3

Cardiovascular Diseases

SIMON F. PEEK AND SEBASTIEN BUCZINSKI

Examination of the Cardiovascular System

The cardiovascular system is assessed by observation of the animal's general state, mucous membrane appearance, and presence of venous distention or pulsation, as well as by examination of arterial pulse quality and rate and auscultation of the heart rate and rhythm.

Inspection of the patient may raise suspicion of cardiac disease if edema is observed in the submandibular space, brisket, ventral abdomen, udder, or lower limbs or if abdominal contours suggest the presence of ascites. Obviously, this requires differentiation from hypoproteinemic states, vasculitis, thrombophlebitis, lymphadenitis, or other less common diseases. Dyspnea, tachypnea, and grossly distended jugular or mammary veins are possible signs of cardiac disease that may be observed during general inspection of the patient. Weakness and exercise intolerance are other signs that require consideration of cardiac disease. In calves, overt congenital abnormalities such as microphthalmos, wry tail, or absence of a tail may also signal the possibility of an accompanying ventricular septal defect (VSD), and ectopia cordis is grossly apparent by inspection of the thoracic inlet or caudal cervical area. However, the majority of congenital heart malformations occur in the absence of other defects. In calves, failure to thrive in comparison with age-matched herdmates, exercise intolerance, and resting tachypnea or dyspnea may suggest a congenital cardiac condition, but confirmation and characterization require auscultation and echocardiography.

During physical examination, the mucous membranes should be evaluated for pallor, injection, or cyanosis. The visual appearance of the oral mucous membranes can vary with normal pigmentation patterns specific to the breed (e.g., Brown Swiss and Channel Islands cattle) and often appear pale to the inexperienced examiner in variably pigmented breeds such as Holsteins. In general, inspection of conjunctival and vulval mucous membrane appearance and refill time is preferable. Cyanosis is rare in dairy cattle with the exception of animals that are dying of severe pulmonary disease. However, cattle having advanced heart failure, right-to-left congenital shunts, and combined cardiopulmonary disease may have cyanotic mucous membranes. Capillary refill time often is prolonged in cattle with advanced cardiac disease.

Close inspection of the jugular and mammary veins for relative distention and the presence of abnormal pulsation is a very important part of every physical examination. Proficiency and practice at palpation of major veins are essential before an examiner can differentiate an abnormal finding from the normal range of variation found in cattle of various ages and stages of lactation. Normally, mammary veins are more sensitive indicators of increased venous pressure than jugular veins and therefore should be palpated routinely during the physical examination. Jugular veins should be observed during the general inspection and again during thoracic auscultation. Jugular veins should not be palpated until the end of the physical examination because many cattle become apprehensive when the neck region is palpated; this apprehension and subsequent excitement could affect baseline parameters or data being collected during the physical examination. This evaluation of the jugular veins, if deemed necessary, should be done at the end of the physical examination during examination of the head.

Mammary veins should be palpated by applying fingertip pressure. First the vein is palpated gently to detect pulsations suggestive of right heart failure; then the vein is compressed against the abdominal wall by gentle fingertip pressure. The amount of pressure necessary to compress the vein against the abdominal wall normally is minimal. When the vein is difficult to compress or, more commonly, seems to roll away from the fingertips, increased venous pressure from right heart failure may be suspected. These evaluations of the mammary veins obviously are subjective techniques but can be helpful adjuncts to other findings when practiced during every physical examination. Although pulsations in the mammary veins are considered abnormal findings suggestive of right heart failure, an occasional healthy older cow with a large udder and rich mammary vein branching may have slight mammary vein pulsation and distention.

Evaluation of the jugular veins for pulsation and distention requires differentiation of the notorious "false"-jugular

pulsation commonly observed in thin-necked dairy cattle from true pathologic jugular pulsation and distention. False or normal jugular pulsation is a product of reverse blood flow from atrial contraction at the end of diastole and expansion of the right atrioventricular (AV) valve during systole. Passive jugular filling during systole also may contribute, as does a "kick," or referred carotid artery pulsation. False jugular pulsation arises as a wave that winds its way from the thoracic inlet to the mandible when the cow has her head and neck parallel to the ground. When the head and neck are raised, the false jugular pulse may only ascend a portion of the cervical area or may disappear. A true jugular pulse fills the whole jugular vein rapidly when the head and neck are parallel to the ground or slightly raised. This rapid filling is similar to filling a garden hose with the end held off when water to the hose is turned on full force. In addition, distention of the jugular veins is more obvious with true jugular distention as found in right heart failure (Fig. 3.1). When confusion exists, the jugular vein may be held off near the ramus of the mandible, blood forced distally toward the thoracic inlet by the examiner's hand, and the vein observed (Video Clip 3.1). Emptying the vein in this fashion will eliminate a false jugular pulse, but a true jugular pulse will refill the emptied vein quickly and indicates right heart failure, increased central venous pressure, or right AV valve insufficiency. Some examiners suggest applying light pressure that partially occludes the jugular vein at the thoracic inlet, thereby mildly distending the jugular vein. This is thought to eliminate false (or normal) jugular venous pulsations from a referred carotid arterial impact. In general, the degree of gross distention of the jugular veins in cattle having right heart failure is more impressive than the degree of pulsation (Video Clip 3.2).

Taking the arterial pulse may be helpful in the assessment of cardiac disease. The middle coccygeal artery is the first artery palpated for pulsation during the physical
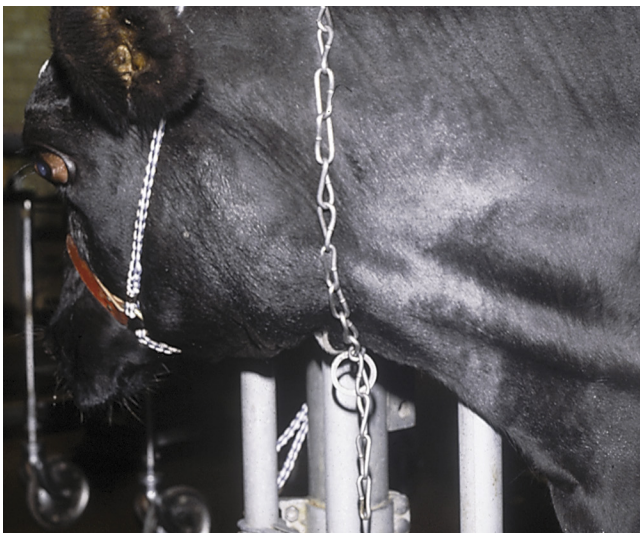
• **Fig. 3.1** Obvious distension of the jugular vein in a cow having heart failure secondary to endocarditis.

examination. The facial artery is used when treating recumbent (hypocalcemic) cattle, and the median artery is the most convenient to palpate when performing simultaneous cardiac auscultation and pulse monitoring. Pulse rate, rhythm, and quality should be assessed. Pulse quality implies considerations of the size, strength, and duration of the pulse wave and distention of the artery. Most cattle with heart failure have decreased pulse strength, unevenness of the pulse, increased pulse rate, or a pulse rate that is different than the heart rate. Abnormalities in pulse rate or rhythm should alert the examiner to the possibility of cardiac arrhythmias.

Proficiency at auscultation of the heart requires some basic knowledge, willingness to auscultate both sides of the thorax carefully during every physical examination, and patience. Many cattle object to stethoscope placement over the sites on the chest wall necessary for cardiac auscultation and adduct the forelimb tightly against the thorax. This is noticed especially on examining the right side, where cardiac auscultation in cattle requires the stethoscope to be placed very cranial in the axillary area around the third intercostal space (ICS). Dairy bulls and large or fat cows have thick chest walls that reduce the intensity of heart sounds. Heart sounds are easier to hear on the left side of normal cattle. The pulmonic valve region is best heard in the left third ICS at a level between the shoulder and elbow. The aortic valve region near the heart base is best heard in the left fourth ICS at approximately shoulder level. The mitral (left AV) valve region coincides with the cardiac apex and is best heard at the left fifth ICS just above the elbow. The right AV (tricuspid) valve is heard far forward in the right third ICS at a level halfway between elbow and shoulder.

Although clinicians generally discuss two heart sounds in normal cattle, it is possible to hear four heart sounds in some cattle as it is with horses. Although the potential for four heart sounds is somewhat confusing and may be impossible to differentiate in most clinical patients, examiners should be aware of these facts and not overinterpret the significance of auscultating more than two heart sounds. The first heart sound (S1) heralds the beginning of systole, is associated with the final halting of AV valve motion after closing, and is best heard at the apex regions coinciding with AV valves in the cow. A slight splitting of S1 into separate mitral and tricuspid valve components is possible but is rarely audible in normal cattle. S1 tends to be of lower frequency and longer duration than S2.

S2 usually is not as loud as S1 and coincides with aortic and pulmonic valve closure. Current theory suggests that valve closing sounds associated with the generation of S2 result from the sudden halt in valve motion when it closes. Asynchronous closure of the aortic and pulmonic valves results in audible splitting of S2 in many normal cattle, especially during the inspiratory phase of the respiratory cycle.

Although S1 and S2 comprise the major heart sounds for cattle, S3 and S4 have been described. Ventricular vibrations at the end of rapid filling in early diastole are thought

to cause S3, a low-frequency sound seldom heard in cattle. S4 sometimes is heard late in diastole and is related to atrial contraction. In cattle with tachycardia, it has been suggested that S4 may in fact closely precede S1 and be mistaken for a split S1. The tripling or quadrupling of heart sounds that resembles a horse's cantering gait is commonly referred to as a gallop rhythm and occurs in the higher range of normal heart rates or when tachycardia exists in some cows. Gallops are diastolic sounds related to atrial contraction (S4 gallop), to ventricular filling (S3), or to both (summation gallop). A prominent and persistent gallop rhythm in a cow with tachycardia may be the first indication of heart disease.

The heart rate of normal adult cattle is 60 to 84 beats/min. Neonatal calves may have normal heart rates as high as 110 to 120 beats/min, but frequently heart rates this high are brought about by the excitement of being handled or in anticipation of being fed. Not everyone agrees on the aforementioned range of normal heart rates for cattle, and several points should be addressed regarding this topic. Oxen and fat, persistently dry cows used only for embryo transfer may have a slower metabolism than lactating dairy cattle. Therefore, somewhat similar to draft horses, these cattle may have heart rates at the low end of the normal range or even less than 60 beats/min. Conversely, healthy but excited, nervous, or aggressive cattle may have heart and pulse rates more than 84 beats/min when approached by any examiner. Therefore, the range of 60 to 84 beats/min really is an average and must be interpreted in light of the patient, its surroundings, and its intended use. Following the work of McGuirk et al. with fasted cattle, a low normal range of 48 beats/min has been proposed. Further studies demonstrated that in normal cattle, a decrease in ruminoreticular fill results in a reflex slowing of the heart rate, predominantly because of an increase in parasympathetic tone. However, fasted healthy cattle seldom are encountered in the world outside of academic settings, and veterinarians are not frequently asked to examine healthy fasted cattle. An exception may be a cow off feed secondary to the classic broken water cup syndrome because she will become anorectic secondary to water deprivation. Sick cattle seldom have a heart rate less than 60 beats/min only because they are anorectic. Sick cattle that do have heart rates less than 60 beats/min usually have a vagal nerve–mediated bradycardia. Therefore, 60 to 84 beats/min is still our preferred normal range for heart rate in adult dairy cattle.

Excited or nervous cattle may have an increased intensity or loudness of the heart sounds in addition to an increased heart rate. Other conditions that increase the intensity of heart sounds may be relative or pathologic. Relative factors include thin body condition, younger animals with thin chest walls, and excitement. Pathologic factors include anemia, the "pounding" heart rate sometimes heard in cattle with endocarditis, and displacement of the heart to a position closer to the thoracic wall by a diaphragmatic hernia or an abscess or tumor in the contralateral hemithorax. "Muffling," or decreased intensity of heart sounds, may occur for relative reasons such as the increased thickness or fat on the chest wall of adult bulls or heavily conditioned

cattle. Muffling also results from pathologic conditions such as pericarditis, pneumomediastinum, diaphragmatic hernia, and displacement of the heart toward the opposite hemithorax by an abscess or tumor in the hemithorax being auscultated. Cattle in shock may have either decreased or increased intensity of heart sounds, depending on the duration and severity of the condition. Whereas "shocky" cows that are weak but still ambulatory tend to have increased intensity of heart sounds, those that are recumbent or moribund have decreased intensity.

Auscultation combined with percussion provides the best subjective means to estimate the position and size of the heart. Heart sounds may radiate over a wider area than normal when transmitted by consolidated lung lobes or pleural fluid or when there is cardiac enlargement.

In calves and thin adult cattle, palpation of the apex beat is possible around the left fourth or fifth ICS at a level halfway between the elbow and shoulder. Palpation of an apex beat on the right side of adult cattle seldom is possible unless profound cardiac disease or displacement of the heart to the right by space-occupying masses has occurred. Deep palpation with the fingertips over the intercostal regions overlying the heart may elicit a painful response in conditions such as endocarditis, pleuritis, traumatic reticulopericarditis, and rib fractures.

As in other species, bovine heart murmurs are classified based on intensity and timing. Intensity may be ranked subjectively on a 1 to 6 basis, with 1 of 6 being a faint, barely detectable murmur; 2 of 6 a soft but easily discernible murmur; 3 of 6 a low to moderate intensity murmur; 4 of 6 moderate in intensity but lacking a thrill; 5 of 6 a loud murmur with a palpable thrill; and 6 of 6 so loud that it can be heard with the stethoscope off the chest and evincing a palpable thrill. Classification relative to timing of the cardiac cycle further defines murmurs as systolic, diastolic, or continuous. Further division is provided by terms such as "early systolic" or "holosystolic." In general, whereas systolic murmurs in cattle reflect AV valve insufficiency or, much less commonly, aortic or pulmonic stenosis, diastolic murmurs reflect aortic or pulmonic valve insufficiency or rarely AV valve abnormalities. Benign systolic murmurs occasionally are heard in excited, tachycardic calves, or cows with anemia, hypoproteinemia, or in those being given rapid intravenous (IV) infusions of fluids. Pathologic systolic murmurs most commonly are found in calves with congenital heart abnormalities such as VSD or tetralogy of Fallot and in adult cows with endocarditis. Continuous murmurs are rare but may be encountered in calves having a patent ductus arteriosus or in cows with pericarditis. The point of maximal intensity for each cardiac murmur may add subjective data as to the valve involved in the cardiac abnormality.

Arrhythmias may be benign, pathologic, or secondary to metabolic disturbances in cattle. Sinus bradycardia and arrhythmia have been confirmed in cattle held off feed, in hypercalcemic adult cattle, and in hypoglycemic or hyperkalemic young calves. Sinus tachycardia may result from excitement, pain, hypocalcemia, and various systemic states such as endotoxemia and shock. Cattle with severe

musculoskeletal pain often have normal heart rates while recumbent but have tachycardia when forced to rise and stand. Persistent tachycardia should be considered abnormal and may reflect cardiac disease unless other systemic or painful conditions coexist.

Hyperkalemia may cause a variety of arrhythmias and is most commonly observed in neonatal calves that develop acute metabolic acidosis associated with secretory diarrhea caused by *Escherichia coli* or acute diffuse white muscle disease. Atrial standstill and other arrhythmias have been documented in diarrheic calves having metabolic acidosis and hyperkalemia. Extreme hyperkalemia (>7.0 mEq/L) may lead to cardiac arrest and should be corrected immediately, especially in calves that may require general anesthesia. Because severe hyperkalemia may be associated with pathologic bradycardias, even without confirmatory blood work, the experienced clinician should be alert to the therapeutic need for fluids that will specifically address hyperkalemia in severely dehydrated, diarrheic calves with discordantly low heart rates for their systemic state. Calves with white muscle disease also may have direct damage to the myocardium, which may be manifested by arrhythmias, murmurs, or frank cardiac arrest. Hypokalemia and hypochloremia in cattle with metabolic alkalosis may predispose to the most common arrhythmia of adult cattle—atrial fibrillation.

Hypocalcemia may be present, or contribute to, cattle having abdominal disorders that lead to metabolic alkalosis. Metabolic alkalosis may be a factor that triggers atrial fibrillation in cattle with normal hearts. Atrial fibrillation causes an irregularly irregular rhythm, with a rate that may be normal or increased (88–140 beats/min), depending on the presence of heart disease or the underlying predisposing condition. Atrial fibrillation is associated with irregular intensity of heart sounds. A pulse deficit may be present in any cow with a rapid or irregular cardiac rhythm, especially when the rate exceeds 120 beats/min. Atrial premature complexes (APCs) may also occur in cows with gastrointestinal (GI) disease and electrolyte abnormalities. APCs may precede or immediately follow atrial fibrillation in some cows. Variation in intensity of the first heart sound during auscultation is characteristic of APCs.

Other causes of arrhythmia in adult cattle include cases of lymphosarcoma with significant myocardial infiltration often causing atrial fibrillation, and ventricular or atrial arrhythmias associated with septic or toxic myocarditis. Intravenous administration of calcium solutions is the major drug-related cause of arrhythmias in cattle, but IV administration of antibiotics or potassium-rich fluids occasionally prompts transient arrhythmias.

Sounds auscultated in patients with pericarditis are variable, often confused with murmurs of valvular origin, and tend to change on a daily basis if affected cattle are available for repeated evaluation. Classic pericardial "friction" rubs occur at different stages of each cardiac cycle unlike murmurs, which tend to occur at a distinct, repeatable, phase of each cardiac cycle. Squeaky sounds, often similar to those made in compression of a wet sponge, may also be heard as a result of pericardial disease. Rubbing sounds caused by contact between fibrin on the visceral and parietal pericardium also may be heard. The heart sounds tend to be muffled, and either free fluid or fluid–gas interfaces may lead to splashing or tinkling sounds or to complete muffling of all sounds. During the acute phase of traumatic reticulopericarditis, the character of the sounds tends to change each day. In those with subacute or chronic disease, muffling of the heart sounds or distinct tinkling or splashing tend to be more consistently present.

Presence of an arrhythmia or murmur alerts the examiner that the heart may be abnormal. However, heart failure may or may not be present. In cattle, right heart failure is more common than left heart failure. The general signs of right heart failure include:
1. Ventral edema—the edema may be diffuse or limited to specific regions such as the submandibular area, brisket, ventral abdomen, udder or sheath, and the lower limbs (Fig. 3.2).
2. Jugular and mammary vein distention with or without pulsations (Fig. 3.3)
3. Exercise intolerance with or without dyspnea
4. Persistent tachycardia
5. Ascites with or without pleural fluid (Fig. 3.4)

• **Fig. 3.2** Submandibular, brisket, ventral, and udder edema in a cow in right heart failure caused by pericarditis.
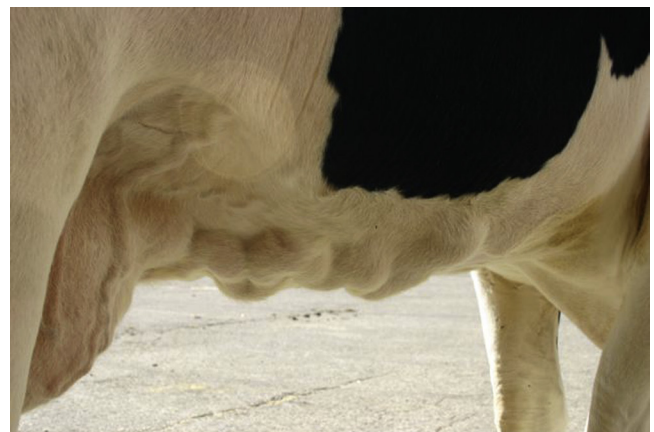
• **Fig. 3.3** Profound mammary vein distention in a 4-year-old Holstein cow with congestive heart failure caused by tricuspid and aortic valve endocarditis. The cow had been markedly hypogalactic for several weeks before this image was taken.
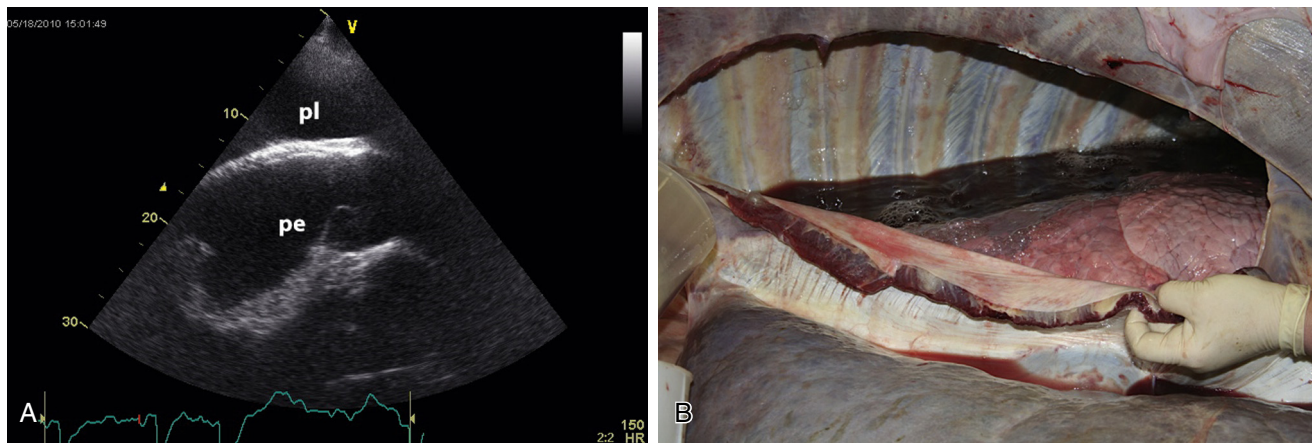
• **Fig. 3.4 A,** Pleural effusion (pl) in addition to pericardial effusion (pe) in a 6-year-old Holstein cow with idiopathic hemorrhagic pericardial effusion and congestive heart failure caused by cardiac tamponade. **B,** Intrathoracic view at postmortem of the same patient demonstrating extravagant pleural fluid.

In addition to the general signs, specific cardiac signs such as a murmur, arrhythmia, or abnormal intensity of heart sounds usually are present and contribute to the diagnosis. Probably the most difficult set of differential diagnoses involves those diseases that result in hypoproteinemia. Hypoproteinemia also causes ventral edema and may cause exercise intolerance and tachycardia. However, hypoproteinemia would not cause jugular and mammary vein distention and pulsation. Therefore, venous distention and pulsation coupled with abnormal heart sounds or rhythm are the key signs when diagnosing heart failure in dairy cattle.

Left heart failure causes dyspnea, pulmonary edema, and exercise intolerance and may lead to cyanosis and collapse or syncope. Specific left heart failure seldom occurs in cattle, but left side failure combined with worsening, antecedent right heart failure may develop as the animal progresses into fulminant congestive heart failure.

Ancillary Procedures

Electrocardiography

The electrocardiogram (ECG) is essential for definitive categorization of arrhythmias in cattle. Vector analysis of ECG tracings to determine cardiac chamber enlargements and other pathology seldom is used in cattle because ventricular myocardial depolarization tends to be rapid and diffuse rather than organized, as in some other species. ECG is also indicated when cattle have variation in heart sound intensity, require monitoring for anesthesia or treatment of cardiac arrhythmias, or show signs of heart failure. Cardiac ultrasonography, however, has largely superseded the ECG as a diagnostic tool in determining chamber enlargement and other cardiac pathology.

The base-apex lead system is most commonly used in cattle. The base-apex lead system results in an ECG with large wave amplitude and is sufficient for evaluating most arrhythmias. The positive electrode is placed on the skin over the left fifth ICS at the level of the elbow, the negative electrode is placed on the skin over the right jugular furrow 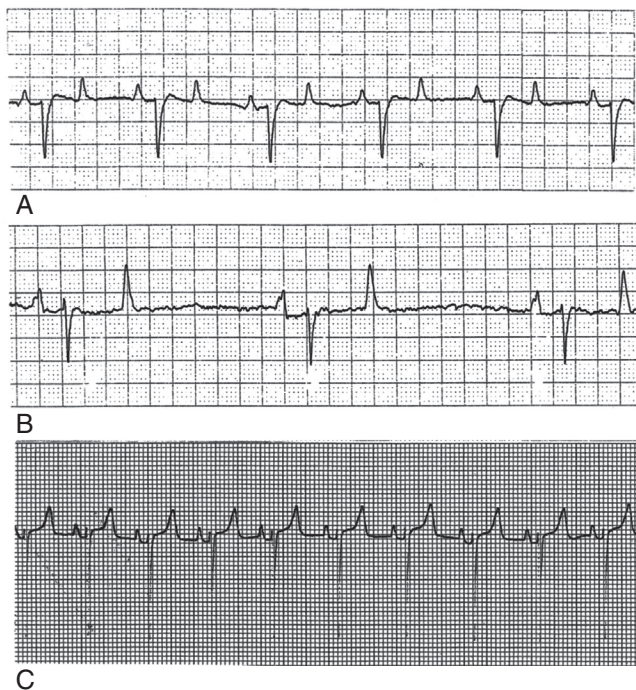roughly 30 cm from the thoracic inlet, and the ground electrode is attached to the neck or withers. The resultant ECG recorded through the base-apex lead system has a positive P wave with a single peak, a QRS complex with an initial positive deflection followed by a large negative deflection, and a variable (positive or negative) T wave (Fig. 3.5).

Echocardiography

Two-dimensional echocardiography and Doppler echocardiography have greatly enhanced our ability to assess cardiac function and visualize anatomic variations and pathologic lesions in cattle. Valvular, myocardial, pericardial, congenital, and acquired lesions can be visualized in real time, measured, and monitored. Qualitative and quantitative assessments of the impact of congenital anomalies and monitoring treatment response of endocarditis, pericarditis, or myocardial lesions are possible with the appropriate equipment and people trained to conduct and interpret a systematic cardiac examination. In short, echocardiography is now an essential component of a full cardiology workup.

Echocardiography for the Evaluation of Heart Disease Detection in Dairy Cattle

Bovine cardiac diseases are most commonly diagnosed when the condition is already advanced and production outcomes have already been affected (decreased milk production, poor reproductive performance, diminished appetite, weight loss or altered growth). The diagnosis of heart disease may be clinically difficult until overt signs of heart failure occur (e.g., peripheral edema, distended jugular veins, or true jugular pulse). However, some cardiac diseases such as endocarditis and VSD may be less commonly associated with clinical signs of heart failure. Routine cardiac auscultation also has its limitations, especially under noisy field conditions or in adults with high body condition score. For these reasons, ancillary tests may be extremely valuable in reaching the definitive diagnosis and to facilitate appropriate case management. Transthoracic echocardiography (TTE) is becoming more available and more readily accessible on farms because of improvements in ultrasound quality, affordability,

• **Fig. 3.6** Performing right transthoracic echocardiography in a farm setting. The probe is placed cranially between the thorax and right forelimb to access the third to fifth ventral intercostal spaces.
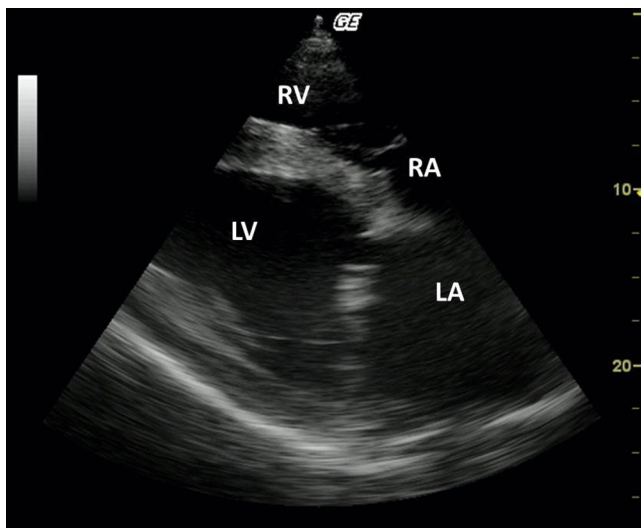
and portability. This imaging technique has the potential to help practitioners reach a definitive diagnosis antemortem, therefore improving case management. Importantly, it can help avoid unnecessary treatments if the prognosis is hopeless as well as differentiate life-threatening conditions (pericarditis secondary to hardware disease) from more benign ones (idiopathic hemorrhagic pericarditis). By contrast with other veterinary species (small animals, horses) in which echocardiographic examination now entails precise calculations of various functional indices or dimensions and can require extensive postgraduate training and expensive equipment and software, bovine echocardiography does not. A great deal of information can be obtained when one knows which views are needed and how to get them. Several of the common cardiac conditions of dairy calves and adult cattle have characteristic ultrasonographic features, and when a veterinarian has become somewhat familiar with the likely image findings for each, a definitive diagnosis can often be reached. Practically speaking, a complete echocardiographic examination can be performed on the farm in about 15 to 20 minutes.

Echocardiographic Technique: Adults and Calves

Transthoracic echocardiography is usually best performed with the individual standing and restrained by a halter. An assistant may also be useful depending on the patient's demeanor to keep the thoracic limb forward during the examination to improve access to the cardiac window on the side in question. The author (SB) generally prefers to put his own leg medial to the forelimb in order to perform a gentle abduction of the cow's limb; this often helps in obtaining better quality images

(Fig. 3.6). TTE is classically performed using "cardiac windows" composed of the ventral third to fifth ICSs on both the right and left sides of the thorax. Ideally, the area is clipped, and ultrasonographic coupling gel is applied. Depending on the context of the examination, a faster technique may be achieved by applying 70% isopropyl alcohol directly to the unclipped skin surface without coupling gel. The author has used this technique increasingly to good effect in recent years. It has the advantage of avoiding unnecessary clipping if there is a high likelihood of sale or culling in the near future and is also more popular with owners of individually valuable cattle during show season! Hair length and body condition (chest wall thickness) can both interfere with the diagnostic quality of images when only alcohol is used. A low-frequency probe (≤3.5 MHz) with good penetration (examination depth >20 cm) is required for adult cows. For calves, a 5 MHz probe is usually adequate because of the smaller size of the thorax. The major limiting factor in performing TTE is the size and shape of the probe compared with the width and accessibility of the relevant intercostal spaces. Many cattle, even those without painful chest walls, resent examination under the elbow and into the axillae, tending to respond by powerful, counterproductive forelimb adduction as the examiner moves the probe forward. Probe rotation, necessary to obtain the standard views, is often challenging, especially in the more cranial ICSs. The phased-array probes (specifically used for echocardiography and therefore more expensive) are optimal; larger sector probes also work quite well but may have limitations for some of the views described in the following section.

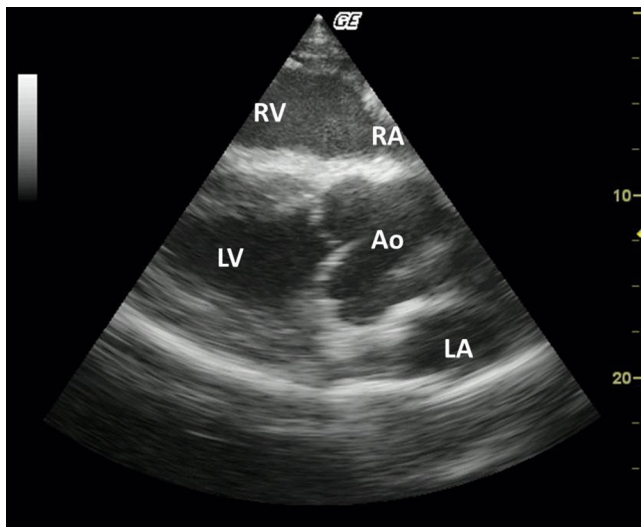### Most Important Echocardiographic Views

The views obtained from the right side are generally the most informative, and the examination should always begin

on this side. In the author's experience, the long-axis views are the most informative and the easiest to recognize. The four-chamber long-axis view is obtained when applying the transducer parallel to the fourth ICS. This view allows observation of the two ventricles and atria as well as the AV valves (Fig. 3.7). A slight clockwise rotation of the transducer allows observation of the left ventricular outflow tract (LVOT) view. This view is of particular value when aortic problems are suspected and for visualization of the membranous part of the interventricular septum (IVS) (Fig. 3.8) which may be absent or incomplete in cases of VSD.

Continuing the rotation of the probe clockwise or movement of the transducer to the third ICS is necessary to observe the right ventricular outflow tract (RVOT). This view is required to evaluate the pulmonary valve and pulmonary trunk (Fig. 3.9). If needed, the probe can be applied perpendicular to the ICS to obtain short-axis views of the heart. However, from a practical standpoint, these views are often not very informative. Views from the left side are of special interest when left heart lesions (e.g., mitral valve anomalies) are suspected. The author does not use these views invariably but only when the right-sided views are inconclusive.

Biochemical Assessment of Cardiac Disease

Although rarely analyzed in ambulatory practice, there have been a number of publications in recent years on the use of cardiac biomarkers for the assessment of myocardial injury in the hospital setting. Borrowing from human cardiology in which cardiac troponins have become an essential part of point-of-care assessment in the management of chest pain and the diagnostic and prognostic data set for myocardial ischemia patients, it is appealing to think that there might be similar value to the measurement of cardiac troponin I (cTnI) in cattle with physical examination or ancillary diagnostic findings suggestive of acute cardiac disease. The obvious difference in prevalence of acute myocardial ischemia between cattle and humans means that the number one indication for cTnI measurement in human patients will never be duplicated in cattle. However, bovine cTnI has been examined in association with congenital heart defects in calves, experimental monensin toxicosis, and a variety of primary cardiac conditions such as endocarditis and pericarditis, as well as in dairy cattle with common, noncardiac production diseases. In each of these published studies, commercial human immunoassays were used, and although different manufacturers' kits have been used in different studies, there is a great deal of structural homology between cTnI among mammalian species, suggesting that these

• **Fig. 3.7** Four-chamber long-axis view. This view allows visualization of the two ventricles (LV and RV), the two atria (RA and LA), and the two atrioventricular valves. The thickness of the mitral valve is often difficult to assess from the right because of distortion at such a high depth.
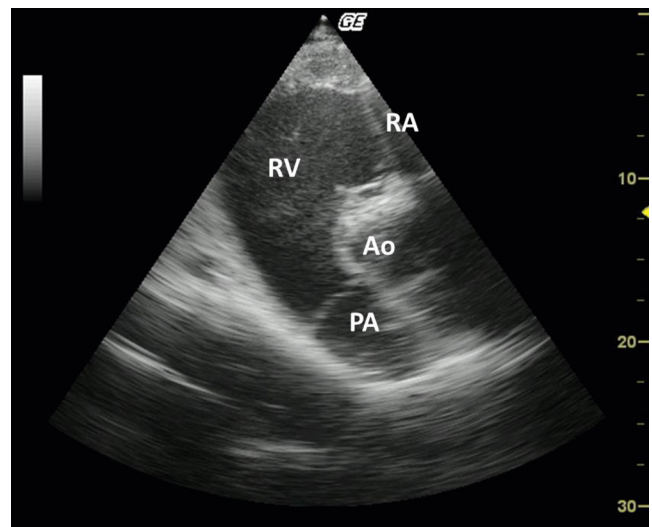

• **Fig. 3.8** Left ventricular outflow tract (LVOT) long-axis view. This view allows visualization of the two ventricles (LV and RV), the two atria (LA and RA), the aortic root (Ao) and the aortic valve. This is the best diagnostic view when one suspects a ventricular septal defect.


• **Fig. 3.9** Right ventricular outflow tract (RVOT) long-axis view. This view is of particular importance to assess the pulmonic valve, pulmonary artery (PA), right ventricle (RV), right atrium (RA), and aorta (Ao).

assays would very likely accurately detect the bovine protein. Consequently, a normal reference range of 0 to 0.05 ng/mL has been suggested in healthy, lactating dairy cattle when a widely available, handheld point-of-care analyzer was used. Other studies have suggested an upper cutoff point of 0.08 ng/mL when a different, laboratory-based immunoassay was used. Cattle with severe, acute myocardial injury, such as that caused by ionophore toxicosis, show marked increases in cTnI to greater than 1 ng/mL over a 1- to 6-day interval after a single, massive overdose. This quantitative increase is paralleled by echocardiographic, electrocardiographic, and histopathologic evidence of marked myocardial necrosis and cardiac dysfunction. Other studies looking at congenital cardiac defects and acquired cardiac conditions of adulthood (pericarditis and endocarditis) have also demonstrated elevations above normal controls, but there is no useful prognostic information in cattle at this point that can be extrapolated from these data. Other, noncardiac primary intrathoracic diseases, such as pneumonia, and noncardiac intrathoracic abscessation, can also be associated with occasional spikes in measured cTnI. In conclusion, although one can identify acute bovine myocardial injury with the use of cTnI measurement, we are currently uncertain of the kinetics of release and half-life of the released protein and how to prognostically interpret single time point values. The half-life of cTnI is very short in other species eg., one hour in the horse.

Specific Cardiac Diseases in Calves

White Muscle Disease

Myocardial damage from vitamin E and selenium deficiency may occur at any site in the heart and may be focal, multifocal, or diffuse (Fig. 3.10). Signs may develop at any time from birth to 4 years of age but are more common in calves younger than 3 months of age. Specific cardiac signs are variable and include arrhythmias, persistent tachycardia, murmurs, exercise intolerance, cyanosis, dyspnea, congestive heart failure signs, and acute death. Signs may be subtle
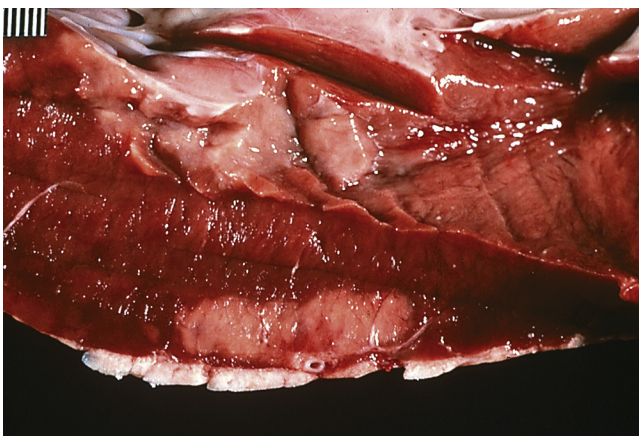
• **Fig. 3.10** A pale focal area of Zenker's degeneration in the myocardium of a calf that died of diffuse white muscle disease.

or dramatic, depending on the magnitude and location of myocardial damage. Sudden death can occur spontaneously, after exercise or even following mere restraint. Other signs of white muscle disease such as stiffness, difficulty in prehension or swallowing, inhalation pneumonia, recumbency, and myoglobinuria may or may not be present. Dyspnea may be directly related to the cardiac lesions or may be caused by Zenker's degeneration in the diaphragm or intercostal muscles. Tachycardia (>120 beats/min) and arrhythmias are the most common specific cardiac signs, but murmurs may be present as well.

Diagnosis can be confirmed by measuring blood selenium values, urine dipstick testing to look for positive "blood" (myoglobin) and protein, and serum biochemistry to evaluate creatine kinase (CK) and aspartate aminotransferase (AST) enzymes. When diagnostic blood samples are obtained after parenteral selenium supplementation, antecedent deficiency can still be confirmed by assaying levels of the enzyme glutathione peroxidase. If the heart is the only muscle involved, serum muscle enzymes may not be greatly elevated; however, the heart seldom is the only "muscle" involved. Because of the necrosis involving the myocardium, acute cases would be expected to have elevated cTnI values.

Treatment should be instituted immediately with vitamin E and selenium injected at the manufacturer's recommended dosage. Although some commercial preparations include label instructions that include IV use, it is suggested that vitamin E and selenium be given intramuscularly (IM) or subcutaneously (SC) to avoid the occasional life-threatening anaphylactic-type reaction seen with these products. The calf should be kept in a small box stall, straw bale enclosure, or hutch so it can move about but not run freely, lest further muscle damage be precipitated. If pulmonary edema is present, furosemide (0.5–1.0 mg/kg) may be given once or twice daily. Concurrent aspiration pneumonia would require intense antibiotic therapy. Vitamin E and selenium injections are repeated at 72-hour intervals for three or four total treatments. Herd selenium status and preventive measures to address the problem should be discussed. Calves that survive for 3 days after diagnosis have a good prognosis.

Hyperkalemia

Cardiac arrhythmias or bradycardia associated with hyperkalemia are primarily observed in neonates having severe, acute diarrhea. Enterotoxigenic *E. coli* causing secretory diarrhea, metabolic acidosis, low plasma bicarbonate values, and hyperkalemia appears to be the most common causative organism. Rotavirus or coronavirus also may be involved in calf diarrhea, but they seldom produce as profound a metabolic acidosis as *E. coli* during the first few days of life.

Less common causes of hyperkalemia include severe diffuse white muscle disease involving heavy musculature of the limbs, ruptured bladders or urachal remnants leading to uroperitoneum, renal failure, urinary obstructions, and nonspecific shock.
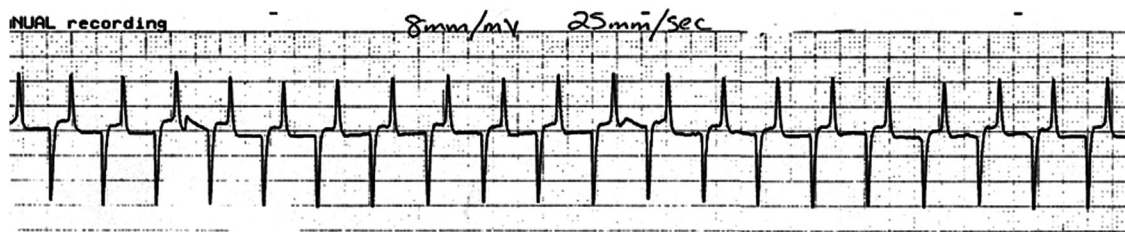
• **Fig. 3.11** Base-apex lead electrocardiographic recording in a calf with a K+ of 8.6 mEq/L. Despite the tachycardia of 130 beats/min, the peaked T waves and flattening of the P waves is very apparent.

Hyperkalemia reduces the resting membrane potential, which initially makes cells more excitable, but gradually (with further elevation in potassium and further reduction in resting membrane potential), the cells become less excitable. Atrial myocytes seem more sensitive to these effects than those within the ventricles. Cardiac conduction is affected, and several characteristic ECG findings evolve in a typical sequence that correlates well with increasing K+ values: ECG changes include peaking of the T wave, shortening and widening of the P wave, prolongation of the PR interval, eventual disappearance of the P wave, widening of the QRS complex, and irregular R-R intervals (Fig. 3.11). Atrial standstill characterized by bradycardia and absence of P waves may occur and has been documented in association with hyperkalemia in diarrheic calves. Further progression may lead to AV block, escape beats, ventricular fibrillation, asystole, and death.

In neonates, hypoglycemia is the major differential diagnosis when bradycardia is present. Septic myocarditis or white muscle disease also may be considered if an arrhythmia is present.

Calves younger than 2 weeks of age that have developed acute diarrhea, are recumbent, dehydrated, and have bradycardia or arrhythmia should be suspected of being hyperkalemic. Obviously only an acid–base and electrolyte analysis and an ECG can confirm this. However, these may not be available in the field. The consequences of underestimating the life-threatening relationship between such elevated K+ levels and pathologic bradycardia in patients are dire.

Calves suspected to be hyperkalemic based on history, physical signs, and arrhythmia or bradycardia, should receive alkalinizing fluids and dextrose. Being neonates, hypoglycemia may contribute to bradycardia when this sign is present. One way to treat metabolic acidosis and hyperkalemia is by IV infusions of 5% dextrose solution containing 150-300 mEq NaHCO$_3$/L. Usually 1 to 3 L is necessary, depending on the magnitude of the metabolic acidosis and bicarbonate deficit. Glucose and bicarbonate help transport K+ back into cells, and the glucose also treats or prevents potential hypoglycemia. After the acute crisis has been resolved, the calf may be safely treated with balanced electrolyte solutions containing potassium. Calves with diarrhea, despite having plasma hyperkalemia, have total body potassium deficits and require potassium supplementation. This may be true even in the acute phase of disease, but when serum K+ is 5.0 to 8.0 mEq/L, this is not the time
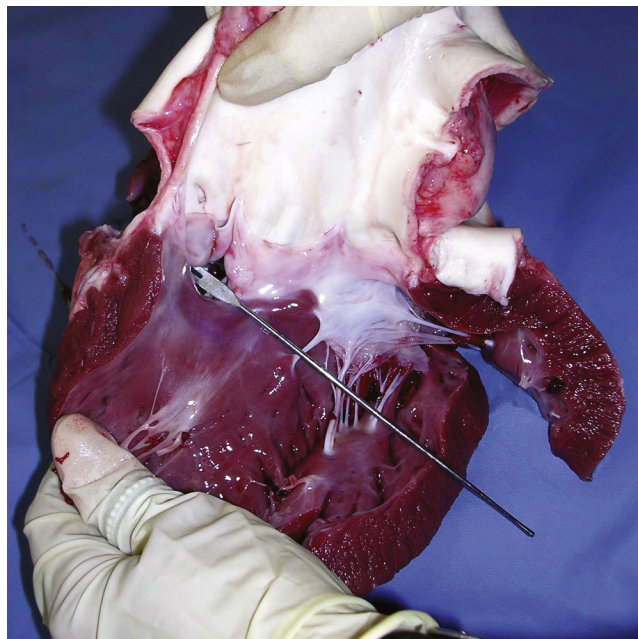
• **Fig. 3.12** Image obtained at necropsy of a calf with ventricular septal defect.

to worry about a "total-body potassium deficit." We have treated hundreds of calves as suggested earlier, and those with a venous blood pH of 7.0 or greater have a good to excellent prognosis unless they have had failure of passive transfer of immunoglobulins and subsequent septicemia. Specific insulin therapy as an adjunct to bicarbonate and glucose to correct hyperkalemia is not necessary in calves.

Congenital Heart Disease

Virtually all forms of congenital cardiac anomaly occur in cattle. Most congenital anomalies appear to be sporadic, but inheritance may play a part in some of the most common malformations. Large retrospective studies indicate that congenital cardiac defects occur in approximately 0.2% of all bovine hearts. The most common congenital anomalies in cattle appear to be VSDs (Fig. 3.12), tetralogy of Fallot, atrial septal defects (ASDs) (Fig. 3.13), and transpositions of the great vessels.

Most congenital cardiac defects cause distinct murmurs. Calves affected with the most common defects such as VSDs, ASDs, tetralogy of Fallot, or aortic or pulmonic stenosis usually have systolic murmurs. Patent ductus arteriosus
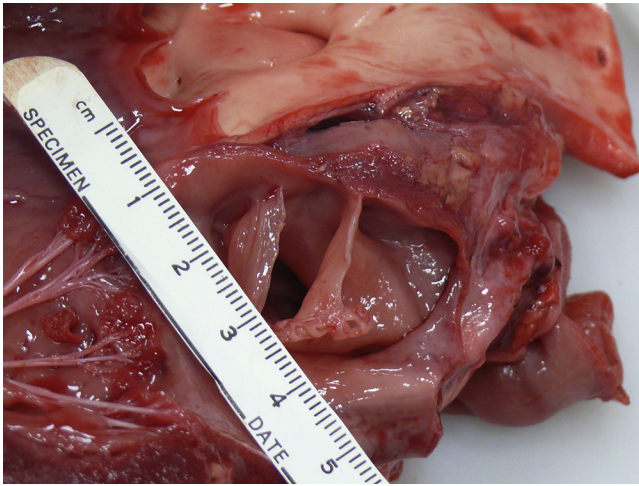
• **Fig. 3.13** Large atrial septic defect in a 3-day-old Holstein calf with multiple congenital heart defects.
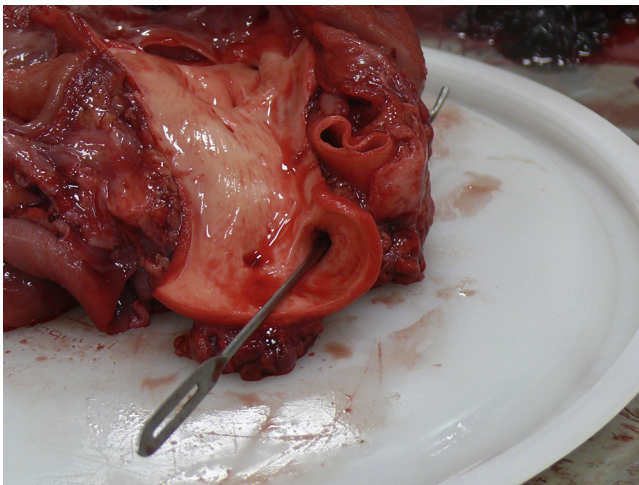
• **Fig. 3.14** Patent ductus arteriosus in the same calf from Fig. 3.13.

(Fig. 3.14), which is rare as a single defect in calves, can cause a systolic or continuous murmur.

Most calves with congenital cardiac defects appear normal at birth but eventually are noticed to have dyspnea, poor growth, or both. Many calves with congenital heart defects are eventually examined by a veterinarian because of persistent or recurrent respiratory signs or generalized ill thrift. The respiratory signs may be real in the form of pulmonary edema associated with heart failure and shunts or be caused by opportunistic bacterial pneumonia secondary to pulmonary edema and compromise of lower airway defense mechanisms. The owners may already have treated the calf one or more times for coughing, dyspnea, and fever, only to have the signs recur. Usually only one calf is affected, thus making enzootic pneumonia an unlikely diagnosis. Regardless of whether pulmonary edema or pneumonia plus pulmonary edema is present, veterinary examination usually detects tachycardia and the cardiac murmur that allows diagnosis. Venous pulsation and distention of the jugular veins may be present, but calves seldom show ventral edema as distinctly as adult cattle with heart failure.


• **Fig. 3.15** Congenital absence of the tail in a 1-day-old Holstein heifer that also had a ventricular septal defect.

Calves with congenital heart defects that do not develop respiratory signs usually still show stunting compared with herdmates of matched age. The degree of stunting varies directly with the severity of the congenital lesions in regard to blood oxygenation but usually becomes apparent by 6 months of age and is very dramatic in calves that survive to yearlings. Some cattle with small defects survive and thrive as adults, but this is rare.

Ventricular septal defects are the most common defects in dairy calves and are found in all breeds. In Guernseys and Holsteins, VSD may be linked to ocular and tail anomalies. Microphthalmos and tail defects, including absence of the tail, wry tail, or short tail, frequently signal VSD (Fig. 3.15). Sometimes ocular, tail, and cardiac defects all are present in the same calf, but it is more common to find either tail or ocular pathology plus VSD. Depending on the size of the VSD, affected calves have a variable life span. Prognosis for most is hopeless because of eventual respiratory difficulty and stunting. However, calves do, in rare instances, survive to productive adult states. The genetics of these multiple defects (eye, tail, and heart) have not been investigated in Holsteins but have been assumed to be a simple recessive trait in Guernseys.

Echocardiography is of particular value in the characterization of congenital cardiac disease. VSDs are preferentially located on the membranous part of the IVS (i.e., close to the aortic valve). For this reason, when performing echocardiography in neonates, it is important to obtain the LVOT view from the right side to correctly scan this area and observe the defect (Figs. 3.16 and 3.17 and Video Clip 3.3). The size of the defect (<2.5 cm) and velocity of blood flow through the defect (>4 m/s) have been mentioned as positive prognostic factors in horses, but no specific comparable study has been performed in cattle. More complex congenital defects such as tetralogy of Fallot may be more challenging to characterize echocardiographically without the help of an experienced operator. ASDs are less common than VSDs but are similarly identifiable from the right side (Fig. 3.18 and Video Clip 3.4).
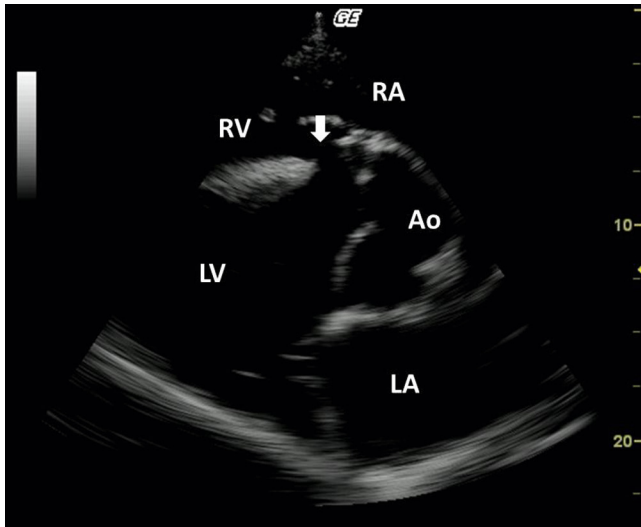
• **Fig. 3.16** Ventricular septal defect in a Holstein heifer, 10 days in milk presented with decreased milk production. The right long-axis left ventricular outflow tract view allows assessment of the membranous part of the interventricular septum. The defect *(arrow)* is observed immediately ventral to the aortic valve. *Ao,* Aorta; *LA,* left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle.
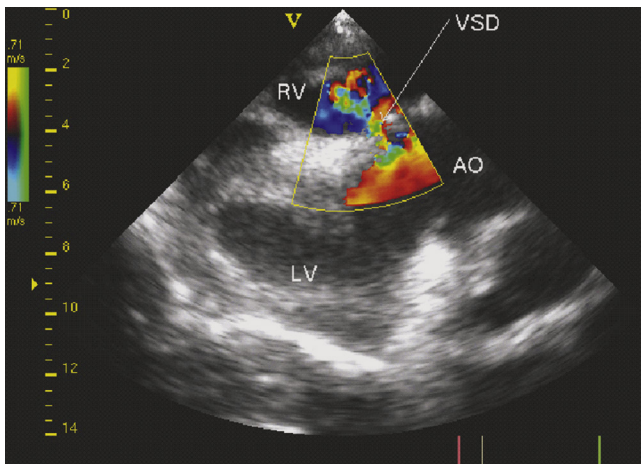
• **Fig. 3.17** Echocardiogram of heifer calf with congenital ventricular septal defect (VSD). *AO,* Aorta; *LV,* left ventricle; *RV,* right ventricle.
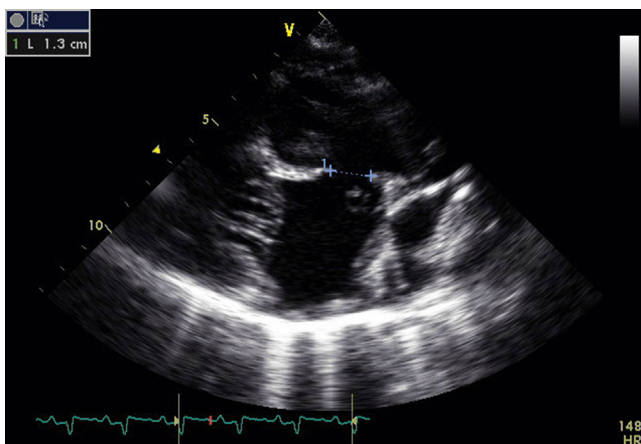
• **Fig. 3.18** Right parasternal long-axis echocardiogram of 2-week-old Holstein calf presented for dyspnea and exercise intolerance. Calipers delineate a large atrial septal defect. (Courtesy of Dr. Rebecca Stepien.)

• **Fig. 3.19** Lymphosarcoma in the heart of a cow that died as a result of multicentric lymphosarcoma. Multifocal areas of yellow-red friable tumor infiltrate are present scattered over the epicardium, great vessels, and right atrium.

Tetralogy of Fallot and other multiple congenital defects that allow right-to-left shunting of blood provoke marked exercise intolerance, cyanosis, and dyspnea and may lead to polycythemia secondary to hypoxia. The prognosis for long-term survival is grave in these calves. Ectopia cordis in a calf creates a dramatic sight, with the heart beating under the skin in the neck, but is extremely rare.

Specific Cardiac Diseases in Adult Cattle

Neoplasia

The heart is one of the common target sites of lymphosarcoma in adult dairy cattle. Many cattle with multicentric lymphosarcoma have cardiac infiltration based on gross or histologic pathology, but fewer of these cattle have clinically detectable cardiac disease. When the heart is a major target site, cardiac abnormalities are more obvious. The heart may be the only organ affected with lymphosarcoma. Therefore, detection of cardiac abnormalities coupled with other suspicious lesions (e.g., enlarged peripheral lymph nodes, exophthalmos, melena, and paresis) simply helps to make a lymphosarcoma diagnosis more definite.

Depending on the anatomic location and magnitude of the tumors, cattle with cardiac lymphosarcoma may have arrhythmias, murmurs, jugular venous distention, jugular venous pulsations, or muffling caused by diffuse cardiac or pericardial involvement. Muffling and splashing sounds are possible if a pericardial transudate or exudate is present. The most common site of tumor involvement is the right atrium, but nodular or infiltrative tumors can be found anywhere in the myocardium, pericardium, or epicardium (Figs. 3.19 to 3.21). The color and consistency of the tumors may vary. Mediastinal lymph nodes also are commonly involved. Cattle with signs of heart disease should be thoroughly examined for other lesions consistent with lymphosarcoma. When multiple lesions exist, the diagnosis is easy. However, cattle examined because of vague signs such as hypophagia
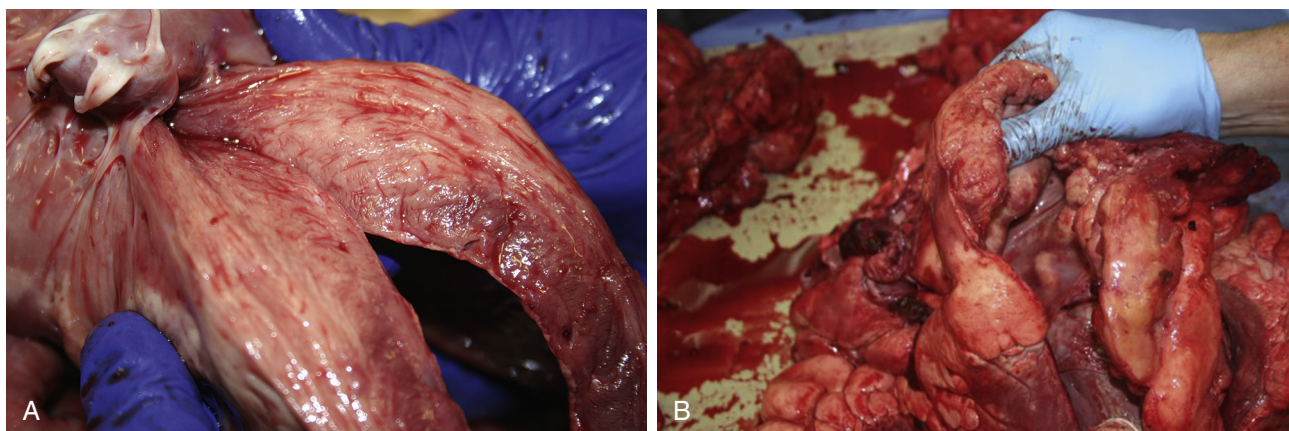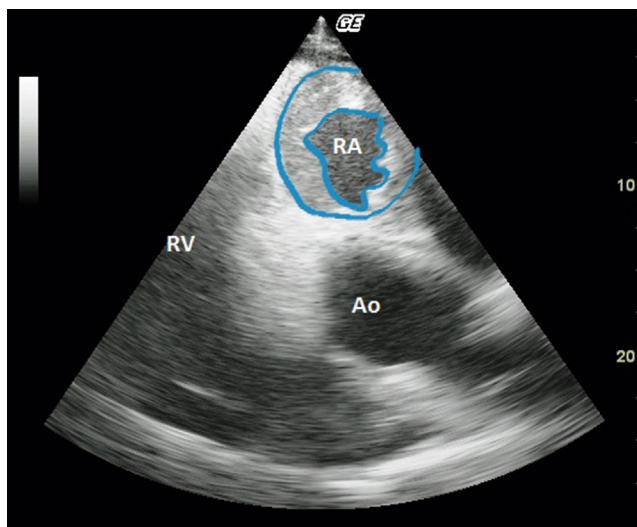
• **Fig. 3.20 A,** Right atrial myocardial infiltration by lymphosarcoma. Note the pale infiltrative neoplasia within atrial wall. **B,** More expansile and proliferative infiltrate within the atrial wall.

• **Fig. 3.21** Extensive epicardial infiltration by lymphosarcoma in a 7-year-old Holstein cow with a history of idiopathic hemorrhagic pericardial effusion. Note cardiac enlargement caused by congestive heart failure.

• **Fig. 3.22** Cardiac lymphosarcoma and right atrial thickening (right ventricular outflow tract view). The thickened and irregular atrial wall is surrounded by blue lines. The cow also presented with a homogenous, anechoic pericardial effusion. Pericardiocentesis and cytology confirmed the neoplastic etiology. *Ao,* Aorta; *RA,* right atrium; *RV,* right ventricle.

and decreased milk production that are found to have tachycardia or other cardiac abnormalities can present diagnostic challenges. Although ECGs and thoracic radiographs have seldom helped make a definitive diagnosis, echocardiography may be very helpful to image nodular or large masses of lymphosarcoma. Common echocardiographic findings include varying degrees of pericardial effusion that usually cannot be accurately distinguished from other causes of pericardial effusion by appearance alone (e.g., needs to be confirmed by pericardiocentesis) or the presence of a mass effect in the right atrial wall or atrial wall thickening (Fig. 3.22). In the case of a mass in the right atrial wall, the other important differential diagnosis would be mural endocarditis, although this is very uncommon. Thoracocentesis and pericardiocentesis to obtain fluid for cytologic evaluation are the most helpful ancillary aids when cardiac lymphosarcoma is suspected (Fig. 3.23). A complete blood count (CBC) and assessment of bovine leukemia virus (BLV) antibody status are indicated, but a positive BLV agar gel immunodiffusion (AGID), enzyme-linked immunosorbent assay (ELISA), or polymerase chain reaction (PCR) test does not ensure an absolute diagnosis because most positive cattle never develop

• **Fig. 3.23** Cytology of pericardial fluid from an adult Holstein cow with epicardial lymphosarcoma demonstrating lymphoblasts.

tumors (see the section on lymphosarcoma in Chapter 16). Therefore, simply assuming a cow with a positive BLV test and heart abnormality detected on physical examination has lymphosarcoma may be an incorrect assumption. A double line-positive BLV-AGID may add further weight to the suspected diagnosis, as would the finding of a persistent lymphocytosis (PL) in a CBC. Clinical identification of masses in other locations or cytology from thoracocentesis or pericardiocentesis provides the best means of definitive diagnosis. If both pleural and pericardial effusions can be identified, then pericardiocentesis will often provide a greater chance of identifying exfoliated neoplastic cells in cases of cardiac lymphosarcoma because pleural fluid accumulation may just reflect a transudate associated with poor cardiac function.

Fever usually is absent in cattle with cardiac lymphosarcoma. Occasionally, cattle with large tumor masses in the thorax or abdomen may have fever because of tumor necrosis or nonspecific pyrogens produced by the neoplasms. Secondary bacterial infections of the lungs or other body systems also may lead to fever, which confuses the diagnosis.

The prognosis is hopeless for cattle with cardiac lymphosarcoma, and most cattle with the disease die from cardiac or multisystemic disease within a few weeks to a few months. Successful attempts at chemotherapy have not been reported to our knowledge. One of the contributors (SB) has successfully prolonged life for up to 6 months in a few cattle with cardiac lymphosarcoma by intermittent pericardial drainage. Occasionally, valuable cattle may justify such treatment to allow a pregnancy to be completed or to be superovulated. However, as with many catabolic conditions, owners should be cautioned that maintaining the dam with advanced heart disease for more than a few weeks may produce a gestationally dysmature fetus even if the pregnancy is carried to term or may seriously affect the cow's ability to superovulate or even produce viable oocytes for in vitro fertilization. There is also the risk of vertical transmission of BLV from dam to fetus in utero, which is greater if the dam has clinically apparent tumors. In one late pregnant cow with severe pericardial effusion caused by lymphosarcoma, we were able to maintain the cow for several weeks by surgically opening the pericardial sac into the pleural cavity, which significantly improved venous return to the heart and the overall condition of the cow, permitting delivery of a healthy calf. The cow was also treated with isoflupredone.

Neurofibroma, although uncommon, frequently causes arrhythmia and variable intensity of heart sounds in affected cattle and bulls. Furthermore, the cardiac arrhythmia may coexist with paresis or paralysis caused by neurofibroma masses in the spinal canal. Because lymphosarcoma more commonly causes paresis coupled with cardiac disease, this combination of signs is more suggestive that lymphosarcoma is present. Although perhaps a moot point because both diseases are fatal, further medical workup of patients with neurofibroma fails to provide confirmation of lymphosarcoma. To date, postmortem examination has been the only means of definitive diagnosis for cardiac neurofibroma. Examiners talented in ultrasonography may be able to diagnose these lesions based on the typically gnarled, raised cords of tumor involving the cardiac nerves. One of the authors (SP) has also seen a single case of a neuroendocrine tumor (chemodectoma) in an adult bull, which presented with signs of congestive heart failure associated with a massive, hemorrhagic pericardial effusion and tamponade (Fig. 3.24).

Myocardial Disease
Infections
Septic Myocarditis
Neonatal septicemia caused by gram-negative bacterial organisms, acute infection with *Histophilus somni*, and chronic infections in any age of cattle resulting from *Trueperella pyogenes* are the most common cause of septic myocardial lesions in cattle. Septicemic calves, calves suspected of having

• **Fig. 3.24 A,** Mature Holstein bull presented with signs of cardiac tamponade caused by hemopericardium associated with a large heart base neuroendocrine tumor (chemodectoma). **B,** Gross postmortem image showing the large heart base tumor and extensive local infiltration. (Courtesy of Dr. Howard Steinberg.)

H. somni infection, and calves with chronic infections should be suspected of having septic myocarditis if an arrhythmia or other signs of abnormal cardiac function develop during their illness. White muscle disease, hyperkalemia, and hypoglycemia should also be considered in the differential. Septicemic calves have a guarded prognosis, and septic myocarditis worsens it. Foci of septic myocarditis in adult cattle with chronic, active infection or abscesses associated with mastitis, localized peritonitis, foot lesions, or chronic pneumonia are more commonly identified by pathologists than clinicians. Although tachycardia is likely to be present, this finding often is assumed to result from the primary illness rather than from myocarditis. As with calves, adult cattle with septic myocarditis may have paroxysmal cardiac arrhythmias that alert the clinician to the diagnosis. Definitive diagnosis has been difficult in the living patient, but increased concentrations of troponin I may be used to help diagnose myocardial disease. An ECG showing atrial or ventricular premature depolarizations in a calf or cow with evidence of sepsis or a walled-off infection can be used to lend credence to the diagnosis. Although bovine echocardiography does not have the same diagnostic utility for myocardial disease as it does for endocardial and pericardial conditions, it can still be of some value, particularly in cases of cardiomyopathy or myocardial mass lesions such as lymphosarcoma and myocardial abscesses. In all cases of myocardial injury, whether it is toxic (ionophore, gossypol, other toxic plants), nutritional (white muscle disease) or inflammatory (*H. somni*), disease progression will ultimately be accompanied by cardiac dilation and resultant nonspecific echocardiographic changes if the animal survives the acute injury. Presumably, the right ventricular hypertrophy that accompanies high-altitude pulmonary hypertension in brisket disease of cattle maintained at elevation in the western United States might also be associated with identifiable echocardiographic abnormalities.

Treatment of the primary disease remains the most important part of managing septic myocarditis. If the primary problem and myocardial lesion can be sterilized, the heart may return to normal function. Myocardial fibrosis and scarring may, however, leave the animal with a permanent arrhythmia and increase the likelihood of cardiomyopathy and eventual congestive heart failure.

Septic myocardial disease of adult cattle, as in calves, usually follows septicemia or chronic infections. Septicemic spread of infectious organisms, thrombi, or mediators of inflammation may be involved in the pathophysiology of myocardial injury that occurs in septic cattle. Although relatively uncommon, development of persistent tachycardia with or without an arrhythmia in a patient with infectious disease may suggest myocarditis. Tachycardia is so nonspecific that most veterinarians attribute the tachycardia to the primary disease rather than secondary myocarditis. Only when the myocardial damage causes signs of heart failure does a diagnosis of myocarditis become easier. Acute death is possible. Arrhythmia, if present, must be assessed using ECG alongside blood electrolytes and acid–base status to rule out atrial fibrillation associated with metabolic abnormalities. Adult dairy cattle

are most at risk for myocarditis with acute septic diseases such as severe mastitis, metritis, pneumonia, and infection caused by *H. somni*. Occasional cases also occur secondary to chronic localized infections such as digital abscesses that predispose to bacteremia. Depending on the size and location of the myocardial lesion, clinical signs range from subclinical to overt heart failure. ECG evidence of ventricular arrhythmias would suggest myocardial damage, but supraventricular arrhythmias are possible as well. Unfortunately, definitive antemortem diagnosis is impossible without advanced echocardiographic or invasive cardiac techniques. Treatment must be directed at the primary disease. Minor myocardial lesions away from nodal and conduction tissue may heal or fibrose asymptomatically, whereas large or multifocal lesions may lead to heart failure, persistent tachyarrhythmia, or sudden death. Although rarer than septic myocardial injury it is also possible to see myocarditis secondary to severe anemia in which an ischemic injury caused by insufficient oxygen delivery to cardiac myocytes has occurred. In this instance, it is also easy to attribute the tachycardia to the primary disease, but the observant clinician may pick up on this possibility when a tachyarrhythmia is auscultated or seen on ECG in an animal with peracute to acute hemorrhage.

Toxins

Ionophores such as monensin and lasalocid are capable of damaging myocardial and skeletal muscle when ingested in toxic amounts. Improper mixing of ionophores into rations is the most common error that may lead to toxicity, but accidental exposure to concentrated products also is possible. Obviously, this is a potential concern for calves and heifers being fed milk replacer or feeds containing ionophores. Fortunately, cattle (except for water buffalo) are much more resistant to the toxic effects of ionophores than are horses, but there is a relatively narrow margin of safety, especially in young calves. Abnormal echocardiographic findings have been reported during experimental intoxication with monensin sodium by Varga and coworkers. Decreased cardiac chamber size and altered left ventricular function were evident from 48 to 120 hours after administration when monensin was fed daily at approximately 25 to 50 times therapeutic levels. The authors noted a significant decrease in the left ventricular shortening fraction as well as a decrease in ejection fraction, which, taken together, are indicators of altered systolic function.

Many poisonous plants are theoretically capable of myocardial injury, but in reality, few are likely to be encountered because of increased confinement of heifers and adult cattle. *Eupatorium rugosum* (white snakeroot), *Vicia villosa* (hairy vetch), *Cassia occidentalis* (coffee senna), *Phalaris* spp., and others are capable of toxic myocardial damage. Gossypol also is capable of causing myocardial damage when fed in toxic amounts. This fact is of special concern given the increased incidence of feeding cottonseed to dairy cattle. Copper deficiency, especially when chronic, occasionally has been linked to acute myocardial lesions, resulting in death ("falling disease" in Australia). Although commonly fed as a byproduct to cattle without ill effect, citrus pulp fed as silage caused granulomatous

cardiac and lymphoid disease in cattle on one farm. Many other organic and inorganic toxins have the potential for causing myocardial damage but create more obvious pathology in other body systems and thus will not be discussed here.

No specific treatment is available for toxic myocarditis. Common sense dictates identification and removal of the toxin from the environment alongside immediate administration of laxatives, cathartics, or protectants to decrease absorption and accelerate intestinal transit. Vitamin E and selenium administration and specific supportive treatment for cardiac disease should be instituted, but the prognosis for animals already demonstrating signs of congestive heart failure is grave.

Parasitic and Protozoan Infections

Cysticerca bovis may cause myocardial lesions, but these appear rarely in dairy cattle in the northern United States. This is the larval form of *Taenia saginata,* the common human tapeworm. Contamination by human sewage of feedstuffs, pastures, or fields puts cows at risk for this disease.

Although *Toxoplasma gondii* is capable of infecting cattle, clinical disease appears rare because cattle rapidly eliminate the parasite from tissue. Cattle are exposed to, and infected by, *T. gondii* via ingestion of feedstuffs contaminated by cat feces.

Sarcocystis spp. are a relatively common cause of myocardial disease in cattle. Although most infestations are asymptomatic, clinical illness characterized by hemolysis, myopathy, myocarditis, weight loss, rattail, and other signs is possible. *Sarcocystis* spp. require two hosts, and carnivores or humans usually are the hosts that shed sporocysts in fecal material that subsequently contaminates cattle feed (see Chapter 16). Cattle then become the intermediate host as intermediate stages of the parasite invade endothelial cells and later stages encyst in muscle, including the myocardium. Subsequent ingestion by carnivores of beef-containing cysts continues the life cycle.

Histopathologic identification of *Sarcocystis* cysts in myocardium of cattle is very common but seldom deemed clinically significant. Certainly, however, heavy exposure to the organism could provoke significant myocardial damage.

Parasitic or protozoal myocarditis usually requires histopathology or serology for diagnosis. Treatment would be best provided by preventive measures to avoid contamination of cattle feeds by carnivore or human feces.

Inherited Myocardial Disease

A dilated cardiomyopathy has been described in Holstein-Friesians in Canada, Japan, and Switzerland. In Switzerland, the disease affects the Fleckvieh and Red Holstein breeds, too. An autosomal recessive mode of inheritance is suggested, associated with a gene-rich locus on bovine chromosome 18, and it has been traced back to a red factor-carrying Holstein-Friesian bull. This condition manifests itself as heart disease between 19 and 78 months of age. Although most cattle develop clinical signs within 4 years of birth, some have lived for 6 to 7 years.

Most cases are presented because of signs referable to heart failure such as ventral edema, exercise intolerance, inappetance, dyspnea, tachycardia, muffled heart sounds, and jugular and mammary vein distention and pulsation. Although tachycardia is fairly consistent, other auscultation findings such as arrhythmias, murmurs, or varying intensity of the heart sounds may occur in individual cases. Hepatomegaly consistent with chronic passive congestion of the liver secondary to right heart failure is also present in some patients.

Echocardiography and ECG recordings are required for diagnosis. Ultrasonography is the best aid to confirm dilated cardiomyopathy.

Long-term prognosis is hopeless, but affected cattle may be helped in the short term by management with cardioglycosides, and furosemide is indicated if pulmonary edema exists. McGuirk suggests digoxin at 0.86 µg/kg/hr as an IV infusion. This obviously requires diligence, IV catheterization, and hospitalization or else a very attentive owner. Alternatively, 3.4 µg/kg IV every 4 hours may be used but creates greater variation in blood levels and increases the risk of digoxin toxicity. Furosemide is used at 0.5 to 1.0 mg/kg twice daily if pulmonary edema is present. Inappetent cattle may benefit from 50 to 100 g KCl orally each day to maintain potassium levels when being treated with digoxin. Ideally, acid–base and electrolyte status should be assessed daily or every other day by blood sample.

Endocarditis

Etiology

Bacterial endocarditis is the most common valvular or endocardial disease in adult dairy cattle. It also is one of the few treatable heart conditions of cattle. Therefore early suspicion, diagnosis, and appropriate treatment improve the prognosis.

Cattle with chronic infections such as septic musculoskeletal conditions, hardware disease, soft tissue abscesses, lactic acid indigestion, chronic pneumonia, metritis or mastitis, and thrombophlebitis are at risk for bacterial endocarditis. In addition, cattle with long-term IV catheters have increased risk of endocardial infections. Bacteremia appears essential to the pathophysiology of bacterial endocarditis in cattle.

T. pyogenes has been the most common organism isolated from the blood and endocardial lesions of cattle affected with endocarditis, but *Streptococcus* spp., *Staphylococcus* spp., and gram-negative organisms may also cause the disease. A recent report identified *Helcococcus ovis*, a facultative gram-positive anaerobe and member of the family *Peptostreptococcaceae,* in up to one-third of bovine endocarditis lesions in a large study from Europe; many of these cases were mixed infections with other more historically typical species such as *T. pyogenes.* The right AV valve (tricuspid) is the most commonly infected valve with the left AV (mitral valve) being the second most common (Fig. 3.25). Other valves or the endocardium adjacent to valves may also occasionally be the site of infection (Fig. 3.26). Owner complaints regarding affected cattle include recurrent fever, weight loss,
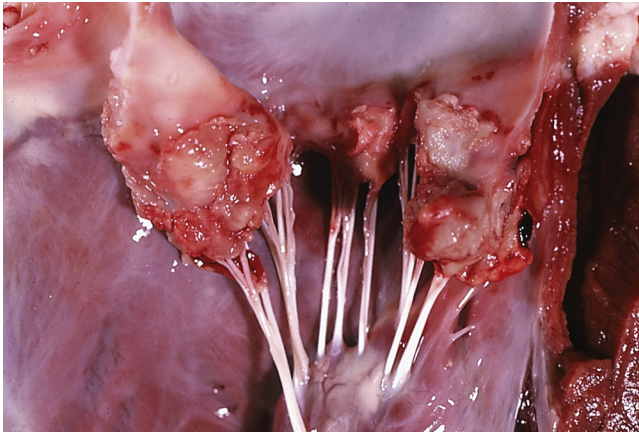
• **Fig. 3.25** Bacterial valvular endocarditis with vegetative lesions in a cow. (Courtesy of Dr. John M. King.)
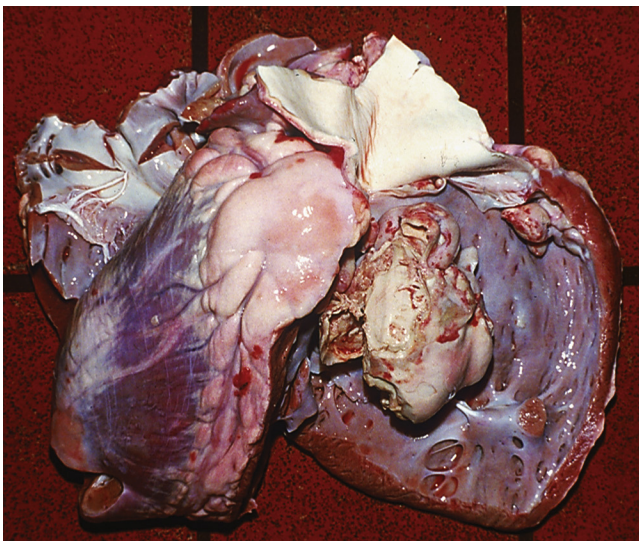
• **Fig. 3.26** Large vegetative endocarditis lesion involving the valves and adjacent endocardium in the ventricle. (Courtesy of Dr. John M. King.)

anorexia, poor production, and sometimes lameness independent of conventional foot or musculoskeletal problems.

Signs

Persistent or intermittent fever, tachycardia, and a systolic heart murmur are the most common signs found in cattle having endocarditis. A "pounding" heart or increased intensity of heart sounds also is common, although the heart sounds may vary in intensity or even be reduced in some patients. Vegetative endocarditis may also occur in the absence of an auscultable murmur, underscoring the diagnostic utility of cardiac ultrasonography in a patient with physical examination findings such as fever and tachycardia with or without arrhythmia that raise suspicion of infectious cardiac disease.

Some cattle with endocarditis appear painful when digital pressure is exerted on the chest wall over the heart region. Fever usually is present, has been present historically, or develops intermittently after initial examination. Some cattle with endocarditis never have fever recorded but do show other signs of illness and a systolic heart murmur or other cardiac signs.

Signs of heart failure may develop along with increased distention and pulsations of the jugular and mammary veins (Fig. 3.27). Tachycardia is a consistent finding, and dyspnea may develop, especially after bacterial showering of the lungs. Arrhythmias are unusual and paroxysmal but may be observed in approximately 10% of patients.

Lameness, often shifting, and stiffness may be observed. Synovitis and joint tenderness sometimes are obvious, but in other patients, exact localization of the lameness is difficult. Bacteremia to joints or epiphyses and immune-mediated synovitis have been suggested as origins of this lameness in patients with endocarditis.

Laboratory Data

Nonregenerative anemia commonly results from chronicity of the primary infection, the endocardial infection, or both. Neutrophilia is common and was found in 24 of 31 cases in one report, and absolute leukocytosis was found in 14 of 31. In this same report, serum globulin values were greater than 5.0 g/dL in 19 of 23 patients with endocarditis that had globulin measured. Elevated globulin was believed to be consistent with the chronicity of infection.

Blood cultures are an important diagnostic test, but echocardiography provides the definitive diagnosis. A patient suspected of having endocarditis should have a series of blood cultures submitted rather than a single time-point sample. Although blood culture results in adult cattle may be negative in as many as 50% of endocarditis patients tested, isolating the causative organism from the bloodstream provides the best opportunity for appropriate and successful treatment with a specific antibiotic. Venous blood cultures should be collected after the jugular vein has been clipped and prepared aseptically. The cow should have been held off systemic antibiotics for 24 to 48 hours before culture, if possible. Although one blood culture attempt is better than none, it is preferable to obtain a series of three to four cultures when economics allow. An appropriate interval between collections of multiple samples has been debated by clinicians for decades. Some clinicians culture only during a fever spike, some at 3- to 30-minute intervals, some at 6- to 8-hour intervals, and some once daily. We prefer to obtain three cultures at 30-minute intervals in febrile patients and at intervals of several hours in nonfebrile patients suspected of having endocarditis.

Diagnosis

Early signs of reduced appetite and production, fever, and tachycardia certainly are not specific for endocarditis. A pounding heart or systolic murmur should suggest the diagnosis and dictate further specific cardiac workup. The diagnosis may be overlooked because of more obvious primary problems such as abscesses, an infected digit or other musculoskeletal infection, suspected hardware disease, or thrombophlebitis because these conditions may also cause fever and nonspecific signs of illness. Therefore heart murmurs, a pounding heart, or
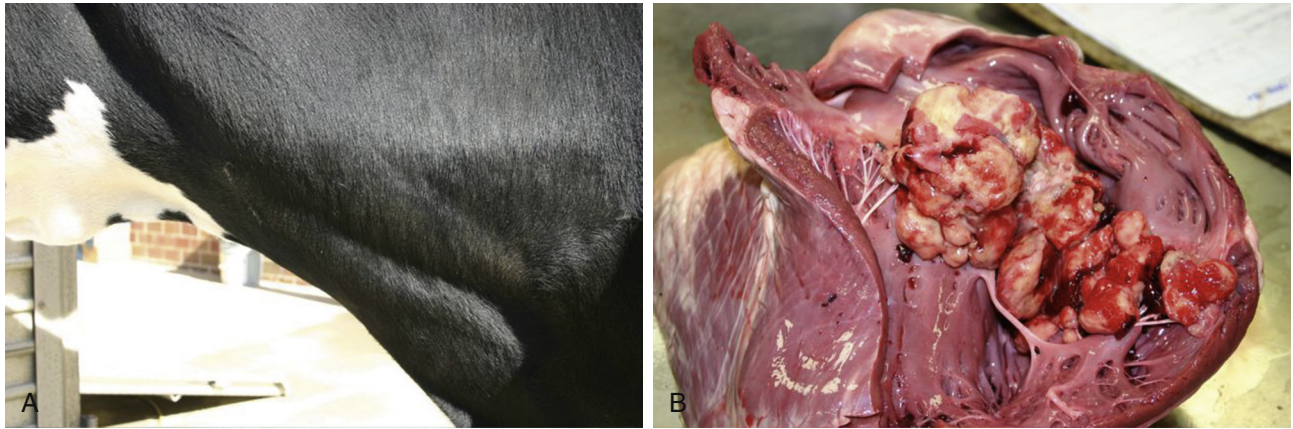
• **Fig. 3.27** Distended jugular vein (**A**) of a mature Holstein cow with extensive endocarditis involving the right atrioventricular valve leaflets and associated endocardium (**B**).

early signs of heart failure in addition to tachycardia merit consideration of the diagnosis of endocarditis. Lameness and stiffness may be difficult to differentiate from primary musculoskeletal disease or the painful stance caused by peritonitis but these can be important clinical signs that aid diagnosis. Because of fever, tachycardia, and sometimes polypnea, cattle having endocarditis often are misdiagnosed with pneumonia or traumatic reticuloperitonitis.

The diagnosis of endocarditis is often suggested by the patient's history and clinical signs. However, a positive blood culture and echocardiography allow definitive diagnosis. Blood cultures, as mentioned previously, may or may not be successful; however, when positive, they allow appropriate selection of antibiotics. Definitive diagnosis based on two-dimensional echocardiography has proved to be one of the most impressive uses of ultrasonography since its more widespread use began about 10 years ago. Veterinarians trained in echocardiography now have a tool to confirm bacterial endocarditis in most patients. The echocardiographic examination should be performed mindful of the fact that endocarditis involves the valvular endocardium in more than 98% of reported cases; mural lesions being extremely rare. As pointed out in a systematic review of published cases by Buczinski et al. (2012), the tricuspid valve is the most commonly affected valve (49.5%) followed by the mitral (29.7%), the pulmonary (13.7%), and aortic (7.5%) valves; information that can be particularly useful in directing the examination when performing echocardiography in cattle with an auscultable murmur. The typical endocarditic lesion will be an irregular valvular thickening with heterogeneous content and a shaggy appearance. Depending on the clinical findings and the resultant, but not invariant, murmur (auscultated in ≈60% of cases), the best views should be selected to image the suspicious valve. Most of time, it is obvious that the valve is abnormal and more than 1 cm thick (Figs. 3.28 to 3.30).

Treatment

Long-term antibiotic therapy is required to cure bacterial endocarditis in cattle. Thus, cattle selected for treatment
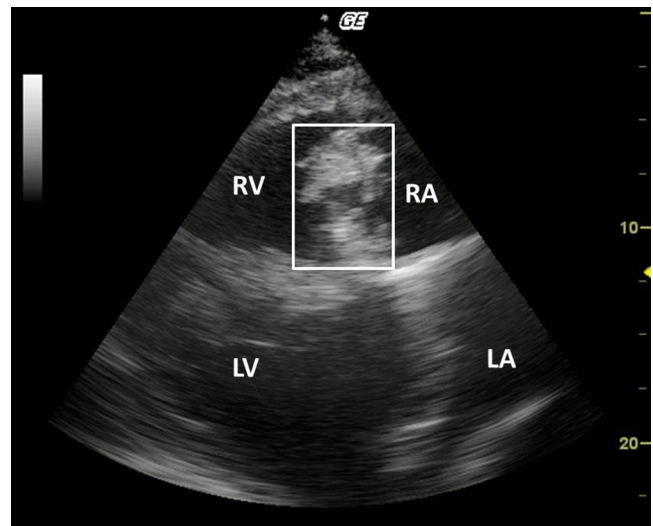
• **Fig. 3.28** Tricuspid valve endocarditis, right, four-chamber long-axis view. The tricuspid valve is irregularly thickened (as outlined by the white box). Secondary right ventricular dilation is suspected based on the relative size of the right and left ventricular (RV and LV) lumina. *RA,* right atrium; *RV,* right ventricle.

• **Fig. 3.29** Echocardiographic image of endocarditis of the tricuspid valve of a cow.
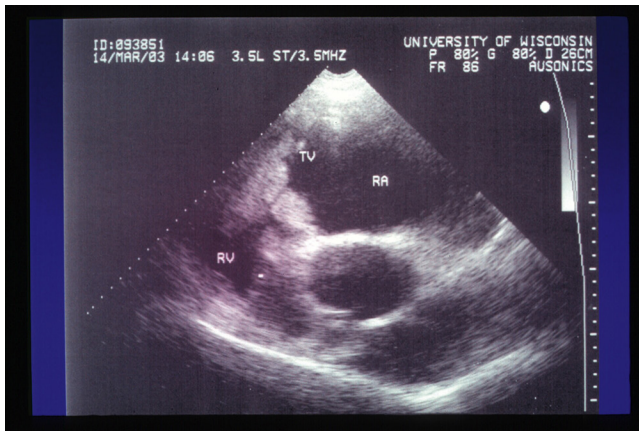
• **Fig. 3.30** Echocardiographic image of vegetative endocarditis of the tricuspid valve (TV) of a mature Holstein cow. *RA,* right atrium; *RV,* right ventricle.

must be deemed valuable enough to justify the cost of antibiotics and discarded milk that will be incurred. A successful blood culture allows selection of an appropriate antibiotic based on sensitivity or mean inhibitory concentration (MIC) values. Because endocarditis in cattle usually is caused by *T. pyogenes* or *Streptococcus* spp., some clinicians assume penicillin will work and do not bother to do blood cultures. This assumption would be a worthwhile gamble if economics dictate that laboratory costs must be minimized.

Therefore, penicillin and ampicillin have historically been the drugs of choice for bacterial endocarditis in cattle caused by *T. pyogenes* and most *Streptococcus* spp. Although ceftiofur has the advantage of limited withdrawal times, depending on formulation, it is more expensive, is not approved for this use and might be overused by some who hope the drug will cure all infections of dairy cattle. Penicillin (22,000–33,000 U/kg twice daily) or ampicillin (10–20 mg/kg twice daily) (both are extralabel dosages) is administered for a minimum of 3 weeks. If gram-negative organisms or penicillin-resistant gram-positive organisms are isolated from blood cultures, an appropriate bactericidal antibiotic should be selected based on MIC or antibiotic sensitivity testing.

Based on work by Dr. Ray Sweeney and others at the University of Pennsylvania, rifampin (rifamycin) has been shown to establish therapeutic blood levels after oral administration to ruminants. Unfortunately, there is significant variability in blood levels between treated cattle, which may limit its treatment potential. Rifampin is a unique antibiotic that gains access to intracellular organisms or walled-off infections by concentrating in macrophages. Rifampin always should be used in conjunction with another antibiotic because bacterial resistance may develop quickly when the drug is used alone. The dosage is 5 mg/kg orally, twice daily for cattle. Although some maintain this dosage is too low, it has seemed effective clinically when used in conjunction with penicillin not only for chronic *T. pyogenes* endocarditis but also for pulmonary abscesses. Therefore, if economics allow, oral rifampin has been reported to improve treatment success in cattle with bacterial endocarditis. Unfortunately, currently within the United States, the Food and Drug

Administration requires that cattle treated with rifampin are not used for either commercial milk or meat production, severely limiting its use. Occasionally, cattle will become significantly anorectic while receiving rifampin (more so than was noted in association with the primary disease), but in many cases, this apparent intolerance to the drug is overcome if administration is discontinued for several days and then reinstituted at the same or lesser dose.

In addition to antibiotic therapy, cattle showing venous distention, ventral edema, or pulmonary edema require judicious dosages of furosemide. Because many patients with endocarditis have reduced or poor appetites, overuse of furosemide may lead to electrolyte depletion (K^+, Ca^{2+}) and dehydration. Therefore when furosemide is used, the drug should be administered on an "as-needed" basis, and 0.5 mg/kg once or twice daily usually is sufficient.

Because cattle with endocarditis often appear painful or stiff and may have either primary musculoskeletal disorders or secondary shifting lameness, aspirin is administered at 240 to 480 grains orally twice daily. Unfortunately, aspirin does not appear to minimize platelet aggregation in cattle and is unlikely to prevent further enlargement of vegetative lesions. Ketoprofen (3 mg/kg IM) has been documented to decrease thromboxane A2 in cattle suggesting it may have some antiplatelet effect. Free access to salt should be denied for cattle showing signs of congestive heart failure.

Antibiotic treatment continues for a minimum of 3 weeks. Positive signs of improvement include increasing appetite and production, as well as absence of fever. The heart murmur persists and may vary as treatment progresses. Resolution of the heart murmur and tachycardia coupled with echocardiographic evidence of resolution of the endocarditis lesions are excellent prognostic signs. Many cows that survive are, however, left with persistent subtle or obvious heart murmurs caused by valvular damage alongside an abnormal echocardiographic appearance to the affected valve. This should not be a concern as long as other signs indicate resolution of infection and heart failure is not present. Cattle with venous distention, ventral edema, or other signs of right heart failure have a worse prognosis than cattle diagnosed before signs of heart failure. However, mild to moderate signs of heart failure should not be interpreted to infer a hopeless prognosis because supportive treatment may alleviate these signs while antibiotic therapy treats the primary condition. Cattle with severe lameness, either as a result or as the cause (i.e., septic joint or tendon) of endocarditis, have a poor prognosis.

The prognosis for patients with endocarditis is guarded at best. Sporadic case reports tend to highlight successfully managed individual cases, but further case series are necessary to suggest accurate recovery rates. Of 31 cattle affected with endocarditis that were admitted to Cornell's hospital between 1977 and 1982, 9 responded to long-term antibiotic (8 penicillin and 1 tetracycline) therapy. Based on these data and the experience of other clinicians, the prognosis is better when the diagnosis is made early in the course of the disease. Repeated echocardiographic examination allows for monitoring and reassessment of the valvular lesions during and
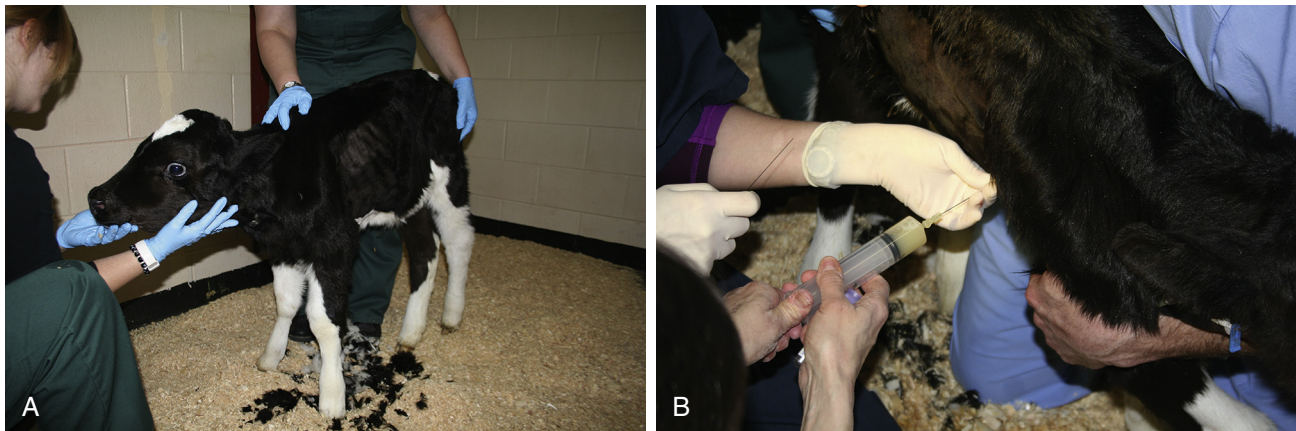
• **Fig. 3.31** Three-week-old Holstein heifer calf with septic pericarditis (**A**). Pericardial sac enlargement was sufficient to allow drainage via the right sixth intercostal space with the calf restrained and the right elbow pulled well forward (**B**).
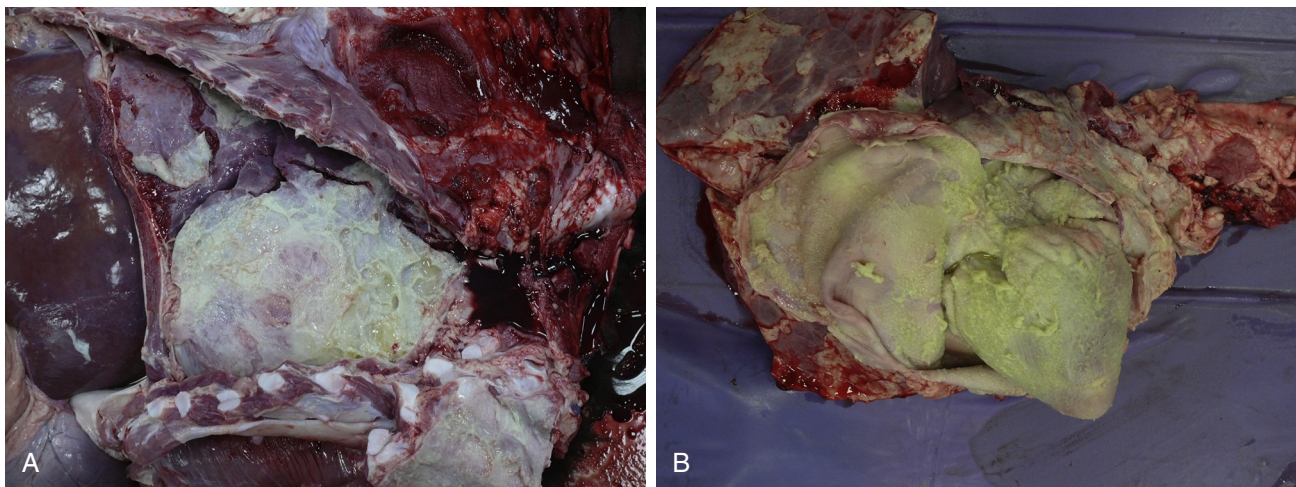
• **Fig. 3.32** Weanling age calf with septic pleuropneumonia (**A**) and septic pericarditis (**B**) associated with *Mannheimia haemolytica* sepsis.

after treatment. With experience and the correct software, ultrasound examination also allows for specific evaluation of cardiac function (e.g., atrial diameter, fractional shortening) that may more accurately assess the degree of cardiac dysfunction and provide valuable prognostic information.

Septic Pericarditis
Etiology

The most common cause of pericarditis in dairy cattle is puncture of the pericardium by a metallic linear foreign body that originated in the reticulum. It is apparent during laparotomy and rumenotomy in cattle that the heart lies very close to the diaphragmatic region of the reticulum. Therefore, traumatic reticuloperitonitis occasionally causes septic pericarditis. Hardware that penetrates the reticulum in a cranial direction may puncture the pericardium or impale the myocardium. It can also infect the mediastinum or puncture a lung lobe. Both the foreign body and the tract of its migration can "wick" bacterial contaminants into the pericardial fluid, resulting in fibrinopurulent pericarditis.

Fibrinous pericarditis can also occur in septicemic calves (Fig. 3.31) or cattle having severe bacterial bronchopneumonia (Fig. 3.32). These forms of pericarditis only occasionally cause clinically detectable fluid accumulation and seldom lead to overt signs of heart failure as are typical in traumatic pericarditis.

Signs

Signs of traumatic pericarditis include venous distention and pulsation, ventral edema, tachycardia, and muffled heart sounds bilaterally (Fig. 3.33). Fever is usually, but not always, present. Tachypnea and dyspnea may be present in patients with septic pericarditis and advanced heart failure. Cattle having traumatic pericarditis are often reluctant to move, appear painful, and have abducted elbows.

Direct pressure or percussion in the ventral chest or xiphoid area elicits a painful response by the cow with traumatic pericarditis. Dyspnea is caused by a combination of lung compression by the enlarged pericardial mass, pulmonary edema, and reduced cardiac output. Auscultation of the heart reveals bilaterally decreased intensity of the heart

• **Fig. 3.33** Anxious expression and severe ventral edema in a cow with traumatic pericarditis.

sounds. This muffling of heart sounds usually coexists with squeaky, rubbing sounds and splashing or tinkling sounds, but these sounds are not present in all cases. A fluid–gas interface created by gas-forming bacterial organisms in the pericardium creates the most obvious splashing sounds. Lung sounds may not be heard in the ventral third of either hemithorax because of the greatly enlarged pericardial sac displacing the lungs dorsally. In addition to these signs, there are two other very important clinical facts associated with traumatic pericarditis in dairy cattle:

1. Most cows with traumatic pericarditis were observed by the owner to be ill 7 to 14 days earlier and may or may not have been diagnosed with traumatic reticuloperitonitis at that time. Frequently, the signs of illness were vague and nonspecific, and veterinary attention may or may not have been requested. Typically, these cattle improve or appear recovered from this previous illness only to become ill again and have signs of cardiac disease. Certainly not all cattle have this two-phased clinical course, and some have peracute pericarditis or traumatic myocarditis and die within hours or days. When the history supports a two-phased clinical disease, it is assumed the cow transiently "felt better" after the foreign body left the reticulodiaphragmatic area and entered the chest, thereby alleviating the peritoneal pain and inflammation. Subsequently, worsening sepsis in the pericardial sac and eventual heart failure causes the second phase of disease that generally moves the owner to seek veterinary consultation.

2. During the acute and subacute phases of traumatic pericarditis, heart sounds may change on a daily basis. Muffling, tinkling, splashing, rubs, murmurs, and other sounds all may be present on one day, absent the next, and present again later. Pathology is dynamic as the relative amounts of fibrin, purulent fluid, and gas in the pericardium change. Chronic cases, on the other hand, tend to have bilateral muffling of heart sounds and a "far away" tinkling as fluid pus is jostled by heartbeats.

Laboratory Data

If the disease is subacute or chronic, neutrophilia is usually present. Cattle afflicted for longer than 10 to 14 days

usually have decreased serum albumin and increased serum globulin; therefore, total protein values are at least high normal and usually elevated. Hyperfibrinogenemia is typically present at all stages of the disease. Other, non-septic causes of pericardial effusion, such as cardiac lymphosarcoma and idiopathic hemorrhagic pericardial effusion, generally have normal fibrinogen and globulin concentrations. Thoracic radiographs, although largely unavailable in the field, often dramatically demonstrate a greatly enlarged pericardium, fluid line, and gas cap above the fluid line. The causative metallic foreign body also may be apparent unless obscured by radiopaque pericardial fluid, fibrin, and the cardiac shadow (Fig. 3.34). Serum liver enzymes may be elevated with pericardial effusions, regardless of the cause, especially when congestive heart failure accompanies the pericardial effusion, often caused by tamponade (Fig. 3.35).

Diagnosis

Although the clinical signs and cardiac auscultation of cattle with traumatic pericarditis usually are sufficient for diagnosis, definitive diagnosis in the field can be accomplished by two-dimensional echocardiography, pericardiocentesis, or both procedures. Thoracic radiographs, if available, also may be definitive. Fluid and fibrin in the pericardial sac are easily visualized with two-dimensional echocardiography (Figs. 3.36 and 3.37). Heavy accumulation of fibrin coats the epicardium and visceral pericardium (Fig. 3.38). This fibrin frequently has the appearance of "scrambled eggs" when seen on postmortem examination (Fig. 3.39). Depending on the severity and stage of the disease secondary ultrasonographic signs of cardiac tamponade can be observed with ventricular collapse during diastole, atrial collapse during ventricular systole or a "swinging heart." Septic pericarditis (either traumatic after hardware disease or secondary to contiguous pulmonary infection), cardiac lymphosarcoma, and idiopathic hemorrhagic pericardial (IHP) effusion are the most common causes of pericardial effusion in cattle. In all cases, a pericardiocentesis under ultrasonographic guidance should be performed to characterize the nature of the pericardial effusion. Other physical examination and clinicopathologic data often heavily suggest the pathogenesis for each of these differentials, but definitive diagnosis is almost always provided by simple cytologic examination of a sample of the effusion.

Pericardiocentesis can be performed with an 18-gauge, 8.75-cm spinal needle or chest trochar of similar length in the left fifth ICS. After clipping and standard preparation of the left thorax, a skin puncture is performed with a scalpel in the fifth ICS just dorsal to the elbow. If continuous drainage is desired, a 20-Fr chest trochar and catheter may be introduced into the pericardium for further drainage. The fluid obtained is purulent and fetid with septic reticulopericarditis. Fibrin clots frequently obstruct flow of the fluid through finer gauge needles or catheters. The purulent fluid greatly exceeds normal values for pericardial fluid (normal; protein <2.5 g/dL, white blood cell count [WBC] ≤ 5000/μL), and neutrophils are the major cellular
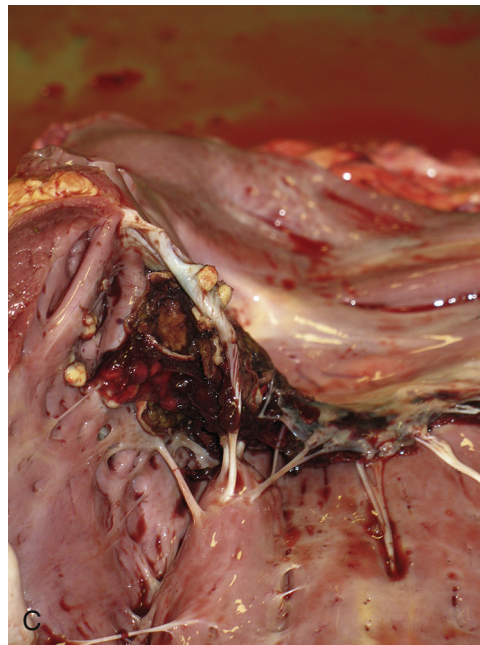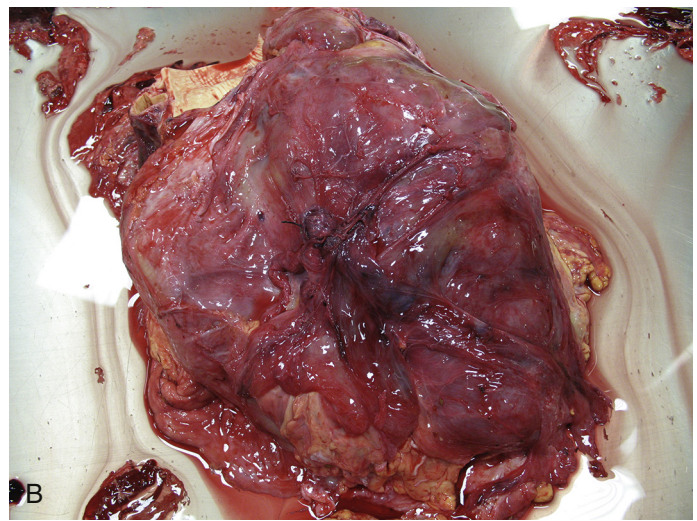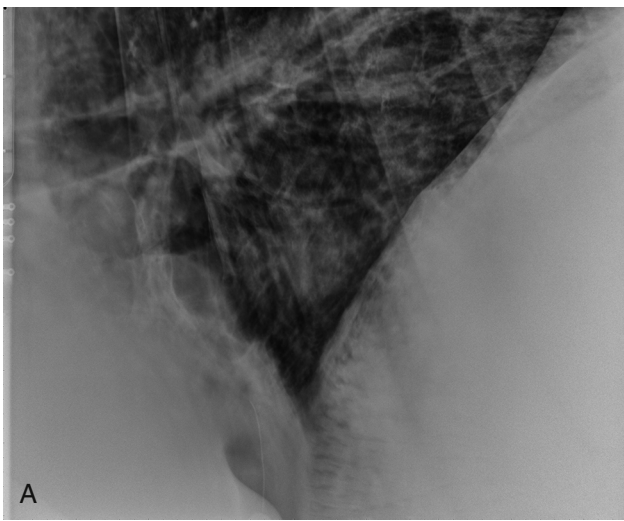
• **Fig. 3.34** Radiographic image (**A**) from an adult dairy cow with reticulopericarditis demonstrating the wire oriented vertically within the enlarged pericardial sac caudal to the heart shadow because of acute penetration. Postmortem appearance of the wire protruding through the outer surface of the pericardium (**B**), and concurrent vegetative endocarditis affecting the same cow (**C**).
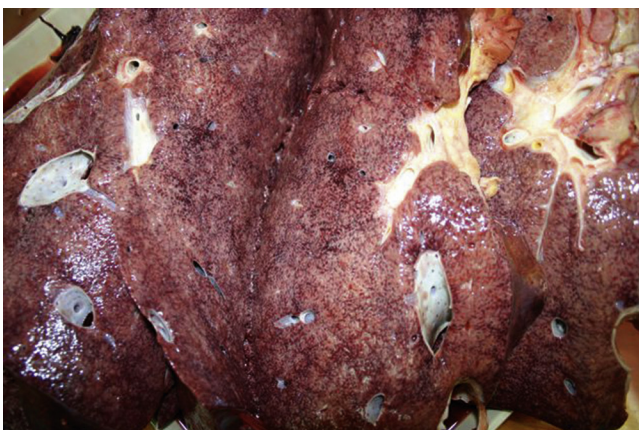
• **Fig. 3.35** "Nutmeg"-like appearance on cut section of a highly congested and enlarged liver from an adult Holstein cow that was euthanized because of congestive heart failure.
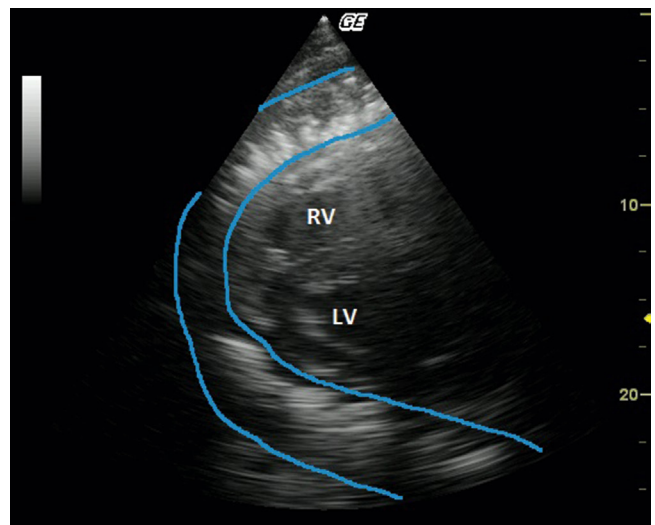
• **Fig. 3.36** Heterogeneous pericardial effusion secondary to traumatic pericarditis. The distended pericardial space is outlined by the *blue lines*. The contents of the pericardial space are heterogeneous compatible with fibrin, pus, and gas, typical of a septic effusion. *LV,* left ventricle; *RV,* right ventricle.

• **Fig. 3.37** Ultrasound image taken from right sixth intercostal space showing an enlarged and thickened pericardial sac containing flocculent and gas-shadowing material associated with septic pericarditis caused by hardware disease in a 6-year-old Jersey cow.
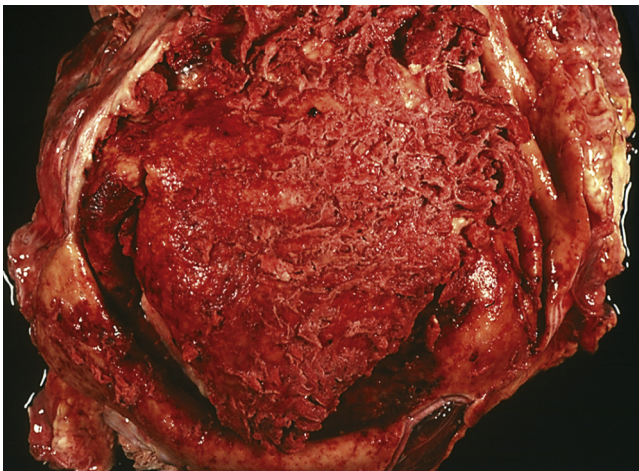
• **Fig. 3.38** Traumatic pericarditis patient's heart and pericardium at necropsy. Purulent fluid has been rinsed away, but the severity of fibrin deposition is apparent because the epicardial surface of the heart is completely covered. The pericardium is also greatly thickened and coated with fibrin. (Courtesy of Dr. John M. King.)
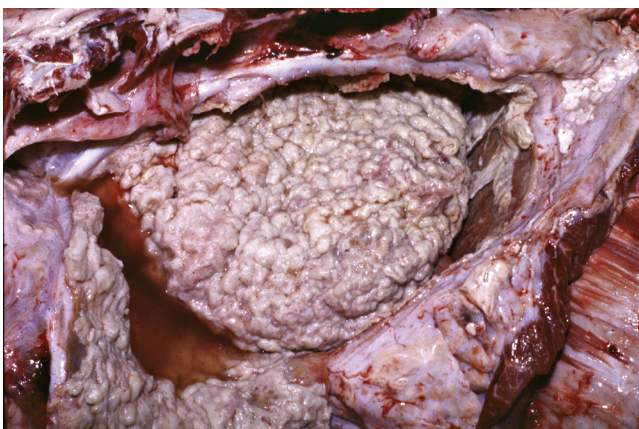
• **Fig. 3.39** "Scrambled egg" appearance of the epicardium and pericardial sac of an adult cow with pericarditis.

component rather than the mononuclear cells normally found in pericardial fluid. Bacteria are easily detected in gram-stained smears of this fluid. With ultrasound guidance, as has become commonplace, it is frequently possible to access the pericardial sac from either the left or the right side (see Fig. 3.31), potentially through several ICSs, so significant is the enlargement and volume of fluid within the pericardium. However, it is advisable that the fifth ICS on the left always be used for diagnostic sampling for cytology. Many cattle with pericardial effusions will also have some degree of pleural effusion, and it can be challenging to differentiate the two spaces ultrasonographically such is the deviation from normal anatomy and the sheer enlargement of the respective spaces. Although septic disease often has comparable cytology in both effusions, this is not always the case for neoplastic disease, nor with idiopathic hemorrhagic pericardial effusion.

The major reason for pericardiocentesis is diagnostic differentiation of traumatic pericarditis from diseases that may create similar signs. Lymphosarcoma with pericardial involvement and fluid accumulation has historically been the major differential diagnosis, but increasing numbers of cases of idiopathic, nonseptic hemorrhagic pericarditis have been documented, in which the clinical signs are similar to those documented with septic pericarditis or neoplastic pericarditis, but the fluid tends to be a sterile hemorrhagic transudate with low to moderate numbers of macrophages, neutrophils, and lymphocytes (see Video Clip 3.5). Cytology of pericardial fluid would clearly differentiate between these diseases. The prognosis for cattle with the idiopathic hemorrhagic condition appears to be better after drainage and antiinflammatory therapy than for pericarditis associated with sepsis or neoplasia (see later section). The presence of flocculent, mixed echogenicity fluid with gas shadowing within the pericardium on ultrasonography is also characteristic for septic pericarditis.

Pericardiocentesis is not without risk. Potential complications include pneumothorax; fatal arrhythmia; cardiac puncture leading to hemorrhage or death; and leakage of pericardial material into the thorax, resulting in pleuritis. Some, but not all, of these complications can be mitigated by performing the procedure using ultrasound guidance. Leakage into the pleural space is possible because most pericarditis patients do not have attachment of the fibrous pericardium to the parietal pleura. Pericardiocentesis performed on one of the author's patients yielded only gas from the needle and was associated with immediate anxiety, dyspnea, and death within 5 minutes. Postmortem examination confirmed that neither hemorrhage nor cardiac injury had occurred. The gas pocket and fluid distending the pericardium had been under positive pressure and may have become somewhat constrictive or altered compensatory mechanisms when suddenly relieved.

Given the poor prognosis usually associated with septic pericarditis, pericardiocentesis is a worthwhile risk to confirm the diagnosis before salvaging a cow suspected to have the disease. The fact that idiopathic hemorrhagic pericarditis

carries a much more favorable prognosis further emphasizes the diagnostic relevance of the procedure in a patient with pericardial effusion.

Treatment

Treatment of traumatic pericarditis in dairy cattle usually is nearly hopeless. Medical therapy with systemic antibiotics and drainage of the pericardial sac rarely, if ever, permanently cures affected cattle. Therefore most therapeutic efforts have included surgical approaches. Thoracotomy and pericardiectomy or pericardiotomy have been performed in many fashions in an effort to provide drainage, search for the foreign body, and prevent fluid or later constrictive damage to the heart (see Video Clip 3.6). Sporadic case reports and third-hand stories attest to the occasional success of pericardiectomy and fifth rib resections, but success is not common. Authors recommending rib-splitting thoracotomy and pericardiectomy reported that five of nine clinical patients recovered. Results from Cornell University, as reported by Ducharme and coworkers, are much more pessimistic with only one of seven surviving following thoracic surgery. Pericardiocentesis followed by fluid drainage may result in clinical improvement with prolongation of life to reach a short-term goal such as calving. Despite a poor prognosis, surgery remains the treatment of choice for valuable cattle with septic reticulopericarditis.

To improve a patient's chances of survival, surgery should be performed as early in the course of the disease as possible. Cattle with severe ventral edema and obvious heart failure are not good candidates for surgery. Removal of the causative wire during the thoracotomy may be difficult but obviously is desirable. Usually the wire is mostly or completely in the thorax and would be difficult or impossible to remove through rumenotomy. However, we have observed patients with acute reticuloperitonitis and acute traumatic pericarditis from a single metallic foreign body that was still lodged in the reticulum and was removed through rumenotomy. These patients had clinically detectable pericardial effusions and radiographic evidence of foreign body penetration of the pericardium. Rumenotomy and intensive bactericidal systemic antibiotics are sometimes sufficient treatment of peracute or acute pericarditis in such cases. If pericarditis worsens despite systemic antibiotics and rumenotomy to retrieve the foreign body, thoracotomy may then be considered. Rumenotomy probably is most indicated in acute cases for which it is hoped that some portion of the metallic foreign object remains in the reticulum. Unfortunately, it is difficult to know this without the benefit of radiographs, and an unsuccessful rumenotomy in the field may further compromise the patient.

It is very disturbing that these "valuable cows" unfortunate enough to develop traumatic pericarditis were not administered a magnet prophylactically at some time in their lives by their owner. The routine administration of a magnet to heifers of breeding age and bulls before 2 years of age should be part of routine herd health in dairy cattle.

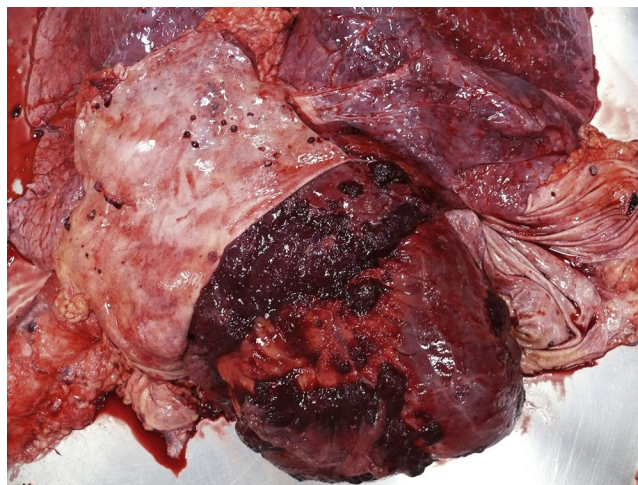## Idiopathic Hemorrhagic Pericardial Effusion
Etiology

Over the past decade, we have seen a seemingly new form of pericardial disease manifest itself in dairy cattle in the northern United States and Canada. The initial reports of the condition were case reports or small case series of individual adult cattle presented to university teaching hospitals with signs of congestive heart failure associated with substantial volumes of hemorrhagic pericardial fluid. Diagnostic workup of these cases demonstrated that cytologically the effusion was neither neoplastic nor septic but merely hemorrhagic and that extended survival times could be achieved with pericardial drainage and parenteral corticosteroid administration. In many cases, the effusion would resolve with such treatment, and cattle would return to milk production or reproductive use for a variable period from several months to years. In the past decade, it has increased in prevalence to the point that at the time of writing, it is now the most common cardiac condition of cattle presenting to the University of Wisconsin's Large Animal Hospital. Subsequent literature has highlighted that many of these cattle go on to develop an unusual form of cardiac lymphosarcoma principally involving the epicardium in the months to years after initial presentation for cardiac disease. Occasionally, cattle have epicardial lymphosarcoma at the time of initial presentation, but we have seen cattle for whom the delay in progression from initial treatment of the nonneoplastic hemorrhagic pericardial effusion to euthanasia for epicardial lymphosarcoma has been in excess of 3 years. The gross appearance of the epicardial neoplasia is quite strikingly different to that seen with classic cardiac lymphosarcoma involving the myocardium. It seems extremely rare for cattle with cardiac lymphosarcoma to have neoplastic infiltration of both myocardial and epicardial locations, although both may show infiltration of thoracic or mediastinal lymph nodes locally. In cases when cattle have been euthanized or died with the disease, without any gross or histologic evidence of lymphosarcoma, the epicardial surface of the heart has a network of highly vascular fibroelastic connective tissue, which is presumably the source of the hemorrhagic effusion (Fig. 3.40). Fulminant cases of epicardial lymphosarcoma have variably florid and highly extensive amounts of this highly vascular connective tissue within which it appears the neoplasia has developed, raising the possibility that it behaves as a "scaffold" for transformed lymphocytes (Figs. 3.41 and 3.42). Affected cattle are reliably BLV positive.

Because this condition is the most treatable of the primary cardiac conditions of dairy cattle, early recognition and appropriate therapy carry the greatest chance of returning the patient to production for an extended period. We have not seen the condition in animals younger than 2 years of age, although first lactation heifers can certainly be affected. It can be seen in either lactating or dry animals, although many are in mid to late lactation at the time of diagnosis. A large retrospective study of 125 cases demonstrated a median age and days in milk of 47 months and 262 days, respectively. Many affected cattle have been producing expected levels of milk
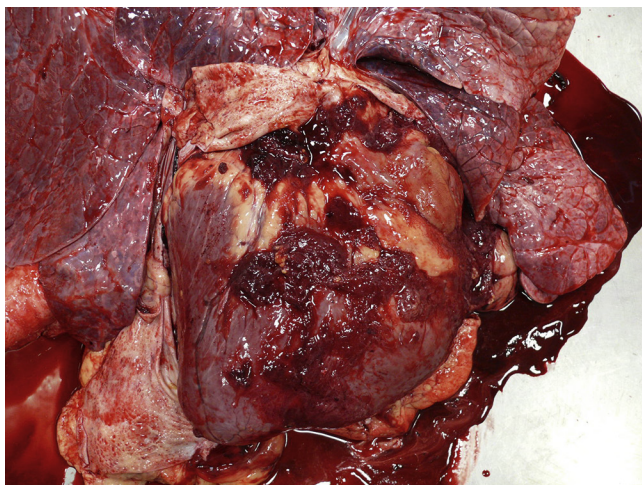
• **Fig. 3.40** Postmortem appearance of the heart of a 2-year-old Holstein heifer euthanized for idiopathic hemorrhagic pericardial effusion. The epicardium is covered with highly vascular, proliferative epicarditis, but there was no neoplastic infiltrate histologically.

• **Fig. 3.42** Pericardial sac opened to demonstrate epicardial lymphosarcoma in a 3-year-old Holstein cow with a 9-month history of idiopathic hemorrhagic pericardial effusion.

• **Fig. 3.41** Postmortem appearance of the heart of a 7-year-old Brown Swiss cow euthanized approximately 2 years after initial presentation and treatment for idiopathic hemorrhagic pericardial effusion. At the time of death, there were lymphoblasts in the pericardial fluid, and histologically, the epicardial surface was diffusely infiltrated by lymphosarcoma.

• **Fig. 3.43** Mild submandibular edema in an 8-year-old Holstein cow presented with muffled heart sounds and idiopathic hemorrhagic pericardial effusion.

herd problem with multiple animals affected over the course of many months.

Signs

The presenting signs typically point toward a cardiac condition with observant producers noticing jugular distention, alongside variably severe submandibular and brisket edema in combination with a seemingly acute reduction in appetite and milk production over 24 to 72 hours (Fig. 3.43). Peripheral vessels such as the superficial mammary veins may also be inappropriately distended and turgid for the stage of lactation. Cattle are typically afebrile or demonstrate only a low-grade fever and have high normal to mildly elevated heart rates. Respiratory rate and effort are usually also mildly increased. Because of the presence and frequently large volume of pericardial effusion, one might expect obvious muffling of heart sounds or a washing-machine type murmur on cardiac auscultation, but it has been our experience that

immediately before diagnosis and are often average- to high-producing animals compared with herdmates. However, the stage of lactation at which animals appear to be commonly affected certainly puts them into a group for whom there may not be such intense health-related oversight unless they are individually valuable or daily milk weights are recorded and checked. In several instances we have investigated this as a

this is not invariable. Certainly, muffling would instantly raise the clinician's suspicion of pericardial disease, but it has been humbling to image the heart of affected cattle ultrasonographically and reveal the extravagant depth of pericardial fluid that had not been anticipated after ordinary stethoscope examination.

Diagnosis

The definitive diagnosis requires exclusion of other causes of cardiac disease and peripheral vein distention, especially septic pericarditis and pericardial effusion associated with more classical cardiac lymphosarcoma. This is most readily achieved by echocardiography and pericardiocentesis. Routine hematology and biochemistry can be useful for exclusionary purposes in that there is an absence of hyperfibrinogenemia, mature neutrophilia, and hyperglobulinemia such as one would expect with septic pericarditis caused by hardware disease. There may well be a significant and persistent lymphocytosis in cattle with this condition who are also BLV positive, which may also be true in cases of right atrial lymphosarcoma. Biochemical abnormalities are infrequent, although many cattle demonstrate elevations in gamma-glutamyl transferase likely associated with passive hepatic congestion of cardiac origin. Pericardial fluid reliably appears bloody, typically has a packed cell volume (PCV) of between 10% and 15%, with a mildly elevated total protein, and a cytologic mixture of nondegenerate neutrophils, macrophages, and small lymphocytes. The latter usually represent the majority of the cells on cytologic examination even if the cow does not have a peripheral lymphocytosis. These small lymphocytes are phenotypically unremarkable in the majority of cases at the time of first diagnosis, but as mentioned earlier, over time this can transition into an obviously lymphoblastic population. Transabdominal ultrasound examination often confirms hepatic congestion, intrahepatic vessel prominence, and commonly a moderate degree of ascites. Thoracic ultrasonography and echocardiography are highly informative and the effusion(s) so marked that either a medium-frequency sector scanner or lower frequency cardiac probe can be used. Echocardiographic findings from either side of the chest include a large volume of predominantly anechoic fluid within the pericardial sac (5–25 cm in depth) (see Video Clip 3.7) often accompanied by a moderate but smaller volume of pleural fluid (see Fig. 3.4). The latter is more likely in individuals with a particularly large volume of pericardial effusion. The epicardial surface of the heart is often coated with more hyperechoic-appearing tissue that projects like fronds of seaweed into the more anechoic fluid within the pericardium, having an ultrasonographic appearance reminiscent of fibrin. The anechoic nature of the pericardial fluid is notably different from that seen with septic pericardial disease, which tends to be more heterogeneous and frequently contains gas shadows (compare Figs. 3.4 and 3.37). Cardiac function is often obviously impaired on echocardiography with poor contractility and low ejection fractions most likely caused by tamponade.

Treatment

Successful treatment of this condition has been achieved both by systemic corticosteroids alone and through a combination of pericardial drainage and systemic corticosteroids. The best results that one author has achieved (SP) in terms of long-term survival have been subsequent to pericardial drainage combined with dexamethasone administration (0.1 mg/kg) over 3 days. In pregnant cattle, isoflupredone acetate at standard, labeled doses can be substituted for the more abortifacient dexamethasone. Understandably, grade cattle may not justify pericardial drainage, and we have experienced good results with steroid use without drainage on the farm, although survival times for commercial cattle treated in this way tend to be measured in terms of months to 1 year. If pericardial drainage is performed, it is wise to concurrently administer an antibiotic such as ceftiofur or ampicillin parenterally.

Cor Pulmonale

Etiology

Conditions of right heart dilatation, hypertrophy, and subsequent failure caused by pulmonary hypertension and increased pulmonary vascular resistance often are referred to collectively as cor pulmonale. This condition is uncommon and sporadic in dairy cattle. Most cases of cor pulmonale occur in cows known to have chronic pneumonia, bronchiectasis, and pulmonary abscesses secondary to bacterial bronchopneumonia, consolidated anteroventral lung lobes from previous pneumonia, or chronic lungworms. Severe chronic interstitial pulmonary disease, although rare, may also result in cor pulmonale in mature cattle with diffuse pulmonary fibrosis. Occasionally, calves with chronic pulmonary disease or those with congenital defects leading to chronic hypoxia and pulmonary hypertension may also develop this problem, but this represents a very small fraction of all calves with even severe or repeated bouts of conventional bronchopneumonia. In calves in which we have observed it, the radiographic and pathologic interpretation of the calf's disease has included both concurrent interstitial disease as well as the more common bronchopneumonia. In cases of cor pulmonale, pulmonary hypertension initially may result from alveolar hypoxia and subsequent precapillary vasoconstriction. Chronic hypoxia and pulmonary hypertension in cattle may provoke hypertrophy of medial smooth musculature within pulmonary arteries and arterioles, causing further work for the right ventricle. We have treated only one adult Holstein cow that had confirmed primary pulmonary hypertension suggesting that it is a very rare condition in the northern and Mid western United States.

The most common example of cor pulmonale is "brisket disease" or "mountain sickness" of beef cattle. This disease can occur in dairy cattle, and in fact Holsteins have been reported to be particularly sensitive. However, on a practical basis, to our knowledge, few dairy cattle in the United States are at risk because of a lack of exposure to high altitudes. Brisket disease may be seen at elevations of 1600 m (5249 ft) above sea level

and tends to have an increasing incidence at elevations above 1600 m. Definite genetic resistance or susceptibility is documented, and affected cattle must be returned to low altitudes early in the course of the disease to survive. Concurrent ingestion of certain plants such as *Astragalus* spp. and *Oxytropis* spp. (locoweed) is known to accentuate and accelerate brisket disease in animals at high elevations.

Pulmonary hypertension secondary to pulmonary and bronchial arteritis recently was observed as an endemic problem in a group of dairy calves. Periarteriolar sclerosis and vasculitis were identified pathologically and explained signs of right heart failure observed in the calves. Although unconfirmed, monocrotaline, a pyrrolizidine alkaloid, was suspected as the cause by the authors.

Signs

Dyspnea, tachycardia, ventral edema, and venous distention and pulsation characterize cor pulmonale. Therefore, the signs are similar to those found in other common heart diseases of cattle and require differentiation from cardiomyopathy, endocarditis, lymphosarcoma, pericarditis, and myocarditis.

Murmurs or a gallop rhythm may be auscultated, depending on valvular function, the degree of myocardial hypertrophy, or cardiac chamber dilation. Heart sounds have normal or increased intensity. Greatest attention should be directed toward the lungs to determine chronic abnormalities (e.g., consolidation determined via auscultation, radiography or ultrasonography, or interstitial disease via radiographs) that may explain the right heart failure. Affected cattle appear more ill as the degree of dyspnea progresses.

Diagnosis

A history of chronic pulmonary disease (or exposure to high altitude), ruling out other cardiac diseases, and finding signs consistent with right heart failure provide suggestive evidence of cor pulmonale. Microscopic examination of stained blood smears may reveal the presence of vacuolation in the cytoplasm of the lymphocytes in cattle with clinical signs caused by locoweed poisoning. Two-dimensional echocardiography may add further evidence if right ventricular hypertrophy and dilatation is proved. Echocardiographic visualization of the pulmonary outflow tract may provide suggestive findings of enlargement and dilation with a diameter similar to that of the aorta. Increased pulmonary arterial pressures, confirmed by cardiac catheterization, are diagnostic but limited to research facilities. Tracheal washes, thoracic ultrasonography, and thoracic radiography may contribute to an understanding of the pulmonary problem in suspected cases, especially cattle with chronic pneumonia, *T. pyogenes* pneumonia, abscesses, or diffuse pulmonary fibrosis. Measurement of arterial blood gas concentrations may confirm the presence of underlying hypoxemia.

Treatment

In cattle affected with primary chronic pulmonary disease, treatment of the primary lung disease coupled with furosemide therapy may be beneficial. Cattle known to have had pneumonia in the past and mild but persistent chronic respiratory signs thereafter may benefit from a tracheal wash to establish cytologic and cultural aids to antibiotic treatment of the chronic lung problem. Baermann's technique should be performed if chronic lungworm infestation is suspected. Cattle at high altitude suspected to have brisket disease should receive oxygen and be moved to lower altitudes.

Furosemide is administered at 0.5 to 1.0 mg/kg twice daily as a diuretic. Although digoxin may be considered in these cases, cattle that require digoxin require hospitalization and incur significant expense. Therefore, use of digoxin seldom is practiced. If digoxin is required for a select case, the recommended dosage is 0.86 µg/kg/hr IV.

Arrhythmias
Etiology

Arrhythmias in adult cattle can be caused by a variety of drugs, myocardial insults, myocardial lymphosarcoma, and metabolic abnormalities. In calves, myocarditis, hyperkalemia, hypoglycemia, and white muscle disease have been discussed previously as factors involved in the pathogenesis of arrhythmias.

Myocarditis may be the most difficult of the adult cow causes to diagnose definitively and therefore is suspected when other known causes are eliminated. Toxic myocardial damage from ionophores and plant toxins, as well as septic or inflammatory mediators (myocardial depressant factor, tumor necrosis factor), must be considered when arrhythmias appear in cattle without GI, electrolyte, or other typical predisposing factors. Cattle with lymphosarcoma of the myocardium, most commonly involving the right atrium, often present with tachyarrhythmias with or without other concurrent signs of cardiac disease on physical examination. It is therefore worthwhile considering this differential whenever the clinician is presented with an adult cow (>2 years of age) that has a tachyarrhythmia (frequently atrial fibrillation) for which no other metabolic, GI, or toxic explanation is forthcoming. Clinical signs consistent with lymphosarcoma in other anatomic locations (abomasum, spinal cord, retrobulbar) are only occasionally found but should be thoroughly investigated. The identification of peripheral lymphadenopathy or PL is supportive, but not definitive.

Calcium solutions are well recognized as being capable of causing cardiac arrhythmias or even death when administered IV to cattle. Both hypocalcemia and hypercalcemia have been associated with arrhythmias, and arrhythmias associated with hypercalcemia are thought to be mediated by vagal stimulation. In fact, arrhythmias associated with hypercalcemia may be abolished by atropine. However, atropine seldom is used for this purpose because of its negative effects on the GI tract of cattle. Atrial fibrillation has been associated with hypocalcemia and has been reported after treatment of cattle with neostigmine (mostly for ileus)
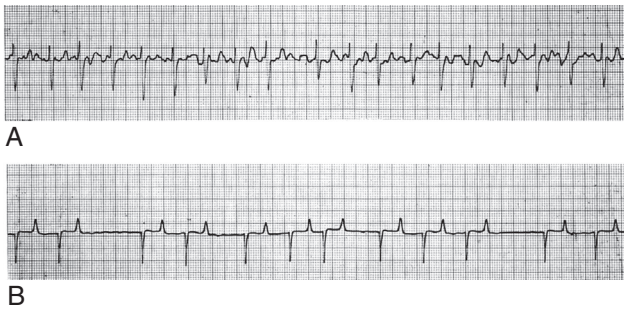
• **Fig. 3.44** Electrocardiographic recording from two different cows showing characteristic changes of atrial fibrillation. Both **A** and **B** demonstrate an irregular rhythm with normal QRS complexes but no P waves. In **A,** the f (fibrillation) waves are coarse, and the heart rate is more rapid than in **B,** which demonstrates relatively fine f waves along with a normal heart rate. In both tracings the intervals between QRS complexes are irregular, a typical feature of atrial fibrillation.

that may have provoked increased vagal tone. Hypocalcemia and hypokalemia in cattle with primary GI diseases seem to be major risk factors for the development of atrial fibrillation and atrial premature contractions (APCs) in adult dairy cattle.

Oxytetracycline in propylene glycol vehicles may cause decreased cardiac output and stroke volume, as well as decreased heart rates and aortic pressures. Systemic hypotension and cardiac asystole also have been observed when these drugs are given IV to awake, healthy calves. It is common knowledge among bovine practitioners that oxytetracycline, especially when prepared in propylene glycol vehicles, should ideally be administered slowly and diluted with saline or dextrose to avoid hypotension, collapse, or death in both calves and adult cattle.

Atrial fibrillation is the most common arrhythmia occurring in adult dairy cattle (Fig. 3.44). One report suggests that APCs in cattle with GI disease may occur as commonly as atrial fibrillation. APCs often were associated with hypocalcemia and sometimes with hypokalemia in that study. APCs probably reflect vagotonia associated with abdominal distention or GI diseases and are characterized using ECG by abnormal premature P waves (P′) from depolarization at an atrial site different from the sinus node. APCs usually result in a normal QRS-T on the ECG unless they enter the ventricle when it is partially refractory or if the AV node is refractory to excitement. In any event, it appears that APCs may precede or predispose to atrial fibrillation. Sporadic irregularities rather than the irregularly irregular rhythm of atrial fibrillation are auscultated during APCs in cattle.

Although atrial fibrillation may occur with or without underlying heart disease, it usually is a secondary event unrelated to primary heart disease. There may be a normal or fast heart rate, depending on the severity of the underlying condition, but the rhythm is always irregular with variation in the intensity of heart sounds and pulse deficits when the heart rate is rapid. There is an absence of P waves and presence of f (fibrillation) waves demonstrated by ECG recordings (see Fig. 3.44).

Signs

Clinical signs related to APCs and atrial fibrillation are nonspecific unless underlying primary heart disease is present, in which case general signs of heart failure also may be observed. Close observation of the jugular vein may reveal occasional abnormal pulsations in cows with APCs. Signs of heart failure, such as venous distention or ventral edema, usually are not present in cattle with atrial fibrillation, except in advanced cases that have progressed to congestive heart failure. Because most cows with either APCs or atrial fibrillation have a primary GI or other medical disorder, the signs vary in each case. Without question, cattle with abomasal displacement and other diseases characterized by abdominal distention are most frequently affected by atrial fibrillation. Specific signs of APCs or atrial fibrillation are associated with cardiac auscultation. Sporadic arrhythmias and variations in the intensity of S1 typify APCs. Although the heart rate varies, perhaps dependent on the primary disease, it often is within the normal range. Atrial fibrillation, on the other hand, leads to more obvious abnormalities in cardiac auscultation. Marked irregularities in rhythm, tachycardia, and dramatic variations in the intensity of heart sounds are obvious. Pulse deficits may be present in cattle with rapid heart rates, and an absence of the S4 has been reported. Although exercise intolerance is possible with atrial fibrillation, cattle seldom show this sign because they are not "raced."

Cattle confirmed to have atrial fibrillation or some other arrhythmia associated with cardiac lymphosarcoma that also have outward signs of congestive heart failure have a guarded to poor prognosis, and such individuals seldom survive more than a few weeks to a few months.

Diagnosis

Although cardiac auscultation is highly suggestive, an ECG is necessary to make a definitive diagnosis of APCs (Fig. 3.45) or atrial fibrillation in cattle (see Fig. 3.44). The increased availability of cTnI testing, usually through local human hospitals, or by using "stall-side" commercial kits (i-STAT) designed initially for people but with diagnostic utility in cattle, provides a useful adjunctive tool for the workup of cattle with suspected myocardial insult. Elevations in cTnI (see earlier section) do not identify the cause of the myocardial injury, and as yet we do not know the kinetics of release or the half-life of the protein in cattle; however, it has become an active focus of current research and the source of several publications. Key ECG findings in each condition are listed below and shown in the figures:

APCs : Abnormal premature P waves (P′);
        Normal QRS-T unless occurring during refractory period of ventricle or AV node; Sporadic

Atrial fibrillation : Absence of P waves;
        F waves may be apparent;
        "Irregularly irregular" rhythm;
        Tachycardia (usually); Pulse deficit
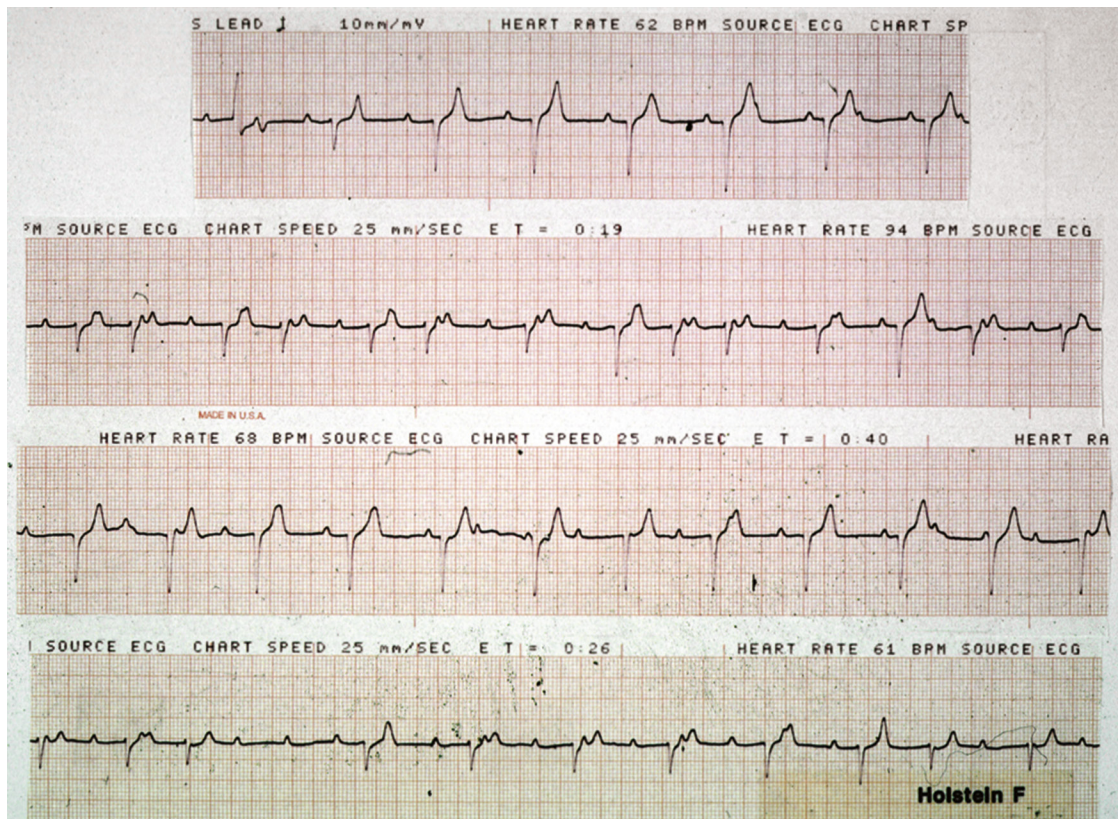
• **Fig. 3.45** Electrocardiographic recording from a cow with atrial premature contractions associated with concurrent gastrointestinal disease.

Treatment

Specific anti-arrhythmic treatment of atrial fibrillation in cattle seldom is necessary because resolution of the patient's primary medical or GI problem generally results in a return to normal sinus rhythm. Medical or surgical treatment of the primary problem coupled with correction of existing acid–base and electrolyte abnormalities is indicated for cattle whose problems include atrial fibrillation.

Routine administration of oral or SC calcium solutions as indicated and oral supplementation with 50 to 100 g of KCl orally, twice daily for 3 to 5 days, are excellent empiric and supportive treatments for cattle with abomasal displacements or other causes of abdominal distention that also have APCs or atrial fibrillation.

Occasionally atrial fibrillation persists several days to several weeks after resolution of the primary problem. Persistent atrial fibrillation raises concerns, lest the long-term condition lead to eventual heart failure. Heart failure has been suspected to result from prolonged (a course of years) atrial fibrillation in horses. Similar suspicions exist in cattle, but we know of no work that confirms this theory pathologically. In addition, cattle with atrial fibrillation that persists more than 1 month after resolution of a GI or medical problem may in fact have myocardial disease causing atrial fibrillation or acquire heart disease because the noncontracting atria will develop progressive dilation that eventually results in tricuspid and mitral valve regurgitation. It also is possible that some cows with persistent atrial fibrillation

had it before the onset of their medical or GI disease. Therefore, discussions of appropriate criteria on which to base treatment are subjective. If medical or surgical therapy for the primary illness fails to resolve the atrial fibrillation, it is difficult to know how much the arrhythmia might contribute to any ongoing inappetence, depression, and decreased milk production. It seems that cattle, similar to horses, can be remarkably tolerant of chronic atrial fibrillation provided there is not concurrent, significant cardiac disease. The fact that chronic atrial fibrillation will ultimately lead to cardiomyopathic changes and deteriorating cardiac function means that there would be circumstances under which an attempt to convert cattle back to sinus rhythm should occur.

If atrial fibrillation persists for 5 days beyond treatment or resolution of the primary problem, it is thought by some that it should be treated with quinidine therapy. This may be premature in cattle that are clinically improved by resolution of their primary problem. It is our opinion that therapeutic intervention in cattle that are improving should be delayed at least 14 days because spontaneous resolution may occur during this time. Failure of cattle to resolve atrial fibrillation spontaneously may result from ongoing medical, GI, acid–base, or electrolyte abnormalities. Treatment with quinidine, or digoxin followed by quinidine, may be expensive and requires careful clinical and ECG monitoring to avoid toxic side effects.

However, if atrial fibrillation persists beyond a reasonable time after resolution of a primary illness or is thought to be

partially responsible for vague signs of illness in a patient or is thought to risk eventual heart failure, treatment may be considered. The following treatment protocols have been suggested:

1. Simple atrial fibrillation that has persisted despite resolution of primary disease:

    Quinidine 48.0 mg/kg in 4 L of saline or lactated Ringer's solution administered at a rate of 1 L/hr IV. Balanced fluids may be given concurrently via the opposite jugular vein.

2. Atrial fibrillation that is complicated by extreme tachycardia or that has not responded to previous quinidine therapy:

    Digoxin 0.86 µg/kg per hour or 11.0 µg/kg thrice daily IV for 4 to 5 days. After this time, quinidine is administered as in (1) above.

    Digoxin—loading dose 22.0 µg/kg once followed by 0.86 µg/kg/hr for 2 to 4 days. After this time, quinidine is administered as in (1) above.

In all treatment protocols, side effects of quinidine such as diarrhea, rumen hypermotility, and tachycardia must be anticipated. Signs of quinidine toxicity may also include arrhythmias other than atrial fibrillation, prolonged QRS complexes, or collapse. If signs of toxicity appear in the form of pronounced tachycardia, the rate of infusion should be slowed or stopped. Intravenous sodium bicarbonate also may be administered. Some cattle are reported to show blepharospasm and ataxia just before conversion to normal sinus rhythm.

Cattle having atrial fibrillation that persists despite attempted conversion therapy may have ongoing primary illnesses, myocardial disease, or vagotonia that interferes with conversion to normal rhythm. Prognosis remains guarded for these patients and for untreated atrial fibrillation patients that remain in atrial fibrillation for more than 30 days after apparent successful resolution of their primary GI or medical disease.

Diseases of the Veins

Thrombosis and Phlebitis

Etiology

Traumatic venipuncture and perivascular reactions to irritating drugs from attempted IV therapy are the major causes of venous thrombosis and thrombophlebitis. Dextrose solutions and calcium solutions that contain dextrose are the greatest offenders because of the tissue reaction that develops around hypertonic dextrose solutions. Tetracycline, phenylbutazone (not to be used in dairy cows older than 20 months of age in the US), and IV sodium iodide also are capable of causing severe thrombophlebitis when inadvertent perivascular leaking occurs.

Traumatic or repeated venipuncture may result in simple thrombosis, thrombophlebitis, or septic thrombophlebitis. Poor restraint, improper preparation of the vein for venipuncture, inexperience in venipuncture, and inappropriate selection of needles for IV therapy increase the risk of injury to veins. The common use of disposable 14-gauge needles for jugular venipuncture in cattle has increased the incidence of venous injury because these needles are only 3.75 cm (1.5 in) long—too short to be placed properly for adult cattle. Furthermore, these same needles are extremely sharp and can lacerate the intima of the vein if the cow moves at all. Prolonged use of indwelling IV catheters risks both thrombophlebitis and septic thrombophlebitis, but catheter materials have improved over recent years such that less thrombogenic polyurethane or antimicrobially coated catheters are available for longer term use and use in patients deemed to be at greater risk for thrombosis. Septic thrombophlebitis of any cause creates a major risk for endocarditis in cattle.

Dehydrated cattle and endotoxic cattle are especially prone to thrombosis during attempts at venipuncture. The normally thick bovine skin becomes even more difficult to penetrate when the animal is severely dehydrated. This is especially true in neonatal calves that are severely dehydrated by diarrhea. Repeated attempts at venipuncture in these patients may injure the vein and cause thrombosis. Endotoxic patients and septicemic patients that are predisposed to coagulopathies may develop venous thrombosis very easily. Platelet activation and other coagulation factors may contribute to venous thrombosis in such cattle, even when an experienced clinician performs venipuncture. In some endotoxic or septic patients, gelatinous or "Jell-O–like" clots appear at the site of venipuncture within seconds of entering the intima of the vein. Further attempts at venipuncture often result in extension of the thrombus along the length of the vessel.

Although the jugular is the most commonly damaged vein in dairy cattle, mammary and tail veins may sustain damage occasionally. It is contraindicated to perform venipuncture in the mammary vein except in dire emergencies or when both jugular veins have been thrombosed. Injury to the mammary vein not only damages the vein but also causes persistent udder edema of both the forequarter and hindquarter on that side and will negatively impact future production or udder symmetry in the case of show animals.

Although most thromboses, thrombophlebitis, and septic thrombophlebitis are iatrogenic because of the aforementioned conditions, occasional cases develop spontaneously. Neonatal calves always are at risk for umbilical vein omphalophlebitis and subsequent septicemic spread of bacteria to distant sites. In adult cattle, the mammary vein is the most common vein to sustain spontaneous thrombosis, and this usually occurs during the dry period. Trauma by other cows butting the patient or simple pressure thrombosis caused by preparturient udder and ventral edema or excessive abdominal weight when lying on hard surfaces may contribute to this condition. Spontaneous thrombosis or rupture of the perineal vein and caudal udder hematoma formation may also occur in the region of the rear udder support and escutcheon (see the section on Udder Hematomas in Chapter 8).

Signs

Signs associated with simple thrombosis include palpable soft or firm clots within the vein. The vein may appear grossly distended by the thrombus or be of normal diameter. When the vein is held off below the thrombus, a fluid wave of blood cannot be ballotted within the vessel. Acute thrombi tend to be soft or "Jell-O–like," but chronic or subacute thrombi may be firm to the touch. Edema may be apparent as a result of poor venous return in areas "downstream" from the thrombus. Therefore, facial edema may appear with jugular thrombosis and ipsilateral udder edema with mammary vein thrombosis. Thrombosis may cause the patient mild pain, but it is not as painful as thrombophlebitis. "Needle tracks" or palpable swelling may be apparent in the skin overlying the site of thrombus formation.

Thrombophlebitis causes more obvious swelling in and around the affected vein. A perivascular component to the swelling and pain are more likely than with simple thrombosis (Fig. 3.46). Palpable warmth to the swelling may be present, and SC edema usually appears downstream from the lesion. It may be difficult to differentiate a sterile thrombophlebitis from a septic thrombophlebitis. In general, fever and inappetence are more common with septic thrombophlebitis. Both may be painful and warm, and when the jugular vein is involved, the patient may be reluctant to raise or lower its neck or eat. Ipsilateral Horner's syndrome develops in some cattle with jugular thrombophlebitis. Thrombophlebitis of the mammary vein causes marked ventral abdominal pain over the site and severe ipsilateral udder and ventral edema (Fig. 3.47). Because septic thrombophlebitis predisposes to bacterial endocarditis in cattle, careful auscultation of the heart is indicated in all cases (Fig. 3.48). Tissue necrosis associated with extremely irritating drugs (e.g., 50% dextrose, 20% sodium iodide, and phenylbutazone) placed perivascularly or resulting in thrombophlebitis eventually will cause sloughing, cellulitis, or sterile abscess formation. Bacterial contamination of such lesions ensures abscess formation and eventual drainage.

Severe thrombophlebitis involving the tail vein may result in sloughing of the entire tail (Fig. 3.49).

Diagnosis

Clinical signs usually suffice for diagnosis. Two-dimensional ultrasound may be used to confirm the diagnosis, assess the extent of thrombosis, and detect fluid or pus accumulations that may be drained in cases of septic thrombophlebitis.

• **Fig. 3.47** Thrombophlebitis of the right mammary vein in a Holstein cow secondary to owner-administered oxytetracycline and dextrose.

• **Fig. 3.48** Septic thrombophlebitis of the right mammary vein that resulted in cellulitis cranial to the udder and septic endocarditis. Attempted blind stitching of an abomasal displacement caused the original venous damage.

• **Fig. 3.46** Thrombophlebitis of the right jugular vein in a cow that had repeatedly been administered dextrose by the owner.

• **Fig. 3.49** Tail slough secondary to perivascular injection of the tail vein.

Treatment

Simple sterile thrombosis requires no treatment other than avoidance of further injury to the vein. In acute cases, cool compresses may be applied to the site overlying the thrombus, but this only minimizes hematoma formation. If simple thrombosis is complicated by perivascular leakage of a treatment that risks thrombophlebitis, SC tissues around the swelling should be injected with normal saline in an effort to dilute the drug deposited in the perivascular region. In addition, warm compresses should be applied to the area several times daily.

Sterile thrombophlebitis is best managed by warm compresses and oral aspirin therapy (240–480 grains orally, twice daily for adult cows). Sterile thrombophlebitis may or may not eventually slough or abscess. Cases caused by irritating drugs are more likely to slough or abscess. Signs of improvement include stabilization or reduction in the degree of swelling, improved appetite and production, and less pain on palpation.

Septic thrombophlebitis requires more aggressive and intensive therapy lest further complications such as endocarditis occur. Warm compresses several times daily, systemic bactericidal antibiotics, and oral aspirin therapy are indicated. Unless culture results from a draining abscess or catheter tip indicate otherwise, procaine penicillin 20,000 to 30,000 U/kg IM or SC twice daily should be chosen because of its activity against *T. pyogenes.* When septic thrombophlebitis associated with IV catheters occurs, the catheter tip should be cultured after its removal from the vein. An effort should be made to avoid further IV therapy in all patients having thromboses or phlebitis because injury to one vessel may predispose to multiple thromboses. When IV therapy is essential for patient management, extensive care and aseptic technique are essential for future placement of IV catheters or injections. Therapy for septic thrombophlebitis usually is long term (several weeks), and relapses are common if therapy is halted prematurely. Occasional cattle with septic thrombophlebitis may have intermittent fever, depression, and inappetence, as well as swelling and pain at the site of venous injury. Such chronic thrombophlebitis is not as common as in horses but may benefit from surgical removal of the affected area of vein. Positive signs for cattle being treated for septic thrombophlebitis include normal temperature; increased appetite and production; reduced pain, swelling, and heat at the site; and decreasing amounts of drainage in cases with sloughing or abscessation.

The prognosis for simple thrombosis is fair. If further injury to the vessel is avoided, some veins recannulate with time. The prognosis for thrombophlebitis is guarded, and most affected veins do not recannulate. In addition, SC edema of the tissue downstream to the vein injury is more common and requires a longer time to resolve. In some cases involving the mammary vein the edema and asymmetry of the udder never completely resolve despite apparent resolution of the thrombophlebitis. This is a particularly frustrating outcome in show cattle.

Prevention

Good restraint, proper technique and equipment, and clinician experience are the best ways to avoid iatrogenic vein injuries. Careful preparation of the selected vein and cutdowns through the skin with small scalpel blades are very important aids when injecting or catheterizing a vein in a known high-risk patient such as a severely dehydrated or endotoxic cow (see Chapter 2). Consideration of catheter type is important, especially in "at-risk" patients and those for whom a long-term indwelling catheter is anticipated. It is the opinion of many veterinarians that the milk vein should be "off limits" for IV injections, particularly in show cattle.

Lacerations
Etiology

Mammary vein lacerations are the most common life-threatening venous laceration in dairy cattle. Sharp objects or barbed wire are the usual cause of injury, and blood loss can be profound unless the animal is attended to quickly.

Signs

Whereas small lacerations or penetrations lead to mild blood loss and hematoma formation, complete lacerations can lead to massive blood loss and exsanguination. Other than the obvious venous bleeding from the site, clinical signs are those associated with blood loss anemia. Weakness, polypnea, tachycardia, anxiety, and pallor of mucous membranes indicate a life-threatening degree of blood loss. Heart rates greater than 120 beats/min and respiratory rates greater than 60 breaths/min usually are associated with severe blood loss. These parameters, coupled with extreme pallor of the mucous membranes and weakness, dictate a need for whole blood transfusion.

Diagnosis

The diagnosis is self-evident. Because blood loss is peracute, the PCV should not be used as a decisive parameter when assessing the need for a whole blood transfusion. Peracute blood loss does not allow time for physiologic reestablishment of plasma volume, and a cow with peracute severe blood loss may die with a normal PCV. Many clinicians rely more on the respiratory rate, heart rate, mucous membrane color, and degree of weakness to judge the severity of the blood loss.

Treatment

Initial treatment includes temporary hemostasis by hemostats, ligatures, clothespins, locking pliers ("mole grips"), or nylon ties followed by a complete physical examination to determine the severity of blood loss. If transfusion of whole blood is indicated (heart rate >120 beats/min, respiratory rate >60 breaths/min, and extreme pallor of membranes), at least 4 L of fresh whole blood should be administered. After transfusion, surgical correction of the laceration with fine sutures or ligation of the vein should be performed.

For mammary vein lacerations if the physical status of the patient tolerates it, the cow should be placed in dorsal recumbency to allow the wound to be explored, extended, and assessed before repair or ligature placement.

Because phlebitis and septic thrombophlebitis are potential complications, systemic bactericidal antibiotics such as penicillin or ceftiofur at standard dosages should be given and continued for 5 to 7 days. A belly wrap applied with self-adherent tape is useful as a pressure wrap after surgery.

Caudal Vena Caval Thrombosis

Caudal vena caval thrombosis secondary to rupture, or outgrowth, of abscesses near the hilus of the liver into the caudal vena cava is the most common clinically impactful consequence of enteric origin liver abscesses in dairy cattle. Thrombi may form at the site of abscess rupture into the caudal vena cava or lodge between the heart and diaphragmatic region of the vessel. Thromboemboli can traverse the right heart to lodge in the pulmonary arterial circulation, potentially leading to acute death, acute respiratory distress, or the more common respiratory sequelae of caudal vena caval thrombosis syndrome with subsequent epistaxis, hemoptysis, anemia, and pneumonia. Endocarditis of the right heart valves is another common sequela. Further discussion of this syndrome is covered in Chapter 4.

Congenital Anomalies

Congenital portosystemic anastomoses have been identified in calves and usually result in poor growth and neurologic signs. They are further discussed in Chapter 13.

Diseases of the Arteries

Rupture

Rupture of major arteries is relatively rare in cattle. Occasional uterine artery tears occur in parturient cattle and are of unknown etiology. Trauma to the artery is suspected and may result from the vessel being trapped in the pelvis as extensive traction is placed on the calf during dystocia. The uterine artery also may experience extreme traction in some severe uterine torsions. Occasional cows having uterine prolapse suffer rupture of the uterine artery and exsanguinate (Fig. 3.50).

Copper deficiency has been suggested but seldom is confirmed as a cause of arterial rupture because it causes degeneration of the tunica elastica within arteries. Deficiency of the enzyme lysyl oxidase, which contains copper, may prevent normal cross-linking of collagen and elastin. Although the aorta seems most at risk for rupture in copper deficiency, Drs. Charles Guard and John M. King have investigated several herds in New York that have had multiple cows die acutely from arterial rupture of the mesenteric arteries or aorta. Histopathology of arteries from affected cattle suggests copper deficiency, but copper levels have not been

• **Fig. 3.50** Fatal uterine artery rupture and self-induced uterine amputation in a cow that stumbled as a result of hypocalcemia and stepped on her prolapsed uterus.

confirmed to be deficient. Therefore, copper deficiency, although suspected, has not yet been proven. Major arterial rupture usually is fatal.

Aneurysms

An example of aneurysmal pathology in adult dairy cattle is presented by pulmonary artery aneurysms that develop proximal to septic thromboemboli in individuals with caudal vena caval thrombosis syndrome. These aneurysms later contribute to hemorrhage into the airways after dissection by septic thrombi that abscess.

We have observed several adult dairy cattle with persistent or intermittent colic that subsequently were shown to have mesenteric arterial aneurysms. Surgical removal of the aneurysm may be possible in some cases, but these cattle are likely to develop arterial rupture and exsanguination eventually. If several cows are affected simultaneously, a toxin such as moldy clover or sweet vernal hay, which can prolong clotting times, should be suspected. For isolated cases, the reason for the abdominal hemorrhage is generally unproven, although copper deficiency has again been proposed as a causative factor.

Arterial Hypertrophy

Hypertrophy of the tunica media of pulmonary arteries and arterioles and subsequent pulmonary hypertension occurs as a response to prolonged hypoxia in high-altitude disease or brisket edema of cattle. This situation leads to right heart failure and is further discussed under cor pulmonale earlier in this chapter.

Vasculitis

Although of nonspecific etiology, vasculitis may occur in conjunction with many infectious, parasitic, and immune-mediated diseases. In dairy cattle, malignant catarrhal fever is a cause of classic generalized vasculitis. Bovine viral diarrhea virus, bluetongue virus, *Salmonella* spp., *H. somni*, and *Erysipelothrix rhusiopathiae* are other potential causes of vasculitis in cattle.

Disorders of the Erythron

Evaluation of the erythron with CBC, stained blood smears, PCV, hemoglobin, and other parameters is primarily useful to clinicians monitoring anemia in cattle. It should be emphasized that the PCV for healthy lactating dairy cattle is lower than in many other species (see Table 1.2). Anemia usually is suspected based on physical examination findings and may be confirmed, quantified, and differentiated as to type based on evaluation of the erythron and leukon. Although a single CBC often allows classification of anemia into a regenerative or nonregenerative category, serial CBC analyses are required to follow trends in the erythron. Blood loss anemia and hemolytic anemia are "regenerative anemias," and anemias caused by chronic disease are termed "nonregenerative." Regenerative simply implies bone marrow response to anemia through increased erythropoiesis. Regenerative anemias in cattle frequently result in overt microscopic evidence of increased erythropoiesis such as increased anisocytosis, polychromasia, reticulocytosis, and occasionally even nucleated red blood cells (RBCs). In addition, an increase in mean corpuscular volume (MCV) and decreased mean corpuscular hemoglobin concentration (MCHC) are typical in regenerative anemias. Complete nonregenerative anemia would occur from a bone marrow disorder such as bracken fern toxicity. Neutropenia and thrombocytopenia would be seen before anemia in bracken fern–poisoned cattle.

Physiologic hemoconcentration occurs with dehydration in calves and adult cattle. Because anemia may be counterbalanced by hemoconcentration, interpretations of PCV in sick cattle must always be made with consideration of the hydration status. True polycythemia (persistent elevation of PCV despite normal hydration) is rare but may occur as a result of familial, geographic, and pathologic conditions. Peracute severe blood loss as might occur in mammary vein lacerations or some abomasal bleeding ulcers does not immediately lower the PCV because physiologic dilution of hematocrit by renal and intestinal absorption of fluid requires at least 12 to 24 hours. Therefore, the degree of acute, obvious blood loss in a patient can be assessed best clinically by evaluating heart rate, respiratory rate, strength in rising and walking, and mucous membrane pallor.

Definitions

Anisocytosis; variation in size of RBC; normal to some degree in cattle; increases in regenerative anemias.

Polychromasia; variable staining (toward blue) in Wright's type stains; indicates "young" RBC or reticulocytes still containing DNA.

Basophilic stippling; blue granules, again indicative of DNA; also may be observed in chronic lead poisoning.

Nucleated RBC; not unusual in cattle with severe but responsive anemia.

Heinz bodies; precipitated hemoglobin deposits on the edge of RBC; observed in some hemolytic anemias. New methylene blue stain is helpful for detecting Heinz bodies and polychromasia in smears.

Poikilocytosis; uncommon in cattle RBC.

Mean corpuscular volume:

$$MCV = \frac{PCV \times 10}{RBC \text{ count in millions}/\mu L}$$

Increase = Usually regenerative anemia

False increase = Blood not spun sufficiently for accurate PCV

Mean corpuscular hemoglobin:

$$(MCH) = \frac{Hb \text{ (g/dL)} \times 10}{RBC \text{ count in millions}/\mu L}$$

Increase = Increased number of reticulocytes

= Hemolysis

Mean corpuscular hemoglobin concentration:

$$MCHC = \frac{Hb \text{ (g/dL)} \times 10}{PCV}$$

Decrease = Responding anemia with reticulocytosis

= Hemolysis

False decrease = Blood not spun down sufficiently

Polycythemia

Relative polycythemia resulting from hemoconcentration is extremely common. Absolute polycythemia results from an absolute increase in PCV (usually ≥60%) that is repeatable, not associated with hemoconcentration, and does not lower in response to fluid therapy. Absolute polycythemia (absolute erythrocytosis) may be primary or secondary. Primary polycythemia, also known as polycythemia vera, is a rare myeloproliferative condition that usually causes excess production of WBCs and platelets as well as RBCs. Plasma erythropoietin is decreased below normal levels in polycythemia vera. Regardless of cause, progressive polycythemia eventually interferes with tissue oxygenation because of hyperviscosity and reduced cardiac output.

Secondary polycythemia is more common than primary polycythemia in cattle and implies a physiologic response to increased erythropoietin. Generally, increased erythropoietin is a response to chronic tissue hypoxia. Therefore, secondary polycythemia tends to occur in animals kept at high altitudes and in calves having congenital cardiac defects with right-to-left shunts. The chronic hypoxia associated with brisket disease or high-altitude disease of cattle is capable of inducing polycythemia (see section on cor pulmonale). Tetralogy of Fallot and other severe congenital cardiac defects that create or progress to right-to-left shunting of blood also may cause secondary polycythemia.

Congenital polycythemia in Jersey cattle has been described as a recessive defect. These cattle are thought to have increased erythropoietin of unknown origin and the condition has been grouped within the secondary polycythemias.

Clinical signs associated with polycythemia are dyspnea, exercise intolerance, tachycardia, tachypnea, and very injected maroon or muddy-red membranes. Calves affected with polycythemia do not grow properly, regardless of whether the cause is cardiac or inherited. Funduscopic examination allows confirmation of hyperviscosity (Fig. 3.51) in the retinal vessels. Retinal vessels are greatly increased in diameter, and the stars of Winslow (choriocapillaries on end) are very obvious. The hematocrit is consistently elevated over 55% and often greater than 60%.

Treatment is impractical in most patients with polycythemia. This is especially true regarding congenital heart defects and inherited forms of the disease. Particularly valuable cattle with high-altitude hypoxia may benefit from phlebotomy and a return to lower altitudes. The practicality of the matter, however, dictates that although extremely dyspneic cattle are most likely to benefit from phlebotomy, these animals may die if restrained. If phlebotomy is accomplished, the PCV should be decreased below 50%, the animal moved to lower altitude, and symptomatic therapy given. Suspected hereditary polycythemia cases should be investigated genetically, and family members should be culled.

Anemia
Blood Loss Anemia

In addition to sporadic trauma and surgical procedures that result in severe blood loss, a long list of differential diagnoses exists for blood loss anemia in cattle. However, several common causes deserve comment.
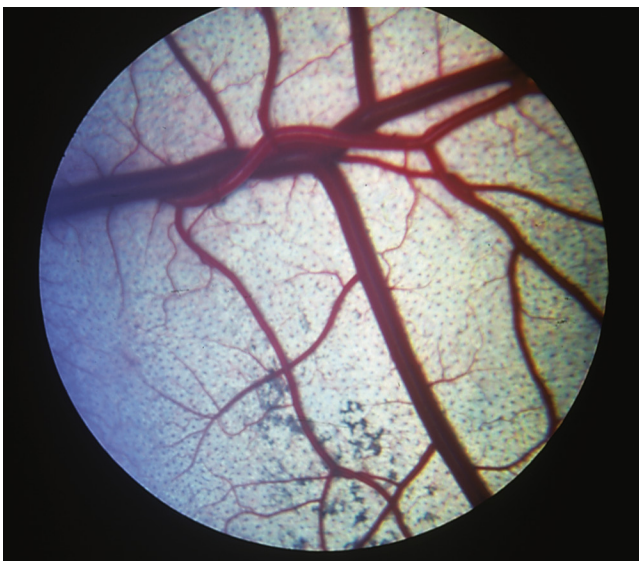
• **Fig. 3.51** Dorsal view of the fundus of a calf that had polycythemia secondary to tetralogy of Fallot. The fundic vessels are greatly accentuated as is typical of hyperviscosity syndrome.

Bleeding abomasal ulcers may cause acute or subacute blood loss in adult cattle. Melena is associated with most abomasal ulcers causing significant blood loss (Fig. 3.52). Bleeding abomasal ulcers that result in clinically significant anemia are not common even though abomasal ulceration is commonly found on necropsy of sick cattle. Bleeding ulcers causing clinical signs of anemia are more common in adult cows than in calves, where perforations are most common. Abomasal bleeding also may occur in association with chronic abomasal displacement in cattle. This combination of chronic abomasal displacement with ulceration is most common in dry cows, bulls, and heifers that are not observed as closely as lactating cattle. Thus the abomasal displacement may have existed for days to weeks before diagnosis. The distention and ileus of the displaced abomasum, coupled with large volumes of hydrochloric acid, contributes to mucosal injury and subsequent ulceration with bleeding.

Lymphosarcoma of the abomasum may cause abomasal ulceration, hemorrhage, and blood loss anemia. The clinical signs may be difficult to differentiate from bleeding abomasal ulcers unless other signs of lymphosarcoma are detected during the physical examination.

Acute splenic rupture caused by infiltration of the spleen by lymphosarcoma may cause severe acute or peracute hemoperitoneum with resultant signs of blood loss anemia.

Caudal vena caval thrombosis syndrome may cause blood loss anemia after abscesses resulting from septic thromboemboli lodged in pulmonary arterioles erode into airways or lung parenchyma. Subsequent hemorrhage results in hemoptysis and epistaxis. Melena or fecal occult blood may be detected if the affected cow swallows sufficient quantities of blood. Epistaxis and blood loss also may occur as a result of granulomatous rhinitis, skull trauma and invasive neoplasia of the upper respiratory tract (usually adenocarcinomas of the respiratory epithelium).

Parasites are another cause of blood loss anemia. Lice are the most common ectoparasite to cause anemia in both calves and adult cattle in the northern United States. In other geographic areas, fleas (*Ctenocephalides felis*) and ticks also may cause significant blood loss. Thanks to modern heifer
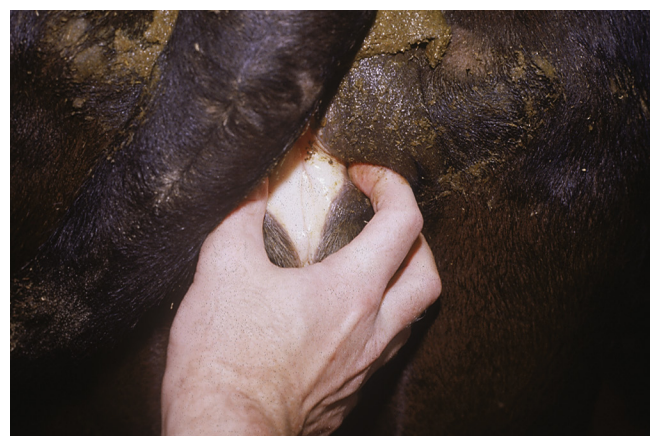
• **Fig. 3.52** Extreme pallor of the vulvar mucous membranes in a cow that had severe blood loss associated with a bleeding abomasal ulcer.

management systems and routine deworming, endoparasites are uncommon but may result in blood loss, especially in pastured heifers. *Eimeria bovis* may cause life-threatening anemia as a result of intestinal blood loss in weanling through yearling age cattle. *Anaplasma marginale* or *Theleria* infection may cause fever, jaundice, and anemia associated with severe extravascular hemolysis. With hemolytic disorders PCV is decreased but there is usually no decrease of plasma protein. By contrast, in severe hemorrhage of more than a few hours duration both PCV and plasma protein concentrations decrease.

Pyelonephritis in cattle may result in anemia by either blood loss (acute and uncommon) or by nonregenerative mechanisms (chronic and common). Cattle having blood loss associated with acute pyelonephritis also may have colic and stranguria as a result of blood clots obstructing the ureters or urethra (see Chapter 11) and usually have fever. Anemia of chronic infection or perhaps that associated with decreased erythropoietin production caused by chronic pyelonephritis may be involved in the anemia observed in such patients. Blood loss anemia, sometimes severe, also occurs in association with thrombocytopenia caused by type 2 bovine viral diarrhea virus (BVDV) infection. Affected animals often have obvious petechial and ecchymotic hemorrhages on their oral, vulval, and conjunctival membranes (see section on thrombocytopenia).

Acquired or congenital defects in hemostasis may cause blood loss and resultant anemia by a variety of mechanisms. When hemostatic dysfunction exists, simple bruising, insect bites, injections, and other minor trauma may cause significant blood loss.

Rupture of the uterine artery during parturition or after uterine prolapse and sporadic rupture of other major arteries are other causes of acute blood loss. Occasionally, vaginal hemorrhage associated with dystocia can be significant enough to cause severe life-threatening anemia. Self-induced trauma or laceration of a prolapsed uterus with subsequent hemorrhage has been observed in dairy cattle. Manual removal of a corpus luteum through rectal palpation to induce heat has fortunately fallen out of favor with bovine practitioners. This procedure occasionally resulted in severe blood loss or exsanguination.

Winter dysentery very occasionally causes severe blood loss from the colon in first-calf heifers. Affected heifers have fresh clots of whole blood and severe dysentery and may require whole blood transfusions.

Nonregenerative Anemia (Anemia of Chronic Disease)

Chronic infections and neoplasms are the most common primary conditions associated with inadequate erythrocyte production or nonregenerative anemia. Chronic pneumonia with abscessation, chronic pyelonephritis, multiple abscesses secondary to musculoskeletal problems, endocarditis, and visceral abscesses may cause nonregenerative anemia. Nonregenerative anemia caused by chronic inflammation is mostly the result of hepcidin release from the liver causing macrophage sequestration and malabsorption of iron resulting in secondary iron deficiency. Serum iron concentration is moderately decreased as is total iron-binding capacity (TIBC) and transferrin. The PCV in these cases is generally not lower than 18%. Primary iron-deficiency anemia may rarely cause severe weakness in milk-fed calves when PCV decreases below 14%. It is characterized as a microcytic and hypochromic anemia. Serum iron is extremely low, and iron-binding capacity is normal or high in affected calves. Treatment with blood transfusion is usually curative.

Cattle with chronic renal disease may have depressed erythropoietin synthesis resulting from renal impairment to help explain their nonregenerative anemia. Chronic protein-losing nephropathies such as amyloidosis and glomerulonephritis also may have a nonregenerative anemia and hypoproteinemia.

Lymphosarcoma may result in anemia through several mechanisms; nonregenerative anemia simply because of diffuse neoplasia, nonregenerative anemia caused by myelophthisis in sporadic adult cattle or calves with the juvenile form of lymphosarcoma, and blood loss anemia resulting from neoplastic ulceration of the abomasum or splenic rupture.

Bone marrow depression by chronic bracken fern intoxication may result in nonregenerative anemia plus blood loss anemia secondary to thrombocytopenia and subsequent hemorrhage (Fig. 3.53). In regions where enzootic hematuria occurs in cattle pastured in bracken fern, blood loss anemia commonly accompanies the bladder lesions. Chronic bovine viral diarrhea virus infection may rarely cause nonregenerative anemia, although BVDV-associated anemia is more commonly associated with acute disease, thrombocytopenia, and blood loss. This is typically associated with a PCV of less than 15%.

• **Fig. 3.53** Necropsy of a 5-month-old Holstein calf found dead in the pasture. Petechial and ecchymotic hemorrhages were immediately visible upon opening the abdomen. Other calves in the pasture were found to have hemorrhages, and complete blood count evaluation revealed severe neutropenia and thrombocytopenia. Bracken fern was plentiful in the pasture and had been eaten by the calves. (Photo courtesy of Dr. Jennifer Nightingale)

Anemia Through Hemolysis

Hemolytic anemias are associated with either intravascular or extravascular erythrocyte destruction (see Chapter 16 for specific causes discussed in more detail). Although extravascular erythrocyte destruction is more common in most species, cattle have several forms of hemolytic anemia caused by intravascular destruction of erythrocytes. A common cause of intravascular hemolysis in calves is water intoxication. Calves watered intermittently that are then given plentiful supplies of water may overdrink to the point that severe decrease in serum osmolality occurs and RBC lysis follows. The presence of hemoglobinuria alongside the history are diagnostic. Low-grade fever also may be present resulting from RBC destruction, and neurologic signs develop in extreme cases. Similarly, IV administration of hypotonic solutions is an occasional complication observed in adults or calves when electrolytes are not added or are added in insufficient quantities to large fluid containers (for example, 20 L of sterile water will reliably cause this problem in an adult cow) before administration. Fever, trembling, hair standing on end, and hemoglobinuria are the four clinical signs that identify the therapeutic error.

Intravascular destruction of RBC occurs in babesiosis (piroplasmosis, tick fever or red water fever) in cattle; this disease has been eradicated from the United States. Fever, anemia, depression, icterus, hemoglobinuria, and other signs associated with anemia can occur in young cattle with leptospirosis. *Leptospira interrogans* Pomona, *Leptospira interrogans* Icterohaemorrhagiae, and *Leptospira interrogans* Grippotyphosa are the most common disease-producing serovars in young cattle. Bacillary hemoglobinuria caused by *Clostridium novyi* type D *(Clostridium hemolyticum)* is another infectious disease that causes intravascular hemolysis in cattle.

One of the authors (TD) has seen *Theileria buffeli* cause intravascular hemolysis in North American dairy cattle. High fever, tachycardia, diarrhea, jaundiced membranes, dark-colored urine, and lymphadenopathy are other clinical findings. Asymptomatic cows may also be in the herd, and the reason why one cow develops severe disease is unknown. Concurrent lymphosarcoma has been sometimes blamed for the onset of *T. buffeli* disease, but *Theileria* spp. can transform lymphocytes to have the appearance of lymphosarcoma, so the association is unclear. The life cycle of *Theileria* includes two intracellular developmental stages; intralymphocytic schizonts and intraerythrocytic piroplasms. Piroplasms can be identified in the red blood cells in stained blood smears but cannot always be differentiated from other blood parasites such as *Babesia* spp. Several hematologic and biochemical changes associated with bovine theileriosis have been reported such as anemia (regenerative), leukopenia, neutropenia, lymphocytosis, and hypo- or hyperproteinemia. Hyperbilirubinemia, increased liver enzymes, and dark urine are all related to the hemolytic process. Treatment with tetracycline and imidocarb has been unsuccessful.

Heinz body hemolytic anemia results from a variety of oxidizing agents that denature hemoglobin. Complexes of globin, a protein, are then observed microscopically as Heinz body inclusions in RBC. Although rare in dairy cattle, Heinz body anemia has been observed in selenium deficiency and in cattle grazing on rye grass (*Secale cereale*), onions, and *Brassica* spp. Hemoglobinuria generally is also observed in cattle with these diseases.

Postparturient hemoglobinuria may develop when lactating dairy cattle are fed a ration deficient in phosphorus. Intravascular hemolysis and hemoglobinuria associated with hypophosphatemia tend to appear during the first month of lactation. A depletion of adenosine 5′-triphosphate (ATP), secondary to phosphorus deficiency, may be involved in the RBC lysis in this condition. A recent report by Grunberg et al suggests that hypophosphatemia is not the actual cause of the hemolytic disorder.

Extravascular hemolysis occurs as a result of immune-mediated RBC destruction in anaplasmosis in cattle. Hemoglobinuria does *not* occur with this form of hemolysis. Severe anemia, jaundice, fever, weakness, weight loss, and decreased production are the typical findings. Autoimmune hemolytic anemia, as described in other species, is rare or has yet to be documented in cattle other than the RBC destruction that occurs with protozoal RBC parasites. *Mycoplasma wenyonii* may rarely cause severe immune-mediated anemia in cattle. Pitting edema of the hind limbs, teats, and udder along with a mild to modest anemia are the characteristic findings. The organisms are seen on the surface of erythrocytes or free in the serum during a Wright's stained cytologic examination. If milk production is affected by the disease, treatment with tetracyclines is generally successful. Autoimmune RBC destruction has been suspected in some cattle with lymphosarcoma, but definitive documentation has not yet been provided. Neonatal isoerythrolysis does not occur naturally in cattle, but the disorder has been observed as a consequence of vaccination of dams against anaplasmosis and babesiosis with products of cattle origin. Subsequent passive transfer of maternal antibodies against specific blood types to calves from these cattle results in some calves showing isoerythrolysis.

The anemia sometimes present in cattle having the inherited disease erythropoietic porphyria ("pink tooth") (see also Chapter 7) is thought to be hemolytic in origin, although several other factors may be involved.

Determination of when an anemic patient requires whole blood transfusion must be made primarily based on the physical examination and secondarily based on PCV. In peracute blood loss, the PCV may be misleadingly high despite obvious pallor, tachycardia, polypnea, weakness, and other general signs that would indicate the need for a transfusion. When acute or subacute (24–72 hr) blood loss causes anemia, the usual PCV associated with the need for transfusion is in the range of 12% to 14%. With subacute or chronic hemorrhage or hemolysis, and assuming normal hydration, a PCV greater than 14% seldom requires an immediate transfusion. A PCV of less than 14% usually coincides with heart rates greater than 100 beats/min, respiratory rates of greater than 60 breaths/min, obvious mucous membrane

pallor, jaundice if a hemolytic process is present, and weakness. Heart rates that are greater than 120 beats/min and pounding, respiratory rates over 60 breaths/min, and obvious pallor all dictate a need for transfusion regardless of the PCV. An increase in blood lactate is a good marker for inadequate tissue oxygenation in cattle with hemolytic anemia and may serve as a transfusion guide.

Chronic blood loss and nonregenerative anemias seldom require transfusions, and the slow, gradual development of anemia seems to allow physiologic compensation for the reduced numbers of RBCs. Cattle with chronic anemias may have PCV values of 9% to 10% without appearing in an anemic crisis.

Diseases of the Leukon

Cattle are unique in regard to their leukogram and its response to various diseases and stresses. Certain conditions, especially peracute inflammatory or endotoxic diseases, cause consistent changes in the leukogram, but other diseases, although infectious in origin, may be associated with normal or variable leukograms that shed little light on the patient's primary problem. Despite having requested leukograms on thousands of bovine patients in academic referral hospitals, we find that the majority of these leukograms, regardless of the cause of illness, have been within normal limits. Despite this fact, the leukogram or, better yet, serial leukograms occasionally may aid greatly in the diagnosis and prognosis for a bovine patient. WBC reference ranges used at the New York State College of Veterinary Medicine for adult cattle are listed in Chapter 1.

Stress and glucocorticoids reliably alter the leukogram to create neutrophilia, lymphopenia, and eosinopenia. The numbers of monocytes appear variable. Concurrent inflammatory diseases may alter this typical "stress leukogram." For example, a cow with acute coliform mastitis that has been treated with dexamethasone may have a normal neutrophil count because of glucocorticoid-induced neutrophilia counterbalancing the expected neutropenia normally found in endotoxemia. This same cow could have a left shift with band (immature) neutrophils present and a lymphopenia in the absence of steroid administration. Cattle and their leukograms are exquisitely sensitive to exogenous corticosteroids. A single injection of 20 mg or more of dexamethasone usually results in a stress leukogram characterized by neutrophilia, lymphopenia, and eosinopenia within 24 hours. Calves occasionally may have neutrophil counts of 20,000/μL or more after administration of dexamethasone. In addition to altering numbers of neutrophils, corticosteroids can also alter the function of neutrophils in a negative fashion. Whereas glucocorticoids are well known for their ability to be immunosuppressive, a single ketosis treatment dose of 0.02 mg/kg dexamethasone is not associated with clinically significant immune function impairment. Neutrophil function may be impaired in cattle with retained fetal membranes and with other common periparturient diseases such as ketosis and fatty liver. Selenium and copper

deficiency are also associated with negative alterations in granulocyte function.

A "degenerative left shift" wherein neutropenia coexists with the appearance of band neutrophils is typical of cattle with severe acute inflammation or endotoxemia. This helpful and, for the most part, consistent leukogram result is seen in dairy cattle affected with severe coliform mastitis, acute *Mannheimia hemolytica* pneumonia, severe salmonellosis, severe postpartum gram-negative mastitis, and perforating abomasal ulcers that cause diffuse peritonitis. A simplistic explanation of this phenomenon revolves around the fact that cattle have a limited bone marrow neutrophil pool to draw on in an acute emergency. Although the degenerative left shift remains a negative prognostic indicator and yet a consistent indicator of severe infection or endotoxemia, it is so typical in cattle that it must be tempered by the patient's signs and response to treatment before using it as the sole basis of a prognosis. Cattle that have a degenerative left shift will often have a return to normal neutrophil numbers within 4 to 7 days after successful treatment of their acute infection. This time lapse may simply reflect the time necessary for resolution of a severe infectious insult. If the infection requires more than 1 week for resolution, rebound neutrophilia usually will occur. Chronic infections may cause a neutrophilia, but many cattle with chronic infections such as visceral abscesses, musculoskeletal infections, chronic peritonitis, and other diseases, frequently have normal neutrophil numbers despite having obvious infection. Neutrophilia seems more likely in resolving acute or subacute infections than in chronic infection. Certainly, some cattle with chronic infections have neutrophilia, but the magnitude of the neutrophilia seldom is dramatic. It is rare to see an adult cow with more than 18,000 to 20,000 neutrophils per microliter unless exogenous corticosteroids have been administered to the animal.

Neutropenia also may be found during severe viral infections such as BVDV infection. Acute BVDV infection causes a leukopenia as a result of neutropenia, lymphopenia, or both. Because acute BVDV infection also adversely affects neutrophil function in addition to sometimes reducing absolute numbers, naive cattle acutely infected with BVDV have a reduced ability to respond to concurrent or secondary infections until they form antibodies and resolve the BVDV infection. The immunosuppressive effect of acute BVDV infection and the potential for greater morbidity and mortality to be associated with concurrent infectious diseases such as salmonellosis or pasteurellosis should not be overlooked diagnostically during a herd outbreak of enteric or respiratory disease.

Absolute lymphopenia occurs in conjunction with stress, exogenous corticosteroid administration, some viral diseases such as BVDV, and some acute severe infections or endotoxemias. Frequently, it is difficult to know whether the lymphopenia is associated directly with the disease or simply represents stress associated with a disease. Although eosinopenia should accompany lymphopenia when the cause is stress or corticosteroid administration, eosinophil

counts have limited value in this regard. Absolute lymphocytosis that is transient is rare in dairy cattle and when present usually is associated with a neutrophilia in patients recovering from acute infection. Lymphocytosis that is persistent and repeatable usually indicates infection with BLV. PL is a condition that develops in association with BLV infection in certain lines of cattle. The Bendixen method of control of BLV was based on elimination of cattle with PL until a more modern understanding of the disease evolved. This method proved successful because it was eventually determined that PL cows have greater levels of viremia than most BLV positive cows without PL and are the predominant virus spreaders within a herd. Cattle that are BLV positive and have PL may be at greater risk of developing lymphosarcoma than cattle that are BLV positive without PL, but this is controversial. In one study, PL was present in as many as one third of cattle infected with BLV. However, these percentages may vary in individual herds because genetic predispositions appear to affect the trait of PL in response to BLV infection. The lymphocytosis in cattle with PL is generally refractory to stress or corticosteroid treatment. Lymphocyte counts may range from 30,000/µL to 150,000/µL in cases of PL associated with BLV infection (Fig. 3.54). True lymphocytic leukemia does occur in a very small percentage of cattle that develop lymphosarcoma after infection with BLV, and in such cases, lymphoblasts may be observed peripherally.

Eosinophils seldom are of diagnostic significance when interpreting the leukon of cattle. Geographic and management variations may alter the "normal numbers" expected as a result of parasite load and other conditions. Eosinopenia concurrent with lymphopenia is consistent with stress or exogenous corticosteroid administration. Eosinophilia is rare in dairy cattle. Eosinophilia is thought to indicate heavy parasitism, histamine release, or occasionally, immune-mediated or allergic diseases. Unfortunately, eosinophil numbers seldom convey useful clinical data. The same is true of basophils.
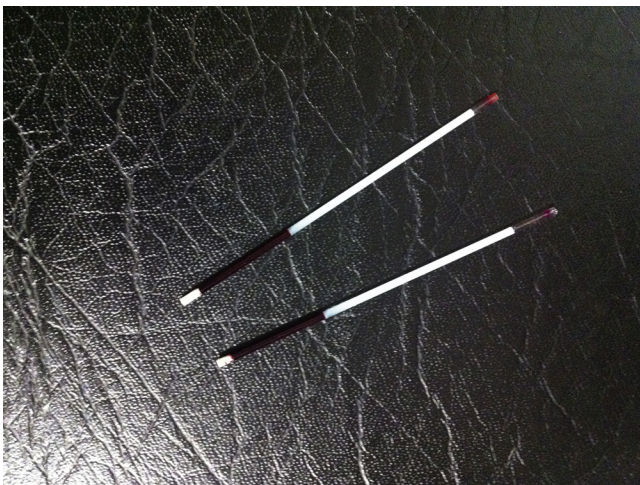
• **Fig. 3.54** Hematocrit tube showing remarkable buffy coat in a bovine leukemia virus–positive, mature Holstein cow with a persistent lymphocytosis of 125,000/µL. (Courtesy of Dr. Sheila McGuirk.)

Monocytosis may be of some value in cattle because it generally is associated with chronic infection. For example, a cow having chronic peritonitis may have a misleadingly normal neutrophil count with no left shift but also may have a monocytosis. Monocytosis, although not specific, should at least raise the clinician's index of suspicion for chronic infection. Although monocytosis is not a consistent finding in the peripheral blood of ruminants infected with *Listeria monocytogenes,* as in humans and rodents so infected, some cattle with listeriosis do have a classical monocytosis. (The name *L. monocytogenes* evolved from the tendency of monogastric animals to have a peripheral monocytosis in response to infection with the organism.)

Bovine Leukocyte Adhesion Deficiency (Bovine Granulocytopathy Syndrome)
Etiology

A fatal syndrome consisting of poor growth, chronic or recurrent infections, and persistent, extreme neutrophilia was first observed in Holstein calves during the latter part of the 20th century. Affected calves had persistent neutrophil counts exceeding 30,000/µL, and some had counts exceeding 100,000/µL. Such calves were initially described subjectively as having a leukemoid blood response that required differentiation from myelogenous leukemia. Despite their neutrophilia, these calves seemed unable to mount a normal defense against common pathogens and minor infections. Although these leukemoid calves sometimes survived for several months, most died before 1 year of age. The true incidence of the disease was impossible to estimate because many "poor-doing" calves eventually die in field situations without ever having a CBC or other diagnostics performed. A genetic immune-deficiency trait was suspected based on clinical observation of the condition in full siblings in a cohort of embryo transfer offspring.

Reports from the United States and Japan on selected calves with the disorder suggested a granulocytopathy, and comparative studies of a canine granulocytopathy in Irish Setters and a leukocyte adhesion deficiency in humans brought about further suspicion of an inherited disorder in these "leukemoid calves." Subsequently this was confirmed and termed bovine leukocyte adhesion deficiency (BLAD) by Kehrli et al. as a genetic disease in Holsteins that represents a severe deficiency of neutrophil Mac-1 (CD11b/CD18). Recessive homozygotes are affected, and heterozygote carriers have intermediate amounts of the Mac-1 β subunit (CD18), but are clinically normal. The molecular basis is a single point mutation (adenine to guanine) at position 383 of the CD18 gene, giving rise to an autosomal recessive mode of inheritance. Despite more than adequate circulating neutrophils, affected calves cannot effectively fight infections because their neutrophils have deficient β2 integrin expression, preventing adherence to vascular endothelium and subsequent migration into tissue sites of inflammation.

Signs

Affected calves have chronic or persistent infections and poor growth (Fig. 3.55). Signs may appear early in life, although some calves live for several months. Relative exposure to a variety of routine pathogens may dictate somewhat the apparent age of onset reported by client histories. Diarrhea and pneumonia are typical signs, but persistent ringworm lesions, persistent keratoconjunctivitis, gingival ulcers, loose teeth, tooth abscesses, poorly healing dehorning wounds, and other lesions also are common. Infections thought to be clinically minor respond poorly or not at all to appropriate therapy. Recurrence of signs and multiple health problems are typical.

Diagnosis

Persistent leukocytosis caused by neutrophilia without a remarkable left shift is a hallmark of the disease. To date most affected calves studied have had greater than 30,000 neutrophils/μL in their peripheral blood. Although myelogenous leukemia is a consideration, neutrophil function tests differentiate these diseases because neutrophils in myelogenous leukemic patients have decreased neutrophil alkaline phosphatase activity. In addition, the truly leukemoid blood picture is characterized as a regenerative left shift, but BLAD calves have primarily a mature neutrophilia. Furthermore, ex vivo tests of adhesion-dependent responses such as chemotaxis and phagocytosis can differentiate between BLAD animals and those with severe, chronic neutrophilia without β2 integrin deficits. Affected calves must be differentiated from calves with chronic abscessation of the thorax or abdomen and calves persistently infected with BVDV that show similar poor growth and apparent reduced resistance to routine pathogens.

Failure to confirm persistent infection with BVDV and ruling out visceral abscessation via radiography, ultrasonography, and serum globulin values support the diagnosis. Definitive diagnosis alongside identification of carriers can be achieved by restriction analysis of PCR-amplified DNA from a suspect individual to allow discrimination between normal, carrier (heterozygote), and affected (homozygote) animals.

Currently, artificial insemination (AI) sires are being tested and identified as either carriers or noncarriers of

• **Fig. 3.55** A normal heifer and two animals affected with bovine leukocyte adhesion deficiency. All three animals were 8 months of age and had been raised on the same farm. (Courtesy of Dr. Robert O. Gilbert.)

BLAD. The routine genetic screening and identification of carriers by AI companies worldwide will eventually lead to the eradication of the disease. It is rare to non-existent now.

Treatment

Treatment is only palliative, and most affected calves die before 1 year of age. The exact age of onset, progression, and true incidence are unknown because most sick calves never have a CBC performed. Theoretically, it is possible that many BLAD calves die early in life and that only those that survive to develop chronic disease associated with poor growth are suspected to have the disease. Because variable expression of the glycoprotein deficiency is possible in homozygote recessives and in heterozygotes, it also is possible that mild forms of disease and prolonged survival occur. The proportionate decrease in β2 integrin expression demonstrated by heterozygotes does not appear to result in any clinical significance however, and heterozygote carriers have comparable growth and performance compared to non-carrier, normal cattle.

Disorders of Coagulation

Inherited

A factor XI deficiency has been described in Holstein cattle and appears to be a recessive trait. Homozygote recessives bleed excessively or repeatedly after injuries or routine surgical procedures such as castration or dehorning. Hematomas commonly occur at venipuncture sites and may lead to venous thrombosis. Routine coagulation profiles may not show in vitro clotting abnormalities in heterozygote carrier cattle even though such animals have less factor XI than normal.

Acquired

Thrombocytopenia

Etiology

Thrombocytopenia is the most common cause of abnormal coagulation in dairy cattle. Cattle normally have between 100,000 and 800,000 platelets/μL of blood. Platelet survival time is thought to be 7 to 10 days, and megakaryocytes in the bone marrow are the precursors of circulating platelets. Thrombocytopenia may result from decreased platelet production, increased platelet destruction, sequestration, or consumption.

Decreased platelet production generally implies a bone marrow insult. Therefore, hemorrhage caused by thrombocytopenia may be the first clinically detectable sign of true pancytopenia. This is the situation with chronic bracken fern toxicity in cattle. Thrombocytopenia and leukopenia tend to be profound long before affected animals become anemic because of the longer normal life span of erythrocytes compared with granulocytes and platelets. Similarly, thrombocytopenia caused by decreased thrombopoiesis has been reported in association with intoxications resulting from ingestion of trichloroethylene-extracted soybean meal,

prolonged furazolidone treatment (in calves), and suspected mycotoxin ingestion in Australian cattle.

Decreased survival of platelets is probably the most common reason for clinical thrombocytopenia. Infectious diseases cause decreased platelet survival via several mechanisms. For example, an immune-mediated thrombocytopenia has been reported in cattle with East Coast fever, and although not specifically immune mediated, the thrombocytopenia that occurs in association with certain strains of type 2 BVDV results from decreased platelet survival after viral infection. Thrombocytopenia in adult cattle and veal calves with natural acute BVDV infection has been observed, and studies confirm a thrombocytopenia beginning 3 to 4 days after experimental infection with some type 2 strains of the virus. Platelet numbers in these cattle then decrease progressively over the next 10 to 14 days (Fig. 3.56). Animals that survive this acute BVDV infection show a return to normal platelet numbers in conjunction with an increase in serum antibody titers against BVDV. It is worth pointing out that this syndrome is a consequence of certain type 2 BVDV strains infecting naive, yet immunocompetent, animals and is not a characteristic manifestation of mucosal disease nor typically seen in persistently infected cattle.

Infectious diseases also may initiate disseminated intravascular coagulation (DIC) with subsequent consumption of platelets. DIC has been suggested as the cause of thrombocytopenia in acute sarcocystosis and can be observed clinically in a variety of septicemic and endotoxic states in cattle. Septic metritis and septic mastitis are the most common endotoxic diseases to cause thrombocytopenia in adult cattle (Fig. 3.57). Thrombocytopenia in these cattle may either be caused directly by DIC or decreased platelet survival for other reasons. In neonatal calves, thrombocytopenia is most commonly observed in association with neonatal calf septicemia due to failure of passive transfer.

Therefore, infectious diseases may result in thrombocytopenia for a variety of reasons. However, these reasons usually affect platelet survival rather than production. Increased destruction, decreased life span resulting from platelet infection, consumption, vasculitis, and unknown factors contribute to thrombocytopenia in association with these infectious diseases. With the exception of BVDV infection and a few other diseases in which thrombocytopenia has been reproduced experimentally, most thrombocytopenia cases are sporadic and associated with a variety of disorders.

Trauma rarely has been associated with thrombocytopenia in cattle and may lower platelet numbers either by consumption or unknown mechanisms. We have confirmed occasional adult cattle with udder hematomas and cattle that are bleeding into a quarter as thrombocytopenic. It is not known whether the thrombocytopenia in these cattle represents cause or effect, but these patients showed no other evidence of systemic disease. One of the editors (TJD) treated a calf with skull and orbital trauma that apparently resulted in profound orbital hemorrhage secondary to thrombocytopenia (Fig. 3.58). The calf completely recovered after a whole blood transfusion and replacement of the proptosed globe.

Immune-mediated thrombocytopenia—or thought to be immune mediated—rarely is observed in ruminants. Perhaps "idiopathic" thrombocytopenia is a better term because clinicopathologic confirmation of true immune-mediated thrombocytopenia seldom is possible in ruminants. Although perhaps more common in goats, idiopathic thrombocytopenia has rarely developed in calves having no evidence of infectious disease, trauma, bone marrow depression, and so forth. Morris states, "The diagnosis of idiopathic thrombocytopenia must be based on small vessel hemorrhagic diathesis and severe thrombocytopenia in a horse with normal coagulation times and no other evidence of DIC." Although this statement refers to horses, it may also pertain to cattle because, in general, specific reagents to detect platelet-associated immunoglobulin G, serum antiplatelet activity, and other confirmatory tests either have not been developed or are unavailable to most veterinarians.

Signs

Petechial hemorrhages on mucous membranes coupled with other signs of hemorrhage that may occur from small vessels anywhere in the body typify thrombocytopenic bleeding. Ecchymotic hemorrhages may accompany the

• **Fig. 3.56** Subconjunctival hemorrhage and hyphema in a calf with thrombocytopenia secondary to bovine viral diarrhea virus infection.

• **Fig. 3.57** Hyphema associated with thrombocytopenia and DIC in an adult cow suffering from acute coliform mastitis.
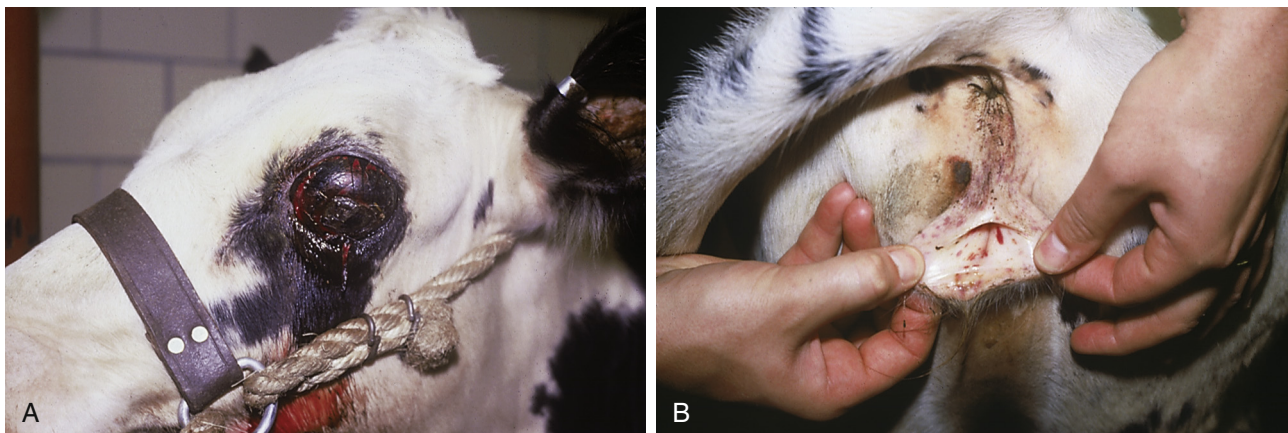
• **Fig. 3.58 A,** Proptosed globe secondary to orbital hemorrhage in a calf with thrombocytopenia after entrapment and struggling. **B,** Petechial hemorrhages visible on the vulvar mucous membranes of the same calf as in Fig. 3.58, A.

petechial hemorrhages on mucous membranes such as the conjunctival, nasal, oral, or vulvar mucosa. Bleeding may occur from the skin at sites of injections or insect bites. Venipuncture causes bleeding, hematoma formation, and possible venous thrombosis. Epistaxis is common in cattle with thrombocytopenia and other signs of bleeding frequently accompany inflammation or injury to specific sites. For example, cattle with thrombocytopenia associated with acute BVDV infection frequently have fresh blood or clots of blood in their feces because of the irritation of diarrhea. Hyphema, scleral hemorrhages, and hematomas may occur secondary to minor trauma, especially in stanchioned cattle. Melena and hematuria also are possible signs.

Clinical bleeding seldom appears until platelet counts drop below 50,000/μL and usually occurs when platelets are less than 20,000/μL. Obviously, stress, trauma, and hydration status may influence the incidence of bleeding at platelet values less than 50,000/μL. Many cattle with confirmed platelet numbers of less than 20,000/μL show no evidence of, or tendency for, bleeding. However, if stressed, traumatized or subjected to multiple injections, venipuncture, bone marrow aspirates, rectal examinations, and so forth, these same cattle will begin to bleed.

Diagnosis

Absolute diagnosis of bleeding resulting from thrombocytopenia depends on:
1. Platelet count (usually <50,000/μL)
2. Ruling out DIC and other coagulopathies

Although it may be difficult in field situations, confirmation of thrombocytopenic purpura necessitates a coagulation panel to confirm normal values for prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time, fibrinogen, and fibrinogen degradation products (FDPs). Bleeding time and clot retraction are abnormal. In essence, DIC is the major differential diagnosis, and the aforementioned tests differentiate primary thrombocytopenia from thrombocytopenia secondary to DIC.

After the diagnosis of thrombocytopenia is confirmed by laboratory studies, clues to the cause of this disorder should be sought. Septicemia, endotoxemia, and recent trauma may be clinically obvious, whereas ingested toxins or parenteral drugs may require careful historical data and evaluation of the patient's environment. When no predisposing factor or cause can be determined, "idiopathic" or immune-mediated thrombocytopenia is the diagnosis by exclusion. Fortunately, this latter category is very rare in cattle.

Bone marrow aspirates or biopsy are indicated whenever the etiology of thrombocytopenia remains obscure, granulocytopenia coexists with thrombocytopenia, or thrombocytopenia has been chronic or recurrent.

Treatment

Thrombocytopenia resulting in clinical bleeding requires therapy with a fresh whole blood transfusion and treatment of any primary condition. Ideally, blood donors should be free of BLV and persistent BVDV infection. The volume of transfused blood is somewhat dependent on the degree of concurrent blood loss and the size of the patient. The standard empiric quantities are a minimum of 1 L for a calf and 4 L for an adult cow, but greater volumes may be essential for severely anemic patients. Blood transfusions are "first aid" for thrombocytopenia, and the success of transfusion completely depends on whether platelet loss or lack of production will continue.

Specific and supportive therapy for primary causes such as endotoxemia, septicemia, trauma, and localized infections may allow a single whole blood transfusion to suffice for treatment of thrombocytopenia secondary to these disorders. Similarly, calves or cattle with acute BVDV infection that are thrombocytopenic and bleeding usually require only one transfusion. These BVDV patients often have their lowest platelet counts approximately 14 days after infection. Immunologically speaking, therefore, they are near recovery, and humoral antibodies are peaking at this same time. Whole blood transfusion and supportive care can save many of these patients.

The prognosis must be grave for patients having both thrombocytopenia and granulocytopenia because a pancytopenic disorder should be suspected. Chronic bracken fern toxicity, furazolidone toxicity in calves, and other conditions that broadly depress bone marrow are difficult to correct. Supportive therapy, whole blood (collected in plastic) or platelet-rich plasma transfusions, and antibiotics to protect against opportunistic infections are indicated in these patients. Bone marrow aspirates are essential to confirm the diagnosis.

If a primary cause cannot be found and idiopathic thrombocytopenia is diagnosed, the clinical course is more difficult to predict. Idiosyncratic drug reactions should be ruled out by history, and drugs having the potential to cause thrombocytopenia should be discontinued. The patient must be monitored with daily platelet counts and physical examination to determine whether bleeding is continuing or a transfusion is necessary as a lifesaving procedure. Fecal occult blood, Multistix evaluation of urine, and inspection of mucous membranes are important means of monitoring idiopathic thrombocytopenic patients. Further whole blood transfusions are often not indicated unless signs of bleeding appear or the patient is showing signs of severe anemia and hypoxia. Idiopathic thrombocytopenia patients that have persistent or recurrently low platelet counts of less than 25,000/μL and bleeding should have bone marrow aspirates evaluated. If the bone marrow is normal, low-dose corticosteroids may be used in an effort to increase platelet numbers by increasing thrombocytopoiesis and counteracting a variety of immune mechanisms that may contribute to platelet destruction. Dexamethasone is preferable in our experience and may be therapeutic at doses as low as 0.05 mg/kg once daily. Most adult patients can be further reduced to 0.02 mg/kg once daily after 5 days. Most patients requiring corticosteroids for suspected immune-mediated thrombocytopenia can be weaned off medication within 30 days and do not tend to relapse.

Disseminated Intravascular Coagulation
Etiology
Disseminated intravascular coagulation is a complex coagulopathy characterized both by bleeding and excessive intravascular thrombosis. This apparent contradiction leads to a dramatic, and usually fatal, clinical progression. It does not occur spontaneously by itself but as a complication of some other primary illness. Cattle experiencing septicemia, endotoxemia, exotoxemia from clostridial infections, and other severe localized infections are at greatest risk for DIC. Septic mastitis and septic metritis are probably the two most common infections to cause DIC in adult dairy cattle. In calves, neonatal septicemia and severe enteritis are probably the two most frequently encountered causes. Fortunately, DIC is uncommon in cattle.

Clinical signs of bleeding and thrombosis represent overstimulation of coagulation within vessels that eventually depletes coagulation factors to such a degree that bleeding evolves as a major sign. Fibrinolysis is excessive, and localized or regional tissue hypoxia occurs as a result of thrombosis.

Subsequent major organ dysfunction (liver, kidney, brain, gut) may ensue. Because a serious primary disease already exists in patients that develop DIC, patients are further predisposed to organ failure and shock.

Products of inflammation (platelet–activating factors) or infectious agents (endotoxin, clostridium α toxin) that encourage procoagulant activity or damage vascular endothelium may activate DIC. However, the exact mechanism by which DIC occurs is unknown, and it is impossible to predict those patients who will have DIC complicate their already potentially life-threatening primary disease.

Signs
Rapid systemic deterioration in conjunction with vascular thrombosis and hemorrhage should cause suspicion of DIC in patients with serious primary inflammatory or GI disease. Hemorrhages may be manifest as petechiae, ecchymoses, hematomas, or bleeding from body orifices. Melena or frank blood clots in the feces may appear, especially in cattle with enteritis. Microscopic or macroscopic hematuria may be present. Bleeding from injection sites and rapid venous thrombosis after venipuncture are typical signs. Epistaxis, hyphema, hemarthroses and visceral hematomas occasionally occur. Renal failure is common (see Chapter 11).

Major organ failure may be caused by reduced perfusion associated with thromboses. Lesser degrees of ischemia may cause renal (infarcts or tubular nephrosis), GI (bleeding), neurologic (bleeding into central nervous system), hemarthroses, or other signs.

As the patient's condition further deteriorates, venous thrombosis may frustrate therapeutic attempts to improve the systemic state.

Diagnosis
Coagulation profiles and platelet counts are essential tests to confirm clinical suspicions of DIC in a patient to differentiate it from other causes of thrombosis and hemorrhage. In all instances, a patient already seriously ill from a primary disease becomes "sicker" and has signs of thrombosis and bleeding. Because both may be caused by similar predisposing causes, DIC must be differentiated from simple thrombocytopenia. Other causes of bleeding such as hepatic failure, warfarin toxicosis, and inherited coagulopathies can only be ruled out by laboratory tests.

The diagnosis of DIC is not made on the basis of a single laboratory value but on a collection of abnormal laboratory results combined with clinical evidence and history of a primary illness known to be associated with DIC in that particular species. Historically, textbooks have discussed the following as being consistent with the diagnosis of DIC:
1. Decreased platelet counts
2. Prolonged PT, APTT, and thrombin time
3. Elevated FDPs
4. Prolonged bleeding time
5. Decreased antithrombin III

In human medicine a diagnostic algorithm can be used that allocates a numerical score based on the severity

of abnormalities in platelet count, FDP (total FDP or D-dimer), PT prolongation, and fibrinogen concentration, alongside the presence of a primary disease known to be associated with DIC. Realistically, it is unusual to have all of these parameters satisfied in a bovine patient suspected of having DIC. For example, the PT and APTT may or may not be outside the normal reference range for the laboratory and if abnormal may be only slightly prolonged. In addition, FDP results in large animals with DIC usually fall in the intermediate (10–40 μg/mL FDP) or suspicious range rather than being obviously elevated. Decreased fibrinogen levels are not typical of DIC in cattle and if identified may actually suggest liver disease. Therefore, clinical cases of bovine DIC may only fulfill two or three of these parameters for diagnosis. Patients fitting many of the textbook parameters usually are in an advanced state and have a grave prognosis. Most bovine DIC patients have thrombocytopenia and intermediate FDP (10–40 μg/mL) results and may have slight prolongation of PT or APTT.

Treatment

Treatment of patients with DIC is perhaps as poorly understood as the disease itself. Without question, intense treatment for the primary condition must continue. Intravenous fluids are essential to counteract hypotension, poor tissue perfusion, and major organ failure. Nonsteroidal antiinflammatory drugs, especially flunixin meglumine (0.5 mg/kg body weight twice daily), may be helpful to patients having underlying gram-negative infections or enteric disorders. Severe thrombocytopenia or continued bleeding dictates replacement of clotting factors even though this may provide further substrate for ongoing coagulation. Therefore, fresh whole plasma or, more likely in the field, fresh whole blood may be indicated.

Other therapies, such as heparin and corticosteroids, have been suggested, but there appears to be no scientific confirmation of their value in treating DIC, and in fact they may have deleterious effects in patients with DIC.

The prognosis for cattle with DIC is guarded to grave. Unfortunately, most patients with confirmed DIC die.

Coumarin Anticoagulants, Dicoumarol Toxicity, and Diffuse Hepatocellular Disease

Etiology

Rodenticides such as warfarin and brodifacoum that are coumarin derivatives, coumarin-containing sweet clover (*Melilotus* spp.) or sweet vernal grass (*Anthoxanthum odoratum*) forages that have become moldy, and diffuse hepatocellular disease may cause hemorrhage resulting from lack of liver origin clotting factors. Coumarin competes with vitamin K1, a precursor of clotting factors II, VII, IX, and X. Excessive fungal growth during improper curing of sweet clover or sweet vernal grass forages causes coumarin to be converted to dicoumarol and results in a decrease in liver production of the aforementioned clotting factors. Diffuse hepatocellular disease also may prevent normal synthesis of these factors, but this is rare and generally seen only in advanced hepatic failure.

Because factor VII has a shorter plasma half-life than factors II, IX, and X, a prolonged PT tends to be the earliest laboratory coagulation abnormality found in patients with coumarin or dicoumarol toxicity. Subsequent prolongation of APTT and activated clotting time occurs as the disease progresses. Obvious external blood loss, hematomas, or occult internal hemorrhages causing profound anemia may appear in affected cattle.

Accidental ingestion of rodenticides containing coumarin derivatives or ingestion of sweet clover forages that are moldy tend to cause sporadic or endemic coagulopathies, respectively.

Toxicity of a given amount of ingested coumarin may be enhanced by hypoproteinemia, drugs that are highly protein bound (thus freeing more coumarin from protein binding), reduced hepatic function, and insufficient vitamin K in the diet.

Clinical signs tend to occur within 1 week of the ingestion of the toxic agent.

Signs

Ecchymotic hemorrhages, hemarthroses, hematomas (especially over pressure points), epistaxis, melena, hematuria, and prolonged bleeding from injection sites or insect bites (Fig. 3.59) all are possible signs. Although not common,
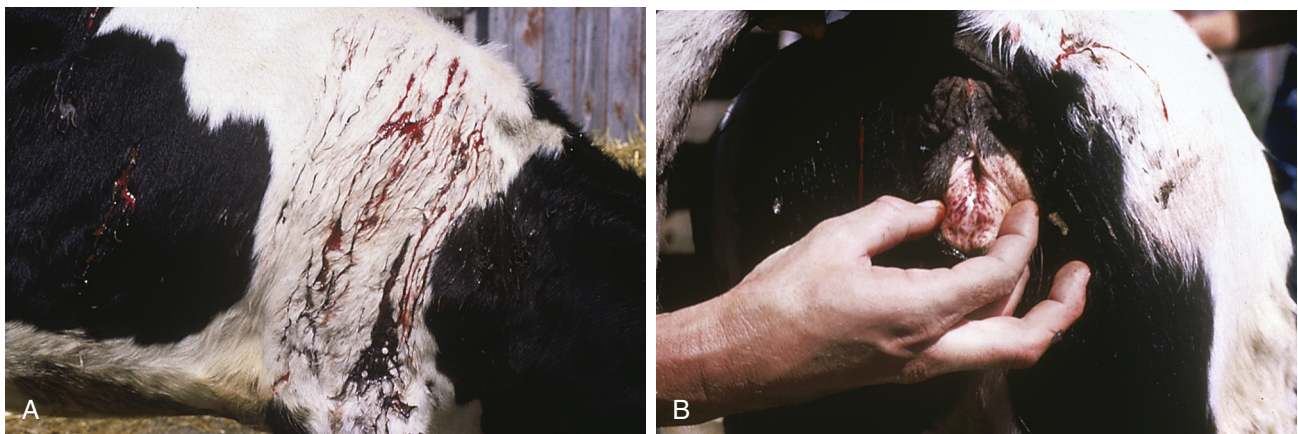
• **Fig. 3.59 A,** Streaks of blood originating from fly bites over the withers area in a calf that had eaten warfarin rodenticide. **B,** Petechial and ecchymotic hemorrhages of the vulvar mucous membranes of the same calf as in Fig. 3.59, A.

petechial hemorrhages may be observed in some patients. In addition, moderate to severe anemia may be apparent resulting from internal or external blood loss and is apparent based on mucous membrane pallor, elevated heart rate, and elevated respiratory rate. Hypoproteinemia also is present when blood loss has been severe. Other less common clinical signs simply reflect bleeding into unusual locations as a result of incidental trauma. For example, seizures or neurologic signs may result from skull trauma. Prolonged bleeding may become obvious after minor surgical procedures such as dehorning in otherwise subclinical cattle.

Diagnosis

Clinical signs, history of exposure to sweet clover or sweet vernal forages, or potential exposure to a coumarin-type rodenticide coupled with a prolonged PT and possibly prolonged APTT support the diagnosis when no other clotting abnormalities are identified. Platelet counts also should be normal. The absence of biochemical evidence of hepatic failure rules out liver disease. Analysis of blood, liver, or feedstuffs for dicoumarol may be available at some diagnostic or toxicology laboratories.

Treatment

All affected animals should receive vitamin K1 (1.0 mg/kg SC or IM). Treatment should be repeated twice daily and continue for at least 5 days. Affected animals that are severely anemic should receive 2 to 6 L of fresh whole blood in transfusions from healthy donor cattle (see also Chapter 2).

Vitamin K3 is not a substitute for K1 and in fact may be toxic. Most vitamin K3 products (menadione sodium bisulfite) have been taken off the market because of toxicity to domestic animals and humans.

Affected feed should be discarded and remaining feed inspected before allowing cattle access to it. Rodenticides should be managed carefully to avoid accidental ingestion.

Causes of Fatal Peracute Hemorrhage in Cattle

Sudden death resulting from exsanguination may result in cattle from a variety of causes. When called to examine or necropsy a previously healthy animal that develops peracute anemia or dies from blood loss, the veterinarian should consider several diseases:

1. Obvious external blood:
   - Laceration of a major vessel such as occurs with mammary vein laceration
   - Caudal vena caval thrombosis with obvious bleeding from the mouth and nose
   - Bleeding from the abomasum with obvious melena
2. Occult or internal blood loss:
   - Manual removal of a corpus luteum during rectal palpation
   - Rupture of the spleen secondary to massive enlargement of the organ with lymphosarcoma
   - Rupture of a uterine or mesenteric vessel (consider both reproductive causes and copper deficiency). Mesenteric vessel rupture may be an endemic herd problem
   - Rupture of vaginal artery during parturition or dystocia; may have some evidence of external hemorrhage from caudal reproductive tract, but blood may "pool" within uterus beyond view
   - Peracute abomasal hemorrhage without obvious melena
3. Toxicity and coagulation disorder such as sweet vernal or sweet clover hay that may interfere with vitamin K–dependent coagulation factors.

Thrombosis

Arterial and venous thromboses are generally associated with septic causes, such as vena caval and related pulmonary thrombosis; jugular and vena caval thrombosis associated with septic phlebitis; uterine, mammary, or intestinal thrombosis associated with infectious or inflammatory diseases of those organs; and septic splenic thrombosis. Endocarditis may result in thrombosis of renal or pulmonary arteries. *Claviceps purpurea,* the cause of fescue foot or ergotism, may cause thrombosis of limb, ear, and tail arteries. Severe frost bite of distal extremities, especially in septic calves, may also cause vascular thrombosis of distal extremities (Fig. 3.60). The prognosis for frostbitten extremities can be determined after rewarming the affected sites and assessing the severity of necrosis and thrombosis. Rewarming the frostbitten area as quickly as possible to salvage as much tissue and function as possible is suggested. The use of circulating water at 40°C is recommended. Do not allow the water to get too hot or too cold. Avoid premature termination of the rewarming process. Remember to treat pain associated with rewarming and provide antibiotic and surgical treatments as needed. Mechanical trauma (from over-vigorous massaging or rubbing), rewarming at too high temperatures, and allowing refreezing are

• **Fig. 3.60** Frostbite of the rear limbs in a septic calf. The foot remained cold and discolored after warming the legs and giving intravenous fluids, which suggested arterial thrombosis. The calf was then euthanized, and thrombosis was confirmed.
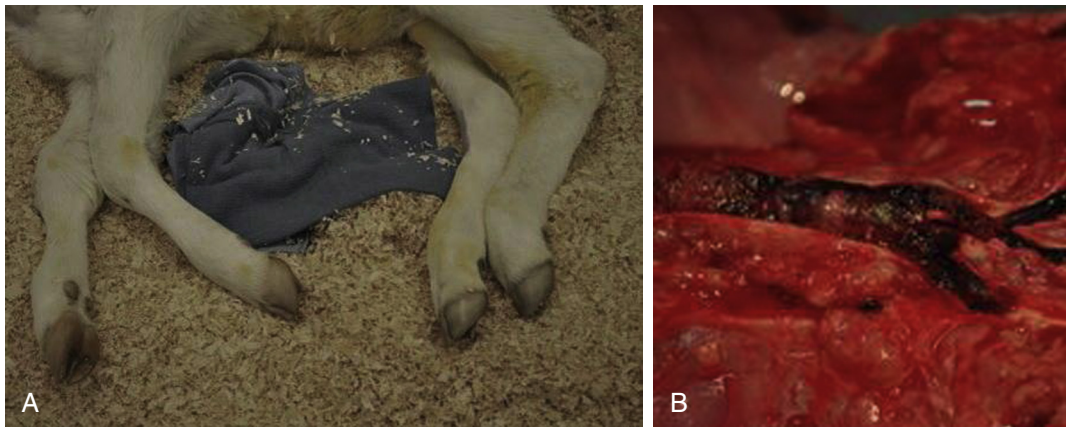
• **Fig. 3.61 A,** A 3-week-old calf with acute onset of progressive posterior paresis that has rapidly advanced to recumbency and the inability to stand. Both distal rear limbs felt cold, there was dark discoloration of the coronary band and hoof, and the calf did not respond to stimuli to the distal extremity. **B,** Necropsy of the calf showing aortoiliac thrombosis.

• **Fig. 3.62** A 14-month-old Brown Swiss heifer with a history of chronic leg swelling but without fever or pain on palpation of the limb. The limbs felt cold to the touch, and pitting was noticeable when pressure was applied to the leg. The owners first noticed the edema when the calf was approximately 2 months of age.

some of the commonest errors in treatment. Anticoagulants such as heparin may be of some value in decreasing further thrombosis but can have side effects; aspirin, however, has minimal effects on coagulation in cattle. Tissue plasminogen activator could be injected proximal to the thrombosis if the thrombosis is acute but it is very expensive.

Aortic and iliac artery thrombosis (Fig. 3.61) may occur in young calves (<6 months of age), resulting in an acute onset of posterior paralysis. The distal limb(s) feel cold below the stifle and may be hyporesponsive to stimuli. Serum CK levels are often 10,000 IU/L to 30,000 IU/L in affected calves. Successful treatment for aortic and iliac artery thrombosis in calves has not been reported.

Lymphatic Disorders

Congenital lymphedema is described in several breeds of cattle, with the description in Ayrshire cattle being the first in veterinary medicine. In some patients, the signs may not be noted until the calf is several months of age, so *primary lymphedema* would be the preferred term for those cases. The disease is characterized by edema of the hind limbs (Fig. 3.62) and sometimes the forelimbs, tail, and prepuce. Lymphatic system lesions may include hypoplasia and aplasia of lymph vessels and prescapular, iliofemoral, and popliteal lymph nodes. Chronic edema is associated with thickening and fibrosis of tissues, making successful treatment highly unlikely.

Acknowledgment

Suggested Readings

Anderson, D. C., Schmalsteig, F. C., Finegold, M. J., et al. (1985). The severe and moderate phenotypes of heritable Mac-1 LFA-1 deficiency: their quantitative definition and relation to leukocyte dysfunction and clinical features. *J Infect Dis*, *152*, 668–689.

Anderson, D. C., & Springer, T. A. (1987). Leukocyte adhesion deficiency: an inherited defect in the Mac-1 LFA-1 and p150, 95 glycoproteins. *Annu Rev Med*, *38*, 175–194.

Araujo, F. R., Silva, M. P., Lopes, A. A., et al. (1998). Severe cat flea infestation of dairy calves in Brazil. *Vet Parasitol*, *80*, 83–86.

Baird, J. D. (1988). Dilated cardiomyopathy in Holstein cattle: clinical and genetic aspects. In *Proceedings: 6th Annual Veterinary Medicine Forum (American College Veterinary Internal Medicine)* (pp. 175–177).

Bartol, J. M., Thompson, L. J., Minnier, S. M., et al. (2000). Hemorrhagic diathesis, mesenteric hematoma, and colic associated with ingestion of sweet vernal grass in a cow. *J Am Vet Med Assoc*, *216*, 1605–1608.

Braun, U. (2009). Traumatic pericarditis in cattle: clinical, radiographic and ultrasonographic findings. *Vet J*, *182*(2), 176–186.

Braun, U., Lejeune, B., Rauch, S., et al. (2008). Ultrasonographic findings in 22 cattle with pericarditis traumatica. *Schweiz Archiv Tierheilk*, *150*(6), 281–286.

Buck, W. B. (1975). Toxic materials and neurologic disease in cattle. *J Am Vet Med Assoc*, *166*, 222–230.

Buczinski, S. (2012). Echocardiographic findings and clinical signs in dairy cows with primary cardiac lymphoma: 7 cases (2007-2010). *J Am Vet Med Assoc*, *241*(8), 1083–1087.

Buczinski, S., Fecteau, G., & DiFruscia, R. (2006). Ventricular septal defects in cattle: a retrospective study of 25 cases. *Can Vet J*, *47*(3), 246–252.

Buczinski, S., Francoz, D., Fecteau, G., et al. (2010a). Heart disease in cattle with clinical signs of heart failure: 59 cases. *Can Vet J*, *51*(10), 1123–1129.

Buczinski, S., Francoz, D., Fecteau, G., et al. (2010b). A study of heart diseases without clinical signs of heart failure in 47 cattle. *Can Vet J*, *51*(11), 1239–1246.

Buczinski, S., Tolouei, M., Rezakhani, A., et al. (2013). Echocardiographic measurement of cardiac valvular thickness in healthy cows, cows with bacterial endocarditis, and cows with cardiorespiratory diseases. *J Vet Cardiol*, *15*(4), 253–261.

Buczinski, S., Tsuka, T., & Tharwat, M. (2012). The diagnostic criteria used in bovine bacterial endocarditis: a meta-analysis of 460 published cases from 1973 to 2011. *Vet J*, *193*(2), 349–357.

Buntain, B. (1980). Disseminated intravascular coagulopathy (DIC) in a cow with left displaced abomasum, metritis and mastitis. *Vet Med Small Anim Clin*, *75*, 1023–1026.

Callan, R. J., McGuirk, S. M., & Step, D. L. (1992). Assessment of the cardiovascular and lymphatic systems. *Vet Clin North Am Food Anim Pract*, *8*, 257–270.

Carlson, G. P. (2002). Diseases of the hematopoietic and hemolymphatic systems. In B. P. Smith (Ed.), *Large animal internal medicine* (3rd ed.). St. Louis: Mosby.

Carlson, G. P. (2002). Heinz body hemolytic anemia. In B. P. Smith (Ed.), *Large animal internal medicine* (3rd ed.). St. Louis: Mosby.

Carlson, G. P., & Kaneko, J. J. (1976). Influence of prednisolone on intravascular granulocyte kinetics of calves under nonsteady state conditions. *Am J Vet Res*, *37*, 149–151.

Constable, P. D., Muir, W. W., 3rd, Bonagura, J. D., et al. (1990). Clinical and electrocardiographic characterization of cattle with atrial premature complexes. *J Am Vet Med Assoc*, *197*, 1163–1169.

Constable, P. D., Muir, W. W., 3rd, Freeman, L., et al. (1990). Atrial fibrillation associated with neostigmine administration in three cows. *J Am Vet Med Assoc*, *196*, 329–332.

Corapi, W. V., Elliot, R. D., French, T. W., et al. (1990). Thrombocytopenia and hemorrhages in veal calves infected with bovine viral diarrhea virus. *J Am Vet Med Assoc*, *196*, 590–596.

Corapi, W. C., French, T. W., & Dubovi, E. J. (1989). Severe thrombocytopenia in young calves experimentally infected with noncytopathic bovine viral diarrhea virus. *J Virol*, *63*, 3934–3943.

Crispin, S. M., Douglas, S. W., Hall, L. W., et al. (1975). Letter: warfarin poisoning in domestic animals. *Br Med J*, *2*, 500.

D'Angelo, A., Bellino, C., Alborali, G. L., et al. (2006). Aortic thrombosis in three calves with Escherichia coli sepsis. *J Vet Intern Med*, *20*, 1261–1263.

Divers, T. J. (2005). Blood component transfusions. *Vet Clin North Am Food Anim Pract*, *21*, 615–622.

Ducharme, N. G., Fubini, S. L., Rebhun, W. C., et al. (1992). Thoracotomy in adult cattle: 14 cases (1979-1991). *J Am Vet Med Assoc*, *201*, 86–91.

Dyson, D. A., & Reed, J. B. H. (1977). Haemorrhagic syndrome of cattle of suspected mycotoxin origin. *Vet Rec*, *100*, 400–402.

Evans, E. T. R. (1957). Bacterial endocarditis of cattle. *Vet Rec*, *69*, 1190–1206.

Evans, I. A., & Howell, R. M. (1962). Bovine bracken poisoning. *Nature*, *194*, 584–585 [London].

Evans, W. C. (1964). Bracken fern poisoning of farm annuals. *Vet Rec*, *76*, 365–369.

Ferrer, J. F. (1979). Bovine leukosis: natural transmission and principles of control. *J Am Vet Med Assoc*, *175*, 1281–1284.

Firshman, A. M., Sage, A. M., Valberg, S. J., et al. (2006). Idiopathic hemorrhagic pericardial effusion in cows. *J Vet Intern Med*, *20*, 1499–1503.

Fox FH: Personal observation, 1968, Ithaca, NY.

Fox, F. H., & Rebhun, W. C. (1983). Warfarin poisoning with complications in a heifer. *Vet Med Small Anim Clin*, *78*, 1611–1613.

Fraser, B. C., Anderson, D. E., White, B. J., et al. (2013). Assessment of a commercially available point of care assay for the measurement of bovine cardiac troponin I concentration. *Am J Vet Res*, *74*, 870–873.

Fregin, G. F. (1970). Arial fibrillation in the horse. In *Proceedings: 16th Annual Convention American Association Equine Practitioners* (pp. 383–388).

Frelier, P. F., & Lewis, R. M. (1984). Hematologic and coagulation abnormalities in acute bovine sarcocystosis. *Am J Vet Res*, *45*, 40–48.

Gabor, L. J., & Downing, G. M. (2003). Monensin toxicity in preruminant dairy heifers. *Aust Vet J*, *81*, 476–478.

Gentry, P. A. (1984). The relationship between factor XI coagulant and factor XI antigenic activity in cattle (factor XI deficiency). *Can J Comp Med*, *48*, 58–62.

Gentry, P. A., & Ross, M. L. (1986). Failure of routine coagulation screening tests to detect heterozygous state of bovine factor XI deficiency. *Vet Clin Pathol*, *15*, 12–16.

Gentry, P. A., Tremblay, R. R. M., & Ross, M. L. (1989). Failure of aspirin to impair bovine platelet function. *Am J Vet Res*, *50*, 919–922.

Giger, U., Boxer, L. A., Simpson, P. J., et al. (1987). Deficiency of leukocyte surface glycoproteins Mo1 LFA-1 and Leu M5 in a dog with recurrent bacterial infections: an animal model. *Blood*, *69*, 1622–1630.

Gilbert, R. O., Grohn, Y. T., Guard, C. L., et al. (1993). Impaired post partum neutrophil function in cows which retain fetal membranes. *Res Vet Sci*, *5*, 15–19.

Goldman, L., & Ausiello, D. (2004). The chronic leukemias. In J. B. Wyngaarden, & L. H. Smith, Jr. (Eds.), *Cecil textbook of medicine* (22nd ed.). Philadelphia: WB Saunders.

Gross, D. R., Dodd, K. T., Williams, J. D., et al. (1981). Adverse cardiovascular effects of oxytetracycline preparations and vehicles in calves. *Am J Vet Res*, *42*, 1371.

Grunberg, W., Mol, J. A., & Teske, E. (2015). Red blood cell phosphate concentration and osmotic resistance during dietary phosphorous depletion in dairy cows. *J Vet Intern Med*, *29*, 395–399.

Gunes, V., Atalan, G., Citil, M., et al. (2008). Use of cardiac troponin kits for the qualitative determination of myocardial cell damage due to traumatic reticuloperitonitis in cattle. *Vet Rec*, *162*, 514–517.

Hagemoser, W. A., Roth, J. A., Lofstedt, J., et al. (1983). Granulocytopathy in a Holstein heifer. *J Am Vet Med Assoc*, *183*, 1093–1094.

Harrison, L. R. (1979). A hemorrhagic disease syndrome of the vealer calf. In *Proceedings: 21st Annual Meeting American Association Veterinary Laboratory Diagnosticians* (pp. 117–125).

Hayashi, T., Yamane, O., & Sakai, M. (1976). Hematological and pathological observations of chronic furazolidone poisoning in calves. *Jpn J Vet Sci*, *38*, 225–233.

Howard, J. L. (1999). Monensin, lasalocid, salinomycin, narasin. In J. Howard, & R. A. Smith (Eds.), *Current veterinary therapy—food animal practice* (4th ed.). Philadelphia: WB Saunders.

Hoyt, P. G., Gill, M. S., Angel, K. L., et al. (2000). Corticosteroid-responsive thrombocytopenia in two beef cows. *J Am Vet Med Assoc*, *217*, 717–720, 674.

Irmak, K., Sen, I., Col, R., et al. (2006). The evaluation of coagulation profiles in calves with suspected septic shock. *Vet Res Commun*, *5*, 497–603.

Jain, N. C. (1986). *Schalm's veterinary hematology* (4th ed.). Philadelphia: Lea & Febiger.

James, L. F., Hartley, W. J., Nielsen, D., et al. (1986). Locoweed oxytropis-sericca poisoning and congestive heart failure in cattle. *J Am Vet Med Assoc*, *189*, 1549–1556.

Jeffers, M., & Lenghaus, C. (1986). Granulocytopaenia and thrombocytopaenia in dairy cattle—a suspected mycotoxicosis. *Aust Vet J*, *63*, 262–264.

Jensen, R., Pierson, R. E., Braddy, P. M., et al. (1976). Brisket disease in yearling feedlot cattle. *J Am Vet Med Assoc*, *169*, 513–520.

Jesty, S. A., Sweeney, R. W., Dolente, B. A., et al. (2005). Idiopathic pericarditis and cardiac tamponade in two cows. *J Am Vet Med Assoc*, *226*, 1555–1558, 1502.

Jubb, K. V. F., Kennedy, P. C., & Palmer, N. (1985). *Pathology of domestic animals* (3rd ed.). (vol. 3). New York: Academic Press, Inc.

Kehrli, M. E., Jr., Schmalstieg, F. C., Anderson, D. C., et al. (1990). Molecular definition of bovine granulocytopathy syndrome: identification of deficiency of the Mac-1 (CB11b/CD18) glycoprotein. *Am J Vet Res*, *51*, 1826–1836.

Kimeto, B. A. (1976). Ultrastructure of blood platelets in cattle with East Coast fever. *Am J Vet Res*, *37*, 443–447.

King JM: Personal communication, 1968, Ithaca, New York.

Krishnamurthy, D., Nigam, J. M., Peshin, P. K., et al. (1979). Thoracopericardiotomy and pericardiectomy in cattle. *J Am Vet Med Assoc*, *175*, 714–718.

Kutzer, P., Schultze, C., Englehardt, A., et al. (2008). Helcococcus ovis, an emerging pathogen in bovine valvular endocarditis. *J Clin Microbiol*, *46*(10), 3291–3294.

Labonte, J., Roy, J. P., Dubuc, J., et al. (2015). Measurement of cardiac troponin I in healthy lactating dairy cows using a point of care analyzer (iSTAT-1). *J Vet Cardiol*, *17*, 129–133.

Lacuata, A. Q., Yamada, H., Nakamura, Y., et al. (1980). Electrocardiographic and echocardiographic findings in four cases of bovine endocarditis. *J Am Vet Med Assoc*, *176*, 1355–1365.

Littledike, E. T., Glazier, D., & Cook, H. M. (1976). Electrocardiographic changes after induced hypercalcemia and hypocalcemia in cattle: reversal of the induced arrhythmia with atropine. *Am J Vet Res*, *37*, 383–388.

Litwak, K. N., McMahan, A., Lott, K. A., et al. (2005). Monensin toxicosis in the domestic bovine calf: a large animal model of cardiac dysfunction. *Contemp Top Lab Anim Sci*, *44*, 45–49.

Mason, T. A. (1979). Suppurative pericarditis, treated by pericardiotomy in a cow. *Vet Rec*, *I05*, 350–351.

McGuirk, S. M. (1991). Treatment of cardiovascular disease in cattle. *Vet Clin North Am Food Anim Pract*, *7*, 729–746.

McGuirk, S. M., & Bednarski, R. M. (1986). Bradycardia associated with fasting in cattle. In *Proceedings: 4th Annual Veterinary Medicine Forum* (2) (pp. 10–29, 10–32).

McGuirk, S. M., Bednarski, R. M., & Clayton, M. K. (1990). Bradycardia in cattle deprived of food. *J Am Vet Med Assoc*, *196*, 894–896.

McGuirk, S. M., Muir, W. W., Sams, R. A., et al. (1983). Atrial fibrillation in cows: clinical findings and therapeutic considerations. *J Am Vet Med Assoc*, *182*, 1380–1386.

McGuirk, S. M., & Shaftoe, S. (1990). Alterations in cardiovascular and hemolymphatic system. In B. P. Smith (Ed.), *Large animal internal medicine*. St. Louis: CV Mosby.

McGuirk, S. M., Shaftoe, S., & Lunn, D. P. (1990). Diseases of the cardiovascular system. In B. P. Smith (Ed.), *Large animal internal medicine*. St. Louis: CV Mosby.

Mellanby, R. J., Henry, J. P., Cash, R., et al. (2009). Serum cardiac troponin I concentrations in cattle with cardiac and non-cardiac disorders. *J Vet Intern Med*, *23*, 926–930.

Morley, P. S., Allen, A. L., & Woolums, A. R. (1996). Aortic and iliac artery thrombosis in calves: nine cases (1974-1993). *J Am Vet Med Assoc*, *209*, 130–136.

Morris, D. D. (1988). Recognition and management of disseminated intravascular coagulation in horses. *Vet Clin North Am Equine Pract*, *4*, 115–143.

Muller, M., Platz, S., Ehrlein, J., et al. (2005). [Bacterially conditioned thromboembolism in dairy cows—a retrospective study of 31 necropsy cases with special consideration of the causative complex] (German). *Berl Munch Tierarztl Wochenschr*, *118*, 121–127.

Nagahata, H., Noda, H., Takahashi, K., et al. (1987). Bovine granulocytopathy syndrome: neutrophil dysfunction in Holstein Friesian calves. *Zentralbl Veterinarmed A*, *34*, 445–451.

Nicholls, T. J., Shiel, M. J., Westbury, H. A., et al. (1985). Granulocytopaenia and thrombocytopaenia in cattle. *Aust Vet J*, *62*, 67–68.

Ogawa, E. R. I., Kobayashi, K., Yoshiura, N., et al. (1987). Bovine postparturient hemoglobinemia: hypophosphatemia and metabolic disorder in red blood cells. *Am J Vet Res*, *48*, 1300–1303.

Otter, A., Twomey, D. F., Crawshaw, T. R., et al. (2003). Anaemia and mortality in calves infested with the long-nosed sucking louse (Linognathus vituli). *Vet Rec*, *153*, 176–179.

Owczarek-Lipska, M., Denis, C., Eggen, A., et al. (2009). The bovine dilated cardiomyopathy locus maps to a 1.0 Mb interval on chromosome 18. *Mamm Genome*, *20*, 187–192.

Peek, S. F., McGuirk, S. M., Gaska, J., et al. (2012). Idiopathic hemorrhagic pericardial effusion as a precursor to epicardial lymphosarcoma in three cows. *J Vet Intern Med*, *26*(4), 1069–1072.

Pipers, F. S., Rings, D. M., Hull, B. L., et al. (1978). Echocardiographic diagnosis of endocarditis in a bull. *J Am Vet Med Assoc*, *172*, 1313–1316.

Power, H. T., & Rebhun, W. C. (1983). Bacterial endocarditis in adult dairy cattle. *J Am Vet Med Assoc*, *181*, 806–808.

Pringle, J. K., Bright, J. M., Duncan, R. B., Jr., et al. (1991). Pulmonary hypertension in a group of dairy calves. *J Am Vet Med Assoc*, *198*, 857–861.

Pritchard, W. R., Rehfeld, C. E., Mizuno, N. S., et al. (1956). Studies on trichlorethylene-extracted feeds. I. Experimental production of acute aplastic anemia in young heifers. *Am J Vet Res*, *17*, 425–429.

Radostits, O. M., Gay, C., Blood, D. C., et al. (2007). *Veterinary medicine. A textbook of the diseases of cattle, sheep, pigs, goats and horses* (10th ed.). London: Saunders. [with contributions by Arundel J.H., Gay C.C].

Rebhun, W. C., French, T. W., Perdrizet, J. A., et al. (1989). Thrombocytopenia associated with acute bovine virus diarrhea infection in cattle. *J Vet Intern Med*, *3*, 42–46.

Reimer, J. M., Donawick, W. J., Reef, V. B., et al. (1988). Diagnosis and surgical correction of patent ductus venosus in a calf. *J Am Vet Med Assoc*, *193*, 1539–1541.

Renshaw, H. W., & Davis, W. C. (1979). Canine granulocytopathy syndrome: an inherited disorder of leukocyte function. *Am J Pathol*, *95*, 731.

Rosenberger G. (1979). *Clinical examination of cattle*. Dirksen G, Grunder H-D, Grunert E, et al (collaborators) and Mack R (translator) (Eds.), Berlin: Verlag Paul Parey.

Roth, J. A., & Kaeberle, M. L. (1982). Effect of glucocorticoids on the bovine immune system. *J Am Vet Med Assoc*, *180*, 894–901.

Roth, J. A., & Kaeberle, M. L. (1981). Effects of in vivo dexamethasone administration on in vitro bovine polymorphonuclear leukocyte function. *Infect Immun*, *33*, 434–441.

Scott, E. A., Byars, T. D., & Lamar, A. M. (1980). Warfarin anticoagulation in the horse. *J Am Vet Med Assoc*, *177*, 1146–1151.

Step, D. L., McGuirk, S. M., & Callan, R. J. (1992). Ancillary tests of the cardiovascular and lymphatic systems. *Vet Clin North Am Food Anim Pract*, *8*, 271–284.

Stockdale, C. R., Moyes, T. E., & Dyson, R. (2005). Acute postparturient haemoglobinuria in dairy cows and phosphorus status. *Aust Vet J*, *83*, 362–366.

Suzuki, K., Uchida, K. E., Niehaus, A., et al. (2012). Cardiac troponin I in calves with congenital heart disease. *J Vet Intern Med*, *26*, 1056–1069.

Sweeney, R. W., Divers, T. J., Benson, C., et al. (1988). Pharmacokinetics of rifampin in calves and adult sheep. *J Vet Pharmacol Ther*, *11*, 413–416.

Takahashi, K., Miyagawa, K., Abe, S., et al. (1987). Bovine granulocytopathy syndrome of Holstein-Friesian calves and heifers. *Jpn J Vet Sci*, *49*, 733–736.

Tennant, B., Asbury, A. C., Laben, R. C., et al. (1967). Familial polycythemia in cattle. *J Am Vet Med Assoc*, *150*, 1493–1509.

Tennant, B., Harrold, D., Reina-Guerra, M., et al. (1969). Arterial pH, PO2, and PCO2 of calves with familial bovine polycythemia. *Cornell Vet*, *59*, 594–604.

Van Biervliet, J., Krause, M., Woodie, B., et al. (2006). Thoracoscopic pericardiotomy as a palliative treatment in a cow with pericardial lymphoma. *J Vet Cardiol*, *8*, 69–75.

Varga, A., Angelos, J. A., Graham, T. W., et al. (2013). Preliminary investigation of cardiac troponin I concentration in cows with common production diseases. *J Vet Intern Med*, *27*, 1613–1621.

Varga, A., Schober, K. E., Walker, W. L., et al. (2009). Validation of a commercially available immunoassay for the measurement of bovine cardiac troponin I. *J Vet Intern Med*, *23*, 359–365.

Vrins, A., Carlson, G., & Feldman, B. (1983). Warfarin: a review with emphasis on its use in the horse. *Can Vet J*, *24*, 211–213.

Weldon, A. D., Moise, N. S., & Rebhun, W. C. (1992). Hyperkalemic atrial standstill in neonatal calf diarrhea. *J Vet Intern Med*, *6*, 294–297.

Wessels, J., & Wessels, M. E. (2005). Histophilus somni myocarditis in a beef rearing calf in the United Kingdom. *Vet Rec*, *157*, 420–421.