elastic arteries, but the lesion can also occur in veins. Known causes include copper deficiency in pigs (Fig. 10-64) because copper is necessary for normal development of elastic tissue and damage from infection with *Spirocerca lupi* in dogs or *Strongylus vulgaris* in horses. Most cases are idiopathic. Dissecting aneurysms are infrequent but have been seen in birds, most notably turkeys (Fig. 10-65). They result from disruption of the intima, which allows entry of blood into the media, and this dissects along the wall. Aneurysms can rupture. Usually the consequences are rapidly fatal because rather large arteries typically are involved. See the discussion on effusions in the section on Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Effusions and also Chapters 3, 7, and 9.

Aortic Rupture and Rupture of Large Arteries. Aortic rupture and rupture of large arteries can be the sequela of severe trauma or occur

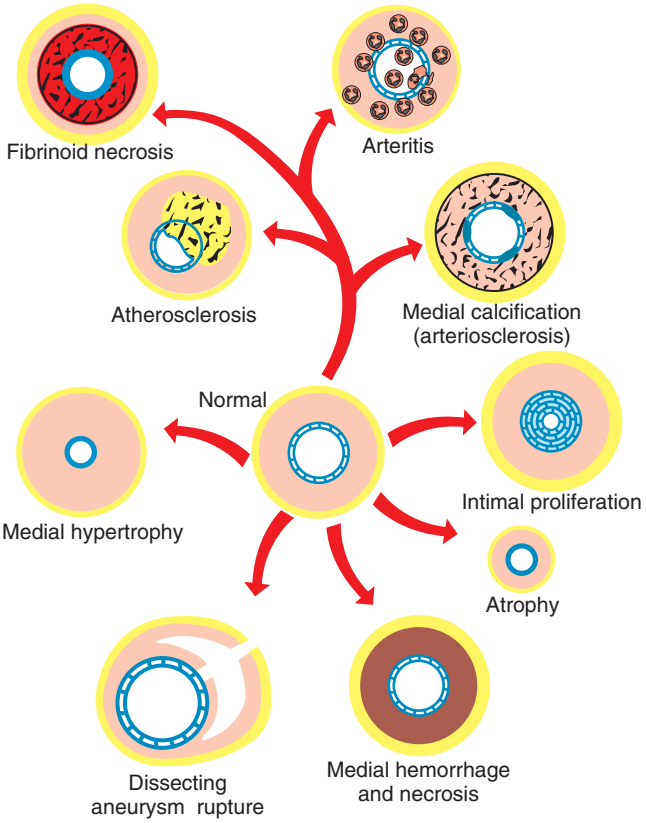


Figure 10-63 Major Arterial Diseases. (Redrawn with permission from School of Veterinary Medicine, Purdue University.)

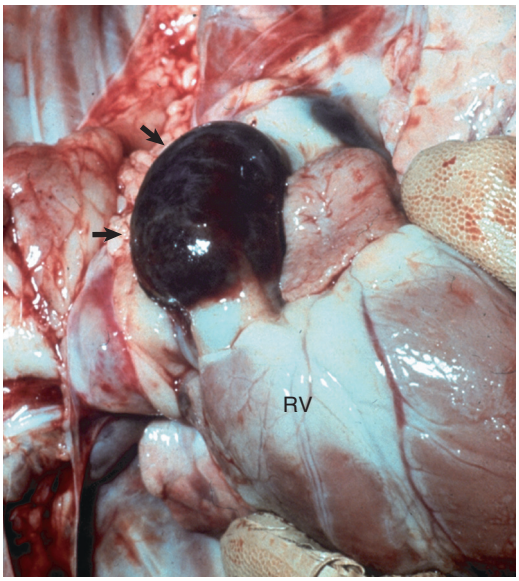


Figure 10-64 Dissecting Aneurysm, Copper Deficiency, Heart, Pulmonary Artery, Right Ventricle *(RV)*, Pig. The dark, blood-filled, bulging segment of the wall of the pulmonary artery *(arrows)* has resulted from disruption of elastic fibers. (Courtesy School of Veterinary Medicine, Purdue University.)

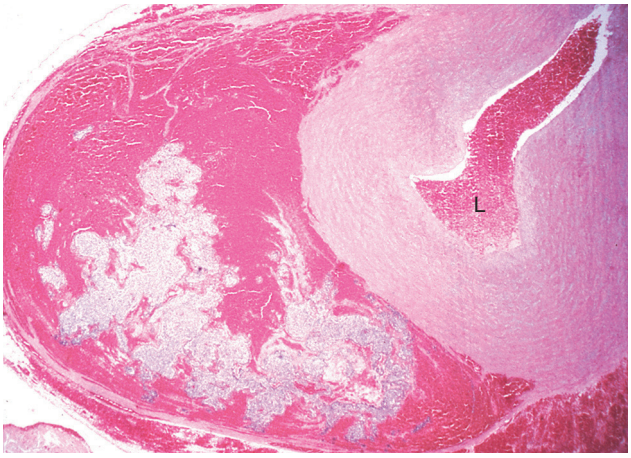


Figure 10-65 Dissecting Aneurysm, Aorta, Turkey. Blood has dissected through the tunica media (in a nearby section of the aorta) and in this section has come to lie in the outer layers of the tunica media and adventitia. *L*, Vessel lumen. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Box 10-15 Most Common Vascular Diseases with Rupture

Aortic rupture: Horse, turkey
Carotid artery rupture: Horse
Thoracic duct rupture: Dog, cat

spontaneously (see Figs. 10-64 and 10-65). Sudden rupture of the ascending aorta or pulmonary artery near the pulmonic valve in horses is associated with notable exertion and severe trauma to the ventral thorax from falling. Death ensues rapidly from cardiac tamponade because the tear is in that portion of the aorta or pulmonary artery within the pericardial sac. In horses, the internal carotid artery can rupture into the adjacent guttural pouch, with subsequent epistaxis. This is a consequence of deep mycotic infection of the guttural pouch. Rupture of the middle uterine artery may occur during parturition in mares and with uterine torsion or prolapse in cows. Aortic rupture, with or without dissection, is an important cause of death in male turkeys. The most common vascular diseases with rupture are listed in Box 10-15.

Gastric Dilation and Volvulus. See the discussion on gastric dilation and volvulus in Chapter 7.

Disturbances of Growth

Neoplastic Transformation

Hemangiosarcoma. Cardiac hemangiosarcoma is an important neoplasm of dogs and can arise either in the heart (primary) or by metastasis (secondary) from sites such as the spleen. This neoplasm is usually seen in the wall of the right atrium and only occasionally involves the right ventricle. The tumor arises from neoplastic transformation of vascular endothelium. Also see Disorders of Dogs, Blood and Lymphatic Vascular Systems, Blood Vessels, Disturbances of Growth, Neoplastic Transformation, Hemangiosarcoma and Hemangioma.

Vascular Melanosis. See the discussion on vascular melanosis in Chapters 1 and 2.

Cell Degeneration and Death. Toxicants that affect vessels are listed in E-Box 10-1.

See Chapter 1. Generalized vascular degenerative diseases in animals are classified into the following three principal groups:

- Arteriosclerosis
- Atherosclerosis
- Arterial medial calcification

Hyaline degeneration, fibrinoid necrosis, and amyloidosis also occur in all animal species.

Arteriosclerosis. Arteriosclerosis is characterized by intimal fibrosis of large elastic arteries, atherosclerosis is characterized by intimal and medial lipid deposits in elastic and muscular arteries, and arterial medial calcification has characteristic mineralization of the walls of elastic and muscular arteries.

Arteriosclerosis is an age-related disease that occurs frequently in many animal species but rarely causes clinical signs. The disease develops as chronic degenerative and proliferative responses in the arterial wall and results in loss of elasticity ("hardening of the arteries") and, less often, luminal narrowing. The abdominal aorta is most frequently affected, but other elastic arteries and peripheral large muscular vessels may be involved. Lesions are often localized around the orifices of arterial branches. Etiologic factors in the development of arteriosclerosis are not well defined, but the significant role of hemodynamic influences is suggested by the frequent involvement at arterial branching sites, in which blood flow is turbulent. Grossly, the lesions are seen as slightly raised, firm, white plaques. Microscopically, initially the intima is thickened by accumulation of mucopolysaccharides and later by the proliferation of smooth muscle cells in the tunica media and fibrous tissue infiltration into the intima. Splitting and fragmentation of the internal elastic lamina are common

Atherosclerosis. Atherosclerosis, the vascular disease of greatest importance in human beings, occurs only infrequently in animals and rarely leads to clinical disease such as infarction of the heart or brain. The principal alteration is accumulation of deposits (atheroma) of lipid, fibrous tissue, and calcium in vessel walls, which eventually results in luminal narrowing. Many studies have established that the pig, rabbit, and chicken are susceptible to the experimental disease produced by the feeding of a high-cholesterol diet; the dog, cat, cow, goat, and rat are resistant. Lesions of the naturally occurring disease have been detected in aged pigs and birds (especially parrots) and in dogs with hypothyroidism and diabetes mellitus that develop an accompanying hypercholesterolemia. Arteries of the heart, mesentery, and kidneys are prominently thickened, firm, and yellow-white (Fig. 10-66, *A*). Microscopically, lipid globules accumulate in the cytoplasm of smooth muscle cells and macrophages, often termed *foam cells*, in the media and intima (see Fig. 10-66, *B* and *C*). Necrosis and fibrosis develop in some arterial lesions. The pathogenesis of atherosclerosis has been extensively studied in human beings. The vascular response-to-injury hypothesis is the current proposed mechanism of injury. The dyslipoproteinemia associated with diabetes or hypothyroidism in the dog results in endothelial injury. A variety of mechanisms, including oxygen free radical production, increase the decay of nitric oxide and decrease its vasodilator activity. The damaged endothelial cell allows lipoproteins to accumulate within the intima, where they are oxidized by free radicals generated by macrophages and endothelial cells. The oxidized products are directly toxic to endothelium and smooth muscle cells. Cellular debris is ingested by macrophages and smooth muscle cells, resulting in the formation of "foam cells." The lesion in dogs differs from that of human beings with respect to the location of lipid, which is abundant throughout the wall of the artery in contrast to human beings, who have lipid accumulation in the tunica intima. The chronic progression of atherosclerosis may result in narrowing of the lumen, ulceration and thrombosis, and hemorrhage or aneurysmal dilation.

Arterial Medial Calcification. Arterial medial calcification is a frequent lesion in animals that often have concurrent endocardial mineralization and involves both elastic and muscular arteries. The causes of arterial medial calcification include calcinogenic plant toxicosis, vitamin D toxicosis, renal insufficiency, and severe debilitation, as seen in cattle with Johne's disease (see Fig. 10-53). Medial calcification occurs spontaneously in horses, rabbits, aged guinea pigs, and in rats with chronic renal disease. Affected arteries, such as the aorta, have a unique gross appearance; they appear as solid, dense, pipelike structures with raised, white, solid intimal plaques (Fig. 10-67). Microscopically, in elastic arteries, prominent basophilic granular mineral deposits are present on elastic fibers of the media, but in muscular arteries, they can form a complete ring of mineralization in the tunica media (Fig. 10-68). Siderocalcinosis (so-called iron rings), the result of deposition of both iron and calcium salts, occurs in the cerebral arteries of aged horses. Lesions in the surrounding brain tissue are generally absent. Siderocalcinosis lesions are considered incidental.

Hyaline Degeneration, Fibrinoid Necrosis, and Amyloidosis. Hyaline degeneration, fibrinoid necrosis, and amyloidosis are vascular lesions of small muscular arteries and arterioles and occur

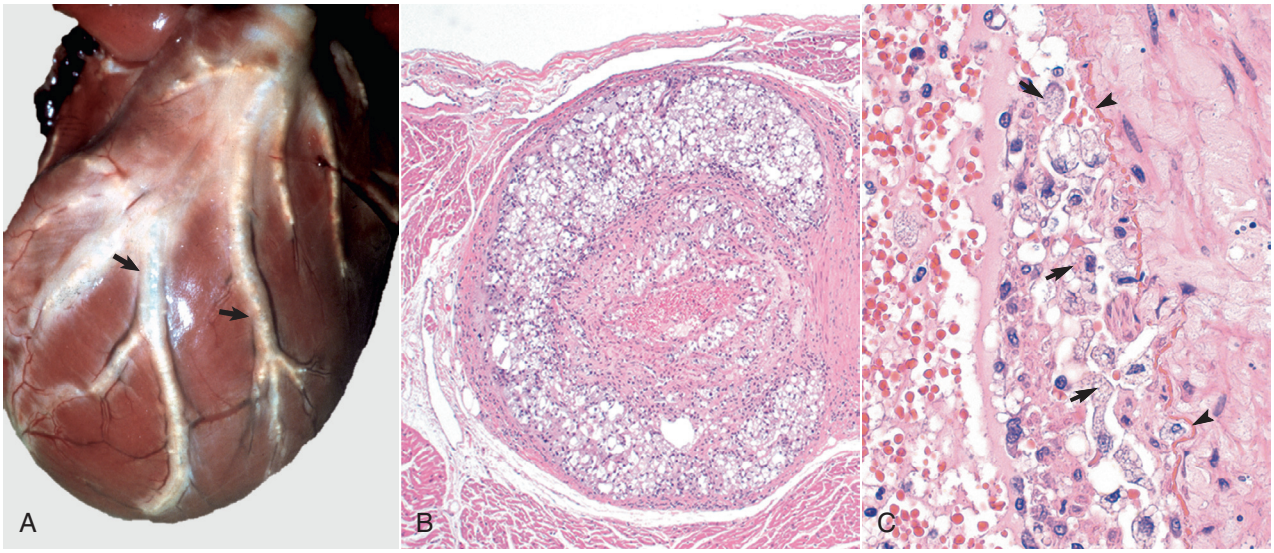


Figure 10-66 Coronary Atherosclerosis, Hypothyroidism, Heart, Left Ventricle, Dog. A, The affected coronary arteries are prominent and cordlike *(arrows)* with thickened walls. The diffuse and focal yellow areas in the walls of the arteries are the sites of atheromatous deposits. **B,** Note the extensive accumulation of lipid-laden (clear vacuoles) macrophages termed "foam cells" throughout the thickened tunica intima and media of this branch of the coronary artery. H&E stain. **C,** Higher magnification of **B.** The tunica intima contains abundant lipid-laden macrophages *(arrows)*. Note the disruption of the endothelium with fibrin on the exposed luminal surface. This condition is highly unstable and is prone to activation of Virchow's triad and the coagulation cascade with the formation of mural thrombi and infarction of myocardium supplied by this artery. The *arrowheads* identify the internal elastic lamina of the tunica intima. H&E stain. (**A** courtesy School of Veterinary Medicine, Purdue University. **B** and **C** courtesy College of Veterinary Medicine, University of Illinois.)

Figure 10-67 Calcification, Vitamin D Toxicosis, Aorta, Rabbit. The aorta is firm and inelastic because of the calcium deposits in the tunica intima and media. (Courtesy School of Veterinary Medicine, Purdue University.)

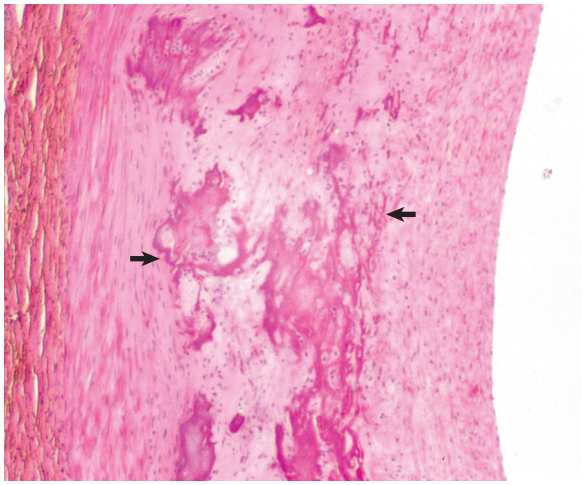


Figure 10-68 Medial Calcification, Aorta, Cow. Note the layer of mineralization *(between arrows)* in the middle of the tunica media. H&E stain. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

in all animal species. These lesions are generally not detected grossly, but in some diseases with fibrinoid necrosis of vessels, hemorrhages and edema are seen in affected organs at necropsy. The microscopic feature shared by these lesions is the formation of a homogeneous eosinophilic zone in the vessel wall (Fig. 10-69; also see Fig. 10-78). Special stains allow differentiation into three types: (1) amyloid confirmed by Congo red and methyl violet; (2) fibrinoid deposits, positive by the periodic acid–Schiff technique; and (3) negative staining of hyaline deposits by these stains. Amyloidosis and hyaline degeneration are often observed in small muscular arteries of the myocardium, lungs, and spleen of old dogs. Lesions in the intramyocardial arteries can cause small foci of myocardial infarction.

Fibrinoid necrosis of arteries is associated with endothelial damage and is characterized by entry and accumulation of serum proteins followed by fibrin polymerization in the vessel wall. These materials form an intensely eosinophilic collar that obliterates cellular detail. This lesion is frequent in many acute degenerative and inflammatory diseases of small arteries and arterioles. Fibrinoid necrosis is seen frequently in dogs with uremia and in dogs with hypertension, although hypertension is an uncommon finding in animals.

Vitamin E–Selenium Deficiency. See the discussion on vitamin E–selenium deficiency in the section on Disorders of Pigs.

Inflammation

Omphalophlebitis ("Navel Ill"). Omphalophlebitis ("navel ill") is inflammation of the umbilical vein that often occurs in neonatal farm animals because of bacterial contamination of the umbilicus immediately after parturition. Bacteria from this site can cause septicemia, suppurative polyarthritis, hepatic abscesses (the umbilical vein drains into the liver), and umbilical abscesses.

Jugular Thrombophlebitis. Jugular thrombophlebitis may be associated with indwelling jugular catheters and is reported to be increased with several concurrent disease conditions, such as hypoproteinemia, salmonellosis, endotoxemia, and large intestinal disease (see Fig. 10-27). The most common diseases with thrombosis and embolism are listed in Box 10-16.

Lymphatic Vessels

Disturbances of Circulation

Effusions

Rupture of the Thoracic Duct. Rupture of the thoracic duct, either as a result of trauma or from spontaneous disruption, causes chylothorax in dogs and cats (see Fig. 9-116). However, many cases of chylothorax occur without injury to the thoracic duct and have been attributed to lesions that interfere with central venous return or produce obstruction of the thoracic duct (right-sided heart failure, neoplasms, granulomas, cranial vena cava thrombosis, or dirofilariasis) or that are idiopathic.

Lymphedema. Lymphedema specifically refers to accumulation of fluid in interstitial space secondary to abnormal lymphatic absorption and should be differentiated from other causes of edema, such as hypoproteinemia, vasculitis, and increased hydrostatic pressure. Lymphatic fluid contains a variable amount of protein that may have an osmotic pressure that allows fluid to be drawn into the interstitial compartment from tissues with a lower osmotic gradient (protein concentration). Lymphedema can be divided into six etiologic categories: overload, inadequate collection, abnormal lymphatic contractility, insufficient lymphatic vessels, lymph node obstruction, and structural defects in lymphatic vessels. Primary lymphedema is caused by aplasia, hypoplasia, or dysplasia of lymphatic ducts, vessels, and/or lymph nodes, whereas secondary lymphedema is an acquired defect due to various disease processes (e.g., neoplasia, radiation, parasites). Primary lymphedema is rare in both dogs and cats, but it is more common in dogs. It can be temporary or permanent, and it usually affects the distal extremities, mainly of the hindlimbs. Secondary lymphedema due to lymphatic filariasis in cats is common in tropical countries and is caused by *Brugia* spp., such as *Brugia malayi* and *Brugia pahangi*. Chronic lymphedema, regardless of its etiology, results in secondary fibrosis, which worsens edema and creates a vicious cycle that leads to chronic progressive lymphedema.

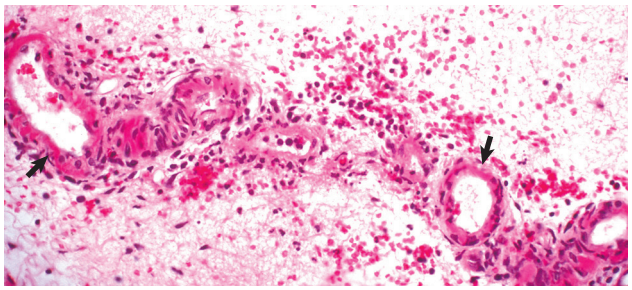


Figure 10-69 Fibrinoid Necrosis of Small Arteries, Edema Disease, Stomach, Submucosa, Pig. Note the circumferential eosinophilic *(arrows)* material in the walls of the arterioles and the extensive edema and mild hemorrhage in surrounding submucosa. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Box 10-16 Most Common Diseases with Thrombosis and/or Embolism in Animals

Pulmonary thromboembolism: Dogs, cats
Aortic thromboembolism in cats and dogs with cardiomyopathy: "Saddle" thrombi
Aortoiliac thrombosis in horses: Verminous or idiopathic
Verminous arteritis in horses: *Strongylus vulgaris*
Septic embolism from lesions of vegetative endocarditis
Fibrocartilaginous emboli: Dogs
Conditions accompanied by DIC (e.g., hog cholera, ICH, FIP, Gram-negative endotoxemia)
Thrombosis of caudal vena cava: Cattle

DIC, Disseminated intravascular coagulation; *FIP,* feline infectious peritonitis; *ICH,* infectious canine hepatitis.

Disturbances of Growth. See the discussion on anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Blood and Lymphatic Vascular Systems.

Neoplastic Transformation. Lymphangioma is a rare benign neoplasm composed of lymphatic channels. Lymphangiosarcoma, the malignant counterpart, occurs more often than the benign neoplasm. Vascular spaces formed by neoplastic lymphatic endothelial cells contain lymph rather than blood. Lymphatic vessels are frequently invaded by primary carcinomas and are a common route of metastasis (see the section on Disorders of Dogs).

Inflammation

Lymphangitis. Lymphangitis is a feature of many diseases (see Box 10-8). The affected vessels are often located in the distal limbs and are thick, cordlike structures (Fig. 10-70). Lymphedema

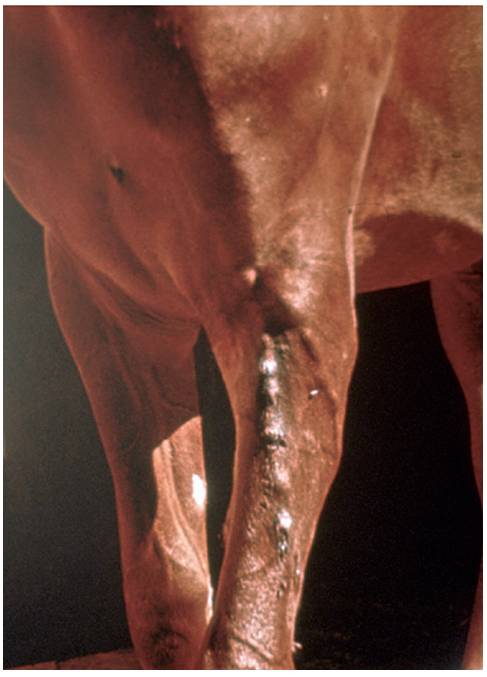


Figure 10-70 Lymphangitis, Forelimb, Lymphatic Vessels, Horse. Note the multiple swellings (cordlike) of the afferent lymphatic vessels in the skin. These lymphatic vessels lie in the subcutis and empty into the caudal superficial cervical (prescapular) lymph node. (Courtesy School of Veterinary Medicine, Purdue University.)

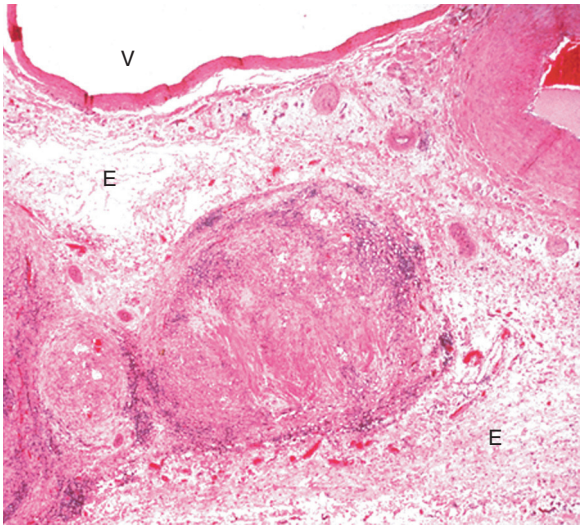


Figure 10-71 Granulomatous Lymphangitis, Johne's Disease, Mesenteric Lymphatic Vessel, Sheep. The lymphatic is occluded by a fibrinous thrombus secondary to the destruction of the endothelium by inflammatory cells including macrophages. Early proliferating fibrous tissue and extensive edema *(E)* surround the lymphatic vessel. The adjacent artery *(upper right)* and vein *(V)* are unaffected. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

can be present. Nodular suppurative lesions of lymphangitis often ulcerate and discharge pus onto the surface of the skin. In Johne's disease, the mesenteric lymphatic vessels are often prominent because of granulomatous lymphangitis, an extension of the enteric infection producing a granulomatous enteritis and lymphangitis (Fig. 10-71).

Disorders of Horses

Myocardium

Cell Degeneration and Death: Toxicoses

White Snakeroot–Induced Myocardial Degeneration. After ingestion, white snakeroot (*Eupatorium rugosum*) causes myocardial degeneration and necrosis (acute injury) followed by fibrosis (reparative response). Tremetol is the toxic compound in white snakeroot; it becomes toxic after microsomal activation of a precursor compound by cytochrome P450 enzymes in the liver. The mechanism used by tremetol to cause injury is unclear, but dysfunction of mitochondrial oxidative phosphorylation by inhibiting the tricarboxylic acid cycle has been suggested. Acute cardiac rhabdomyocyte degeneration and necrosis are discussed in detail in the section on Responses to Injury: Myocardium, Myocardial Necrosis and also in Chapter 15. Reparative responses are discussed in Chapter 3. Macroscopic lesions include pale white to tan areas and linear streaks throughout the myocardium; microscopic lesions include multifocal myocardial degeneration and necrosis with vacuolation of myocardial cytoplasm; loss of cross-striations; fragmentation of rhabdomyocytes; hypereosinophilia, coagulation, and clumping of the sarcoplasm; and nuclear pyknosis and karyolysis. The pericardium may contain a modified transudate with fibrin.

Ionophore-Induced Myocardial Degeneration. See the discussion on ionophore-induced myocardial degeneration in the section on Disorders of Domestic Animals.

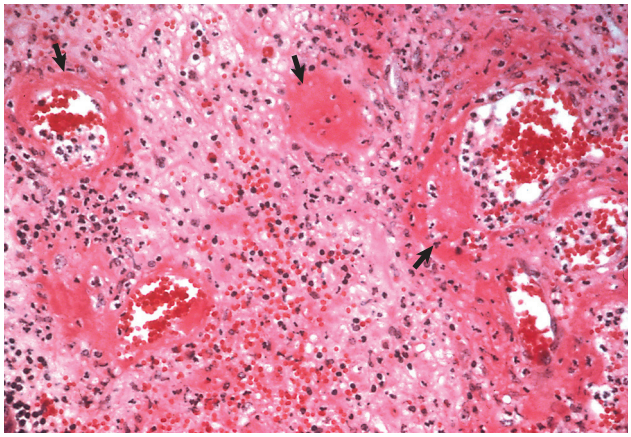


Figure 10-72 Acute Arteritis, Equine Viral Arteritis, Small Intestine, Submucosa, Horse. Small arteries have fibrinoid degeneration (circumferential eosinophilic material *[arrows]*) with leukocytic infiltration of the tunica media. The surrounding loose connective tissue is edematous and infiltrated by numerous leukocytes. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Pericardium and Epicardium

Inflammation

Fibrinous Pericarditis. Hematogenous spread of specific organisms may result in fibrinous pericarditis in the horse. These include *Actinobacillus*, streptococcal, and mycoplasma infections. Sterile swabs of the pericardial exudates are recommended to identify the causative organism. Equine herpesvirus types 1 and 2 and influenza virus infections may result in fibrinous pericarditis. Fibrinous pericarditis has been reported in horses with mare reproductive loss syndrome following exposure to the Eastern tent caterpillars.

Blood and Lymphatic Vascular Systems

Blood Vessels

Inflammation

Equine Viral Arteritis. Equine viral arteritis is a systemic viral infection with a tropism for vascular endothelial cells. In this disease, affected small muscular arteries have lesions of fibrinoid necrosis, extensive edema, and primarily mononuclear infiltration with thrombosis (Fig. 10-72). Grossly, the vascular injury is reflected by hemorrhage and severe edema of the subcutaneous tissues, lymph nodes, and intestinal wall and mesentery accompanied by notable accumulation of serous fluids in body cavities and pulmonary edema.

African Horse Sickness: Subacute Cardiac Form. African horse sickness is an insect-borne (*Culicoides* spp.) viral disease of *Equidae* that is endemic in Africa, the Middle East, India, and Spain. The occurrence is seasonal because the insect vectors thrive in hot, wet conditions. The febrile disease may produce high mortality (up to 95%) and appears in several clinical forms, including the subacute cardiac form described here, as well as an acute respiratory form with massive pulmonary edema. The pathogenesis is initiated by the introduction of the virus by bites of the insect vector. The virus proliferates in local lymph node, and viremia ensues. The virus has a tropism for endothelial cells, monocytes, and macrophages, and increased vascular permeability, edema, hemorrhage, and microthrombosis are produced. The gross lesions are extensive subcutaneous and intermuscular edematous swelling of the head and neck. Massive hydropericardium is present with accompanying epicardial and endocardial ecchymotic hemorrhages. Histopathologically, endothelial degeneration and necrosis occur with the edema. In the myocardium, hemorrhage, edema, and focal myocardial necrosis

with inflammatory cell infiltrates are present (see Chapter 4 and Fig. 4-40).

Cranial Mesenteric Arteritis and Thrombosis. Cranial mesenteric arteritis and thrombosis results from fourth-stage larval migration from *Strongylus vulgaris* (Fig. 10-73). Infection of horses by *Strongylus vulgaris* is now less common because of widespread use of highly efficacious antiparasitic drugs. During its larval development, the parasite migrates through the intestinal arteries, and the most severe lesions are generally found in the cranial mesenteric artery near its origin. The affected vessel is enlarged, and its wall is firm and fibrotic. The intimal surface often has an adhering thrombus often admixed with larvae. Microscopically, the affected vessel has extensive infiltration of inflammatory cells and proliferation of fibroblasts throughout the wall. As a consequence, thromboembolism of the intestinal arteries frequently occurs and can produce colic, but the abundant collateral circulation to the equine intestinal tract makes intestinal infarction an unusual event.

Aortoiliac Thrombosis. Aortoiliac thrombosis is characterized by extensive and progressive thrombosis thought to be caused by migration of fourth-stage larval migration from *Strongylus vulgaris*. Aortoiliac thrombosis results in posterior weakness following exercise with recovery following rest. See the previous section on cranial mesenteric arteritis and thrombosis.

Jugular Thrombophlebitis. See the discussion on jugular thrombophlebitis in the section on Disorders of Domestic Animals: Blood and Lymphatic Vessels, Blood Vessels, Inflammation.

Cell Degeneration and Death

Arterial Intimal Calcification. Arterial intimal calcifications (intimal bodies) are distinctively small, mineralized masses within the subendothelium in small muscular arteries and arterioles of horses (E-Fig. 10-24). They have no deleterious effect.

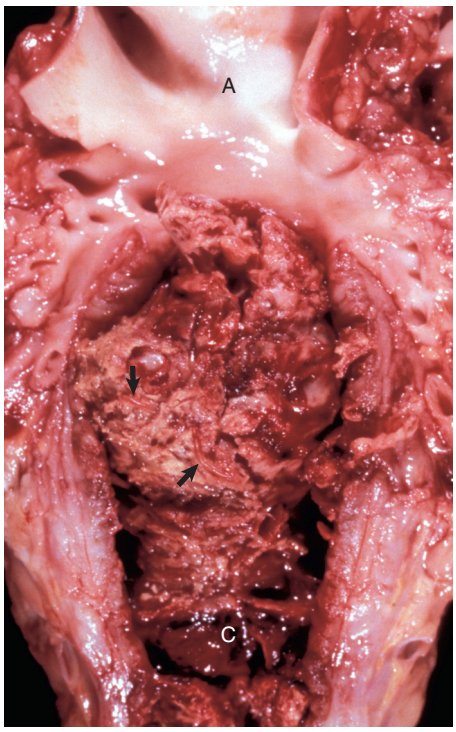


Figure 10-73 Verminous Arteritis and Mural Thrombosis, Strongylosis, Abdominal Aorta *(A)* and Cranial Mesenteric Artery, Horse. A pale friable thrombotic mass, in which several *Strongylus vulgaris* larvae *(arrows)* are embedded, is attached to the wall of the cranial mesenteric artery *(C)*. (Courtesy College of Veterinary Medicine, University of Illinois.)

Lymphatic Vessels

Inflammation

Glanders Disease (Farcy): Cutaneous Form. Glanders disease (Farcy) is a contagious disease of horses, donkeys, and mules caused by infection with *Burkholderia* (*Pseudomonas*) *mallei*. Once worldwide in distribution, it is now seen in eastern Europe, Asia, and northern Africa. The disease occurs in several clinical forms, and the cutaneous form with involvement of lymphatic vessels is described here. The pathogenesis is initiated by ingestion of contaminated food and water. The organisms enter through the pharynx and are disseminated to the skin hematogenously. The gross lesions of the skin appear as multiple ulcerated nodules that follow infected lymphatic vessels. Most frequent in the limbs, the ulcerated lesions discharge suppurative exudate onto the skin surface. Swollen tortuous cutaneous lymphatic vessels are visible between the ulcerative lesions. Microscopically, the skin nodules represent pyogranulomatous inflammation extending from cutaneous lymphatic vessels with suppurative lymphangitis (see Fig. 4-25).

Miscellaneous Cutaneous Lymphangitides. The cutaneous lesions affecting lymphatic vessels in less common cutaneous lymphangitides are as follows (see Box 10-8):

1. Ulcerative (likely caused by *Corynebacterium pseudotuberculosis* and other cutaneous bacteria)
2. Sporadic (cause unknown)
3. Epizootic lymphangitis (*Histoplasma farciminosum*)
4. Melioidosis (*Burkholderia pseudomallei*)

These lesions mimic those of Glanders disease, and differentiation occurs by impression smears and microbiologic cultures and analyses. The skin of the legs, head, neck, and/or flanks has raised firm nodules (≈1 to 2 cm in diameter), draining nodules, and draining fistulous tracts, often arranged in linear bands (beaded appearance) that follow the flow of lymphatic vessels. These lesions contain or drain pus, which is often thick and white-yellow in color. Microscopically, lesions are characterized by suppurative to pyogranulomatous inflammation. Infectious microorganisms are often present in the exudate (see Fig. 4-25).

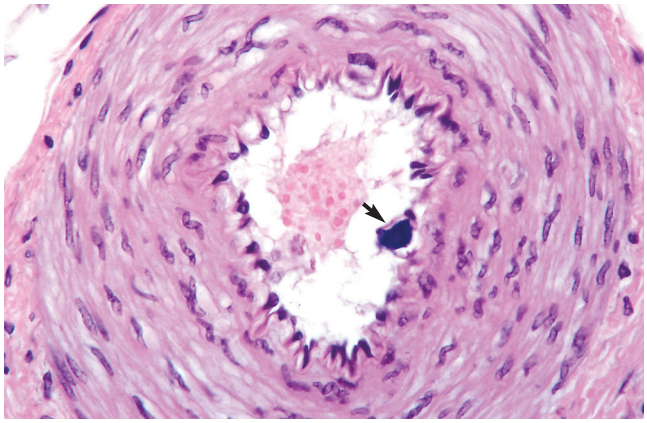
Chronic Progressive Lymphedema in Draft Horses. Chronic progressive lymphedema (CPL) occurs in many draft horse breeds and is a debilitating condition. A definitive cause is not known; however, a genetic disorder of elastin metabolism resulting in dysfunction of the lymphatic vessels in the distal extremities with multiple contributing factors including secondary bacterial infections is suspected. The distal limbs are swollen with pitting edema, thickened, scaling skin with exudation, erosions, and ulcerations. Microscopically, dermal lymphatic vessels are markedly dilated within the edematous dermis. In chronic cases, the dermis may become markedly thickened with fibrous connective tissue as a result of the chronic edema. The overlying epidermis may be acanthotic with intraepidermal pustules, erosions, and ulcerations. Folliculitis and deep dermal abscesses may be present. Staining for elastin fibers demonstrates a disorganized and excessive network of elastin fibers within the superficial dermis. Lymphatic vessels within the deep dermis lack normal elastin fibers.

Disorders of Ruminants (Cattle, Sheep, and Goats)

Myocardium

Disturbances of Growth

Dilated Cardiomyopathy. See the discussion on cardiomyopathies in the section on Disorders of Domestic Animals: Myocardium, Disturbances of Growth, Hypertrophy and Atrophy.



E-Figure 10-24 Intimal Body *(Arrow)*, Intestine, Muscular Artery, Horse. Intimal bodies are distinctive small, mineralized masses within the subendothelium of small muscular arteries and arterioles of horses. They are an incidental finding and have no pathologic significance. H&E stain. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

Lymphoma (Lymphosarcoma). See the discussion on neoplastic transformation in the section on Disorders of Domestic Animals: Myocardium, Disturbances of Growth.

Inflammation

Blackleg Myocarditis. Hemorrhagic myocarditis occurs together with the hemorrhagic inflammation typically found in skeletal muscle of cattle with blackleg (*Clostridium chauvoei*) (Fig. 10-74). See the discussion on myocarditis in the section on Responses to Injury: Myocardium, Inflammation; sections on disorders of individual animal species; and also Chapter 15.

East Coast Fever (*Theileria parva*). East Coast fever is a tick-transmitted protozoal disease of cattle, sheep, and goats in Africa caused by *Theileria parva*, which causes myocardial necrosis and inflammation (E-Fig. 10-25).

Foot-and-Mouth Disease. Foot-and-mouth disease can cause myocarditis in young lambs and piglets. Focal myocardial necrosis and apoptosis with infiltration of mononuclear inflammatory cells are scattered throughout the myocardium. Myocarditis may precede the typical vesicular lesions (see Chapters 4, 7, and 9).

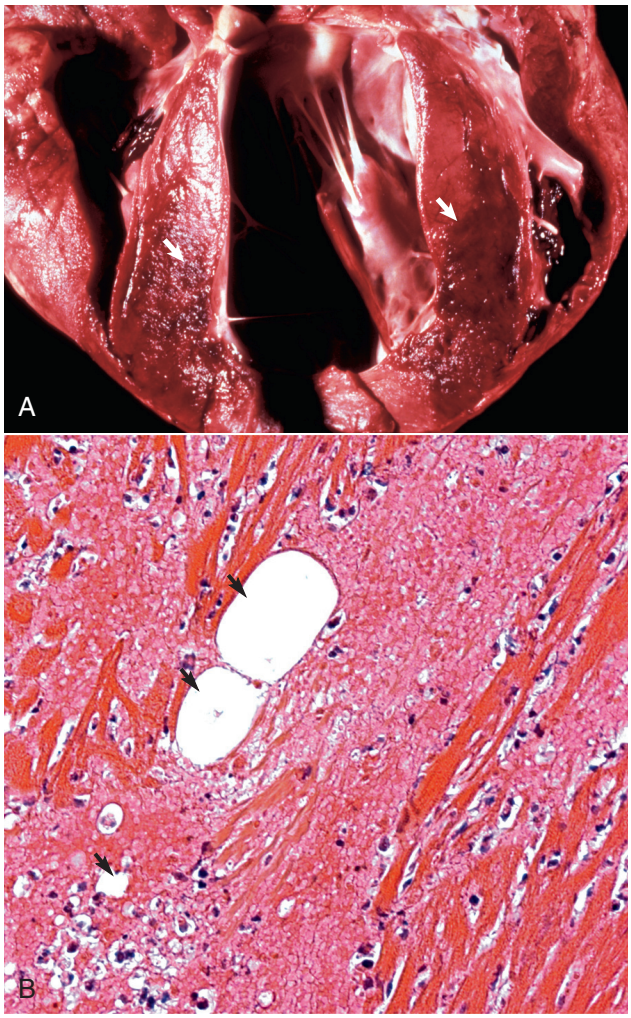


Figure 10-74 **Necrohemorrhagic Myocarditis, "Blackleg," Heart, Steer. A,** Note the area of hemorrhagic myocarditis *(arrows)* in the wall of the ventricular myocardium. This disease is caused by *Clostridium chauvoei*, and lesions are most common in skeletal muscle. **B,** Necrohemorrhagic myocarditis, heart, cow. Note the myocardial necrosis, serocellular interstitial debris, and the clear spaces *(arrows)* representative of gas bubbles. (**A** courtesy Dr. J. Simon, College of Veterinary Medicine, University of Illinois. **B** courtesy Atlantic Veterinary College, University of Prince Edward Island.)

Eosinophilic Myocarditis. Eosinophilic myocarditis and the accumulation of eosinophils in the inflammatory response are the result of some parasitic infections such as sarcocystosis (see Chapter 15).

Cell Degeneration and Death: Toxicoses

Gossypol-Induced Myocardial Degeneration. See the discussion on gossypol-induced myocardial degeneration in Disorders of Domestic Animals: Myocardium, Cell Degeneration and Death, Toxicoses.

Excess Vitamin D and Calcinogenic Plants. See the discussion on mineralization in the section on Disorders of Domestic Animals: Endocardium and Heart Valves, Cell Degeneration and Death, Endocardial Mineralization; in others sections of this chapter; and also Chapters 1 and 15.

Endocardium and Heart Valves

Disturbances of Growth

Valvular Hematomas. Valvular hematomas (hematocysts, valvular telangiectasia) frequently are observed on the AV valves of postnatal ruminants (see Fig. 10-51, *A*). These lesions, which may regress spontaneously by the time the animals are several months of age, do not produce any functional abnormalities. Lesions are bulging, blood-filled cysts, several millimeters in diameter, on the AV valves.

Valvular Lymphocysts. Valvular lymphocysts may also occur and appear as yellow serum-filled cysts on the AV valve cusps (see Fig. 10-51, *B*).

Inflammation

Vegetative Valvular Endocarditis. Endocarditis is usually the result of bacterial infections in which the affected valves have large, adhering, friable, yellow-to-gray masses of fibrin termed *vegetations*, which can largely occlude the valvular orifice (see Fig. 10-54, *A*). Microscopically, the lesion consists of accumulated layers of fibrin and numerous embedded bacterial colonies underlain by a zone of infiltrated leukocytes and granulation tissue (see Fig. 10-54, *B*). See the discussion on vegetative valvular and mural endocarditis in the section on Disorders of Domestic Animals: Endocardium and Heart Valves, Inflammation, and also Chapter 3.

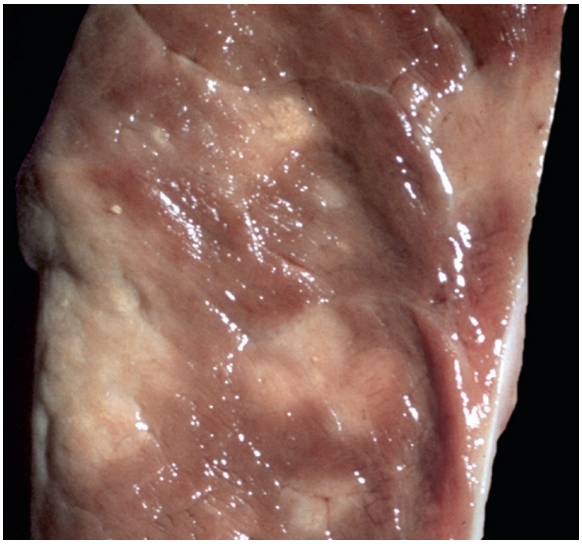
Cell Degeneration and Death

Endocardial Mineralization See the discussion on mineralization in the section on Disorders of Domestic Animals: Endocardium and Heart Valves, Cell Degeneration and Death, Endocardial Mineralization; in others sections of this chapter; and also Chapters 1 and 15.

Pericardium and Epicardium

Inflammation

Fibrinous Pericarditis. Hematogenous spread of specific organisms may result in fibrinous pericarditis. Mannheimiosis, blackleg, coliform septicemias, contagious bovine pleuropneumonia, sporadic bovine encephalomyelitis, and in utero *Brucella* spp. and *Arcanobacter pyogenesis* fetal septicemias may all produce fibrinous pericarditis. In sheep, Mannheimiosis and streptococcal infections most commonly result in fibrinous pericarditis. In goats, *Mycoplasma*



E-Figure 10-25 Myocarditis, East Coast Fever, Heart, Cow. The multiple white-beige areas in the left ventricular wall are infiltrates of mononuclear inflammatory cells. (Courtesy School of Veterinary Medicine, Purdue University.)

mycoides subspecies mycoides produces a fibrinous pericarditis. Sterile swabs of the pericardial exudates are recommended to identify the causative organism. See the discussion on pericarditis in Disorders of Domestic Animals: Pericardium and Epicardium, Inflammation and also Chapters 7 and 9.

Suppurative Pericarditis (Traumatic Reticulopericarditis). Suppurative pericarditis is seen mainly in cattle as a complication of traumatic reticuloperitonitis ("hardware disease"). Foreign bodies, such as nails or pieces of wire that accumulate in the reticulum, occasionally penetrate the reticular wall and diaphragm, enter the adjacent pericardial sac, and introduce infection. Some affected cattle survive for weeks to months until death ensues from congestive heart failure and septicemia. Grossly, the pericardial surfaces are notably thickened by white, often rough, shaggy-appearing masses of fibrous connective tissue that enclose an accumulation of white to gray, thick, foul-smelling, purulent exudate (see Fig. 10-62). See the discussion on pericarditis in the section on Epicardium and Pericardium, Disorders of Domestic Animals, and also Chapters 7 and 9.

Blood and Lymphatic Vascular Systems

Blood Vessels

Inflammation: Infectious Diseases

Thrombotic Meningoencephalitis. *Histophilus somni* (formerly *Haemophilus somnus*) causes a systemic vasculitis in cattle resulting in meningoencephalitis. Mural thrombi from local vascular injury rather than thromboemboli from distal sites of vascular injury, such as the lungs, are the major type of thrombus in this disease. Gross lesions in the central nervous system (CNS) are characteristic of infarcts (see Fig. 14-89, A). Microscopic lesions are initially vasculitis and vascular necrosis, which are followed by thrombosis and infarction (see Fig. 14-89, B). Septic vasculitis, the initial event, is followed by edema and an influx of neutrophils and macrophages in and around vessel walls and adjacent parenchyma. Colonies of small Gram-negative bacilli are frequent in thrombi, in and around affected vessels, and in areas of necrosis. *Histophilus somni* can also cause a necrotizing myocarditis, frequently in the left ventricular papillary myocardium.

Thrombosis of the Caudal Vena Cava. Thrombosis of the caudal vena cava occurs in association with rupture of hepatic abscesses into either the hepatic vein or the caudal vena cava. The hepatic abscess inflammation extends into the adjacent large hepatic veins and results in formation of a septic thrombus in the caudal vena cava. Rupture and release of the contents of the abscess into the lumen can cause multiple septic emboli in the pulmonary capillaries and unexpected death of the affected animal, often preceded by severe hemoptysis.

Foreign Parasitic Diseases. Foreign parasitic diseases important in tropical regions of the world are characterized by the presence of parasites in the lumens of veins. These diseases in cattle and water buffalo include schistosomiasis (blood fluke infection—*Schistosoma* spp.) in which adult parasites are present in the mesenteric and portal veins, and the resulting phlebitis is characterized by intimal proliferation and thrombosis.

Omphalophlebitis ("Navel Ill"). See the discussion on omphalophlebitis ("navel ill") in the section on Disorders of Domestic Animals: Blood and Lymphatic Vascular Systems, Blood Vessels, Inflammation, and also Chapter 8.

Johne's Disease. Lesions of Johne's disease affecting blood and lymphatic vessels and characterized by intimal mineralization and granulomatous lymphangitis, respectively, are discussed in greater detail in Chapters 4, 7, and 13.

Anthrax. Anthrax in herbivores often occurs as an acute febrile highly fatal septicemic disease. Although global in distribution, the disease is enzootic in certain areas. The etiology is *Bacillus anthracis*, a large rod-shaped spore-forming bacterium. The pathogenesis of the disease in affected herbivores is exposure by ingestion of contaminated food (especially bone meal) and water. The organisms produce a variety of lethal toxins that provoke local edema and tissue necrosis and increased vascular permeability associated with lymphangitis and lymphadenitis. Herbivores that die from septicemic anthrax have dark, thick unclotted blood oozing from body orifices. These cases should NOT be subjected to necropsy to avoid massive contamination of the environment by the spores of the organism. Instead, a blood smear should be collected and examined for the presence of the diagnostic bacilli. If a case is necropsied by mistake, the diagnostic findings are massive splenomegaly (so-called blackberry jam spleen), disseminated serosal hemorrhages, and swollen edematous lymph nodes. Microscopic findings (histopathologic evaluation is NOT recommended) include massive numbers of typical large rod-shaped organisms in the blood, congestion, hemorrhage, lymphangitis, and lymphadenitis (see Chapter 4, Fig. 4-23; Chapter 7, Fig. 7-135; and Chapter 13, Fig. 13-57).

Neospora caninum. See the discussion on *Neospora caninum* in Chapter 4.

Malignant Catarrhal Fever. See the discussion on malignant catarrhal fever in Chapter 4.

Bovine Virus Diarrhea. See the discussion on bovine virus diarrhea in Chapters 4 and 7.

Bluetongue. See the discussion on bluetongue in Chapters 4 and 7.

Disorders of Pigs

Myocardium

Cell Degeneration and Death

Mulberry Heart Disease. See the discussion on mulberry heart disease in the next section on Blood and Lymphatic Vascular Systems, Blood Vessels, Cell Degeneration and Death, Dietary Microangiopathy: Mulberry Heart Disease.

Inflammation: Infectious Diseases

Viral Myocarditis

Encephalomyocarditis. Encephalomyocarditis virus is a cardiovirus of the Picornaviridae. The type B strain can affect several species including human beings, but pigs are most often affected. Pigs of any age can be affected. Gross lesions can include multifocal areas of pallor. Multifocal areas of myocardial necrosis with infiltrations of mononuclear inflammatory cells are observed microscopically. Other viruses that can cause myocarditis in pigs include porcine parvovirus and porcine circovirus 2 associated with postweaning multisystemic wasting syndrome.

Endocardium and Heart Valves

Inflammation

Endocarditis. Endocarditis is commonly found in pigs and results from a bacterial septicemia. The most commonly isolated organisms are *Streptococcus* spp. and *Erysipelothrix rhusiopathiae*. Confirmation of the definitive organism requires bacterial isolation. Affected valves have large, adhering, friable, yellow-to-gray masses of fibrin termed *vegetations*, which can largely occlude the valvular orifice (see Fig. 10-54). Microscopically, the lesion consists of accumulated layers of fibrin and numerous embedded bacterial colonies underlain by a zone of infiltrated leukocytes and granulation tissue

(see Fig. 10-54, *B*). See the discussion on valvular and mural endocarditis in the section on Inflammation; Disorders of Domestic Animals: Endocardium and Heart Valves, and also Chapter 3.

Pericardium and Epicardium

Inflammation: Infectious Diseases

Fibrinous Pericarditis. Fibrinous pericarditis may accompany Glasser's disease (*Haemophilus parasuis*) (Fig. 10-75), streptococcal infections, enzootic mycoplasma pneumonia, and salmonellosis. Sterile swabs of the pericardial exudates are recommended to identify the causative organism. See the discussion of pericarditis in the section on Disorders of Domestic Animals: Pericardium and Epicardium, Inflammation, and also Chapters 3, 7, and 9.

Porcine Polyserositis (Glasser's Disease, *Streptococcus suis* II). See Fig. 10-75; also see the discussion of edema disease in the next section and in Chapters 4 and 7.

Blood and Lymphatic Vascular Systems

Blood Vessels

Cell Degeneration and Death

Dietary Microangiopathy: Mulberry Heart Disease. Dietary microangiopathy of pigs or "mulberry heart disease" is produced by a deficiency of vitamin E and/or selenium and the resultant effect on the microvasculature, which is characterized by fibrinoid necrosis, and thromboses of small vessels resulting in microhemorrhages. The hemorrhage results in major discoloration of the epicardial surface of the heart, particularly the right atrium said to resemble a mulberry (Figs. 10-76 and 10-77). In addition to the epicardial hemorrhages, hydropericardium often ensues. Massive hemorrhagic hepatic necrosis (hepatosis dietetica) is also produced with vitamin E and/or selenium deficiency (see Fig. 8-74). With either form of the disease, fibrinoid necrosis of small muscular arteries and arterioles is widespread and is accompanied by endothelial damage and fibrin thrombi in capillaries, especially capillaries of the myocardium (Fig. 10-78; E-Fig. 10-26). This complex of vascular lesions has been termed *dietary microangiopathy*.

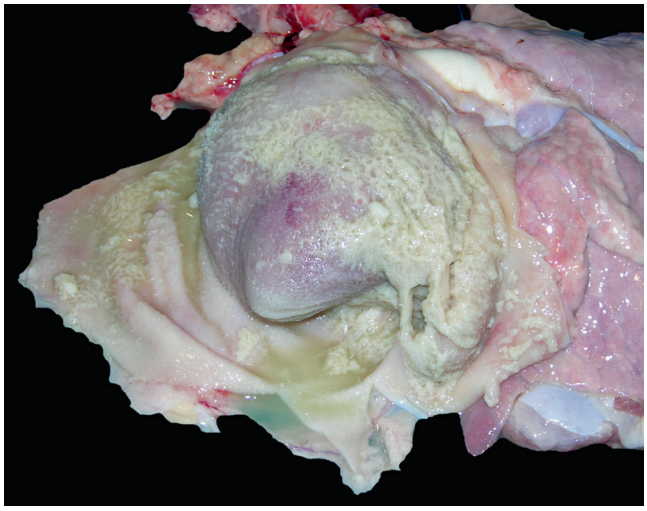


Figure 10-75 Fibrinous Porcine Polyserositis, Glasser's Disease, Pericardium and Epicardium (Pericardial Cavity), Pig. A fibrinous pericarditis is typical of Glasser's disease (*Haemophilus parasuis*). Streptococcal infections, enzootic mycoplasma pneumonia, and salmonellosis can also cause this lesion. (Courtesy Dr. D. Driemeier, Federal University of Rio Grande do Sul, Brazil.)

Fibrinoid Necrosis of Blood Vessels. Fibrinoid necrosis of arteries and veins (see Fig. 10-69) is particularly frequent in pigs and is an important diagnostic feature in cases of vitamin E–selenium deficiency (heart), edema disease (gastric submucosa), cerebrospinal angiopathy, porcine circovirus II vasculopathy, and organic mercury toxicosis (meninges). See the previous section on Dietary Microangiopathy: Mulberry Heart Disease.

Inflammation: Infectious Diseases

Edema Disease (Cerebrospinal Angiopathy). Infections with certain strains of hemolytic *E. coli* produce a cytotoxin that targets vascular endothelium, resulting in fibrinoid necrosis of arterioles and resultant edema. Lesions are often prominent in the arterioles of the gastric submucosa (Fig. 10-79). Vascular changes occurring in the

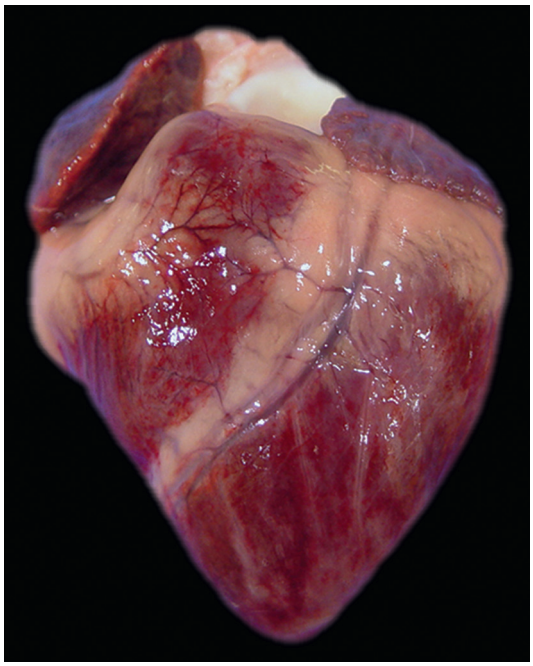


Figure 10-76 "Mulberry Heart Disease," Suffusive Hemorrhage, Epicardium, Right Ventricle, Heart, Pig. Red areas of suffusive hemorrhage ("mulberry-like") are present on the epicardial surface of the right ventricle. (Courtesy Dr. L. Miller, Atlantic Veterinary College.)

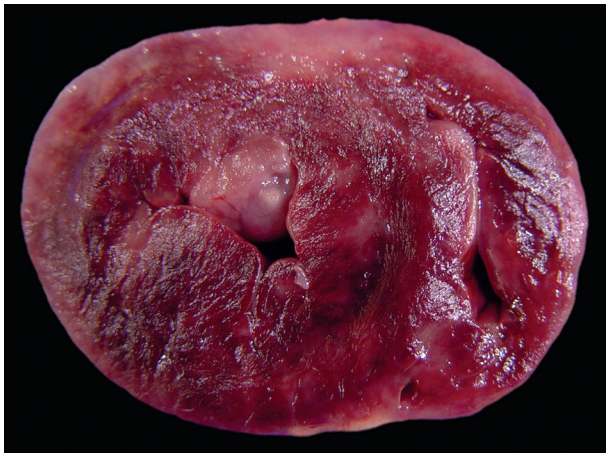
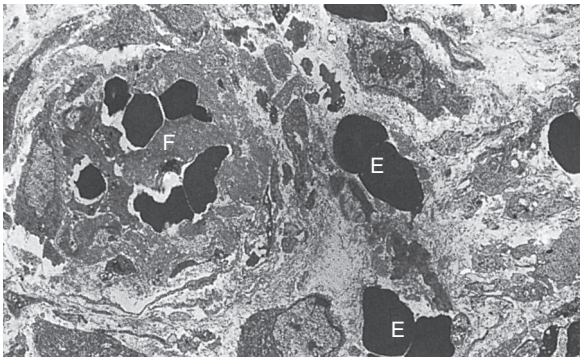


Figure 10-77 "Mulberry Heart Disease," Hemorrhage and Necrosis, Left and Right Ventricular Myocardium, Transverse Section, Pig. Red and pale mottled areas are caused by hemorrhage and necrosis, respectively. (Courtesy Dr. L. Miller, Atlantic Veterinary College.)



E-Figure 10-26 **Fibrinoid Necrosis, "Mulberry Heart Disease," Vitamin E–Selenium Deficiency, Heart, Section of Myocardium, Pig.** The affected arteriole *(left)* has intraluminal masses of fibrin *(F)* and entrapped erythrocytes. Fibrin masses are present in the vessel wall, and the adjacent interstitium has edema and hemorrhage. Note scattered erythrocytes *(E)*. TEM. Uranyl acetate and lead citrate stain. (Courtesy School of Veterinary Medicine, Purdue University.)

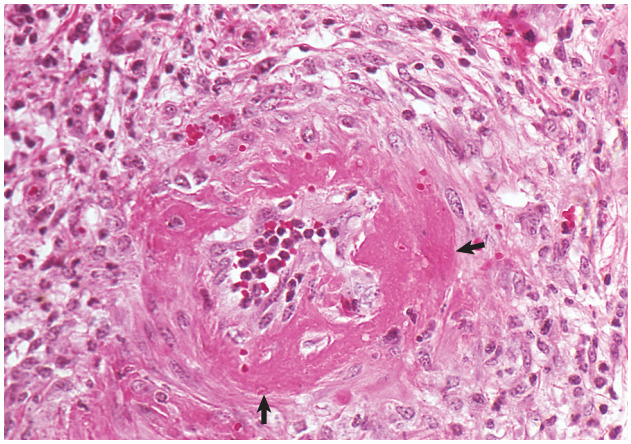


Figure 10-78 Vitamin E–Selenium Deficiency ("Mulberry Heart Disease"), Fibrinoid Necrosis, Myocardial Arteriole, Heart, Pig. Note the circumferential eosinophilic deposits *(arrows)* in the wall of the arteriole. H&E stain. (Courtesy Dr. J. Simon, College of Veterinary Medicine, University of Illinois.)

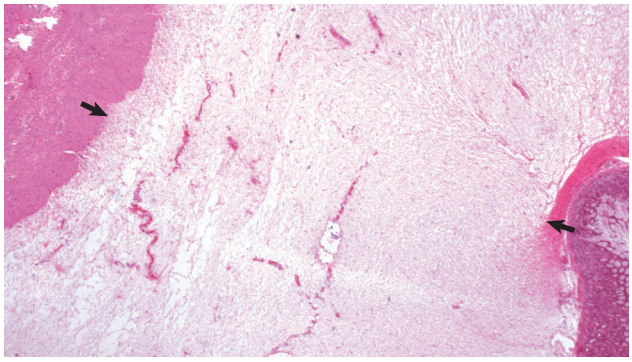


Figure 10-79 Submucosal Edema, Edema Disease, Stomach, Submucosa, Pig. The submucosa *(between arrows)* is distended with edema fluid. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

CNS are known as cerebrospinal angiopathy and can produce clinical signs of disease of the nervous system (E-Fig. 10-27; also see Fig. 10-69; Chapters 4, 7, and 11; and Figs. 7-169 and 7-170).

Erysipelosis (Erysipelothrix rhusiopathiae). Cutaneous lesions in erysipelosis are caused by *Erysipelothrix rhusiopathiae* and are the result of bacterial embolization to the skin during sepsis. Lesions consist of square to rhomboidal, firm, raised, pink to dark purple areas (Fig. 10-80; see Fig. 17-70) caused by vasculitis, thrombosis, and ischemia (infarction). The rhomboidal shape likely represents an area of skin supplied by a thrombosed vessel (see Chapter 17).

Porcine Polyserositis (Streptococcus suis II). *Streptococcus suis* II is one of several bacteria that can cause the disease porcine polyserositis. Gross lesions include vasculitis leading to variable quantities of a gray-white friable material (fibrin) on serosal surfaces (fibrinous polyserositis) of the lungs (fibrinous pleuritis), heart (fibrinous pericarditis [see Fig. 10-75]), and abdominal cavity (fibrinous peritonitis). The bacterium gains access to and spreads systemically through the blood vascular system. Lesions suggest this bacterium may have a tropism for vascular endothelial cells of serosae, and bacterial endotoxins may contribute to vascular injury and permeability changes leading to the leakage of fibrinogen and its polymerization to fibrin on serosal surfaces and in some cases to microthrombus formation and disseminated intravascular coagulation (DIC) in other organ systems (see Chapters 4, 7, and 9).

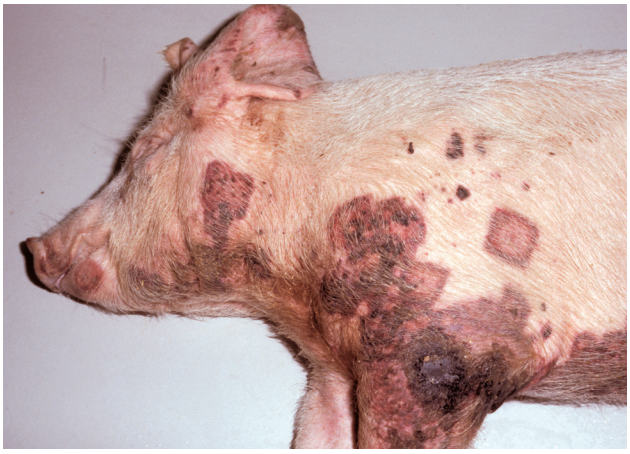
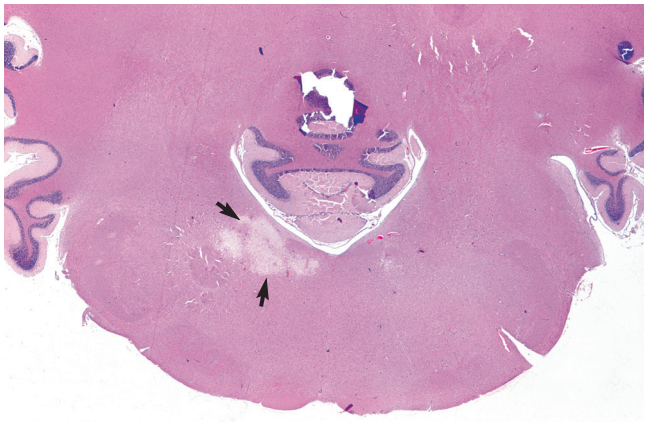


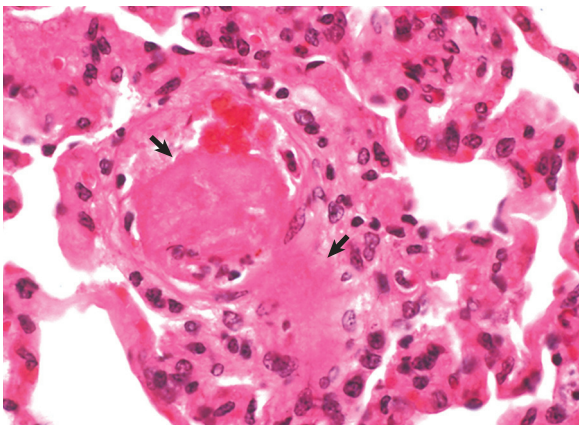
Figure 10-80 Cutaneous Infarcts, Diamond Skin Disease, *Erysipelothrix Rhusiopathiae* Septicemia, Skin, Pig. Emboli of *Erysipelothrix rhusiopathiae* have lodged in cutaneous vessels and caused a localized vasculitis, which has resulted in thrombosis followed by ischemia and cutaneous infarction. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

African Swine Fever (Wart Hog Disease, African Pig Disease). African swine fever is a highly contagious febrile hemorrhagic disease of pigs associated with a DNA virus. The clinical and pathologic features are very similar to those of classic swine fever (hog cholera). The disease is enzootic in Africa, and outbreaks have occurred in Europe, South America, and the Caribbean region. The pathogenesis of the disease is via entry in the upper respiratory tract. The virus proliferates in the tonsils and lymph nodes of the head and neck with subsequent viremia and dissemination to the entire body. Transmission to domestic swine is via ingestion of infected tissues of warthogs and bush pigs, which develop an unapparent infection, or by the bite of infected soft ticks (*Ornithodoros moubata*). The distinctive hemorrhagic lesions are attributed to disruption of the clotting mechanism and thrombocytopenia. The gross lesions are characterized by widespread congestion, edema, and hemorrhage. Hemorrhagic visceral lymph nodes and splenomegaly are present along with petechial hemorrhages of the renal cortices, epicardium, and other serosal surfaces. Pulmonary edema and hydrothorax also occur. Microscopically, viral-induced vascular alterations include congestion, hemorrhage, and edema with fibrin microthrombi (E-Fig. 10-28). The virus produces widespread necrosis of lymphocytes and macrophages (see Fig. 4-42).

Hog Cholera/Classic Swine Fever (Swine Fever, Swine Plague, Schweinpest). Hog cholera (also termed *classic swine fever*) is a highly contagious febrile hemorrhagic disease of swine produced by an RNA virus. The disease is enzootic in South America, Central America, Caribbean countries, Asia, and Europe. The pathogenesis of the disease is initiated by inhalation of the virus from direct contact with infected pigs or by ingestion of uncooked infected pork. The virus traverses the oral mucosa, replicates in the tonsils, and initiates viremia. The virus selectively damages endothelial cells, cells of the immune system (lymphoreticular cells and macrophages), and epithelial cells. The characteristic hemorrhagic lesions are associated with increased vascular permeability, thrombocytopenia, and DIC. The gross lesions are characterized by widespread petechial hemorrhages, especially of the renal cortices, urinary bladder, larynx, gastric mucosa, and epicardium with accompanying hemorrhage in lymph nodes and skin. A distinctive finding is hemorrhagic infarction of the spleen and "button ulcers" of the colonic mucosa.



E-Figure 10-27 **Vasculitis with Infarction *(Arrows)*, Neuroparenchyma, Edema Disease (Enterotoxemic Colibacillosis), Brainstem, Pig.** Some strains of *Escherichia coli* produce a Shiga-like toxin that causes necrosis of smooth muscle cells in small arteries and arterioles in the central nervous system (CNS), leading to vasculitis and infarction. The toxin binds to specific receptors on endothelial cells (see Chapter 4), and this binding can initiate a chain of inflammatory and immunologic reactions that lead to vascular damage. H&E stain. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)



E-Figure 10-28 **Fibrin Thrombi, Disseminated Intravascular Coagulation, Lung, Alveolar Septal Capillaries, Horse.** Fibrin thrombi *(arrows)* occlude two alveolar capillaries. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

Microscopically, endothelial damage is evident as hydropic degeneration and cellular proliferation. Affected vessels may have fibrinoid necrosis with fibrin deposition in the media and intima. Circulatory alterations include congestion, hemorrhage, thrombosis, and infarction. The brain has a diffuse nonsuppurative encephalitis (see Fig. 4-41).

Porcine Anthrax. See the discussion on anthrax in the section on Disorders of Ruminants (Cattle, Sheep, and Goats), Blood and Lymphatic Vascular Systems, Blood Vessels, and also Chapter 4.

Disorders of Dogs

Myocardium

Disturbances of Growth

Developmental Errors: Congenital Anomalies. See the discussion on anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies.

Cardiomyopathies. Also see the discussion on cardiomyopathies in the section on Disorders of Domestic Animals, Disorders of Domestic Animals: Myocardium, Disturbances of Growth, Hypertrophy and Atrophy.

Dilated (Congestive) Cardiomyopathy. Dilated or congestive cardiomyopathy is an important cause of congestive heart failure in dogs. Some affected dogs have low tissue concentrations of taurine, but supplementation has not proved beneficial. Affected dogs often are males of large breeds, such as Doberman pinschers, Portuguese water dogs, Dalmatians, Scottish deerhounds, Irish wolfhounds, Saint Bernards, Afghan hounds, Newfoundland dogs, Old English sheepdogs, Great Danes, and boxers, although smaller breeds, such as English cocker spaniels, may be affected. The disease often has a familial pattern in the affected breeds and appears to be inherited as an autosomal recessive or X-linked recessive trait. At necropsy, lesions of congestive heart failure are present and the hearts are rounded because of biventricular dilation (see Figs. 10-43 and 10-44). The dilated cardiac chambers often have a diffusely white, thickened endocardium. Microscopic and ultrastructural alterations are nonspecific, can be either mild or absent, and may include interstitial fibrosis and fatty infiltration and changes of myocyte degeneration, including the occurrence of so-called attenuated wavy fibers. See the discussion on cardiomyopathies in the section on Disorders of Domestic Animals, Disorders of Domestic Animals: Myocardium, Disturbances of Growth, Hypertrophy and Atrophy.

Cardiac Neoplasms. Cardiac neoplasms comprise primary and secondary (metastatic) tumors. Primary cardiac tumors include hemangiosarcoma (most frequent), thyroid/parathyroid ectopic carcinomas, mesotheliomas, thymomas, granular cell tumor, sarcomas (osteosarcomas, chondrosarcomas, fibrosarcomas/fibromas, rhabdomyosarcomas/rhabdomyoma, neurofibrosarcomas/neurofibroma, and malignant mixed mesenchymal tumor), and chemodectomas (heart-base tumors). Secondary cardiac neoplasms are metastases from distant, primary tumor sites. In a study that included 80 dogs with primary and/or secondary cardiac neoplasms, 36% of dogs had evidence of cardiac metastases.

Inflammation: Infectious Diseases

Canine Parvovirus Myocarditis. Lymphocytic myocarditis is usually a lesion of viral infections and is well illustrated by the lesions of parvoviral myocarditis of puppies. Dogs with parvoviral myocarditis die unexpectedly and have generalized lesions of acute congestive heart failure but lack lesions in the intestine, the primary site of viral damage in approximately 95% of clinical cases. The heart is pale and flabby and has disseminated interstitial lymphocytic infiltrations and scattered myocytes with large, basophilic, intranuclear viral inclusion bodies in dogs that survive fibrosis (Fig. 10-81).

Trypanosoma cruzi. *Trypanosoma cruzi* is the protozoan hemoflagellate that causes American trypanosomiasis (Chagas' disease). The kissing bug (family Reduviidae, subfamily Triatominae) transmits the disease. Infection with *Trypanosoma cruzi* causes fatal chronic myocarditis. Acute disease is characteristic in dogs younger than 1 year of age. Affected dogs develop lymphohistiocytic myocarditis resulting in right-sided congestive heart failure with ascites, lymphadenomegaly, and hepatosplenomegaly. Grossly, the cardiac muscle contains multiple yellow-white myocardial streaks and spots that are often accompanied by hemorrhage. Chronic lymphocytic and plasmacytic myocarditis that leads to right-sided congestive heart failure typically affects older dogs. Grossly, the heart is bilaterally enlarged, thinned and flaccid, and contains fibrous plaques (areas of fibrosis).

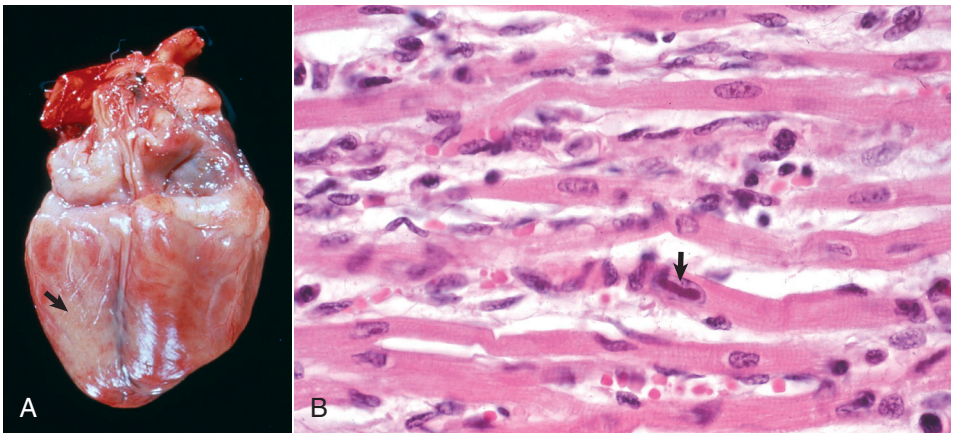


Figure 10-81 **Parvovirus Myocarditis, Heart, Dog. A,** Note the multifocal pale areas *(arrow)* in the ventricular myocardium. **B,** Parvovirus infection, section of myocardium. An intranuclear basophilic inclusion body is in a myocyte *(arrow)*. H&E stain. (**A** courtesy Dr. B. Weeks, College of Veterinary Medicine, Texas A&M University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia. **B** courtesy School of Veterinary Medicine, Purdue University.)

Cell Degeneration and Death

Neurogenic Cardiomyopathy (Heart-Brain Syndrome). Neurogenic cardiomyopathy (heart-brain syndrome) is a syndrome in dogs characterized by unexpected death 5 to 10 days after diffuse CNS injury (usually hit by car). Affected dogs die of cardiac arrhythmias caused by myocardial degeneration and necrosis. Grossly, the myocardium has numerous discrete and coalescing pale white streaks and/or poorly defined areas of myocardial necrosis—most often involving the papillary muscles of the left ventricle (Fig. 10-82). Neurogenic cardiomyopathy is thought to be caused by overstimulation of the heart by autonomic neurotransmitters and systemic catecholamines released at the time of trauma. It is unknown why there is a 5- to 10-day delay in the development of myocardial necrosis. See Chapter 14 for a discussion of heart-brain syndrome.

Endocardium and Heart Valves

Disturbances of Growth

Valvular Anomalies and Dysplasia. See the discussion on valvular anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves.

Cell Degeneration and Death

Myxomatous Valvular Degeneration (Valvular Endocardiosis). Myxomatous valvular degeneration (valvular endocardiosis) is the most common cardiovascular disease in dogs, and it is the most common cause of congestive heart failure in old dogs. Other names for this disease include endocarditis valvularis chronica fibrosa (nodosa), chronic valvular endocarditis, chronic valvular disease, billowing sail distortion of the mitral valve, endocardiosis, chronic mitral valve fibrosis, senile nodular sclerosis, mucoid degeneration, chronic myxomatous valve disease, and degenerative mitral valve disease. Myxomatous valvular degeneration (MVD) is an age-related cardiac disease of middle-aged to old dogs, especially small, toy, and medium-sized breeds. Males of affected breeds develop the disease at an earlier age than females. MVD appears to have a polygenic inheritance in dachshunds and Cavalier King Charles spaniels. The Cavalier King Charles spaniel breed has a unique susceptibility, with more than 50% prevalence by 4 years of age and 100% prevalence by 10 years of age. Other breeds with high incidence include the cocker spaniel, Lhasa apsos, bichons, Yorkshire terriers, shih tzus, dachshund, poodle, Pomeranian, miniature schnauzer, Chihuahua, fox terrier, Boston terrier, and Pekingese. At autopsies (syn: necropsies) of 3245 dogs, gross lesions occurred on the mitral valve alone (57.3%), mitral and tricuspid valves (26.6%), tricuspid valve alone (7.5%), aortic valve alone (2.1%), pulmonic valve alone (0.4%), and in combinations (6.1%). The lesions in MVD become progressively worse with age. Affected valves are shortened and thickened (nodular), either focal or diffusely, and appear smooth and shiny (Fig. 10-83) rather than rough and granular, as is usual in cases of valvular endocarditis.

MVD is grossly classified into four groups as follows: type 1, a few small discrete nodules in the area of contact that are associated with areas of diffuse opacity in the proximal portion of the valve; type 2, larger nodules that are evident in the area of contact, which tend to coalesce with their neighbors, along with areas of diffuse opacity that may be present; type 3, large nodules that coalesced

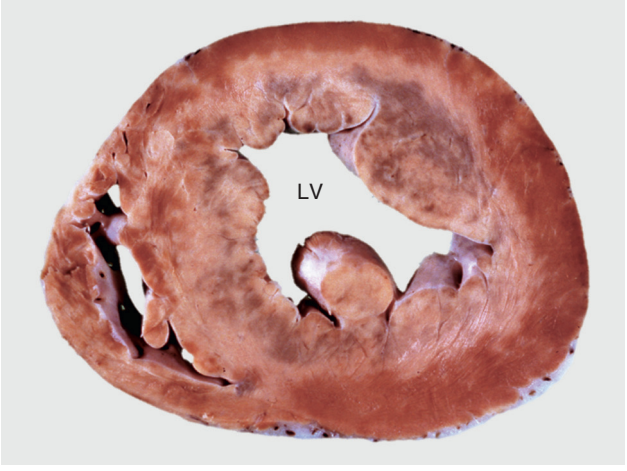


Figure 10-82 Myocardial Necrosis, "Heart-Brain Syndrome," Heart, Transverse Section of Ventricles, Dog. Necrotic areas are pale beige to white and are concentrated in the inner half of the wall of the left ventricle *(LV)* and in the ventricular septum. (Courtesy School of Veterinary Medicine, Purdue University.)

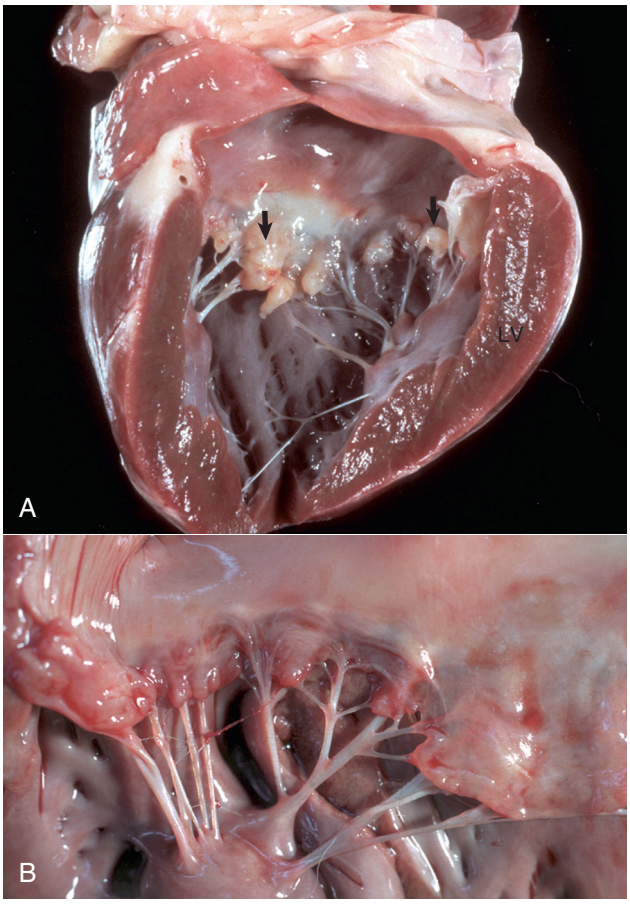


Figure 10-83 Myxomatous Valvular Degeneration (Valvular Endocardiosis), Left Atrioventricular Valve, Heart, Dog. A, The cusps of the mitral valve are thickened by white, smooth nodules *(arrows)*. *LV,* Left ventricular free wall. **B,** Note the characteristic smooth and shiny (endocardial) surface of the valve and nodules. This differentiates myxomatous valvular degeneration (endocardiosis) from the rough and granular surface of chronic bacterial endocarditis. The pink staining of the valve is caused by postmortem imbibition of hemoglobin. (**A** courtesy Dr. J. Wright, College of Veterinary Medicine, North Carolina State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia. **B** courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

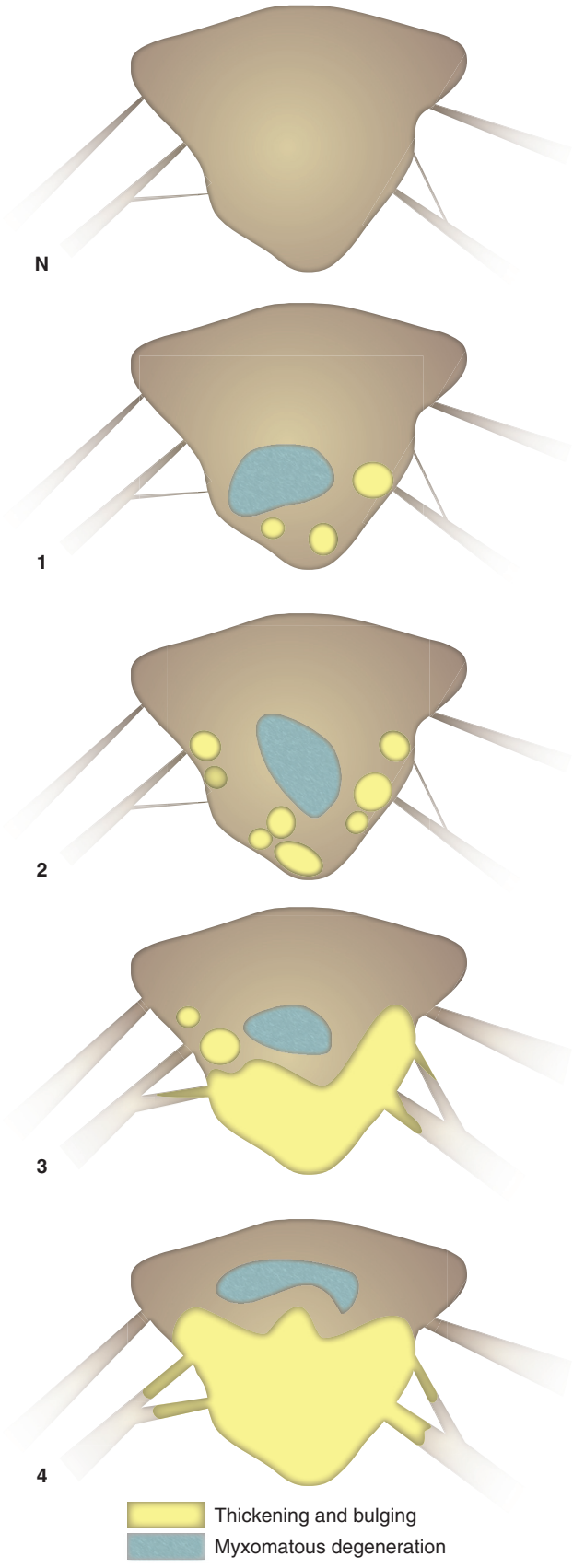


Figure 10-84 Natural Progression of Myxomatous Valvular Disease in the Mitral Leaflet. Myxomatous valvular disease is grossly classified into four groups (1-4). Type 1 has a few discrete nodules (minimal changes); type 2 has larger nodules in contact areas (mild changes); type 3 has large, coalescing nodules forming plaquelike deformities (moderate changes); and type 4 has obvious distortions of the valve (severe changes). The light-colored areas represent areas of nodular or diffuse thickening and ballooning of the valve cusp and proximal chordae tendineae. The dark-colored areas represent areas of diffuse opacity due to accumulation of neutral fat within the spongiosa layer. *N*, Normal valve. (Redrawn from Figure 2 from Borgarelli, M, Buchanan JW: Historical review, epidemiology and natural history of degenerative mitral valve disease, *J Vet Cardiol* 14(1):93-101, 2012.)

into irregular, plaque-like deformities that extend to involve the proximal portions of the chordae tendineae; and type 4, there is gross distortion and "ballooning" of the valve cusp, and the chordae tendinea are thickened proximally (Fig. 10-84). These lesions result in valvular insufficiency with subsequent atrial dilation and development of atrial "jet lesions." The jet lesion is a raised, rough, firm streak of endocardial fibrosis resulting from long-term trauma by a jet of blood leaking through the damaged valve in the closed position. Histologically, the valves are divided into four layers: atrialis, ventricularis, spongiosa, and fibrosa. The atrialis and ventricularis layers face the respective cardiac chambers and consist of endothelium and immediate subendothelial tissue containing fibroblasts, scattered collagen fibers, and a thin layer of elastic fibers. The spongiosa layer is loose connective tissue with interstitial cells and minimal fibers. The fibrosa consists of dense collagen that is continuous with the collagen core of chordae tendineae. Histopathologic lesions in MVD predominate in the distal third of the valve leaflets, and the incidence and severity increase with age. Lesions include progressive expansion of the spongiosa layer and disruption of the fibrosa layer.

Microscopically, the thickened valves have notably increased myofibroblastic proliferation and deposition of acid mucopolysaccharides (Fig. 10-85). It is important not to confuse normal age-related valve thickening in asymptomatic dogs with true pathologic thickening. Therefore a "clinical relevant diagnosis" would be more certain when the mitral valve and chordae tendineae are thickened and/or ruptured or when left heart chambers are enlarged or there are left atrial jet lesions. Severe complications of MVD include occasional rupture of chordae tendineae, occasional splitting or rupture of the left atrial wall that can result in hemopericardium, or acquired atrial septal defects. Frequent accompanying myocardial alterations include arteriosclerosis of intramyocardial arteries and multifocal myocardial necrosis and fibrosis. Progression of MVD is associated with an increase in plasma N-terminal pro-B-type natriuretic peptide concentration and an altered serotonin (5-hydroxytryptamine) signaling pathway.

Inflammation

Endocarditis. Endocarditis is occasionally observed in dogs. Bacterial septicemias result in inflammation of cardiac valves. Bacteria most commonly isolated include *Streptococcus* spp., *Bartonella* spp., and *Escherichia coli*. The mitral valve is most commonly involved and is associated with polyarthritis. Infections with *Bartonellosis* may only have inflammatory changes involving the aortic valve leaflets. *Erysipelothrix tonsillarum* (formally known as *Erysipelothrix* serovar 7) is occasionally isolated. Confirmation of the definitive organism requires bacterial isolation and/or identification by

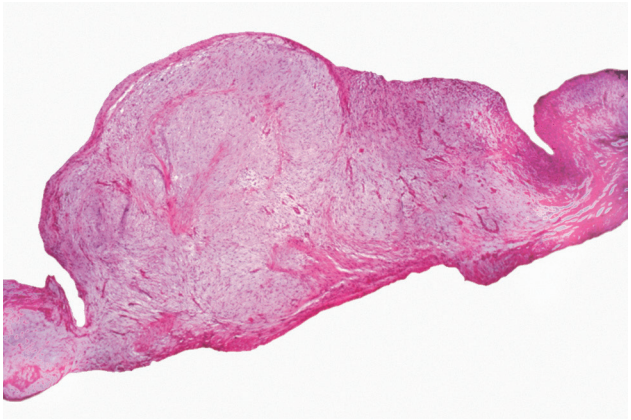


Figure 10-85 Myxomatous Valvular Degeneration (Valvular Endocardiosis), Cusp of Right Atrioventricular Valve, Heart, Dog. The valve is thickened and nodular from an increase in myxomatous tissue supported by a fibrous stroma. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

molecular tools. See the discussion on vegetative valvular and mural endocarditis in the section on Disorders of Domestic Animals: Endocardium and Heart Valves, Inflammation, and also Chapter 3.

Pericardium and Epicardium

Disturbances of Circulation

Idiopathic Pericardial Effusion (Hemorrhagic Pericardial Effusion). Idiopathic pericardial effusion is one of the most common causes of canine pericardial effusion and accounts for approximately 19% of all canine pericardial effusions. Large or giant breeds, such as the Great Dane, Saint Bernard, Great Pyrenees, German shepherd, and golden retriever, are most often affected. It is a diagnosis of exclusion after all other potential causes (neoplastic, traumatic, infectious, metabolic, cardiac, and coagulopathy) have been ruled out. Idiopathic pericardial effusion can be hemorrhagic or serosanguinous. The pericardium is thickened by diffuse fibrosis; neovascularization; areas of lymphocytic, plasmacytic, and histiocytic infiltrates; and areas of mesothelial hyperplasia alongside regions void of parietal mesothelium. See the discussion on effusions in the section on Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Effusions, and also Chapters 3, 7, and 9.

Blood and Lymphatic Vascular Systems

Blood Vessels

Disturbances of Growth

Anomalies and Dysplasia. See the discussion on anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies.

Neoplastic Transformation

Hemangiosarcoma and Hemangioma. Cardiac hemangiosarcoma (HSA) is an important neoplasm of dogs and can arise either in the heart (primary) or via metastasis (secondary) from primary sites such as the spleen. In a recent study, HSA frequently occurred in older golden retrievers, followed by Maltese dogs and miniature dachshunds. Mass lesions of HSA were found more commonly in the right auricle and right atrium, and the right atrial masses were significantly larger than the right auricular masses, potentially accounting for their higher antemortem detection rate by echocardiography. Grossly, protruding red to red-black blood-containing masses are located on the epicardial surface (Fig. 10-86) and may also protrude into the atrial lumen. Rupture can produce fatal hemopericardium and cardiac tamponade. Microscopically, the neoplasms are composed of scattered, elongated, plump neoplastic endothelial cells, which may or may not form vascular spaces containing blood (Fig. 10-87). Pulmonary metastases are frequent. Immunohistochemistry staining for factor VIII-related antigen or CD31 (an endothelial marker) confirms the tumor cells are endothelial in

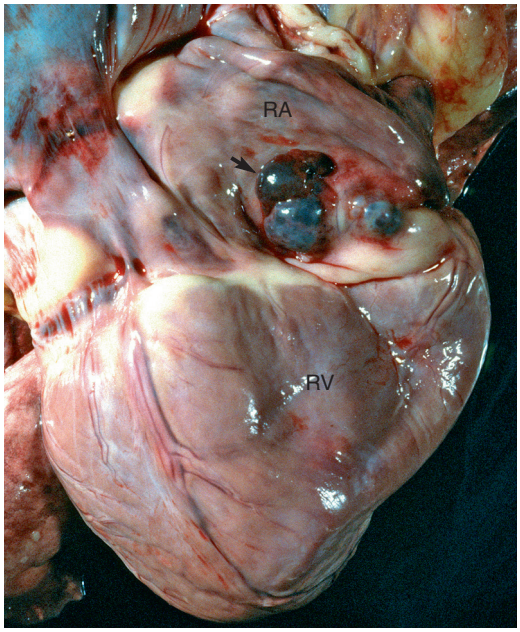


Figure 10-86 Hemangiosarcoma, Heart, Right Atrium, Dog. A dark-red hemangiosarcoma protrudes from the wall of the right atrium *(RA)*, a predilection site in the dog for this tumor *(arrow)*. *RV,* Right ventricle. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

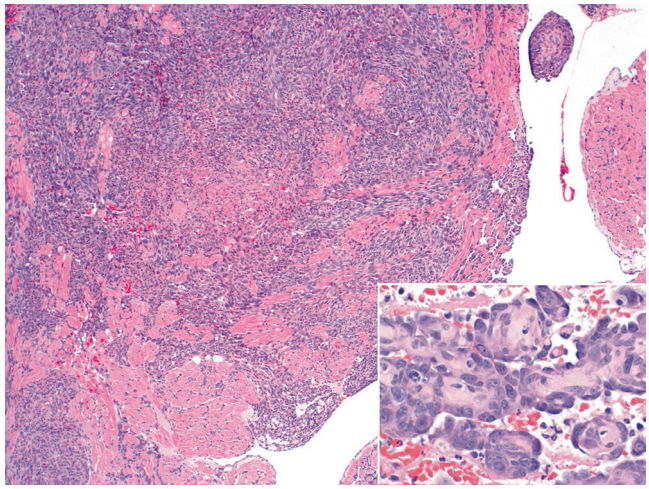


Figure 10-87 Hemangiosarcoma, Heart, Right Atrium, Dog. Malignant endothelial cells have invaded the myocardium of the right atrium, thus giving it the bluish granular appearance (cell nuclei) at low magnification. The high magnification *(inset)* shows these endothelial cells with large, round-to-oval nuclei forming poorly delineated and haphazardly arranged vascular channels. These cells can also "pile up" and be arranged in clusters or solid sheets. Mitotic figures can be prominent and numerous (not shown here). A golden-brown pigment (hemosiderin) can form secondary to erythrophagocytosis of damaged or effete erythrocytes (not shown here). H&E stain. (Courtesy Dr. J.F. Zachary, College of Veterinary Medicine, University of Illinois.)

origin. Hemangiomas are benign neoplasms often found in the skin of dogs (Fig. 10-88). These red, blood-filled masses are well circumscribed.

Heart-Base Tumors. See the discussion on cardiac neoplasms in the section on Disorders of Dogs, Myocardium, Disturbances of Growth; on neoplastic transformation in the section on Disorders of Domestic Animals, Blood and Lymphatic Vascular Systems, Blood Vessels, Disturbances of Growth; and also see Fig. 10-48.

Cell Degeneration and Death

Medial Necrosis and Hemorrhage. Medial necrosis and hemorrhage is a distinctive lesion produced in muscular arteries and arterioles of dogs and rats by a wide variety of vasoactive drugs. These vascular lesions, detected during evaluations of new compounds, produce grossly apparent hemorrhage, especially in the epicardium. Microscopically, acute damage is evident as necrosis of smooth muscle cells in the tunica media with surrounding erythrocytes. Healing lesions have fibrosis of the vessel wall and perivascularly.

Segmental Arterial Mediolysis. Segmental arterial mediolysis is a distinctive lesion produced in muscular arteries and arterioles of dogs and rats that most often occurs in the splanchnic muscular and coronary arteries and causes catastrophic hemorrhages. The pathology can be induced experimentally by administration of ractopamine, a synthetic β_2-adrenoceptor agonist to dogs. Exposure to α_1-adrenergic receptor agonists or β_2 agonists induces the release of norepinephrine from the peripheral nervous system. Epinephrine is thought to induce injury at the adventitial medial junction through medial muscle apoptosis. Microscopically, acute damage is evident as necrosis of smooth muscle cells in the tunica media with surrounding erythrocytes. Healing lesions have fibrosis of the vessel wall and perivascularly.

Fibrocartilaginous Embolism. Fibrocartilaginous embolism of the spinal cord vasculature and resultant infarction of the spinal cord supplied or drained by the obstructed blood vessel lead to posterior paresis or paralysis. Affected dogs are typically middle-aged large or giant breeds, but occurrence in young Irish wolfhounds has been reported. The mechanism of formation of the arterial or venous emboli is still unclear, but movement within the spinal vasculature of fibrocartilaginous fragments from degenerated intervertebral disks is generally considered to underlie the presence of these unusual emboli (Fig. 10-89; E-Fig. 10-29).

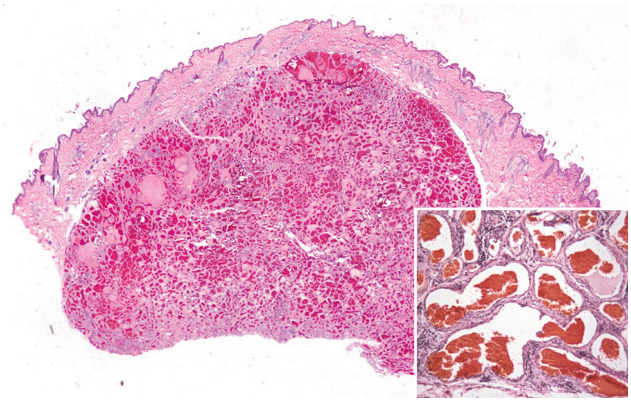


Figure 10-88 Cutaneous Hemangioma, Skin, Dog. The subcutis contains a well-demarcated mass formed by vascular channels lined by a single layer of well-differentiated endothelial cells. *Inset,* Higher magnification of the well-differentiated endothelial cells lining the vascular channels. H&E stain. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

Pulmonary Artery Thromboembolism. Pulmonary artery thromboembolism (Fig. 10-90) is often a life-threatening condition and in dogs has an incidence of 0.9% over a 10-year period. A wide variety of predisposing conditions may result in altered blood flow, hypercoagulability, or endothelial damage. These include sepsis, immune-mediated hemolytic anemia, neoplastic disease, protein-losing nephropathy/amyloidosis, disseminated intravascular coagulation, cardiac disease, hyperadrenocorticism, dirofilariasis, and use of intravenous catheters. The thrombus in the pulmonary arteries lyses within a few hours and therefore may be absent at the time of autopsy (syn: necropsy) in approximately 15% of cases, as was indicated by one study. Because of extensive collateral pulmonary arterial circulation, the presence of a large thrombus in the pulmonary artery or its main branches makes a clinically relevant diagnosis of pulmonary artery thromboembolism more certain, unless antemortem ancillary tests such as pulmonary angiography and ventilation/perfusion scanning are strongly supportive of it.

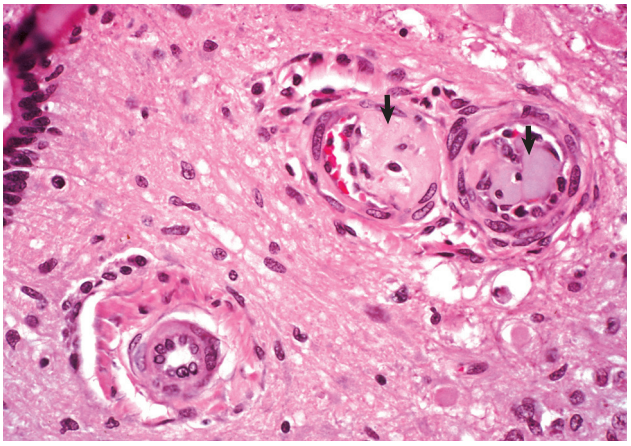


Figure 10-89 Fibrocartilaginous Emboli, Spinal Cord, Pig. The basophilic masses *(arrows)* occluding small arteries *(cross sections)* in the spinal cord gray matter adjacent to the central canal *(top left margin)* are fibrocartilaginous emboli. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)

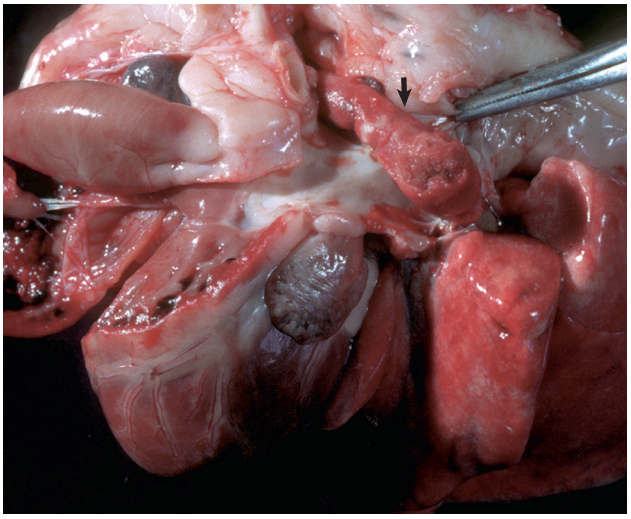
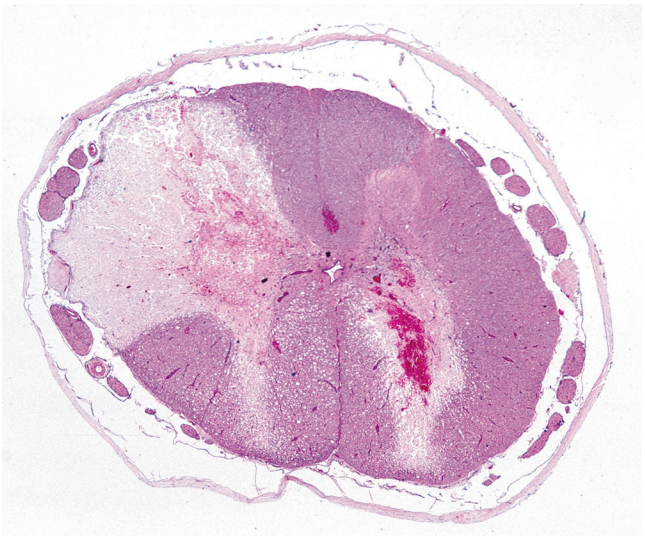


Figure 10-90 Arterial Thrombus, Pulmonary Artery, Dog. Arterial thrombi are composed primarily of platelets and fibrin because the rapid flow of blood tends to exclude erythrocytes from the thrombus, and thus arterial thrombi are usually pale beige to gray *(arrow)*. (Courtesy Dr. D.A. Mosier, College of Veterinary Medicine, Kansas State University.)



E-Figure 10-29 **Fibrocartilaginous Emboli, Multifocal Infarction, Spinal Cord, Dog.** Note the poorly stained *(pale red to clear)* areas in the left half of the spinal cord affecting both dorsal and ventral gray horns and all funiculi. The ventral gray horn is affected on the right side. These areas are infarcts caused by occlusion and blockage of blood flow in arterioles supplying blood to these areas by fibrocartilaginous emboli. Emboli are thought to cross from the venous side to the arterial side of the circulatory system in vascular anastomoses that form in metaplastic and degenerative cartilage as occurs in intervertebral disk disease. H&E stain. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)

Arterial Thromboembolism and Thrombosis. Arterial thromboembolism and thrombosis occur in dogs and arise from injury to vascular endothelium, propagated via the coagulation cascade (see Chapter 2). In dogs, the most common site is the aortoiliac trifurcation (Fig. 10-91), in which a thromboembolus extends from the caudal aorta distally to the external and internal iliac arteries. Embolization of the subclavian and brachial arteries also results in lameness of the forelimb, albeit less commonly. Other sites include embolization of the coronary arteries in the heart, renal arteries, and intestinal arteries. Aortoiliac thromboembolism in dogs has been reported with infection by *Spirocerca lupi* and *Blastomyces dermatitides* and in association with various disease conditions, such as protein-losing nephropathy, hypothyroidism, hypercortisolism, diabetes mellitus, and aortic neoplasia.

Thrombosis of the Femoral Artery. Thrombosis of the femoral artery, with resulting partial to complete occlusion, has been reported in Cavalier King Charles spaniels. Affected dogs generally do not develop hindlimb ischemia, in contrast to human patients with this condition, because of extensive collateral circulation and thrombus recanalization. It is a common but clinically insignificant pathology in Cavalier King Charles spaniels that is suspected to result from a probable weakness in the femoral artery wall.

Inflammation

Heartworm Dirofilariasis (Dirofilaria immitis). Dirofilariasis (heartworm disease) may occur in 35% to 45% of dogs and 2% of cats in areas of high infection rates, such as within 150 miles of the Atlantic and Gulf coasts from Texas to New Jersey and along the Mississippi River and its major tributaries. The extent of cardiac alterations is related to the number of adult parasites present. Initially, the parasites accumulate in the pulmonary arteries (Fig. 10-92), and as the numbers increase, they are present in the right ventricle, then in the right atrium, and finally may occupy the vena cavae. Pulmonary hypertension results from vascular blockage and pulmonary vascular lesions produced by the parasites, and right ventricular hypertrophy follows. Right-sided heart failure may eventually develop. The pulmonary arteries containing parasites initially have an infiltration of the intima (termed *endarteritis*) by eosinophils, with subsequent development of an irregular fibromuscular proliferation of the intima visible grossly as a rough granular or shaggy appearance of the luminal surface (see Fig. 10-92; E-Figs. 10-30 and 10-31). Live or dead parasites can be present within these vascular lesions and be accompanied by thromboembolism and pulmonary infarction. The pleura of the caudal lung lobes may contain multifocal areas of hemorrhage, hemosiderosis, and fibrosis. The presence of a massive number of adult worms may result in filling the right heart extending into venae cavae, resulting in venal caval syndrome. This syndrome results in sudden collapse, liver failure, intravascular hemolytic anemia, shock, and death if the adult worms are not removed surgically.

Polyarteritis: "Beagle Pain Syndrome." Polyarteritis is a disease that occurs sporadically in many animal species and is an important disease of aged rats called *polyarteritis nodosa* (E-Fig. 10-32). Many recent reports have described the occurrence of polyarteritis in a disease termed *idiopathic necrotizing polyarteritis* (idiopathic canine polyarteritis, juvenile polyarteritis syndrome) involving multiple arteries, including the coronary and meningeal arteries in dogs, most often pet and laboratory beagle dogs ("beagle pain syndrome"). Clinically, affected dogs typically show recurrent episodes of fever, body weight loss, and occasionally cervical pain manifested by a stilted gait and stiff neck with a hunched body posture. However, some affected dogs do not display clinical signs of disease. The lesions are usually attributed to an immune-mediated vascular injury. Small and medium-sized muscular arteries in a wide variety of organs, including the heart, meninges, epididymis, and thymus, are selectively involved and grossly appear thick and tortuous, have associated focal hemorrhage, and develop aneurysms and thrombosis. Microscopically, the early lesions include fibrinoid necrosis and

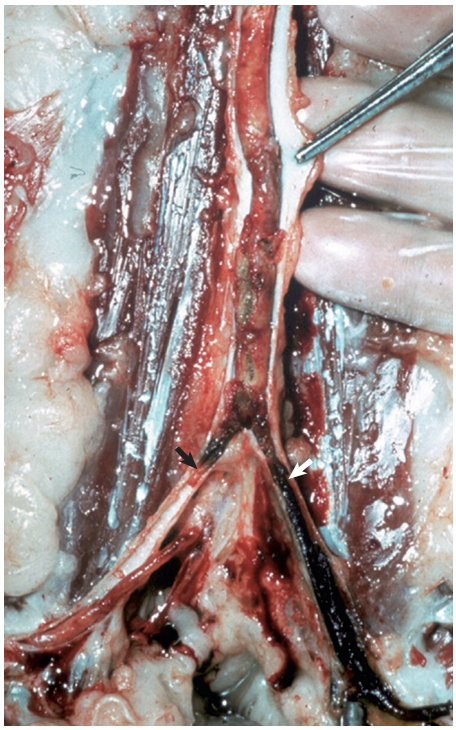


Figure 10-91 Aortic Thrombosis, Aorta and External Iliac Arteries, Dog. The tan thrombus occluding the caudal abdominal aorta is a cranial extension of the red saddle thromboembolus at the aortic bifurcation and in the external iliac arteries *(arrows)*. (Courtesy School of Veterinary Medicine, Purdue University.)

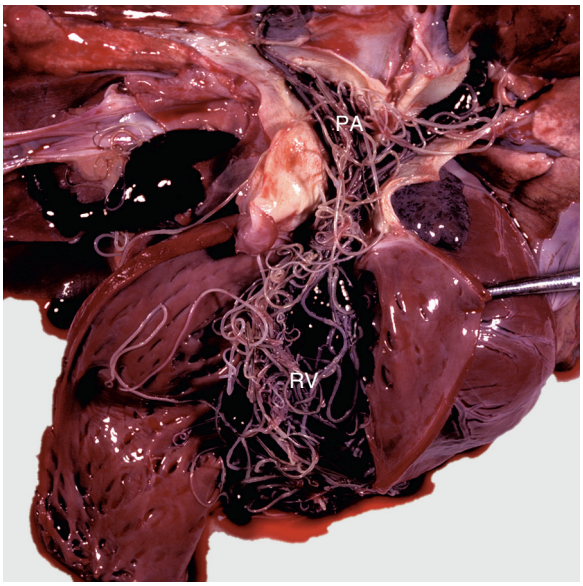
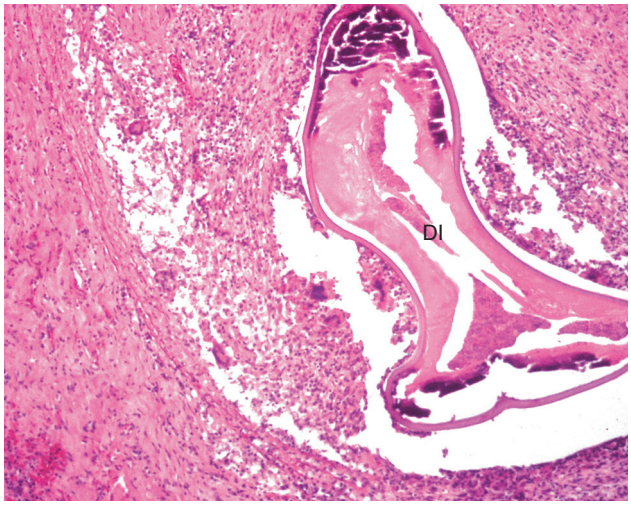
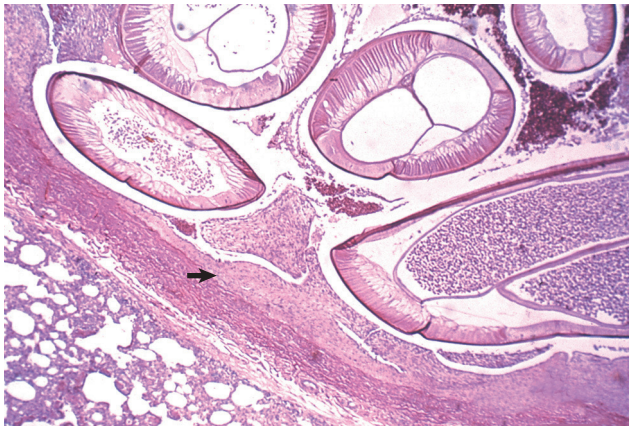


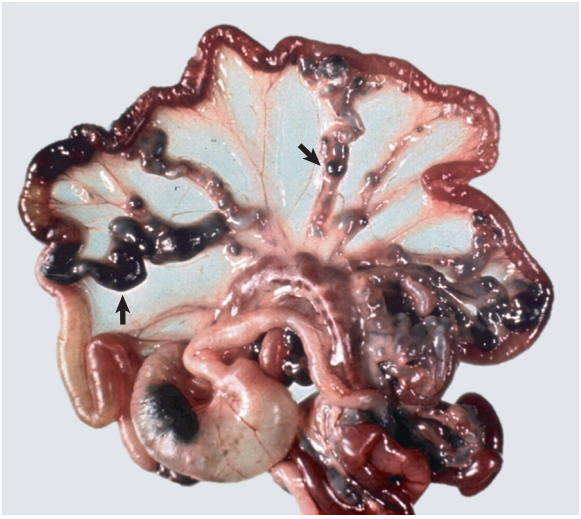
Figure 10-92 Dirofilariasis, Heart, Opened Right Ventricle, and Pulmonary Artery, Dog. Numerous adult *Dirofilaria immitis* are present in the right ventricle *(RV)*, right atrium, and pulmonary artery *(PA)*. (Courtesy Dr. M.D. McGavin, College of Veterinary Medicine, University of Tennessee.)



E-Figure 10-30 Verminous Arteritis, Dirofilariasis, Pulmonary Artery, Dog. A dead adult *Dirofilaria immitis (DI)* parasite in the lumen of the pulmonary artery is surrounded by pyogranulomatous inflammatory cells adhered to the wall *(left)* of the artery. Note the loss of the endothelial cells on the left side of the artery. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-31 Chronic Endarteritis, Dirofilariasis, Lung, Pulmonary Artery, Dog. Several intact adult *Dirofilaria immitis* are in the lumen. Note the thickened fibrotic intima *(arrow)*. H&E stain. (Courtesy School of Veterinary Medicine, Purdue University.)



E-Figure 10-32 Polyarteritis Nodosa, Mesenteric Arteries, Rat. The affected segments of the arteries are thick, red, hemorrhagic, and tortuous *(arrows)*. (Courtesy School of Veterinary Medicine, Purdue University.)

leukocytic invasion of the intima and media (E-Fig. 10-33). In chronic lesions, inflammatory cells and fibrosis involve all layers of the vascular wall.

Lymphatic Vessels

Disturbances of Circulation

Primary Lymphedema. Primary lymphedema is a rare pathology in dogs that often involves the distal hindlimbs, and it results from aplasia/hypoplasia of superficial lymphatic vessels and/or draining lymph nodes of the distal hindlimbs. Antemortem, dogs are being presented with nonpainful pitting edema of the distal hindlimbs. At autopsy (syn: necropsy) there is lymphatic hypoplasia and/or absence of popliteal lymph nodes with distal secondary lymphatic hyperplasia. Marked delay in lymphatic filling in lymphangiography, in lymphoscintigraphy, or in the patent blue violet dye absorption test are antemortem ancillary test results that strongly support the diagnosis of primary lymphedema.

Primary Intestinal Lymphangiectasia. Primary intestinal lymphangiectasia is a rare intestinal pathology of dogs that results in severe protein-losing enteropathy. The Lundehund breed is predisposed. Clinically, dogs are presented for wasting, diarrhea, and ascites. Lacteals in the intestinal villi are fused, blunted, and have markedly distended tips, whereas lymphatic vessels throughout the wall of the intestine, and occasionally mesentery and mesenteric lymph nodes, are distended with milky opaque fluid (i.e., chyle) (see Fig. 7-14). In dogs, the role of obstruction of lymphatic vessels or their structural integrity (i.e., hypoplasia) in the pathogenesis of this disease is still unclear. Secondary intestinal lymphangiectasia is much more common and results from obstruction of lymphatic drainage by inflammation or neoplasia.

Disorders of Cats

Myocardium

Disturbances of Growth

Anomalies and Dysplasia. See the discussion on anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Myocardium.

Cardiomyopathies. See the discussion on cardiomyopathies in the section on Disorders of Domestic Animals, Disorders of Domestic Animals: Myocardium, Disturbances of Growth, Hypertrophy and Atrophy.

Endocardium and Heart Valves

Disturbances of Growth

Valvular Anomalies and Dysplasia. See the discussion on valvular anomalies and dysplasia in the section on Disorders of Domestic Animals, Developmental Errors/Congenital Anomalies: Endocardium and Heart Valves.

Inflammation

Endomyocarditis. Endomyocarditis is a disease of cats of undetermined cause. The affected areas are thickened and often in the area of the outflow of the left ventricle. Lesions consist of a mixed population of inflammatory cells, which extends into the adjacent myocardium. Chronic lesions have marked, often visible fibrous connective tissue with fewer inflammatory cells within the endocardium.

Pericardium and Epicardium

Disturbances of Circulation

Effusions. See the section on Disorders of Domestic Animals, Disorders of Domestic Animals: Pericardium and Epicardium, Disturbances of Circulation, Hemopericardium and Hydropericardium.

Pericardial Effusions

Hemopericardium. Rodenticide toxicity and systemic consumption of clotting factors from disseminated intravascular coagulation are the most common causes of hemopericardium in cats.

Hydropericardium. Cats develop hydropericardium most commonly from congestive heart failure. Neoplasms, including heart-base tumors, mesotheliomas lymphoma, rhabdomyosarcoma, and fibrosarcoma, can produce hydropericardium. Uremia, through systemic damage to blood vessels, may result in hydropericardium.

Inflammation

Pericarditis. Feline infectious peritonitis (FIP) is a cause of fibrinous pericarditis in cats. The etiological agent is mutated feline enteric corona virus, and in that case pericarditis is a local manifestation of a multisystemic and generalized disease process.

Blood and Lymphatic Vascular Systems

Blood Vessels

Disturbances of Growth

Medial Hypertrophy of Pulmonary Arteries. Medial (tunica media) hypertrophy of pulmonary arteries is a disorder of cats of unknown cause (see Fig. 10-26); however, a response to antigens during nematode infections may be involved.

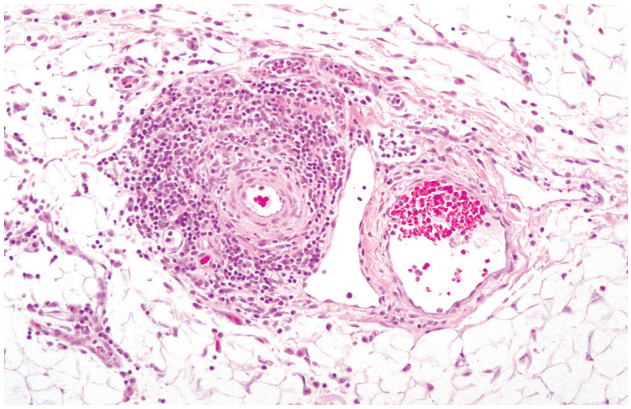
Inflammation

Pulmonary Artery Thromboembolism. See the discussion on pulmonary artery thromboembolism in the section on Disorders of Dogs.

Arterial Thromboembolism. Arterial thromboembolism (ATE) is defined as obstruction usually followed by infarction of arterial beds by embolic material derived from a thrombus from a distant site and in the presence of intact endothelial surface (to be distinguished from arterial thrombosis). The most common cause of ATE in cats is cardiomyopathy in which a large thrombus is formed in the enlarged left atrium. However, other conditions, such as protein-losing nephropathy/enteropathy, sepsis, DIC, and endocrinopathies, should be considered in the diagnostic workup. The fate of the infarcted area depends on the ability to establish collateral blood flow, thus bypassing the occluded artery. In cats and dogs, the most common site is the aortic trifurcation ("saddle embolus"), and the right subclavian artery is the second most common cause of ATE in cats with cardiomyopathy. Renal, splanchnic, and cerebral circulations can also be affected on occasion. In a saddle embolus, occlusion of limb(s) blood flow results in ischemic neuromyopathy of the limb(s). Grossly, distal limbs below the stifle are most severely affected, and the affected limb is often dark red to blue and edematous due to hemorrhagic ischemic necrosis.

Feline Infectious Peritonitis. Feline infectious peritonitis is a severe viral infection that produces phlebitis in various organs. This lesion appears to result from deposition of immune complexes, which subsequently induce an inflammatory reaction in affected vessels (see Chapters 4, 7, and 11).

Heartworm-Associated Respiratory Disease. *Dirofilaria immitis* infection in cats occasionally results in heartworm-associated respiratory disease. Cats are more susceptible than dogs to infection with *Dirofilaria immitis*, although many do not have adult worms or have only a few (one to four worms). Grossly, there may be a visible shaggy or roughened appearance to the large lobar arteries, especially the right caudal lobar artery. The pulmonary arteries develop villus endarteritis with medial hypertrophy (see Fig. 10-26). Initially, small pulmonary arteries may become embolized and infarcted,



E-Figure 10-33 **Periarteritis and Arteritis (Polyarteritis—"Beagle Pain Syndrome"), Beagle Dog.** Note the accumulation of lymphocytes and macrophages around the arteriole. H&E stain. (Courtesy Dr. P.W. Snyder, School of Veterinary Medicine, Purdue University.)

leading to small areas of hemorrhage and necrosis in the lung and sudden death in some cats. Many cats that survive this initial phase develop collateral blood supply, but histologically they have multiple small pulmonary arteries with villus endarteritis and multifocal areas with type II pneumocyte hyperplasia, which is indicative of chronic alveolar injury. The most common clinical manifestation is an asthma-like syndrome potentially from inflammatory mediators that are released by numerous eosinophils and other leukocytes that cuff affected small pulmonary arteries.

Foreign Parasitic Diseases. Foreign parasitic diseases important in tropical regions of the world are characterized by the presence of parasites in the lumens of veins and lymphatic vessels. These diseases include infection of cats in South America by *Gurltia paralysans*, infection of cats in tropical regions with *Brugia* spp., and infection of pulmonary vessels by *Dirofilaria immitis*. Cats infected with *Gurltia paralysans* have spinal cord damage from thrombophlebitis in the lumbar veins, associated with the presence of adult parasites in affected vessels. *Brugia* spp. infect lymphatic vessels and lead to secondary lymphedema.

Lymphatic Vessels

Disturbances of Circulation

Lymphedema. See the section on Disorders of Domestic Animals, Disorders of Domestic Animals: Blood and Lymphatic Vascular Systems, Lymphatic Vessels, Disturbances of Circulation, Lymphedema.

Suggested Readings

Suggested Readings are available at www.expertconsult.com.

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