Sixth Edition

Jubb, Kennedy, and Palmer's

Pathology of DOMESTIC ANIMALS

Volume 3

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DOMESTIC ANIMALS

Volume 3

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Preface

In this sixth edition of *Pathology of Domestic Animals*, we continue the long tradition of surveying the literature and updating the information in this reference textbook in light of our own practical experience in the pathology of the major domestic mammals. True to the spirit of the first edition, this text is designed to explain the pathogenesis of common and not-so-common diseases, define the distinguishing features of these various conditions, and put them in a context relevant to both students and working pathologists. Knowledge has been generated incrementally since the publication of the fifth edition, particularly with respect to improved understanding of pathogenesis at the molecular level, as well as through the use of improved diagnostic tools, including the frontier of whole genome sequencing. My thanks to the contributors to this edition for their rigorous perusal of the literature in their areas of interest, for their addition of insightful information to their chapters, and for their inclusion of many new figures.

NEW TO THE SIXTH EDITION

The most noticeable, and I think very welcome, change in the sixth edition is the addition of full-color figures throughout the text. Nearly all of the images from prior editions have been replaced. These new images clearly depict the diagnostic features of hundreds of conditions.

We have also added a new chapter, "Introduction to the Diagnostic Process," to the usual lineup of chapters in these 3 volumes. The goal of this new chapter is to illustrate the whole-animal perspective and detail the approaches to systemic, multi-system, and polymicrobial disease.

The complete index is again printed in each volume as an aid to readers. "Further reading" lists have been pruned in the print book to save space. All references are available on any electronic version of the text as well as on the companion website that accompanies the purchase of any print book. These online references link to abstracts on PubMed.com.

COMPANION WEBSITE

In addition to updating the graphic design of these volumes, the print version of *Pathology of Domestic Animals* now has a companion website, accessible at:
PathologyofDomesticAnimals.com

Included on the companion website are:
- A complete image collection, including 325 bonus, electronic-only figures that have been called out in the text. These figures are identified in the printed version as "eFigs."
- An expanded list of useful references, each linked to the original abstract on PubMed.com.

I hope that we have captured significant changes and have synthesized this new knowledge to provide a balanced overview of all topics covered. Keeping pace with evolving agents and their changing impacts is a never-ending challenge. We have used current anatomical and microbial terminology, based on internationally accepted reference sources, such as the Universal Virus Database of the International Committee on Taxonomy of Viruses (http://www.ncbi.nlm.nih.gov/ICTVdb/index.htm). Microbial taxonomy is, of course, continually evolving, and classifications and names of organisms can be expected to be updated as newer phylogenetic analyses are reported. Debate continues, for example, over the taxonomy of *Chlamydophila/Chlamydia* spp. And change will continue.

We have attempted to contact all contributors of figures from previous editions and from various archives and apologize to any whom we were unable to contact or who were overlooked. If any individual recognizes an image as one of his/her own or as belonging to a colleague, we would be happy to correct the attribution in a future printing.

Grant Maxie
Guelph, Ontario, 2015

These volumes are dedicated to Drs. Kenneth V.F. Jubb (1928-2013)[1],
Peter C. Kennedy (1923-2006)[2], and Nigel C. Palmer,
and to my family—Laura, Kevin, and Andrea.

Drs. Palmer, Jubb, and Kennedy while working on the third edition in Melbourne, 1983. (Courtesy, University of Melbourne.)

[1]http://www.vet.unimelb.edu.au/news/2013/memorial.html
[2]http://senate.universityofcalifornia.edu/inmemoriam/peterckennedy.htm

Cardiovascular System

Wayne F. Robinson • Nicholas A. Robinson

DISEASES OF THE HEART

GENERAL CONSIDERATIONS

The heart is structured and functions to fulfill a singular role, which is to move sufficient volumes of blood to all organs in the body to meet the varying metabolic needs of the organism. For this purpose, the heart can be described as an *in-series, 2-stage, rate-variable, one-way pump.* From this characterization, the heart must provide sufficient force to eject the blood it receives, respond to the host's needs by varying the amount of blood ejected per unit time, and finally, ensure one-way flow without impediment of forward flow as well as prevent backflow. As befits a biological pump, the heart is a physically active organ that rhythmically contracts and relaxes which, over an average 10-year lifetime of a dog, beats in the vicinity of 400 million times and receives and ejects ten million liters of blood—by any measure, a remarkable and sustained performance.

If the structure or function of any of the components of the pump are compromised or fail, it will result in either diminution, or at worst, complete cessation of function. Additionally, if each component of the heart as a pump is examined and understood, it then facilitates the understanding and categorization of the causes and effects of component dysfunction. We are concerned predominantly with the diseases that interfere with the *heart's rate and rhythm, its strength of contraction, and the flow of blood through the heart*. Heart disease may be clinically detectable and, when sufficiently severe, may give rise to heart failure, or may be only evident on postmortem (eFig. 1-1).

Under the anatomic units of the *pericardium, endocardium, and myocardium,* we will first consider the normal form and function of the heart, the morphologic patterns of disease, its pathophysiology, and finally, its reaction to injury and its specific diseases.

Normal structure and function

Located within the mediastinum, the heart is enclosed in the fibroserous **pericardial sac,** which is lined by a serosal membrane and contains several milliliters of clear serous fluid that acts as a lubricant.

The heart consists of a right and left side; each side consists of an atrium and a ventricle. The ventricles function as 2 pumps in series. Venous blood from the body enters the **right atrium,** passes into the **right ventricle,** and is pumped through the pulmonary artery into the lungs to be oxygenated and to give up its carbon dioxide. Oxygenated blood returns via the pulmonary veins to the **left atrium,** enters the **left ventricle,** and is then pumped to the body via the aorta. **Heart weight** varies with species, age, sex, nutritional status, and fitness level of the animal; averages about 1% of body weight in newborns; and decreases to 0.3-0.8% in juveniles and adults.

Ventricular thickness varies greatly. Left ventricular free wall and interventricular septum are normally 2-4 times thicker than the right ventricular free wall. *An increase in*

myocardial mass is termed **hypertrophy;** *an increase in chamber volume is termed* **dilation.** *An overall increase in the external dimensions of the heart is termed* **cardiomegaly.**

The 4 cardiac valves are structured to allow *unimpeded unidirectional blood flow, to prevent backflow, and to withstand pressure, especially those of the left side of the heart.* The **atrioventricular (AV) valves,** supported by tendinous cords (chordae tendineae) and papillary muscles of the ventricles, allow flow from the atria into the ventricles and prevent backflow into the atria. The right AV (RAV, tricuspid) valve has 3 valve cusps (2 cusps in the dog). The left AV (LAV, bicuspid, mitral) valve in most species consists of 2 cusps. The **pulmonic and aortic semilunar** (crescent moon-shaped) **valves** each have 3 cusps, and they allow flow into the pulmonary artery and aorta, respectively, and prevent backflow into the ventricles. The nodules *(nodules of Arantius)* in the center of the free edges of the semilunar valve cusps are normal structures. Valve cusps are normally thin and translucent. The free edges of the valve cusps *(coaptation region)* normally overlap during closure, and therefore fenestrations of the valve edges are usually insignificant. Normal valve function depends on coordinated actions of the respective annulus and leaflets, and in the case of AV valves, the tendinous cords, papillary muscles, and ventricular walls.

The cardiac muscle and valves are supported at the base of the heart by the **cardiac skeleton,** *which consists of 4 fibrous rings, the fibrous triangle, and the fibrous or membranous part of the ventricular septum.* The fibrous triangle fills the space between the AV openings and the base of the aorta; it consists of dense fibrous connective tissue in pigs and cats, fibrocartilage in dogs, hyaline cartilage in horses, and bone *(os cordis)* in large ruminants.

The **blood supply to the heart** is primarily via 2 major coronary arteries. The *left and right coronary arteries* arise, respectively, behind the left and right cusps of the aortic valve at the base of the aorta. The left coronary artery gives rise to the left descending and the left circumflex coronary arteries. The epicardial coronary arteries give rise to the intramural arteries that penetrate the myocardium. Most coronary arterial blood flow occurs during ventricular diastole, when the coronary microcirculation is not compressed by myocardial contraction.

The **myocardial conduction system** consists of modified cardiac myocytes that initiate and conduct an electrical impulse (Fig. 1-1). The **sinus node** (sinoatrial node, SA node) is located subepicardially at the junction of the cranial vena cava and the right auricle. Because cells in the sinus node are not capable of remaining in a depolarized state, after each repolarization, their membranes permit leakage of sodium and potassium until they reach a stage of depolarization (the critical threshold), when they rapidly depolarize. The impulse from this pacemaker *(the dominant pacemaker)* in turn causes atrial depolarization and contraction, and travels through internodal bundles to the **AV node** located in the interatrial septum just cranial to the coronary sinus. The impulse slows while traversing the AV node before traveling via the **AV bundle** (bundle of His) to the **left and right bundle branches,** or crura, through the **Purkinje fibers.** These *modified myocardial cells* ramify within the myocardium and transmit the depolarizing impulse to ventricular myocytes.

Although each component of the conduction system has different rates of diastolic depolarization, the sinus node has the most frequent rate and is therefore dominant. The frequency of depolarization of the sinus node is in turn modified
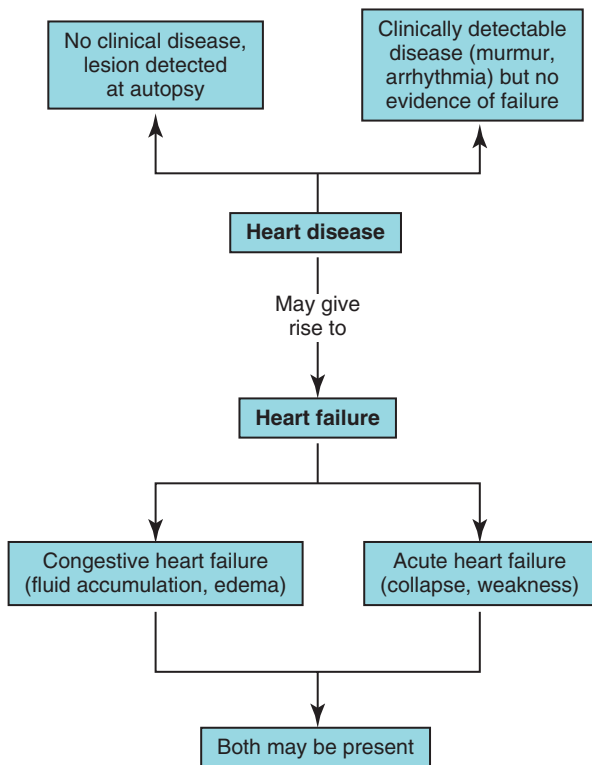
eFigure 1-1 Relationship between **heart disease and heart failure**. Heart disease may be present without attendant clinical signs or may give rise to either acute or congestive heart failure. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.)
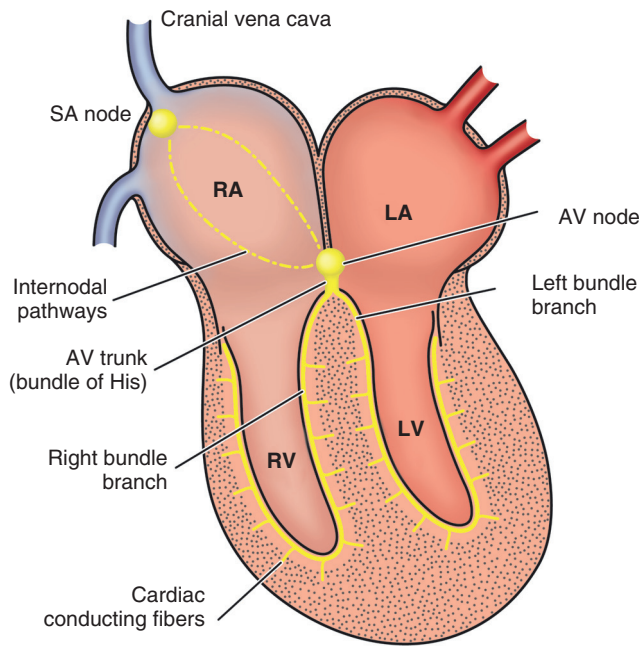
Figure 1-1 **The myocardial conduction system.** Major species differences include ramification of the cardiac conduction fibers, which can reach the subepicardium in some species (not shown). *AV,* atrioventricular; *LA, left atrium; RA,* right atrium; *LV, left ventricle; RV,* right ventricle; *SA,* sinoatrial. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.)

by the autonomic nervous system. *Atrial and ventricular myocytes do not normally exhibit the property of automaticity.* However, when atrial or ventricular myocytes are injured, they may repeatedly depolarize independent of a stimulus from the conduction system and may become dominant pacemakers. There are diseases that specifically affect the conduction system producing *dysrhythmias* (abnormalities of rate and rhythm), but it is the dysrhythmias resulting from disease injuring the atrial and ventricular myocytes that are most common. The cardiac wall has 3 layers:

1. The **epicardium,** the outermost layer
2. The **myocardium,** the thick muscular middle layer
3. The **endocardium,** the innermost layer, which is continuous with the tunica intima of the great vessels entering and leaving the heart

The **epicardium,** or visceral pericardium, consists of a thin layer of mesothelium resting on elastic fiber-rich connective tissue that merges with that of the myocardium. The epicardium is continuous with the **parietal pericardium,** which consists of an inner mesothelial layer and a thick layer of collagen and elastic fibers. The cavity between the visceral and parietal pericardium contains serous fluid that lubricates the surfaces and reduces friction between the epicardium and pericardium during cardiac motion. Although the **pericardial sac** is not a vital organ, its proper function includes prevention of sudden cardiac dilation, assurance of equal end-diastolic transmural pressures throughout the ventricles, limitation of right ventricular stroke work, hydrostatic compensation for gravitational or inertial forces, reduction of friction, and maintenance of cardiac alignment and streamlined cardiac flow.

The **myocardium,** the generator of the force required to eject blood from the atria and ventricles, consists of striated muscle cells—**cardiac myocytes**—embedded in a well-vascularized connective tissue framework. Individual myocytes, which account for about ⅔ of the myocardial volume, are intimately joined at intercalated discs to function as a unit. Each cardiac myocyte consists of a single, central nucleus; mitochondria; abundant contractile elements (myofibrils), predominantly composed of actin, myosin, tropomyosin, and troponin; sarcoplasmic reticulum that stores calcium needed for the initiation of contraction; and the cell membrane (sarcolemma) and T tubules needed for impulse conduction. Myocytes may be binucleate in some species, for instance, dogs, and are commonly multinucleate in pigs (4-16 nuclei per cell). The actin and myosin filaments comprise contractile units called **sarcomeres,** which are demarcated by Z lines. Mitochondria occupy about 20-30% of the volume of cardiac myocytes versus 2% in skeletal muscle, reflective of the great dependence of cardiac muscle on aerobic metabolism. Sarcomere length varies from 1.6-2.2 μm; *ventricular dilation increases sarcomere length, which enhances contractility (Frank-Starling relationship).* Atrial cardiac myocytes are typically smaller than ventricular cardiac myocytes, predominantly because they operate in a low-pressure system where less force is required to eject blood. There are consequently many fewer myofibrils and mitochondria per cell, but they contain specific granules encasing the hormone **atrial natriuretic factor** (ANF) which is released on dilation or stretching of the atria.

The cardiac **interstitium** contains blood vessels and fibroblasts in a diverse extracellular matrix that consists of collagens, proteoglycans, noncollagenous glycoproteins, growth factors and cytokines, and extracellular proteases. The collagen network of the heart is arranged into 3 interconnected regions: the collagenous weave of the *endomysium* around individual fibers, the *perimysium* around groups of fibers, and the *epimysium* around the whole muscle. This fibrillar collagenous network of the myocardium prevents overstretching of myofibers, transmits myofiber-generated force to the chamber, and provides tensile strength and stiffness to the chamber. The collagenous struts that connect adjacent myofibers provide proper alignment during contraction. Struts that connect myocytes to capillaries help to maintain capillary patency during high intraventricular pressure.

The **endocardium** lines the heart and consists of a monolayer of *endothelium* on a continuous basement membrane, covering the *inner subendothelial layer* of dense collagen, and the *outer subendothelial layer* composed of collagen, elastin, and blood and lymph vessels. The **atrioventricular (AV) valves** are endocardial infoldings with a layer rich in elastin on the atrial side *(atrialis);* a central layer *(fibrosa)* of dense irregular connective tissue covered by layers of elastic fibers; and, on the ventricular side, loose connective tissue *(spongiosa).* The central collagen of the AV valves is continuous with the dense collagen of the *chordae tendineae,* which are attached to the ventricular papillary muscles. The **aortic and pulmonic semilunar valves** consist of a *ventricularis* layer of collagen and radially aligned elastin on the ventricular side, a central *spongiosa* layer of water and glycosaminoglycans, and a *fibrosa* layer of collagen and elastin arranged in a circumferential direction on the great vessel side of the valves to resist back-pressure of blood. Valve cusps are predominantly avascular.

The **coronary arteries** feed a dense capillary network that supplies the myocardium, endocardium, epicardium, cardiac

skeleton, and bases of the cardiac valves. Blood collected by venules and veins is drained into the right atrium via the *coronary sinus*. Lymphatic capillaries draining the cardiac connective tissue are continuous with larger lymph vessels in the endocardium and epicardium. Sympathetic and parasympathetic innervation is extensive in the atria, and particularly around the SA and AV nodes.

Morphologic patterns of heart disease

The 3 broad anatomic divisions of the heart—the mural and valvular endocardium, the myocardium, and the pericardium—exhibit differing features in the face of disease. It is not that the usual suspects that affect all organs are not in play. Inherited disease, infectious agents, toxins, nutritional deficiencies, and neoplasia all affect the heart, but it is the combination of the structure of the heart, the biological characteristics of the cells comprising the heart, and their response to injury, in concert with the host's general response to injury, that results in the display of the particular features of heart disease. It should be remembered that the heart may also show evidence of disease as an integral part of diseases of another organ system or systemic disease.

The mural and valvular endocardium and the heart valves proper

Valvular abnormality from any cause can lead to disturbances of blood flow through the heart either by altering the normal unidirectional pattern of flow, or by impeding blood flow into or out of the chambers. Alterations in hemodynamics reflect changes in systolic workloads characterized by changed pressure loading during contraction *(afterload)*, or changed volume loading during diastole *(preload)*. Most valvular disorders impose only a single preload or afterload on the heart. This encompasses those valvular disorders that cause either **insufficiency** *(failure to close)* or **stenosis** *(narrowing, failure to open)*. Some of the congenital heart abnormalities, such as patent ductus arteriosus and tetralogy of Fallot, have multiple preload and afterload effects. The general rules are (eFig. 1-2):
1. Valvular insufficiency increases the preload on the ventricle.
2. Semilunar valvular stenosis, outflow tract stenosis, and hypertension increase the afterload on the ventricle.
3. AV valvular stenoses and pericardial disorders decrease the preload on the ventricles.

   Subendocardial hemorrhage is a frequent accompaniment to a myriad of diseases of the heart, but more particularly, with systemic disease, where the heart is just another surface where hemorrhage can be observed. **Subendocardial mineralization** occurs as either a dystrophic or metastatic phenomenon. **Additions to valves and/or the mural endocardium** result from disturbances to the health of the endothelial lining of the mural and valvular endocardium, and because of the location, can have wide-ranging consequences. The most severe and extensive occurs with microorganisms, particularly bacteria, that arrive via the systemic circulation that adhere to endothelium and/or subendocardium after the endothelium has been damaged or eroded. The cascade of events that follow, especially the incitement of thrombosis, results in a mass of platelets, fibrin, and inflammatory cells (vegetations) accumulating on the exposed surfaces, impeding blood flow through the heart and predisposing to thrombotic emboli lodging in end-arteries in organs throughout the host. Although healing may occur, the healed valve is rarely returned to its

original state and is often left thickened, shrunken, and distorted. Affected valves may be either insufficient or stenotic or both, but one or the other usually predominates. **Distortions of the structure** of heart valves in the absence of vegetations and with an intact valvular endothelium are commonly encountered. Valves can be effaced, displaced, shrunken, thickened, or, in the case of the AV valves, no longer firmly anchored to the papillary muscles. All result, to a greater or lesser extent, in a diminution of effective unidirectional blood flow. Probably the best examples of distortions in architecture are those seen in congenital heart disease, such as valvular aortic and pulmonic stenosis, left and right AV valvular stenosis or insufficiency. Similar lesions can be seen in acute or healed valvular endocarditis and degenerative diseases of the AV valves, such as endocardiosis in dogs. **Abnormal chamber or great vessel communication** is of special interest because of the altered hemodynamics that ensue in the transition from fetal to postnatal life. Predominantly congenital in origin, it is often the result of incomplete closure of fetal communications between the atria, ventricles, and great vessels following birth. Acquired arteriovenous communication can also occur.

The myocardium

The myocardium may be primarily and specifically affected by a particular disease, but it may also be just another organ involved in systemic disease. The morphologic manifestations of myocardial disease reflect some of the characteristics of the myocardium, such as the predominance of contractile proteins in each cardiac myocyte; the exquisite compartmentalization of calcium required for regular and orderly contraction; its high requirement for energy for regular contraction; its end-arterial blood supply, predisposing the myocardium to infarction; and the very limited capacity of cardiac myocytes for regeneration. Cardiac myocytes, however, have a remarkable capacity to increase in mass (hypertrophy) in response to an increase in either physiologic or pathologic workload.

As do all tissues, the myocardium has a limited set of reactions to injury, but the pattern and distribution of lesions may aid in arriving at a morphologic and etiologic diagnosis. The stage of irreversible damage to a myocyte, at least in ischemia, is determined by structural and functional changes in the mitochondria. Irreversible damage occurs after only 30 minutes of ischemia, whether or not flow is restored.

Shortly after birth, most cardiac myocytes lose their ability to *regenerate*. Once the neonatal period passes and a particular myocyte or group of myocytes is lost, there is usually no replacement. There is, however, recent evidence to show that there is a low level of cardiac myocyte turnover throughout life. On the death of myocytes, there is progressive scavenging of the necrotic or apoptotic remnants of the myocytes and replacement by fibrosis. Remaining myocytes do have the capacity for *compensatory hypertrophy*.

Myocardial injury may be functionally manifest as either irregularities in the rate or rhythm of impulse formation and conduction (dysrhythmias), or as depression in the force of myocardial contraction. **Dysrhythmias** are usually associated with acute, nonlethal, often focal injury to cardiac myocytes. **Contractility disturbances** occur when there are either *insufficient numbers* of ventricular myocytes for effective contraction, as occurs in massive ischemic necrosis of ventricular myocytes following blockage of a major coronary artery, or when there is *generalized ineffective contraction* of normal numbers of myocytes. Generalized, ineffective myocardial
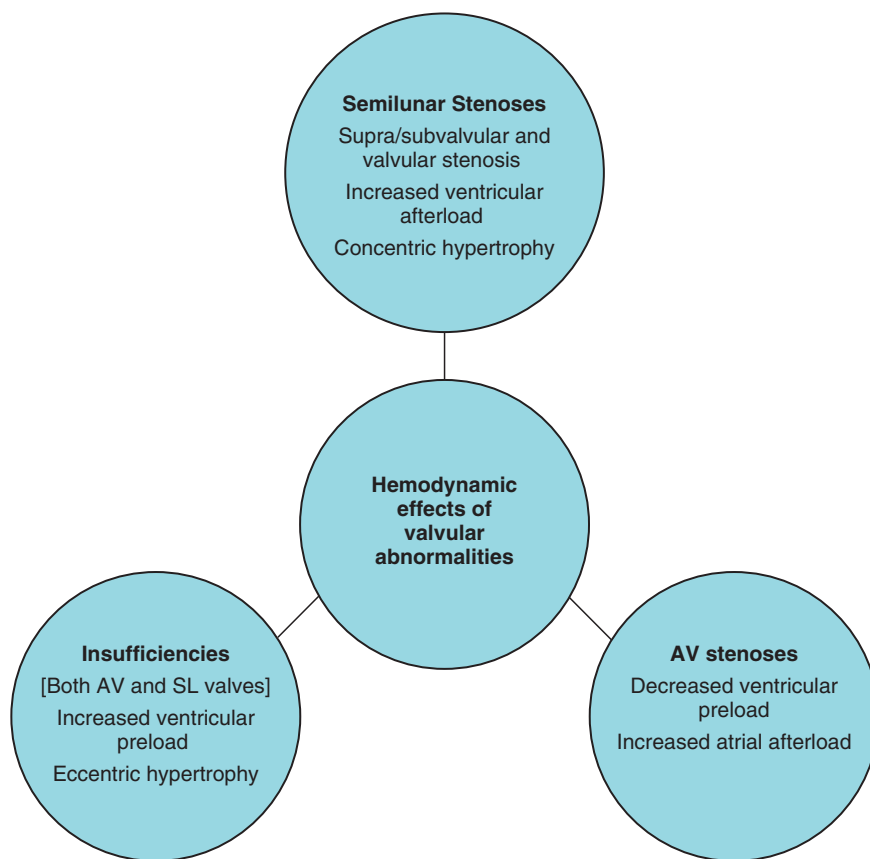
eFigure 1-2 Hemodynamic effects of **valvular abnormalities**. *AV,* atrioventricular; *SL,* semilunar. (Courtesy Vasileios Psychas.)

contraction is most commonly seen as a feature of dilated cardiomyopathies. The basis of generalized ineffective contraction is complex and reflects the many contributing factors to the normal functioning of cardiac myocytes. For example, with the cardiomyopathies, there are a number of disorders that have as their origin inherited defects in either contractile proteins, cytoskeletal proteins, or mitochondrial proteins, all leading to a lowering of the effectiveness of contraction.

A number of grossly observable permutations and combinations assist in arriving at a diagnosis that involves the myocardium. An **increase in ventricular wall thickness or mass** should lead the investigator to search for a cause of increased workload performed by the heart, such as a stenotic valve, or a shunt between chambers or great vessels, which produce an increased afterload on the heart. If no obvious cause for the increased mass can be discerned, a primary myocardial disease, such as hypertrophic cardiomyopathy, should be considered. **A dilated ventricular lumen accompanied by a normal to thin ventricular wall** leads toward consideration of an increased preload on the heart, such as AV or semilunar valvular insufficiency or a vascular shunt. In the absence of an inciting cause, dilated cardiomyopathy should be considered. **Focal pale areas** in an otherwise normally appearing myocardium suggest destruction of cardiac myocytes alone, cellular infiltration alone, or a combination of the two. The most common causes include bacterial and viral infections as well as nutritional deficiencies and toxins that induce necrosis of cardiac myocytes. Metastatic neoplasms should also be considered. Although rare in domestic animals, a special type of focal, well-circumscribed area of paleness with a reddened periphery is indicative of a **recent infarct** following thrombosis of a coronary artery. **Focal scarring/fibrosis of the ventricular wall** is characteristic of a healed infarct or replacement fibrosis of necrotic cardiac myocytes. **Discrete nodules in the chamber walls,** especially of the ventricles, are typical of bacterial/fungal/parasitic infections. Frank abscessation is more typical of bacterial infection, whereas nodules with caseous centers ringed by well-demarcated fibrous tissue suggest intermediate stage parasitic infection.

The pericardium

The inability of the pericardium to stretch rapidly to accommodate additional fluid in the pericardial sac leads to clinically significant disease. Fluid accumulation prevents adequate filling of the chambers during diastole, lowering stroke volume and cardiac output. This is also central feature of a resolving or resolved pericarditis.

- **Blood, often clotted blood,** within the pericardial sac is often the result of a ruptured atrium, ventricle, great vessel, or coronary artery. Unclotted blood in the pericardial sac, of unknown cause, occurs in dogs.
- **Clear fluid in the pericardial sac** should lead to an investigation of causes of hypoproteinemia and as part of a number of infectious diseases.
- **Fibrinous/purulent exudates** in the pericardial sac usually indicate acute bacterial/mycoplasmal infection. The presence of pericardial and epicardial fibrosis often indicates a prolonged and ineffective attempt at repairing acute fibrinous and purulent pericarditis.

Pathophysiologic patterns of heart disease

When the heart is diseased, there is a restricted array of alterations in function that can be categorized as follows.

Disturbances of impulse formation or impulse conduction

Diseases affecting the sinus node of the heart's specialized conduction system can lead to an increase, decrease, or absence of *impulse formation*. Any disease affecting the conducting fibers—the intra-atrial conduction pathways, the AV node, the common bundle, right and left bundle branches, or Purkinje fibers—can result in a decrease or an absence of *impulse conduction*. These are manifest as various forms of *bradyarrhythmias* (heart block), such as sinoatrial arrest; first-, second-, and third-degree heart block; and left and right bundle branch block.

By far and away the most significant and most common disturbances of *impulse formation* are those that arise from injury to atrial and ventricular myocytes. Common causes include electrolyte disturbances, coronary arterial thrombosis or embolism, nutritional deficiencies, bacterial and viral infections, and toxins, especially plant toxins. The predominant alterations in heart rate and rhythm are an increased rate and an erratic rhythm (tachyarrhythmias). It should be noted that arrhythmias arise from the inappropriate depolarization of injured components of the conduction system or cardiac myocytes (ectopic pacemakers) that are often in close proximity to necrotic/apoptotic myocytes. The major pathophysiologic effect of disturbances of the heart's rate rhythm or conduction is erratic filling and contraction, leading to a depression in cardiac output. Disturbances of both impulse formation and impulse conduction can be readily classified through the use of electrocardiography.

Depressed myocardial contractile strength

This category is essentially one of either a *decrease in ventricular myocardial contractile critical mass*, such as in massive myocardial necrosis, or, in a heart that has *sufficient ventricular myocardial mass*, but where there is a *disturbance in the effectiveness of contraction*. The latter occurs in a number of dilated cardiomyopathies, especially in dogs and cats.

Impeded blood flow

This occurs with stenosis (narrowing) of the AV or semilunar valves, resulting in either a restriction of blood flow from one chamber to another (atrium to ventricle), or from a ventricle to the major arteries. This places an increased systolic workload (afterload) on the affected chamber. The lesion is not invariably pure in nature. Stenotic valves can also be mildly regurgitant, but it is the stenosis that predominates. Stenosis can either be congenital or acquired. More common forms of acquired impedance of blood flow include acute valvular endocarditis with thrombosis or healed endocarditis with resultant distorting fibrosis of the valves.

Regurgitant blood flow

This is associated with lesions of the AV and semilunar valves in which the valve structure is so effaced that it becomes insufficient and cannot prevent backflow of blood from ventricle to atrium or from a great vessel back to its ventricle. With regurgitation, the heart responds by increasing its stroke volume, which places an increased diastolic load (preload) on the heart. The lesion can be congenital, such as congenital mitral insufficiency, or acquired, such as healed endocarditis or the degenerative AV valvular condition endocardiosis, in dogs. Again, some primarily insufficient valves can be mildly stenotic, but in these cases, the insufficiency predominates.

Abnormal pattern of blood flow (shunted blood flow)

Although these can be acquired, they are much more commonly congenital in origin. They can be simple communications between the great vessels (patent ductus arteriosus), the atria (patent foramen ovale/atrial septal defect), or the ventricles (ventricular septal defect). The pathophysiology can be complicated where the defect results in increases in both preload and afterload on particular chambers. A special case of shunted blood flow occurs with the transposition of the great vessels.

Restricted atrial/ventricular filling

Pericardial disease, either acute or chronic, can restrict chamber filling during diastole, as can some of the hypertrophic cardiomyopathies. In essence, the compliance of either the pericardium or the myocardium is reduced, which prevents full diastolic relaxation of the ventricles. The major pathologic effect is one of increased central venous pressure leading to congestive heart failure, which can be predominantly right-sided or left-sided, depending on which chamber is most affected.

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HEART FAILURE

Heart failure *is the end point of a number of causes, rather than a specific disease*, and denotes a situation in which all compensatory mechanisms have been exhausted, and the heart is unable to meet the demands of the animal. The syndrome is characterized by *diminished cardiac output ("forward failure")*, or *damming back of blood in the venous system ("backward failure")*, or both. The heart can fail because of **impaired pump function** or because of **increased cardiac work demands**; both mechanisms may be operative in some cases. The heart can fail as a pump because of

1. Decreased myocardial contractility, or loss or replacement of myofibers, or
2. Decreased distensibility *(compliance)*, or
3. Dysrhythmia (abnormal heart rate and/or rhythm)

Increased cardiac work demands on one or both ventricles result from disturbed hemodynamics, in the form of sustained *pressure overload* (e.g., obstructed flow in aortic valvular stenosis) or *volume overload* (e.g., regurgitant flow in mitral valvular regurgitation).

Congestive heart failure *is characterized by vascular congestion and edema fluid within the interstitium of tissues and body cavities*. Not all cases of heart failure are of the congestive type. Although in congestive heart failure the clinical manifestations are more or less constant, in **acute heart failure,** there may be intermittent weakness and syncope caused by a substantial change in heart rate or rhythm, resulting in a precipitous drop in cardiac output. The effect of acute heart failure is often sudden unexpected death, often with minimal lesions. **Circulatory failure, or shock,** *denotes a state of inadequate peripheral vascular perfusion* and is used to describe a state that may or may not be the result of heart failure. It is characterized by a drop in effective circulating blood volume. Common causes are acute internal or external hemorrhage, dehydration, or endotoxic shock. Shock can of course lead to acute heart failure.

Based on clinical manifestations, heart failure may be predominantly either left-sided failure or right-sided failure. **Left-sided failure** *results in left atrial dilation, pulmonary congestion and edema*, and clinical signs of dyspnea and cough. A prominent feature of chronic left-sided heart failure is the presence of hemosiderin-laden macrophages ("*heart failure cells*") in pulmonary alveoli, the result of diapedesis of red cells into the alveoli. **Right-sided failure** *results in excessive right atrial pressure and systemic venous congestion*, expressed as jugular distension, hepatic and splenic enlargement, ascites, and peripheral edema. **Cor pulmonale** *is defined as right heart failure secondary to pulmonary disease*, such as chronic obstructive pulmonary disease, dirofilariasis, or pulmonary thromboembolism. Because the cardiovascular system is closed, failure of one ventricle will ultimately lead to failure of the other, culminating in global or **biventricular failure.**

Although there are many causes that lead to intermittent or permanent lowering of effective cardiac output, there is a limited set of responses to this by the animal. The major compensatory mechanisms include the **intrinsic cardiac responses** *of dilation and hypertrophy*, and the **systemic responses,** *which include increased heart rate and peripheral resistance, redistribution of blood flow, venular constriction, and increased blood volume.* In each case, the compensatory responses are at least temporarily beneficial and are directed toward increasing cardiac output to meet the metabolic needs of the animal. The range within which the compensatory mechanisms result in an increase in cardiac output is wide. Indeed, the increase may be up to 5 times the basal rate. As cardiac output falls below the requirements of the animal, signs of congestive heart failure appear. These may be intermittent or prolonged, depending on the nature of the defect.

An untoward side effect of the systemic responses is increased capillary hydrostatic pressure that leads to the accumulation of **edema fluid.** This can involve the systemic or pulmonary veins. *Right-sided lesions*, such as right atrioventricular (AV) valvular insufficiency, pulmonic stenosis, or pulmonary hypertension, result in peripheral-dependent edema (e.g., submandibular edema ["bottle-jaw"], brisket edema), ascites, hydrothorax, and hydropericardium. *Left-sided defects*, such as left AV or aortic valvular insufficiency, cause pulmonary edema as the predominant finding.

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Figure 1-2 **Cardiac dilation** in a lamb. Left ventricular dilation with effacement of papillary muscles and severe subendocardial fibrosis. (Courtesy Vasileios Psychas.)

Intrinsic cardiac responses in heart failure

Cardiac dilation

Dilation is a response to an increased workload in both physiologic and pathologic states. Increasing the end-diastolic volume, and hence stretching the myofibers, can increase the contractile force of the heart and increase the stroke volume and cardiac output. This is known as the **Frank-Starling relationship,** or heterometric autoregulation. Transient cardiac dilation is an acute response to increased demands, for instance, increased exercise. Continued stretch increases contractile force to a limit, after which increased stretch will result in a decrease in tension developed. The limit of stretch in most species appears to be a sarcomere length of 2.2-2.4 μm. Chronic dilation of a ventricle can occur through addition of sarcomeres and hence lengthening of myocytes.

Various disease conditions can cause an increased diastolic workload (preload) and hence dilation of the heart, such as arteriovenous shunts, and AV and semilunar valvular insufficiencies (Fig. 1-2). *Acute volume overload of a chamber is expected to lead to dilation, whereas chronic volume overload is one stimulus to the development of cardiac hypertrophy.*

Cardiac hypertrophy

Cardiac hypertrophy is a reversible increase in the mass and a minimal increase in the number of myocardial cells, and is a compensatory response to an increase in mechanical work or to trophic signals. In general, **chronic pressure overload** *leads to myocardial hypertrophy, whereas* **chronic volume overload** *leads to combined ventricular dilation and hypertrophy.* Hyperplasia, or increase in the number of cells, has recently been shown to occur in response to workload, although the capacity of the myocyte to divide decreases rapidly prior to birth, and little mitotic activity is observed after the first few weeks of life.

At this juncture, it is important to distinguish between hypertrophy that is physiologic and hypertrophy that is pathologic in nature. **Physiologic hypertrophy** is a response to exercise or pregnancy and results in a mild increase in heart weight, not >10-20% normalized to body weight. It is an extension of the normal growth process, is without deleterious effect and occurs without the induction of the molecular stress fetal gene program that is associated with the development of pathologic

hypertrophy. Physiologic hypertrophy is initiated by ligands that include thyroid hormone, insulin, insulin growth factor 1, and growth hormone. Additionally, cardiac function is maintained or enhanced and is reversible. On the other hand, with **pathologic hypertrophy,** there may be up to a 4-fold increase in mass, depressed cardiac function, and the induction of a molecular fetal stress cardiac gene program. Of particular note is the initiation of hypertrophy by mechanical work through the activation of stretch-sensing transducing proteins located in the plasma membrane, within the cardiac Z line, or by adhesion complexes. The following discussion will be concerned only with the process of hypertrophy following a defined change in workload or stimulation. The presence of hypertrophy in the absence of an observable increase in workload will be considered to be primary and is discussed under the cardiomyopathies.

In pathologic hypertrophy, the mass and size of the heart are increased through a restricted number of hypertrophic stimuli resulting in the activation of a limited number of intracellular signal transduction pathways that alter gene expression. The initiating actions include mechanical stimuli (stretch) or trophic stimuli (polypeptide growth factors; vasoactive agents, such as angiotensin II and α-adrenergic agonists), all of which increase the rate of protein synthesis; the amount of protein, especially contractile proteins; the size of myocytes; and the number of sarcomeres and mitochondria. The hypertrophic response is accompanied by selective upregulation of several immediate early-response genes and embryonic forms of contractile and other proteins. The phenotype of the hypertrophic myocyte may be changed by this expression of embryonic genes, for instance, induction of atrial natriuretic factor occurs in ventricular myocytes, and late response genes, such as β-myosin heavy chain and skeletal α-actin, may be expressed (a switch from adult to fetal/neonatal forms). Other genes are also activated and selectively regulated in hypertrophy, including immediate early genes or proto-oncogenes that encode early regulatory factors *(c-jun, c-fos, egr-1),* growth factors (transforming growth factor-β, insulin-like growth factor, fibroblast growth factor), vasoactive agents (α-adrenergic agonists, endothelin-1, angiotensin II), and components involved in receptor-mediated signaling pathways, such as protein kinase C.

In pathologic states, hypertrophy is an adaptive response of limited benefit, where myocytes have impaired intrinsic contractility, impaired ventricular relaxation, and decreased compliance, which cause increased end-diastolic pressure and limited exercise performance. Once further muscle mass cannot meet the demands posed by increased workload, heart failure ensues. Degenerative changes occur in myofibers, including loss of myocardial contractile elements. Limitations to continued hypertrophy and the reasons for eventual myocardial failure include inadequacy of the vascular supply to the enlarged fibers, diminished oxidative capacity of mitochondria, altered protein synthesis and degradation, and cytoskeletal alterations. The capillary density in hypertrophic myocardium typically does not keep pace with myofiber size, intercapillary distances increase, and fibrous tissue is deposited in the interstitium *("reactive interstitial fibrosis").* Also, the altered isoforms of proteins produced by expression of fetal genes may be less functional than adult forms. Myocyte hypertrophy occurs only if increased protein synthesis exceeds the rate of degradation. Similarly, hypertrophy of the ventricle occurs only if growth of individual myocytes exceeds the

apoptotic loss of myocytes; excessive apoptosis can contribute to failure of a hypertrophic heart. This postulate is supported by experimental work with receptor-mediated Gαq signaling of cultured rat cardiac myocytes (Gαq is the α subunit of the Gq family of G proteins, guanine nucleotide–binding proteins, which transduce signals); moderate levels of Gq signaling stimulate cardiac hypertrophy, whereas high-level Gq activation results in cardiac myocyte apoptosis.

There are distinctive anatomic patterns of hypertrophy that accompany the increase in workload. **Concentric cardiac hypertrophy,** *that is, an increase in mass of the ventricle without accompanying increase in end-diastolic volume,* characterizes increased systolic loads *(increased afterloads),* such as aortic stenosis, pulmonic stenosis, and pulmonary hypertension in patent ductus arteriosus. There is often a decrease in the volume of the ventricular lumen (Fig. 1-3). An increase in diastolic load *(increased preload),* typically produced by AV or semilunar valvular insufficiencies or by arteriovenous shunts, results in **eccentric cardiac hypertrophy,** *which is an increase in myocardial mass accompanied by increased end-diastolic volume (dilated chamber).* Because of dilation, the thickness of the involved ventricular wall is usually no more than normal and may be less (Fig. 1-4).

In relation to altered hemodynamic loads placed on the heart, AV valvular stenosis or pericardial fibrosis restrict ventricular filling, leading to a decrease of the load on the myocardium (Fig. 1-5).

The gross appearance of the hypertrophic heart depends on the chamber affected and the nature of the insult. In general, hypertrophy of the right side of the heart makes the heart broader at its base; hypertrophy of the left side increases the organ length; bilateral hypertrophy produces a more rounded shape than normal.

In *concentric hypertrophy,* there is increased thickness of the wall of the affected chamber, and a marked increase in the size of the papillary muscles and the trabeculae carneae (Fig. 1-6). Although the hypertrophy may emphasize one or other chamber, the whole heart is involved. When the right ventricle is involved, the moderator band (trabecula septomarginalis) may be much thickened. Extreme hypertrophy of one chamber

Increased ventricular afterload (Pressure overload)
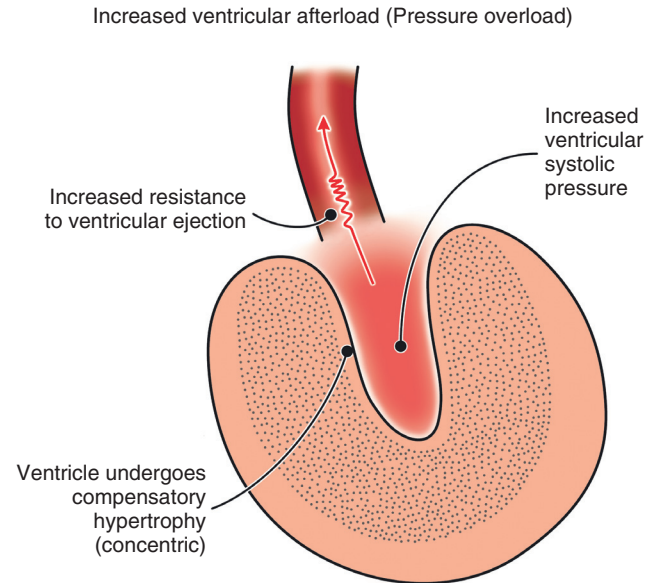
Figure 1-3 Increased ventricular afterload. The involved ventricle undergoes concentric hypertrophy following increased resistance to ventricular ejection. End-diastolic volume may be reduced. The shaded area shows the outline of a normal ventricle. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.)

Increased ventricular preload (volume overload)
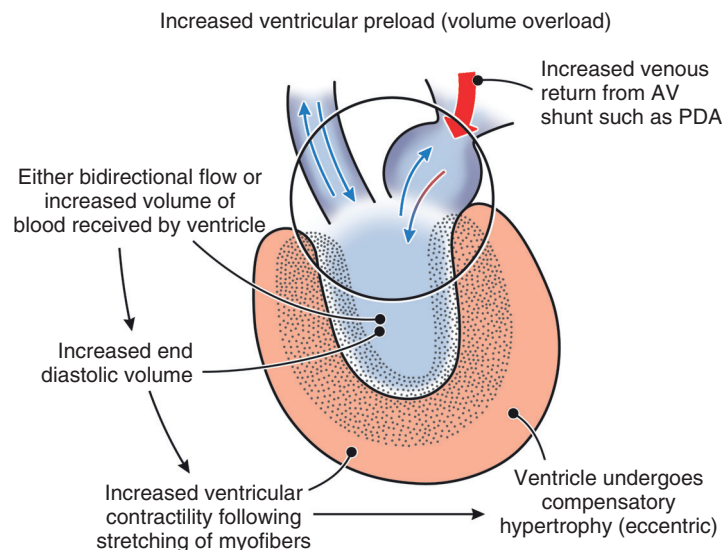
Figure 1-4 Increased ventricular preload. Increased ventricular preload may result from (1) bidirectional flow from insufficient atrioventricular (AV) or semilunar valves, or (2) increased volume of blood from intracardiac or extracardiac arteriovenous shunts. The ventricle dilates and undergoes eccentric hypertrophy. The shaded area shows the outline of a normal ventricle. *PDA,* patent ductus arteriosus. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.)
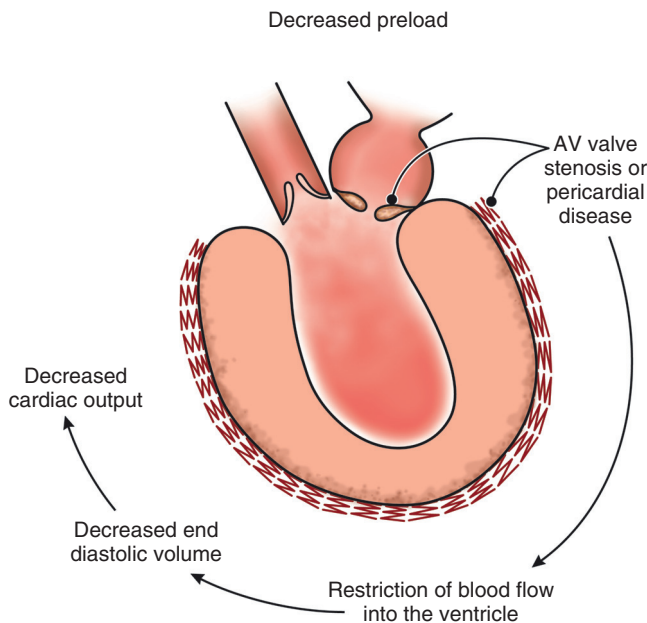
Figure 1-5 **Decreased ventricular preload.** Decreased ventricular preload follows atrioventricular (AV) valvular stenosis or myocardial restriction, such as pericardial fibrosis. End-diastolic volume decreases because of restricted inflow. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.)

Figure 1-6 **Concentric left ventricular hypertrophy.** The ventricular free wall and interventricular septum are thickened, and the lumen of the ventricle is reduced, in this cross-section of ventricles from a dog.

Figure 1-7 **Eccentric left ventricular hypertrophy** in dilated cardiomyopathy in a dog. The lumen of the left ventricle is increased relative to the thickness of the walls of the ventricle.

may encroach on the diastolic capacity of its opposite number. Microscopically, the myocytes are enlarged, but the increase in the size of fibers is not uniform and is not always easy to discern on routine microscopy.

In *eccentric hypertrophy and dilation*, the heart tends to be globose, and even though the mass is increased, the wall is usually thin. The papillary muscles may also be attenuated (Fig. 1-7).

In both types of hypertrophy, the endocardium may be diffusely opaque as a result of subendocardial fibrosis, and this alteration may be the best indication of dilation in the atria, in which dilation and hypertrophy can be difficult to assess.

An example of concentric cardiac hypertrophy occurs in cats with **hyperthyroidism** (thyrotoxicosis), a condition usually resulting from the presence of thyroid hyperplasia or adenoma. The thyroid glands in these cases are unilaterally or bilaterally enlarged, nodular, pink to dark brown, and may contain cysts. Microscopically, the thyroids usually exhibit a mixture of hyperplastic areas, adenomatous nodules, and normal follicles (see also disorders of the thyroid gland in Vol. 3, Endocrine glands). The pathogenesis of ventricular hypertrophy in this disease is not clear, but may involve the direct action of thyroid hormones on myocardium, enhanced myocardial adrenergic receptor number or affinity, peripheral vasodilation, and work hypertrophy in response to increased peripheral tissue demands for oxygen and dissipation of heat. The hearts in most cases are symmetrically hypertrophied; however, some exhibit asymmetric hypertrophy. The left ventricular lumen is usually reduced in size. Affected myofibers are enlarged, but are not in disarray in the great majority of cases. The hypertrophy is reversible on return to euthyroidism.

Systemic responses in heart failure

The *extracardiac features of heart failure* stem from 2 basic pathophysiologic changes: **fluid accumulation** and **tissue or organ ischemia.** Depending on the cause of the heart failure, both effects may be present, but it is more usual for one to predominate.

Fluid accumulation results from the retention of sodium and water, which primarily involves the kidneys, and also involves atrial natriuretic factor released from the heart (eFig. 1-3A). The influence of the failing heart on the kidneys stems from its inability to supply them with an adequate flow of blood. Blood flow through different parts of the kidneys depends on the vasomotor tone of blood vessels within the
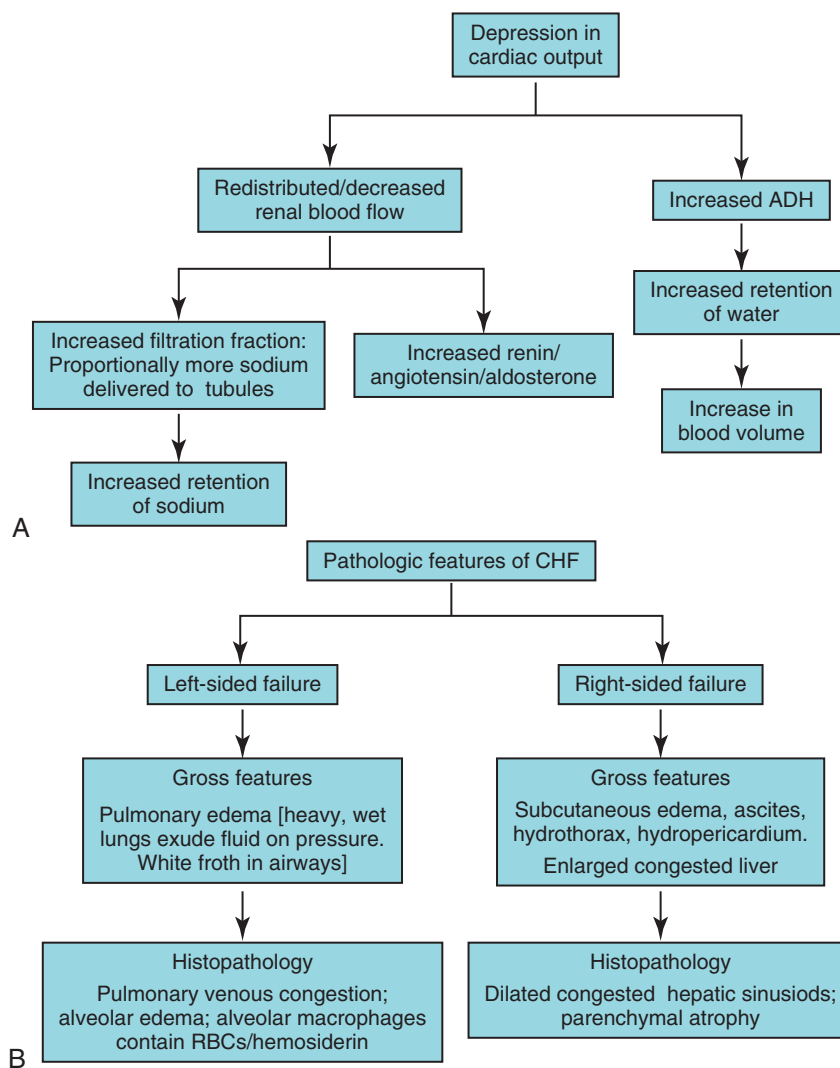
eFigure 1-3 **Congestive heart failure**. **A.** Pathogenesis of heart failure. This involves sodium and water retention by the kidney following reduced blood flow/redistribution of blood flow to the kidney. Increased antidiuretic hormone (ADH) activity also contributes to the retention of water. All lead to an increase in blood volume. (Modified from Robinson WF, Huxtable CRR, eds. Clinicopathologic Principles for Veterinary Medicine. Cambridge, UK: Cambridge University Press, 1988. Reprinted with permission.) **B.** Pathologic features of congestive heart failure (CHF). *RBCs*, red blood cells.

parenchyma. It is considered that many, if not all, of the intra-renal blood flow changes in heart failure follow increased activity of the sympathetic nervous system.

The kidneys receive approximately 20% of the output of the left ventricle, almost all of which flows through the renal cortices. One of the earliest changes following a drop in cardiac output is redistribution of blood flow within the kidney. There is reduced flow through the outer renal cortex and increased flow within the outer renal medulla. This results in readjustment of the *filtration fraction*, which is the ratio of glomerular filtration rate (GFR) to renal blood flow. Contrary to expectations, there is a *less* than proportionate drop in GFR compared with renal blood flow, resulting in an *increased* filtration fraction. As a consequence, proportionally more sodium moves through the glomerular filter, leading to pro-portionally more sodium being delivered into the proximal convoluted tubule. Because the rate of sodium resorption remains constant, a greater number of sodium ions are resorbed. Also, because of the increased filtration fraction, local plasma osmotic pressure in the efferent arteriole increases, causing greater resorption of sodium and water.

The alteration in renal blood flow in heart failure also increases the activity of the **renin-angiotensin-aldosterone** system, producing more sodium resorption from the distal convoluted tubule. There is also increased water-retaining activity by **antidiuretic hormone.**

A mechanism within the heart also regulates blood volume, blunting the activity of aldosterone and the renin-angiotensin system. **Atrial natriuretic factor** (ANF), with natriuretic and diuretic properties, is present in granules in some of the atrial myocytes. If the atrial pressure is elevated or the atria are distended, ANF is released and causes natriuresis, vasodilation, suppression of the renin-angiotensin-aldosterone axis, and decreased arterial blood pressure. *In terms of homeostasis, ANF has effects opposite to those of aldosterone, thus providing a balance to fluid regulation.* Although plasma ANF is signifi-cantly increased in dogs with chronic left AV valvular insuf-ficiency, it is not clear whether the metabolic effects of aldosterone or ANF predominate, but it would appear that the effects of aldosterone over-ride those of ANF.

It should be noted that none of the hormones mentioned produce the edema of congestive heart failure if administered alone. In addition, once a new steady state has been reached, the hormonal state returns to relatively normal limits. Last, *the mechanisms that are brought into play are not exclusive to the syndrome of heart failure. Any* situation that leads to a drop in effective circulating blood volume will activate the sodium- and water-retaining mechanism. The fundamental difference between these states and congestive heart failure is that the total blood volume in heart failure is already more than adequate, but the *effective blood volume* is much dimin-ished because of the poor cardiac output. The volume changes in heart failure should be viewed as an integrated response by the body to compensate for the inability of the heart to respond to the normal hemodynamic needs of the body.

The expansion of blood volume has both a beneficial and a detrimental effect. By increasing blood volume, venous return is enhanced and, in turn, cardiac output and tissue perfusion are improved. However, this is to the detriment of the balance between capillary hydrostatic pressure and plasma osmotic pressure. This leads to an increase in the amount of fluid in the interstitial spaces and body cavities.

Syndromes of circulatory failure

Circulatory failure, the term implying severe systemic conse-quences, falls into 3 general categories: *cardiac syncope, periph-eral circulatory failure, and congestive heart failure*.

Cardiac syncope

Cardiac syncope is characterized clinically by profound changes in blood pressure and heart rate with bradycardia or tachycardia, either of which may result in inadequate output of blood. Both may occur in the presence or absence of organic heart disease.

In one form of cardiac syncope, hypersensitive or hyperac-tive reflexes, for which the vagus nerve is the efferent limb, may result in reflex inhibition of the heart rate, manifest as extreme bradycardia or as asystole. The sudden deaths that result from acute pleural irritation or the tracheal irritation of aspirated vomitus fall into this group, and obviously there may be no organic heart lesion.

In a second form of cardiac syncope, the heart rate is extremely rapid, and the cardiac output severely reduced. Such may occur in paroxysmal tachycardia, atrial flutter or fibrillation, and ventricular fibrillation.

Third, in organic heart disease with complete obstruction of impulse conduction from the atrium to the ventricle (complete heart block), syncope may occur if there is suffi-cient delay before the ventricle assumes an independent rhythm.

Finally, cardiac syncope may terminate a syndrome of con-gestive cardiac failure when the cardiac reserve is depleted and the heart cannot increase its output sufficiently to meet sudden increases in peripheral needs.

Peripheral circulatory failure

Peripheral circulatory failure is characterized by reduction in the effective circulating blood volume with insufficient venous return and reduced cardiac output. Acute hemorrhage and shock are examples of this form of circulatory failure.

Congestive heart failure

The combination of compensatory mechanisms, brought into play to maintain cardiac output, is in general successful. However, there is also the planting of the seeds of destruction. Both the local increase in venous hydrostatic pressure and the increased sodium and water retention by the kidneys tend to promote the development of interstitial edema. Depending on the inciting abnormality, it is usual for one side of the heart to fail before the other, but it must be remembered that the cardiovascular system is a closed circuit and that failure of one side will eventually embarrass the other (eFig. 1-3B).

Left-sided heart failure is ushered in by progressive dilation of the left ventricle and atrium, although this progression may be marked by exacerbations and remissions if hypertrophy is given time to develop. The major extracardiac manifestations of left-sided failure arise from the damming back of blood in the lungs and the diminution in cardiac output. The *pulmo-nary venous congestion* is transmitted back to the capillaries of the alveolar wall, and edema fluid accumulates in the inter-stitial tissue and the alveolar spaces. The consequent reduction in pulmonary vital capacity and impaired gaseous exchange of cardiogenic pulmonary edema result in hypoxic stimulation of the carotid sinus and medullary respiratory centers so that *reflex dyspnea* occurs. A *wheezing bronchial cough* is common and is presumed to be due to irritation of the respiratory
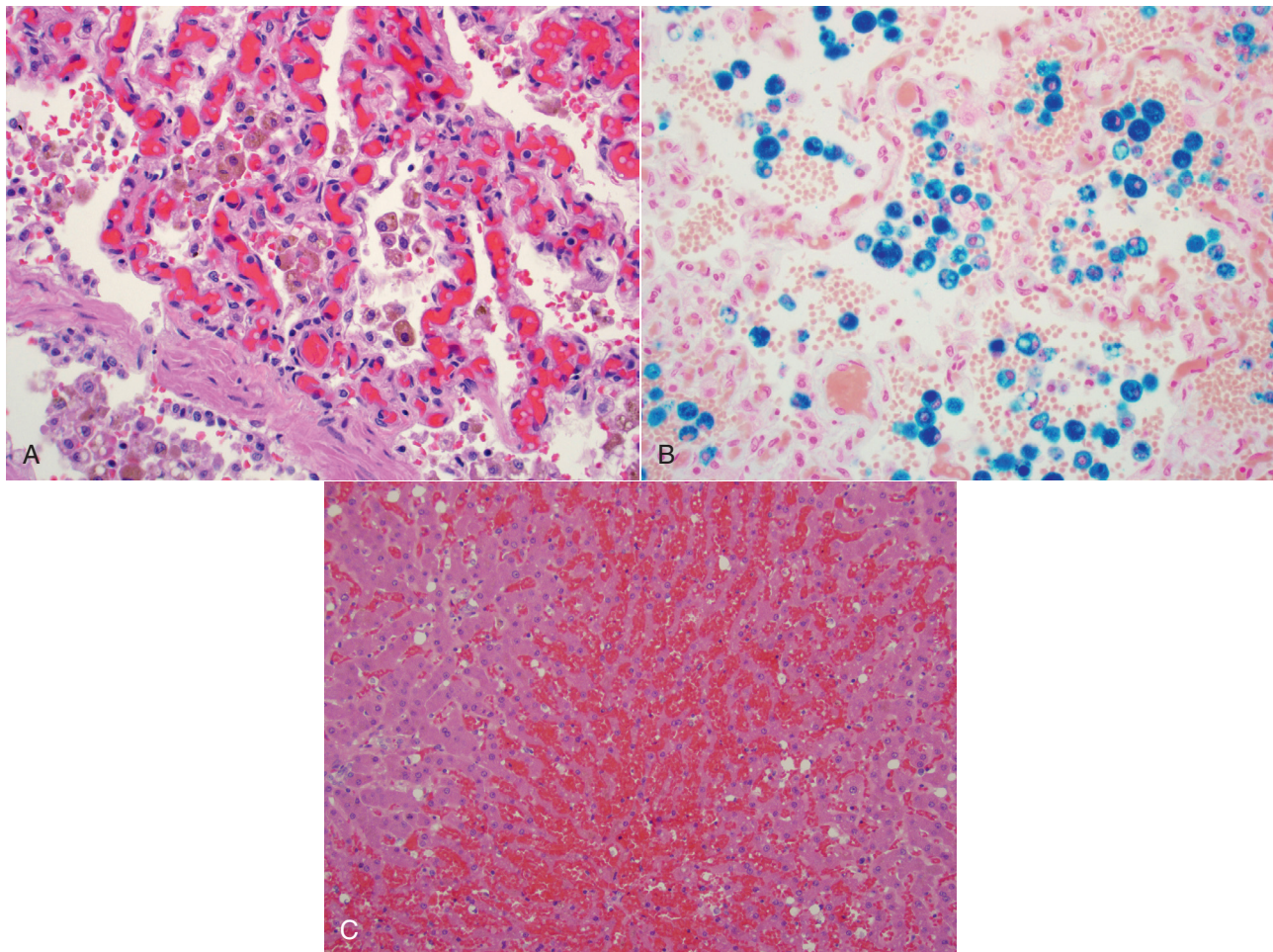
Figure 1-8 Congestive heart failure. **A.** Left-sided congestive heart failure in a dog. Pulmonary alveolar capillaries are congested, and there is hemorrhage into alveoli that contain hemosiderin-laden macrophages ("heart-failure cells"). H&E. **B.** Same section as (**A**) stained with Prussian blue to highlight the abundance of iron derived from hemosiderin in alveolar macrophages. **C.** Chronic passive congestion of the liver, leading to zonal hepatocyte atrophy, in right-sided congestive heart failure in a dog. H&E.

mucosae by the edema fluid. Cyanosis may be present but is more often the rule in right ventricular failure.

At postmortem, the **lungs** are usually of normal color, but may be light brown, and are heavy and wet. Stable, white froth is present in the airways, and fluid exudes from the cut surface. Because of its low protein content, there is little evidence of the abundant fluid on microscopic examination. The alveoli contain erythrocytes and a scattering of macrophages, some of which contain hemosiderin. It may be necessary to use a differential stain for iron to confirm the presence of these so-called "*heart-failure cells*" or siderophages (Fig. 1-8A, B). They are more numerous in chronic disease, and hemosiderin within their cytoplasm may be sufficient to produce tawny discoloration of the lungs.

In **right-sided heart failure,** the major extracardiac manifestations depend on increased hydrostatic pressure in the systemic and portal venous systems, and the reduction of flow from the lungs to the left ventricle. Renal complications occur more frequently in right-sided than in left-sided heart failure, leading to increased blood volume, peripheral edema, and more marked azotemia.

There is some species difference in the **distribution of edema** in congestive heart failure. In ruminants and horses, *dependent subcutaneous edema* is expected; in the other species, excess subcutaneous fluid is scant or absent. In dogs, the predominant accumulation of fluid is in the *peritoneal cavity.* In cats, it is in the *thorax.*

Grossly, the **liver** is enlarged and congested and has a "nutmeg" appearance on section because of *chronic passive congestion* (Fig. 1-8C). Microscopically, the sinusoids are dilated, with atrophy of the parenchyma about the central veins. In more severe or acute cases, the parenchyma in this location may undergo degeneration or necrosis. It is exceptional for an animal with congestive failure to live long enough for severe fibrosis and nodularity to occur. Impaired hepatic function is not usually a significant part of the clinical course, although jaundice may be observed.

Congestion of the **stomach and intestines** is evident, and this may impair their function, which is manifest usually as diarrhea. In horses, the subserosal lymphatics, particularly of the large bowel, are often readily discernible, dilated, and filled with edema fluid. The systemic and portal veins are distended,

and the **spleen** is enlarged and congested. However, this latter finding is masked if the animal in question has been euthanized using barbiturates.
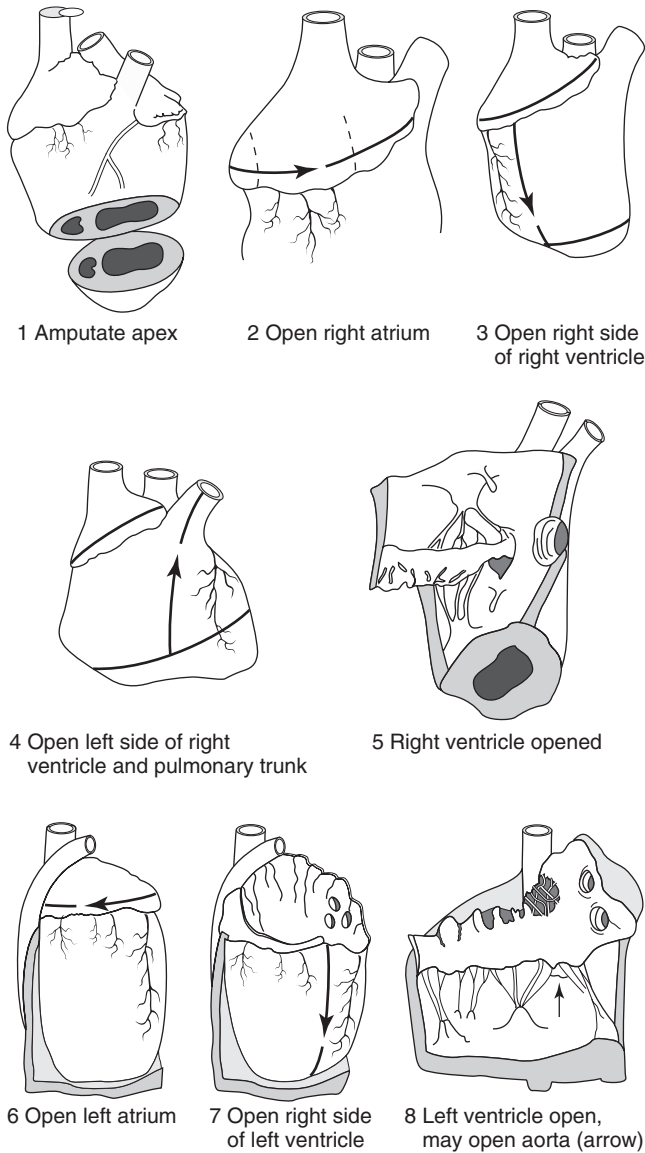
EXAMINATION OF THE HEART

In a **gross postmortem examination** of the heart, it is important to examine 4 major areas: pericardium, myocardium, mural and valvular endocardium, and the great vessels. A useful system is to follow the route of blood flow through the heart, that is, an inflow-outflow method of dissection (Fig. 1-9A, eFig. 1-4). This technique may require modification in the case of cardiac anomalies. Examination of the heart in the planes used for echocardiographic examination could be beneficial.

• The initial examination of the heart and great vessels is best made with the organs in situ to assess abnormalities of size and position.
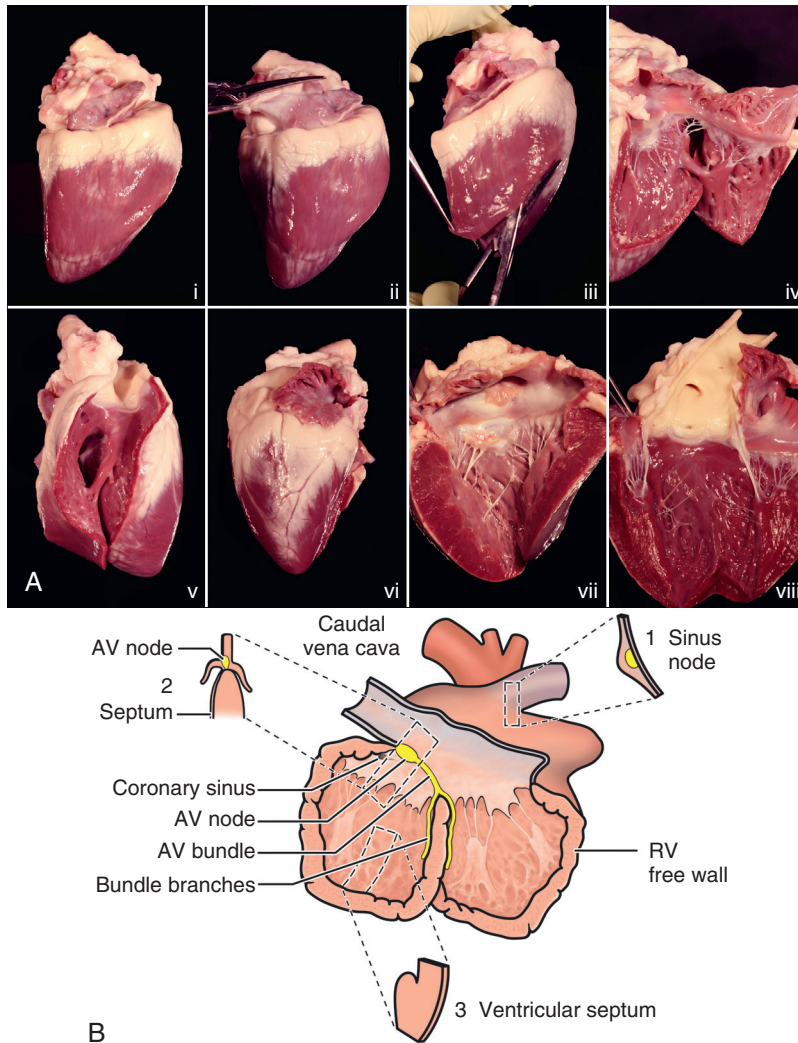
Figure 1-9 **Examination of the heart. A.** Gross examination. (i) Heart oriented to show right atrium/ventricle facing. (ii) Incision made transversely from caudal vena cava to right auricular appendage. (iii) Incision commenced in right atrium into junction between right ventricle and interventricular septum. (iv) Right ventricle opened to display right atrioventricular valve. (v) Incision continued to display right ventricular outflow tract and pulmonic valve. (vi) Heart oriented to display left atrium (transversely incised from pulmonary vein to left auricular appendage) and left ventricular free wall. (vii) Left ventricle free wall incised from base to apex displaying the left atrioventricular valve. (viii) Left ventricular outflow tract and aortic valve displayed by incision through left atrioventricular valve. Goat. **B.** Microscopic examination of the heart. The cardiac conduction system can be assessed via **block 1,** in which the *sinus node* is located subepicardially in the terminal groove at the junction of the cranial vena cava and right auricular appendage, and **block 2,** in which the *atrioventricular* (AV) node is located subendocardially on the right side of the interatrial septum, just cranial to the coronary sinus: Serial sections through this block will reveal the AV node, the common bundle, and the origins of the bundle branches. A block through the *left ventricular free wall, including papillary muscle,* or **block 3,** through the ventricular septum, is the minimal representative sample to take from a grossly normal heart. *RV,* right ventricle.

1 Amputate apex

2 Open right atrium

3 Open right side of right ventricle

4 Open left side of right ventricle and pulmonary trunk

5 Right ventricle opened

6 Open left atrium

7 Open right side of left ventricle

8 Left ventricle open, may open aorta (arrow)

eFigure 1-4 Gross examination of the heart (see text for details). (1) Transect apex of heart and examine ventricular walls. (2) Open right atrium from caudal vena cava to the tip of the right atrial appendage. (3) Follow blood flow through right ventricle. (4) Cut right ventricular free wall adjacent to septum and out pulmonic valve. (5) Right ventricle and pulmonary trunk opened; moderator band transected. (6) Open left atrium. (7) Open left ventricle toward the apex. (8) Left ventricle opened and left atrioventricular valve exposed; aorta may be opened as indicated by arrow.