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CHAPTER 36

Diseases of the Cardiovascular and Hemolymphatic Systems

Christopher Cebra and David Sisson

The Cardiovascular System

Clinical Evaluation

Physical Examination

Physical examination of the cardiovascular system involves examination of mucous membranes for color, refill time, and moistness; thoracic palpation and auscultation, assessment of arterial pulse quality via the median or medial saphenous arteries; assessment of jugular filling; and palpation of the ventrum for edema. Common ancillary tests include blood analysis, blood pressure measurement, thoracic radiography, electrocardiography, and echocardiography. The areas suitable for cardiac auscultation lie conveniently within the short-fleeced axilla, under the forelimb above the elbow. On the left side, the pulmonic valve is heard best over the third intercostal space, under the triceps brachii, whereas the aortic valve area is located more dorsally at the fourth intercostal space. The mitral valve area is located more ventrally on the left hemithorax at the costochondral junctions over the fourth or fifth intercostal space, and the tricuspid valve is heard best on the right hemithorax over the fourth intercostal space at the caudal edge of the triceps brachii. Areas over all valves should be palpated for the presence of a thrill. Healthy adult camelids in the Oregon State University herd have resting heart rates between 48 and 72 beats per minute (beats/min), with rare individuals spiking up to 84 beats/min. This range is slightly lower than the 60 to 90 beats/min or higher rates that are sometimes cited. Adults with higher heart rates are likely to be excessively stressed, volume depleted, or otherwise compromised. Neonates typically have heart rates varying from 90 to 120 beats/min, although rates up to 140 beats/min may be found in some newborns. Juveniles typically will have heart rates less than 100 beats/min by age 1 month, and this declines to the adult range by age 1 year.[1]

The first and second heart sounds should be heard clearly on the left side of the thorax in all but the most obese camelids. These sounds are more difficult to discern on the right side but should be audible in an adequately restrained camelid in a quiet environment. With careful auscultation, soft third and fourth sounds are discernible in some healthy camelids. Loud S3 or S4 heart sounds are usually indicative of serious cardiac disease, reflecting the presence of ventricular enlargement and ventricular dysfunction. Physiologic and innocent murmurs are often identified in adult and immature camelids. Anemic, systemically ill, and even apparently healthy camelids may exhibit soft, nonpathologic systolic murmurs (≤grade 3 of 6) over the left heart base. These murmurs are usually crescendo–decrescendo, ejection-type murmurs occupying midsystole, with preservation of the first and second heart sounds. Scansen and co-workers recently identified high-velocity and turbulent flow in the branch pulmonary arteries of several young crias and offered an elegant explanation for some of the innocent murmurs identified in immature camelids.[2] The murmur and the flow disturbances resolved within a few months, which suggests that this finding is benign, therein resembling the condition of peripheral pulmonary stenosis seen in human infants. Often, however, the precise cause of these soft murmurs is not apparent even with the aid of color flow echocardiographic evaluation.

Loud systolic murmurs are abnormal and may be detected in camelids with septal defects, outflow tract obstructions, and insufficiency of the atrioventricular (AV) valves. The systolic murmur of a ventricular septal defect may be either band shaped or crescendo–decrescendo and is typically best heard on the right side of the chest. Heart murmurs resulting from outflow tract obstruction are typically crescendo–decrescendo or diamond-shaped and are usually best heard at the left heart base. The regurgitant murmurs of AV valve insufficiency are typically band shaped or plateau shaped and are best heard at the left or right apex, depending on the valve affected. Regurgitant murmurs tend to be longer (pansystolic) than systolic ejection murmurs (holosystolic), so both the first and second heart sounds are usually obscured in camelids with AV valve insufficiency. In comparison with horses and dogs, insufficiency of the AV valves occurs much less commonly in llamas and alpacas. Diastolic murmurs are also relatively rare, almost always clinically significant, and are usually caused by insufficiency of the aortic valve, or more rarely, the pulmonic valve. Such murmurs are usually best heard at the heart base on the left side of the thorax. The continuous murmur of a posterior descending artery (PDA) is also best heard at the left heart base as in other species. It is important to recognize that many significant congenital and acquired cardiac lesions in camelids result in no discernible murmur. For example, camelids with a large ventricular septal defect (VSD) and pulmonary hypertension may not evidence a murmur but will often have accentuated splitting of the second heart sound because of asynchronous closure of the semilunar valves. Thus, it must be appreciated that auscultation alone is not entirely reliable for ruling out the presence of cardiac disease.

The lymphatic system is often conveniently assessed by examining the size of peripheral lymph nodes, particularly when they are enlarged because of inflammation or neoplasia. Moreover, it is not uncommon to identify disorders of the lymphatic system by inference when lymph accumulates in a body cavity or regional pitting is noted in an extremity. The easiest lymph nodes to find in normal camelids include the prescapular nodes located near the base of the neck and the superficial inguinal nodes located in the inguinal region close to the ventral body wall. Other peripheral nodes are difficult to locate in healthy camelids because they often comprise a collection of small nodules. Emaciation or pathologic

node enlargement facilitates successful palpation of the submandibular, retropharyngeal, and popliteal nodes, which are often very hard to identify in healthy animals.

Electrocardiography

Electrocardiograms (ECGs) are primarily recorded to elucidate the nature of an auscultated rhythm disturbance. A standardized six-lead ECG may be easily obtained in the standing camelid by attaching two electrodes above the olecranon on the forelimbs and the remaining two electrodes just above the patellas on the hindlimbs. Leads are attached with alligator clips and wetted with alcohol. Clipping the fleece is usually not necessary. It is often preferable to obtain ECGs in young crias by restraining them in right lateral recumbency. In either circumstance, ECG tracings are most easily interpreted when a paper speed of 50 millimeters per second (mm/s) is selected for the recording. It is useful to complement the limb leads with a rhythm strip that is recorded by using a base–apex lead; the rhythm strip is obtained by repositioning the right front leg electrode to the base of the neck on the right and by moving the left front leg electrode to a location over the cardiac apex on the left side of the chest. This lead often provides the largest amplitude complexes thereby facilitating cardiac rhythm analysis.[3]

Normal ECG reference values for camelids have been reported in several published studies (Figure 36-1).[4–6] In the recent report by Kraus and coworkers, heart rate was seen to vary from 60 to 100 beats/min with a mean heart rate of 80 beats/min.[6] The mean (+/− standard deviation [SD]) duration of the electrical events were reported as follows: P waves: −40 milliseconds (ms; +/− 12); PQ interval: 150 ms (+/− 33); QRS complex: 50 ms (+/− 8); Q–T interval: 360 ms (+/− 60); ST segment: 230 ms (+/− 46). QRS morphology was found to be extremely variable. The mean polarity of the QRS complexes was negative in 60% of the lead I recordings, in 56% of the lead II recordings, and in 51% of the lead III recordings. The QRS complex was least variable for lead V10, where the QRS complexes were positive in 88% of the animals examined. The amplitudes of the R and S waves tended to be low in the limb leads, as often noted in herbivores. Values obtained from mean electrical axis (MEA) estimations were extremely variable but were directed mainly to the right and in a cranial direction. In contrast to humans and small animals, ECG recordings obtained from camelids provide little information about the overall size of the heart or the enlargement of specific chambers. The Purkinje fiber network of camelids penetrates completely through the wall of the ventricles from the endocardium to the epicardium, as in sheep, resulting in a pattern of activation that effectively obscures the hallmarks of chamber enlargement seen in humans and smaller mammals such as the dog and the cat.[4,7] In our experience, neither the recorded voltage nor the estimated MEA appears to be useful for the detection of chamber enlargement.

Cardiac rhythms observed in healthy camelids include sinus rhythm and, more commonly, sinus arrhythmia with an occasional animal showing first or low grade second-degree heart block, presumably as a result of high vagal tone. In anxious animals, an occasional premature supraventricular beat may also be noted.[4] With the exception of sinus bradycardia and sinus tachycardia, cardiac arrhythmias and conduction disturbances are infrequently detected in camelid species. However, a variety of rhythm disturbances are occasionally observed in animals that are experiencing environmental adversity, are systemically ill, or have serious underlying

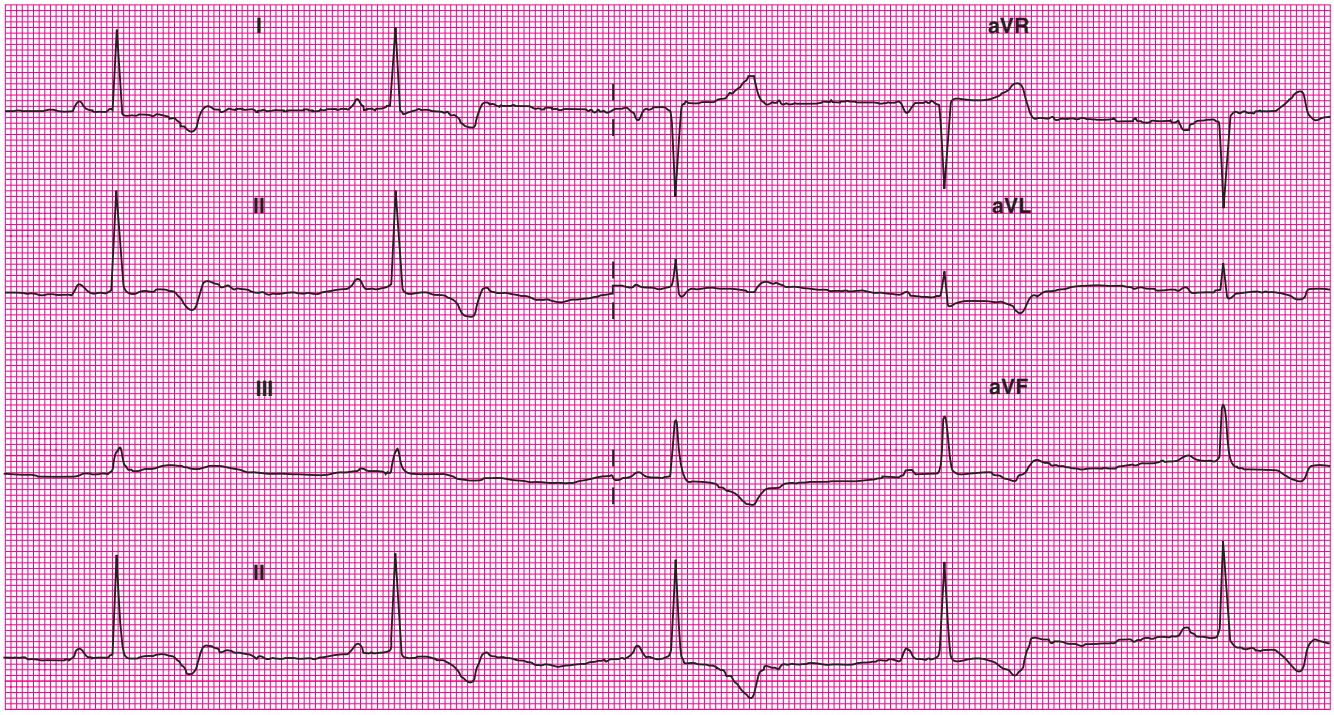

Figure 36-1 As in other species with extensive arborization of Purkinje fiber throughout the myocardium, marked variability of R wave amplitudes and the mean electrical axis is seen. This 6-lead electrocardiogram was recorded from a normal adult male alpaca.

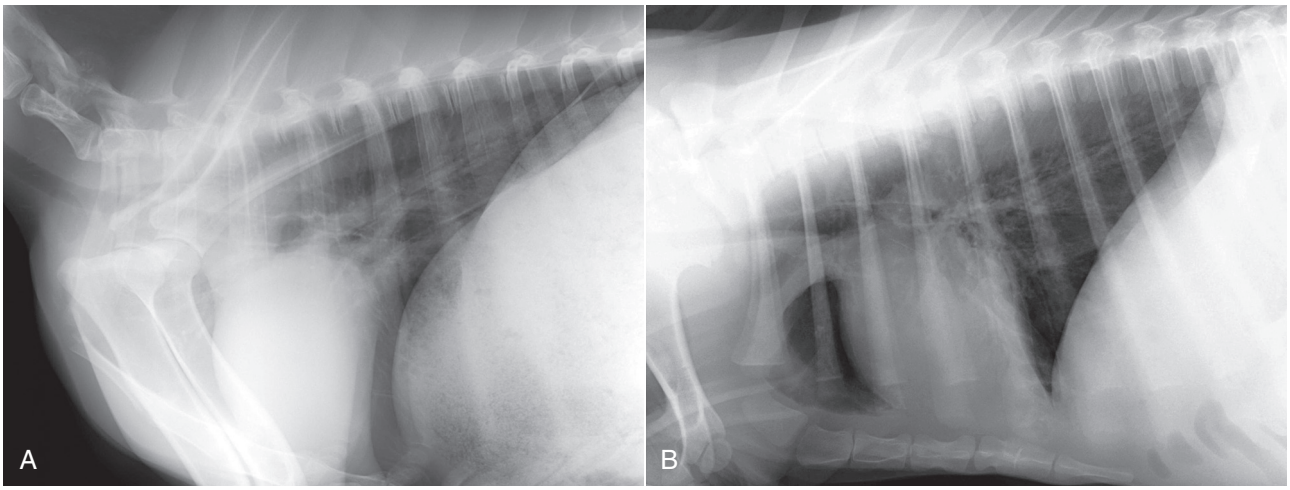

Figure 36-2 A standing lateral thoracic radiograph of a healthy mature alpaca (*A*) is contrasted with a radiograph of an alpaca cria obtained in lateral recumbency (*B*) with the forelegs pulled forward to better visualize the cranial margin of the cardiac silhouette.

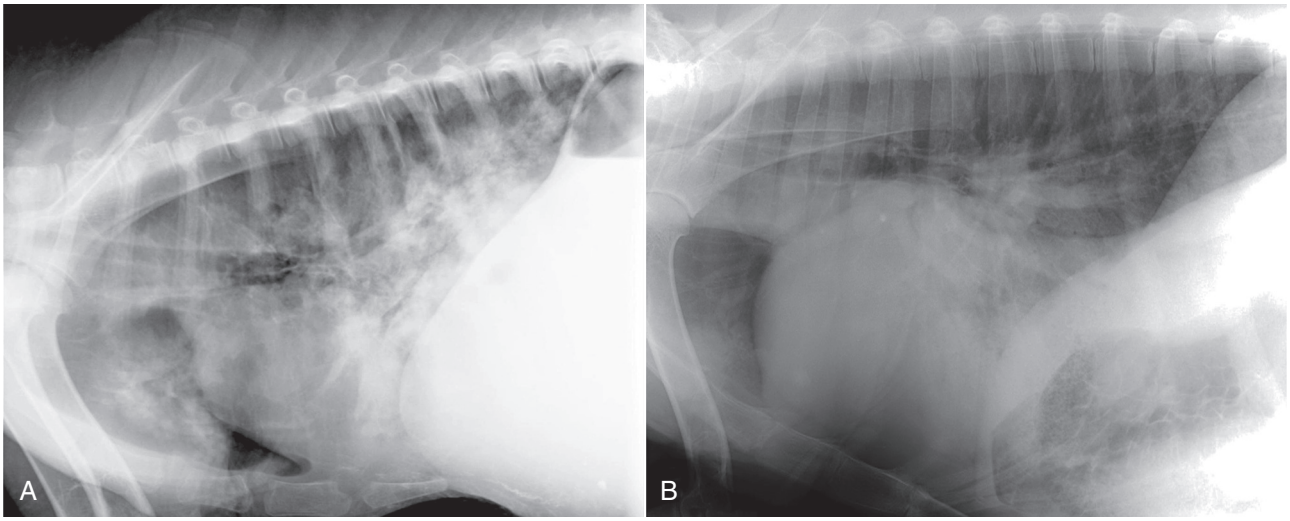

Figure 36-3 Thoracic radiography is particularly useful for distinguishing respiratory distress caused by pneumonia (*A*) from left-sided congestive heart failure (*B*). (*B, From McClane M, et al: Listeria associated mural and valvular endocarditis in an alpaca, J Vet Cardiol 10:141-145, 2008.*

congenital or acquired heart disease. Observed rhythm disturbances include premature atrial and ventricular depolarizations, supraventricular and ventricular tachycardia (SVT or VT), atrial fibrillation (AF), high-grade and complete AV block, and preexcitation.[3,8]

Thoracic Radiology

Thoracic radiographs should be obtained as part of the clinical evaluation whenever cardiac disease is suspected. It is, of course, always important to integrate physical examination findings, laboratory determinations (such as arterial blood gas [ABG] analysis), and thoracic imaging studies to arrive at an accurate diagnosis. Practical considerations in adult animals often limit thoracic radiographic imaging to a standing lateral view (Figure 36-2), but this single view is usually adequate to distinguish primary airway or pulmonary parenchymal disease from pulmonary compromise caused by left-sided heart failure (Figure 36-3). Thoracic radiography is also useful for identifying pleural effusion, its severity, and its likely cause. In this regard, it is complementary to thoracic ultrasonography. In neonates, thoracic radiography is particularly useful for distinguishing heart disease from the far more common pulmonary parenchymal diseases associated with immaturity or infection. It is often possible to obtain lateral and dorsoventral radiographs in young crias, and two-view studies are advisable whenever they can be accomplished without causing undue stress to the animal. Chemical restraint should also be considered to optimize the quality of the imaging study when the condition of the animal permits. This often causes less duress compared with physical restraint.

The base of the heart is normally tilted slightly cranially in llamas and alpacas, and the cardiac long axis is normally oriented parallel to the ribs and perpendicular to the thoracic spine. The carina is typically located at the fourth rib or in the

fourth intercostal space. The ratio of heart height to the height of the thorax, both measured along the cardiac long access, ranges from 0.68 to 0.74 in healthy adult llamas, and 0.65 to 0.84 in alpaca crias.[8,9] Cardiomegaly is usually obvious in camelids with serious heart disease and is typically revealed by an increase in cardiac width beyond three intercostal spaces, an increase in heart height beyond three fourths the height of the thorax, and elevation of the trachea with reduction in the angle of divergence from the thoracic spine below the reported normal range of 10° to 19° (mean 14.4° + 2.0°) in adult llamas, and 9° to 22° (mean 14.2° + 3.6°) in alpaca crias.[8,9] Using a modification of the Buchanan vertebral heart score (VHS) system, Mattoon and colleagues have provided scaled criteria for identifying cardiomegaly in llamas.[8] According to this method, the height plus width of the normal adult llama heart ranges from 7.7 to 9.1 "vertebral lengths" (mean VHS = 8.4) or 2.75 to 3.55 times the distance from the cranial aspect of T3 to the caudal aspect of T5. In crias, the ratio of cardiac height plus width to T3-T5 has been reported as 3.12 ± 0.21, which is very similar to adult animals. Left heart enlargement is usually easily identified on the lateral radiograph, but reliable identification of right heart enlargement is often more problematic. In young crias, dorsoventral thoracic radiography allows for more sensitive detection of right heart enlargement. In crias, the mean cardiac height plus width to T3-5 ratio on dorsoventral radiography has been reported as 2.5 ± 0.25 and the cardiac to thoracic width ratio as 0.80 ± 0.06. Ambiguous radiographic findings can often be clarified by an echocardiographic evaluation, which is much more accurate for identifying specific patterns of chamber enlargement.

The pulmonary vasculature should be routinely and systematically evaluated on thoracic radiography, and discrepancies in the absolute and relative size of the arteries and veins should be noted. In young crias, the ratio of the right cranial pulmonary artery to third rib has been reported as 0.42 + 0.11 and the ratio of the right cranial pulmonary vein to third rib as 0.45 + 0.11. In adult llamas, the ratio of the right cranial pulmonary artery to the height of T4 is reported as 0.28 ± 0.04 and the ratio of the right pulmonary vein to the height of T4 as 0.30 ± 0.04. Thus, in normal camelids, the cranial lobar pulmonary veins are similar in size or only slightly larger than the accompanying arteries. Developing left heart failure should be considered when the pulmonary veins are substantially larger than the arteries. When interstitial or alveolar perihilar infiltrates are identified together with enlarged pulmonary veins and an enlarged left atrium, congestive heart failure (CHF) is likely. In animals suspect for congenital heart disease, pulmonary overcirculation, resulting from a left-to-right–shunting PDA or VSD, is typically evidenced by concurrent enlargement of the cranial lobar arteries and veins together, with an overall increase in the opacity of the lungs. Right-to-left shunts, in turn, are usually evidenced by diminutive pulmonary vessels and reduced opacity of the lung fields. Evaluation of caudal vena caval size is also easily accomplished on lateral radiography, and this assessment takes on added importance in camelids when right heart failure is suspected, since jugular venous distension cannot be readily evaluated by physical examination. As a general rule, the diameter of the caudal vena cava should not exceed the height of the body of the fourth thoracic vertebrae.

Echocardiography

Echocardiography is essential for the evaluation of all congenital heart diseases and most acquired heart diseases and is particularly well suited for the detection of pericardial effusion. The techniques used to perform echocardiography in camelids do not differ substantially from those used in other large animal species. Low-frequency transducers, ranging from 2 to 3.5 megahertz (MHz), are required to adequately examine adult animals. In crias, either a 5-MHz or a 7.5-MHz transducer provides the necessary resolution required for optimally imaging immature patients. Uncooperative subjects should be sedated if their clinical condition is sufficiently stable. Interrogation of the heart is typically accomplished from a combination of imaging windows located at the ventral aspect of the fourth or fifth intercostal space on the right side of the thorax and at the cardiac apex on the left. To obtain optimal images from the right side, it is very helpful to have the right forelimb positioned as far forward as the animal will accommodate so that the ultrasound transducer can be positioned as far cranial and dorsal as the lung permits. From this location, two-dimensional images should be obtained in six short-axis imaging planes through the left ventricle: (1) through the cardiac apex, (2) at the level of the papillary muscles, (3) the chordae tendineae, (4) the mitral valve, (5) the heart base at the level of the aorta and left atrium, and, if possible, (6) at the level of the main pulmonary artery as it bifurcates at the origin of the left and right pulmonary arteries (Figure 36-4). Two long-axis imaging planes should be recorded from this same location by rotating the transducer counterclockwise to obtain an image plane that optimizes a view of the left ventricular outflow tract and another imaging plane optimizing a view of all four chambers of the heart together with the mitral and tricuspid valves (Figure 36-5). Echocardiography may also be used to examine the heart of the fetus for malformations (Figure 36-6).

With modern echocardiography, M-mode images can be derived (postprocessed) from the digitized two-dimensional images (Figure 36-7). Alternatively, two-dimensional imaging may be used to guide the orientation of the M-mode beam to obtain the desired imaging location. Relevant measures of chamber size may be made from either the two-dimensional or M-mode images permitting the calculation of a variety of functional indices. Normal M-mode echocardiographic measures that are available are based on one study of 23 healthy llamas weighing 110 to 166 kg (mean = 138 kg) and another study of 27 healthy alpacas weighing 43 to 101 kg (mean = 68 kg).[3,10] The reported normal ranges are very wide, reflecting the inclusion of animals with widely differing body weights. M-mode echocardiographic data from a small population of crias (12 alpacas and 5 llamas) were also recently made available.[3] Left ventricular (LV) fractional shortening (%FS), calculated as the % change in LV short-axis diameter from end-diastole to end-systole, is the most commonly used index of systolic function. As a rule of thumb, %FS should be 25% or greater in healthy camelids, regardless of age, breed, or sex.

Two-dimensional color flow Doppler imaging is a particularly useful and cost-effective imaging modality for the evaluation of camelids with congenital or acquired heart disease. Not only can the architecture of the heart be easily visualized and accurately measured, but flow disturbances within the heart and great vessels can be easily appreciated and

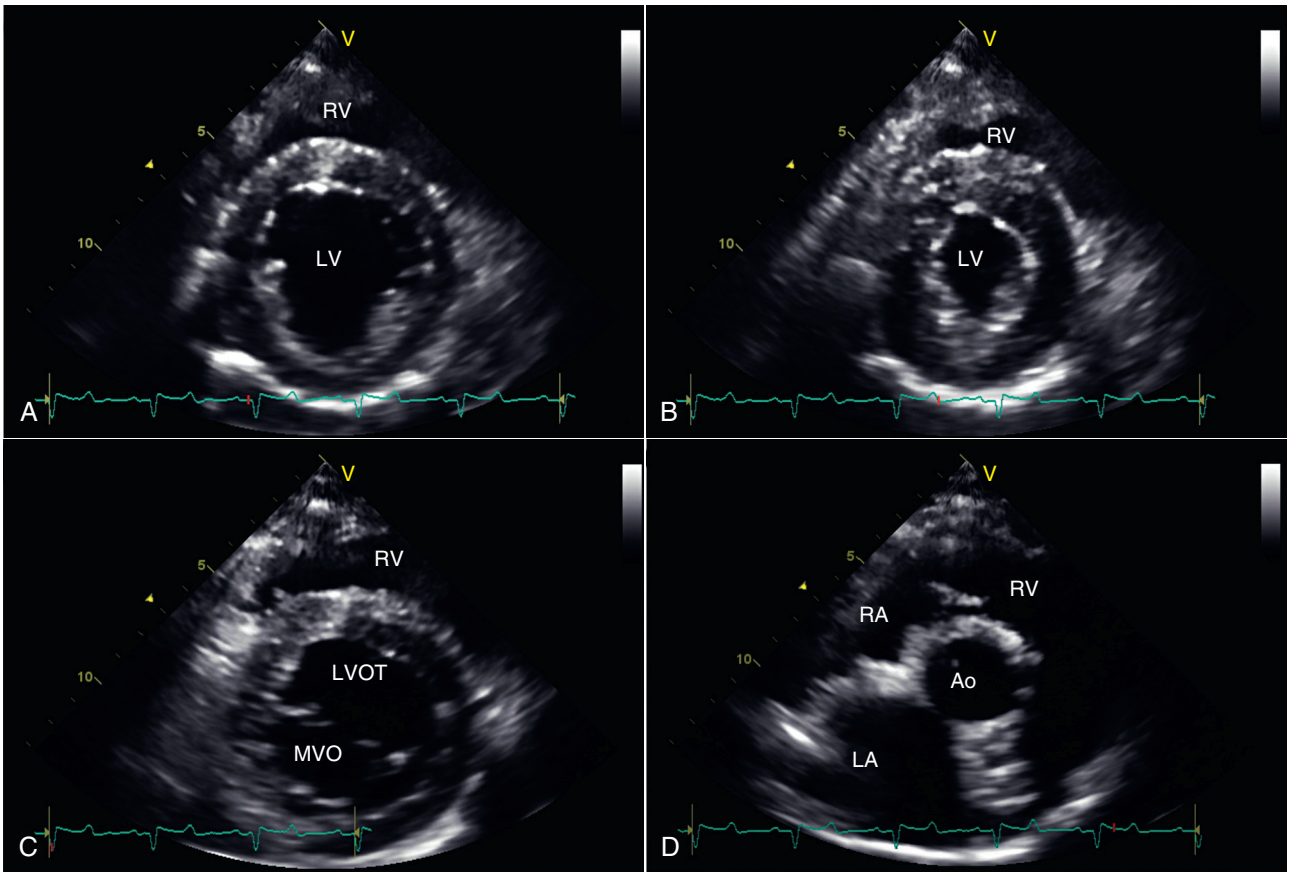

Figure 36-4 Right parasternal, short-axis, two-dimensional echocardiographic views of an adult alpaca heart at the level of the chordae tendineae are shown at end diastole (*A*) and end systole (*B*). Also shown are short-axis views at the level of the mitral valve (*C*) and at the heart base (*D*) at the level of the aorta and left atrium. *Ao*, Aorta; *LA*, left atrium; *LV*, left ventricle; *LVOT*, left ventricular outflow tract; *MVO*, mitral valve orifice; *RA*, right atrium; *RV*, right ventricle.

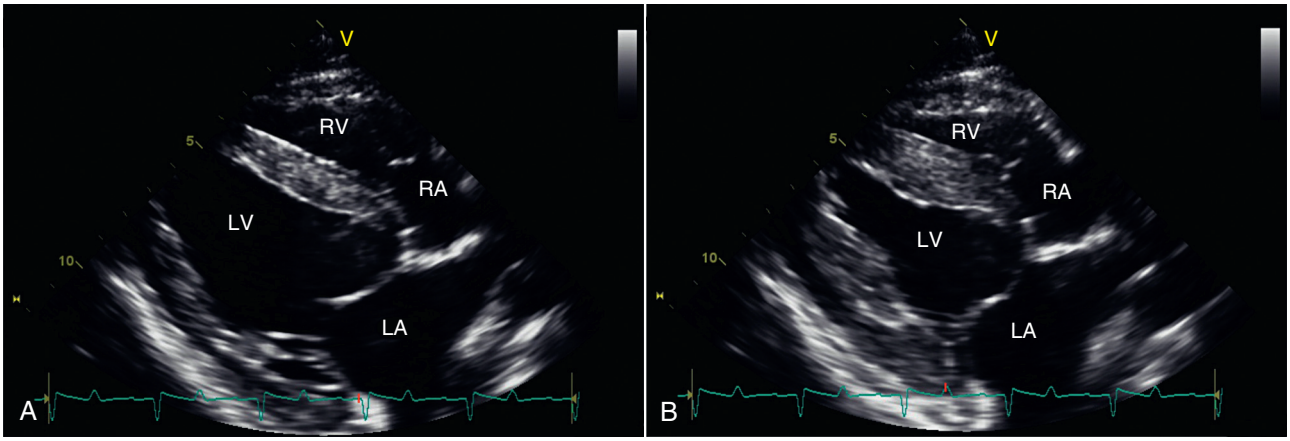

Figure 36-5 Right parasternal, long-axis, four-chamber, two-dimensional echocardiographic views of an adult alpaca heart are shown at end diastole (*A*) and end systole (*B*). *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

quantified. Images are initially obtained from the right side of the thorax, where flow disturbances in the vicinity of the pulmonic, aortic, mitral, and tricuspid valves can often be appreciated. From this location, accurate flow velocity determinations via spectral Doppler can be achieved only for flow through the pulmonic valve, as such measures require the interrogating ultrasound beam to be parallel with the direction of flow. Nonetheless, it is often possible to document flow disturbances resulting from aortic, mitral, and tricuspid valvular insufficiency or from a VSD via the right parasternal long axis views (Figure 36-8). Echocardiographic imaging from the left apical region on the left side of the chest allows the generation of four-chamber and five-chamber views of the heart, the latter referring to the inclusion of the four cardiac chambers plus the LV outflow tract together with the proximal aorta. This view is particularly useful for evaluating the velocity of blood

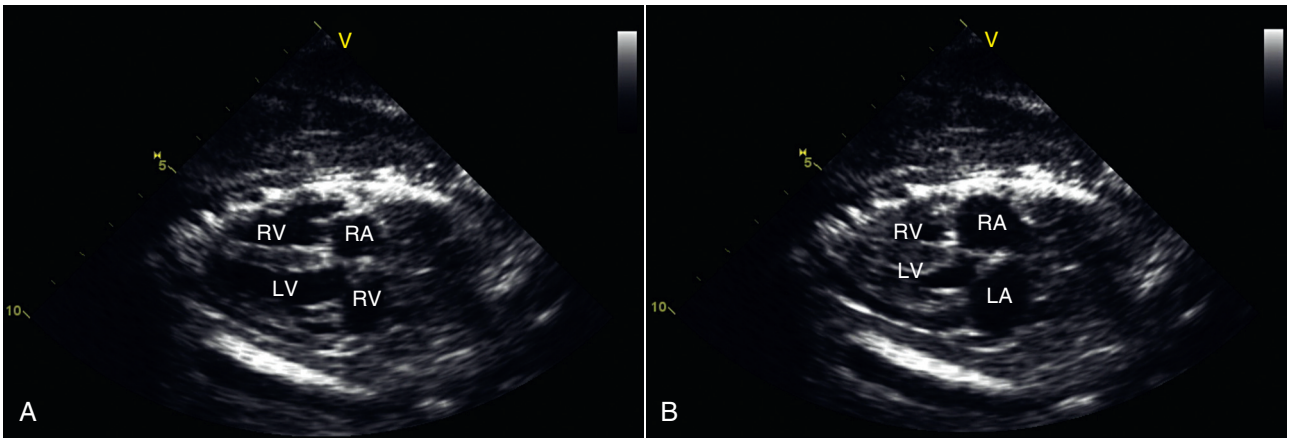

Figure 36-6 These echocardiographic images show four-chamber, two-dimensional views of an alpaca fetal heart at end diastole (*A*) and end systole (*B*). Such evaluations can be useful for establishing viability of the fetus and for identifying cardiac malformations prior to birth.

flow as it moves away from the transducer while flowing out through the aortic valve. Increased flow velocity usually indicates outflow tract obstruction, but mildly increased flow velocities may also be observed with left-to-right shunts and other causes of increased stroke volume. Quantification of valvular stenosis and insufficiency via the modality of spectral Doppler velocity recordings has supplanted cardiac catheterization as the preferred method for determining disease severity. Transvalvular flow velocities recorded in healthy llamas and alpacas are very similar to those reported for dogs and cats. It is noteworthy that often very small jets of valvular insufficiency are present in the immediate vicinity of all the cardiac valves in healthy camelids, and such observations should not be considered indicative of valve disease.[11]

Arterial Blood Gas Analysis

ABG analysis is useful for determining whether a suspected cardiac abnormality has led to significant right-to-left shunting of blood. Right-to-left shunting allows deoxygenated venous blood to enter the aorta without passing through the lungs, reducing the partial pressure of oxygen (PaO_2) below reference values. Affected animals have a decreased activity level or tolerance for exercise. To differentiate shunting from other causes of hypoxemia, presupplemental and postsupplemental oxygen concentrations may be compared; shunts prevent an increase in PaO_2, whereas oxygenation increases with most other causes of hypoxemia. Serial ABG analyses may be used to track failure, as some animals with left-to-right shunts or a mixture of oxygenated and deoxygenated blood entering the aorta will have a worsening of hypoxemia as left heart failure progresses.

ABG analysis is also a useful diagnostic test in poor-doing animals, particularly neonates and juveniles. Some of these animals will have a covert cardiac defect or acquired valvular disease that does not cause a prominent murmur. Finding hypoxemia, particularly when it does not respond to supplemental oxygen, may be the first clue to direct the diagnostic efforts toward the heart.

Techniques for obtaining arterial samples are described in Chapter 37.

Congenital Heart Defects

The most commonly reported abnormalities of the camelid cardiovascular system are congenital heart malformations. Boon and co-workers summarized the prevalence of congenital heart disease in llamas presented for evaluation at Colorado State University (24 of 663 total camelid admissions = 3.6%) and from data obtained from the Veterinary Medical Data Base from 1986 to April 1993 (35 of 2167 = 1.6%).[10] Heart malformations have been reported to comprise 6.4% of all camelid congenital defects and were identified in 2.2% of camelids that were necropsied.[12] It is important to be mindful that a substantial percentage of crias with congenital heart disease have more than one anatomic cardiac defect, emphasizing the need for a meticulous cardiovascular examination. Various reasons have been put forward for the perceived high prevalence of congenital heart disease in camelid populations compared with what is seen in other domestic hoofstock. The most plausible explanations focus on the proposed heritability of most congenital heart defects and the founder effect of a small gene pool for camelids in those countries where sizeable camelid herds have been built up from a relatively limited number of imported camelids, as well as bottlenecks in their native populations.

A large variety of congenital heart defects has been described in camelids, including VSD and atrial septal defect (ASD), vascular ring anomalies, endocardial cushion defects, patent ductus arteriosus (PDA), tetralogy of Fallot (ToF), pseudotruncus arteriosus, persistent truncus arteriosus, transposition of the great vessels (TGV), pulmonic stenosis, double outlet right ventricle, mitral and tricuspid valve dysplasia, and tricuspid valve atresia.[3,10,12–19] Nineteen cases of congenital heart disease in llamas were identified from 1980 to 1990 at the University of California, Davis, and of these, 11 had VSDs, 4 had TGV, 2 had ASDs, 1 had ToF, and 1 had PDA (Dr. W.P. Thomas, personal communication). Fifteen cases of congenital heart disease have been identified in alpacas at the Oregon State Veterinary Teaching Hospital over the last 6 years including 4 with VSD, 4 with vascular ring anomaly, 2 with TGV, 1 with pseudotruncus arteriosus, 1 with ToF, 1 with hypoplastic left ventricle, 1 with coronary sinus to right atrial fistula, and 1

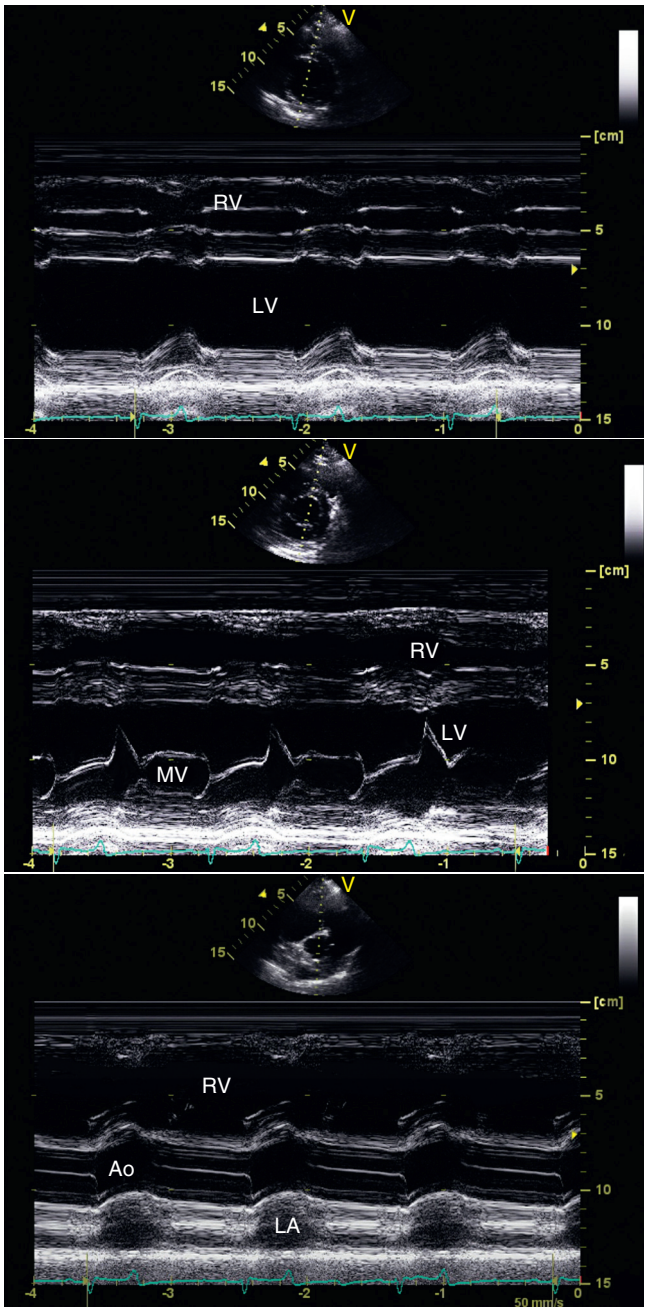

Figure 36-7 These M-mode echocardiographic scans were obtained at the level of the chordae tendineae (*top*), the level of the mitral valve (*middle*) and at the base of the heart (*bottom*). *Ao*, Aorta; *LA*, left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

with peripheral pulmonary artery stenosis. The high prevalence of vascular ring anomaly in this last population reflects greater awareness of this disorder, and a particular interest in this condition at this institution.

Ventricular Septal Defects

VSDs are far and away the most common congenital anatomic heart defects encountered in camelids.[3,10,12,14] VSDs often occur as isolated abnormalities, but they sometimes represent only one component of a more complex cardiac malformation. Accompanying congenital heart defects identified in camelids

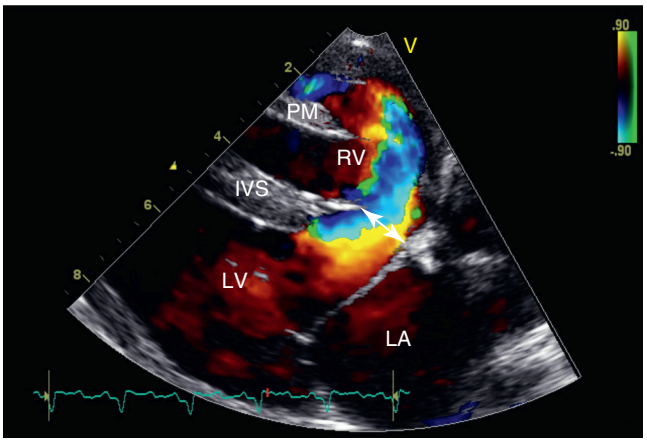

Figure 36-8 This right parasternal, long-axis, four-chamber, color flow echocardiographic image illustrates a large left-to-right shunting high ventricular septal defect (*arrow*) at the base of the interventricular septum (*IVS*). *LA*, Left atrium; *LV*, left ventricle; *PM*, right ventricular papillary muscle; *RV*, right ventricle.

with a VSD include ASDs, endocardial cushion defects, the various components of ToF, tricuspid valve atresia, TGV, and pulmonary artery hypoplasia. Moreover, VSD may be accompanied by other congenital musculoskeletal, urogenital, and facial abnormalities such as a cleft palate.

The consequences of VSDs depend on size, location, and the presence of other concurrent cardiac malformations. In the majority of affected animals, the VSD is small, and long-term survival without clinical manifestations can be rightly anticipated. Large, isolated VSDs may result in clinical disability either from CHF or as a consequence of pulmonary hypertension. VSDs occur most often in a perimembranous location at the cranial margin of the septal leaflet of the tricuspid valve and just below the supraventricular crest. Less often, VSDs are located immediately below the pulmonic valve in a supracristal, subarterial location. If the aortic annulus is undermined by a VSD positioned high in the interventricular septum, heart failure may develop as a consequence of aortic valve insufficiency resulting from distortion of the right or noncoronary cusps. Not uncommonly, one or more VSDs are identified in the muscular portion of the interventricular septum, where they are referred to as *muscular* or *trabecular VSDs*.

In most affected animals, the systolic murmur of a VSD is best heard on the right cranial thorax. Often, an accompanying palpable systolic thrill exists in the same location. The intensity of the murmur is poorly predictive of the size of the lesion, as smaller defects may create greater turbulence through high pressure jets compared with larger defects with more profound hemodynamic consequences. In some affected animals, the point of maximum intensity of the murmur is located at the left heart base, but a right-sided murmur is almost always still identifiable. When the defect is located in the muscular portion of the interventricular septum, the murmur may be heard in a more caudal location on the right side of the thorax near the cardiac apex. On those occasions where aortic insufficiency develops as a consequence of an undermined aortic root, an additional diastolic murmur may be heard in association with the VSD murmur, producing a characteristic "to and fro" type of cardiac murmur. With sufficiently large defects, the volume-overloaded left heart dilates,

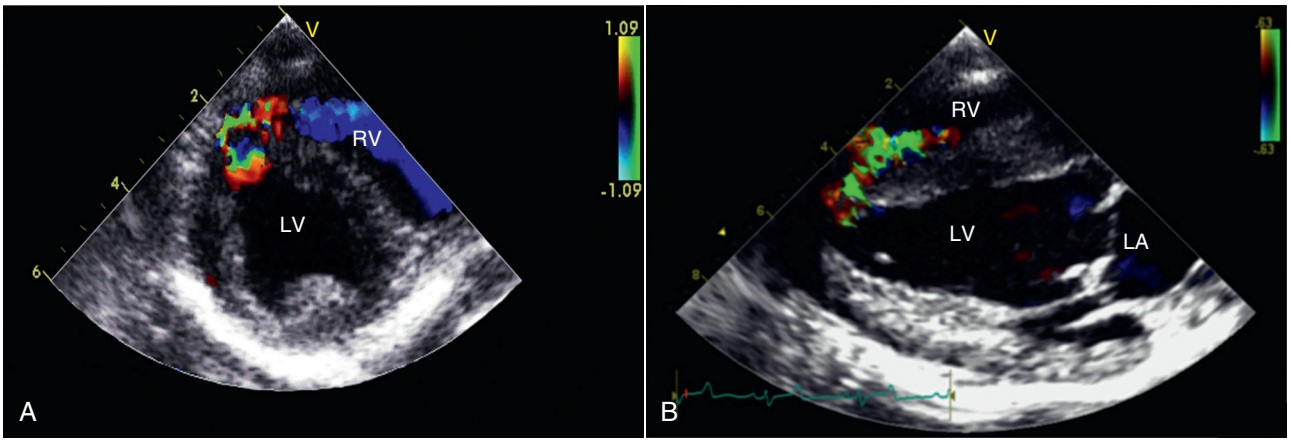

Figure 36-9 This right parasternal, short axis (*A*) view and accompanying long-axis, four chamber color flow echocardiographic image (*B*) illustrate a small left-to-right shunting muscular ventricular septal defect at the apex of the interventricular septum (IVS) in an alpaca cria. *LV* = left ventricle; *RV* = right ventricle; *LA* = left atrium.

develops mitral insufficiency, and eventually fails. In animals with very large defects, plexiform lesions develop in the pulmonary arterioles, resulting in the development of irreversible pulmonary hypertension. The resulting reversal of the shunt results in arterial desaturation, exercise intolerance, and central cyanosis. In such cases, no detectable heart murmur may be present.

When the shunt is sufficiently large, thoracic radiography may reveal changes suggestive of a VSD, including evidence of left-sided or biventricular heart enlargement in combination with pulmonary overcirculation, manifested as enlarged pulmonary arteries and veins. However, a definitive diagnosis is usually not possible without resorting to echocardiography (Figure 36-9). Color flow Doppler echocardiography is the preferred method to confirm the diagnosis, allowing visualization of the VSD and estimation of the direction and volume of the resulting shunt. Doppler echocardiography is also particularly useful for detecting pulmonary hypertension or coexisting pulmonic stenosis and for estimating right ventricular and pulmonary artery pressures. VSDs range in size from a few millimeters to the entire expanse of the septum. Most defects are between 0.5 and 1 centimeter (cm) in diameter and located in the membranous portion of the septum in an infracristal location. About one third of VSDs are located above the crista superventricularis. Less often, VSDs are found in the muscular portion of the interventricular septum, particularly near the cardiac apex. It is not uncommon to discover several muscular defects in an affected animal. Given the variability of the location of VSD in camelids, it is important to inspect the entire interventricular septum using a variety of unconventional imaging planes whenever a right-sided murmur is auscultated in a young camelid.

Small VSDs discovered in very young crias may spontaneously close or may never shunt enough blood to cause clinical complications. In general, affected camelids that survive into adulthood without clinical manifestations are unlikely to develop signs later in life. Hence, camelids with small defects do not require treatment. Periodic monitoring by echocardiography is advisable if the integrity of the aortic valve appears threatened or if evidence of significant chamber enlargement exists at the time of initial diagnosis. Common complaints for animals with large VSDs include poor growth, increased time spent in recumbency, and exercise intolerance marked by open-mouthed breathing or recumbency after physical exertion. Treatment of camelids with large VSDs and impending or existent heart failure has largely been limited to the administration of diuretics. Should an owner be particularly intent on optimizing care, a variety of VSD occlusion devices, designed for human use, are available. Once clinical disease is present, progression of the clinical signs usually leads to a decision to euthanize within a few months. The heritability of VSDs has not been established in camelids but conscientious breeders should consider this possibility, even when the VSD is small and not otherwise an important health concern.

Patent Ductus Arteriosus

PDA is not a particularly common congenital heart defect of camelids and has not been identified as an important cause of left heart failure or clinical disability. On occasion, a small PDA is seen as an isolated finding or in association with a persistent right aortic arch, where it contributes to the formation of a constricting vascular ring. More often, a PDA is discovered as part of a more complex defect, where it plays an important role in providing adequate blood flow to the pulmonary circulation when normal perfusion is impaired by right ventricular outflow tract obstruction. In those cases, a continuous (machinery) heart base murmur may be present and accompany other murmurs associated with other cardiac defects.

The exact time of ductus closure in healthy neonatal camelids has not been established with certainty, but it is not unusual to auscultate a soft continuous murmur at the left heart base in crias at 3 or 4 days of age. Color flow Doppler echocardiography often demonstrates a small transductal jet during this period. It is rare to detect such murmurs or to ductal flow by echocardiography after age 1 week.

Atrial Septal Defects and Patent Foramen Ovale

ASDs are far less common causes of clinical disease compared with VSDs, and anecdotal postmortem evidence suggests that they are altogether uncommon in camelids. Several different

types of ASD are recognized. Ostium primum ASDs, located in the lower portion of the interatrial septum, may occur as isolated defects or as a manifestation of a complete endocardial cushion defect, sometimes referred to as an *atrioventricular septal defect*. Ostium secundum ASDs develop in the middle of the interatrial septum, in the region of the fossa ovalis, and are the most common type of ASD. Sinus venosus ASDs occur in the uppermost region of the interatrial septum, typically in association with anomalous pulmonary venous drainage. In crias, the foramen ovale is patent at birth and usually closes within the first 2 weeks of life. In the absence of cardiac enlargement, a patent foramen ovale (PFO) is generally regarded to be of little consequence, as the higher left atrial pressure results in physiologic closure of this potential communication between the atria. Significant shunting across a PFO only becomes problematic when another cardiac disorder causes an increase in atrial pressure and atrial enlargement sufficiently severe to allow shunting similar to that seen with a small secundum type ASD. We have also seen a 12-year-old alpaca with a PFO and bilateral CHF, in which we suspected the defect may have played a contributory role to the severity of its condition.

Interestingly, the soft systolic ejection murmur of a left-to-right shunting ASD resembles the innocent or physiologic murmurs often heard in young crias as well as the soft murmur of mild pulmonic stenosis. Thus, murmurs resulting from ASDs are best heard at the left heart base and rarely exceed grade 3 of 6. Such murmurs are the result of an increased stroke volume passing through the right ventricular outflow tract rather than the quiescent shunting of blood within the atria. Fixed splitting of the second heart sound may sometimes be noted and is a useful clue to the presence of an ASD. Right-to-left shunting through a PFO may be seen in crias with pulmonary and tricuspid stenosis, pulmonary and tricuspid atresia, and other congenital heart defects resulting in elevated right atrial pressure. Small and even moderate-sized ASDs are generally well tolerated. Clinical signs are uncommon unless the defect is quite large or accompanied by other cardiac abnormalities. In the former circumstance, signs of right heart failure may develop during the first few years of life. To date, no treatments beyond supportive care have been reported.

Congenital Valve Stenosis and Insufficiency

Semilunar valve stenosis has been reported in camelids, but such defects are uncommon. We have evaluated several alpacas with moderate isolated pulmonic valve stenosis. More often, lesions of the pulmonary outflow tract comprise one of several anatomic defects such as ToF (see "Cyanosis-Producing Defects" below). Aortic stenosis appears to be particularly uncommon in camelids. Congenital aortic and pulmonic valvular insufficiency are also apparently very rare, as is dysplasia of the mitral or tricuspid valves.[17] Mitral dysplasia causes respiratory compromise and exercise intolerance when severe, whereas tricuspid defects result in jugular distention, jugular pulses, pleural effusions, and ascites. Hematocysts are sometimes observed on the AV valves at necropsy, but such lesions rarely result in valvular insufficiency. Confirmation of a suspected congenital valvular defect is best accomplished by echocardiography. No reports describing the treatment of such defects in camelids have been published.

Cyanosis-Producing Congenital Heart Defects

Complete endocardial cushion defects have been reported in a number of camelids, including a pair of llamas with a common dam.[16] This malformation, sometimes referred to as an *AV septal defect* or *AV canal*, consists of lesions involving those structures formed by the endocardial cushions, including the lower portion of the atrial septum and upper portion of the ventricular septum, the septal leaflet of the tricuspid valve, and the anterior leaflet of the mitral valve. The consequence of this combination of lesions is admixture of oxygenated and unoxygenated blood within a "single chamber" compounded by the volume loads resulting from AV valvular insufficiency. A systolic murmur is typically present in such cases and may often be heard on both sides of the chest. Affected camelids usually display clinical signs within the first weeks or months of life. These signs include weakness, cyanosis, lethargy, exercise intolerance, increased time spent in recumbency, decreased nursing, open-mouthed breathing, dyspnea, and poor growth. Engorged jugular and other peripheral veins, pleural effusion, ascites, and passive congestion of the abdominal organs may be present. Echocardiography reveals the communicating heart chambers (Figure 36-10). Color flow Doppler echocardiography reveals dramatic lesions with bilateral AV valve insufficiency and shunting through the combined ASD and VSD. All chambers of the heart are enlarged, but the right side is often enlarged to the extent that it provides the apex of the heart. Severe systolic dysfunction is typically present and pulmonary hypertension may also be evident. Although one llama appears to have survived adequately for 1 year at less than 300 meters (m) above sea level, other affected camelids have shown clinical signs at a young age. Once clinical signs develop, the affected animal usually dies or is euthanized within a few weeks or months. Interestingly, one affected 2-year-old llama began to show signs only after spending a year at high altitude. Diuretics have been used to palliate the clinical signs, but they do not have much effect on the progression of the disease or the eventual outcome. The occurrence of this defect in two related camelids raises the likelihood of a genetic cause, but the heritability of this defect remains speculative.

ToF is another well documented cyanosis-producing cardiac defect occurring in camelids and is characterized by pulmonary stenosis with hypoplasia of the pulmonary arteries, a high VSD, an enlarged and dextropositioned aorta, and right ventricular hypertrophy. This constellation of findings is the result of maldivision of the conotruncal septum during embryonic development. Extreme variants of this abnormality include those cases in which the pulmonic valve and the main pulmonary artery are completely atretic, creating the appearance of a "pseudo" truncus arteriosus (Figure 36-11). In such cases, pulmonary perfusion is accomplished by a PDA connecting the aorta to the right and left pulmonary arteries. Acyanotic forms of ToF are also seen when the pulmonic stenosis lesion is mild and right ventricular systolic pressures are not elevated above the pressure in the left ventricle. Echocardiography is particularly useful for identifying the complex anatomy of all the components of these complex congenital heart defects. Effective treatment requires surgical repair of the observed defects and, to our knowledge, this has not been accomplished in camelids.

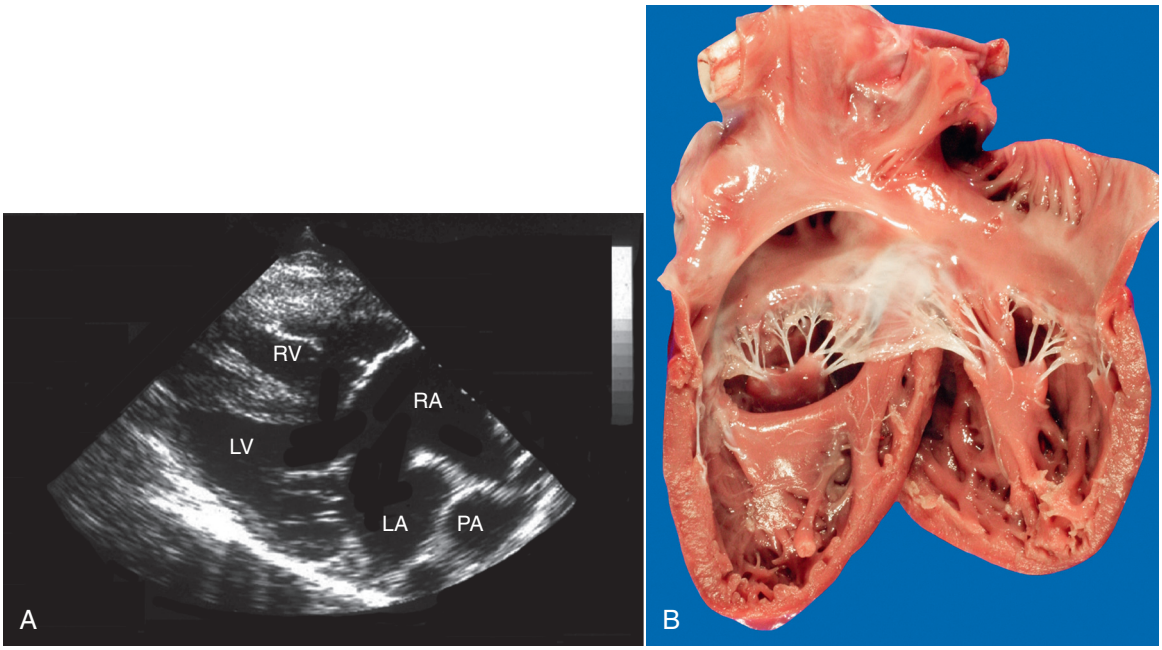

Figure 36-10 **A**, An echocardiogram of a large atrioventricular (*AV*) canal defect in a young llama. **B**, A necropsy specimen of another llama with complete AV canal. *(B courtesy of WP Thomas.)*

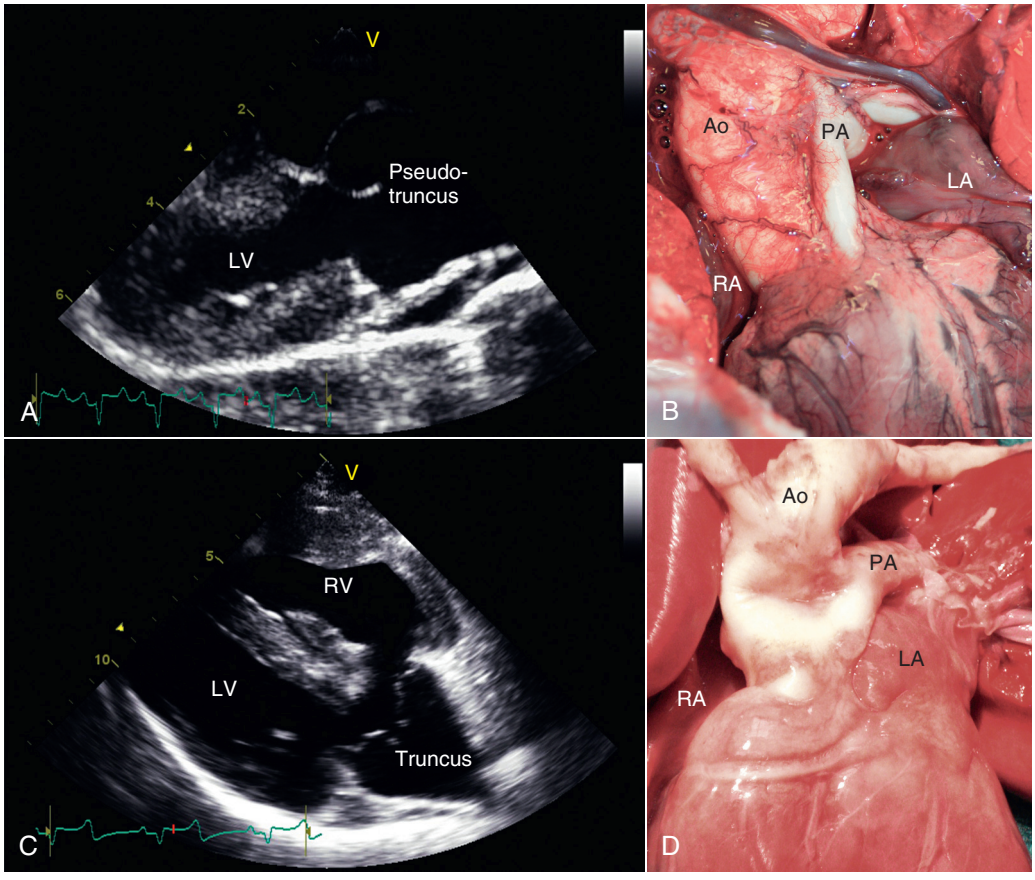

Figure 36-11 A pseudotruncus arteriosus, which is an extreme variant of tetrology of Fallot, is shown in an affected alpaca cria via echocardiography (*A*) and at necropsy (*B*). Note the close resemblance to an actual truncus arteriosus defect in a different alpaca cria, shown via echocardiography (*C*) and at necropsy (*D*). *Ao*, Aorta; *LA*, left atrium; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RV*, right ventricle.

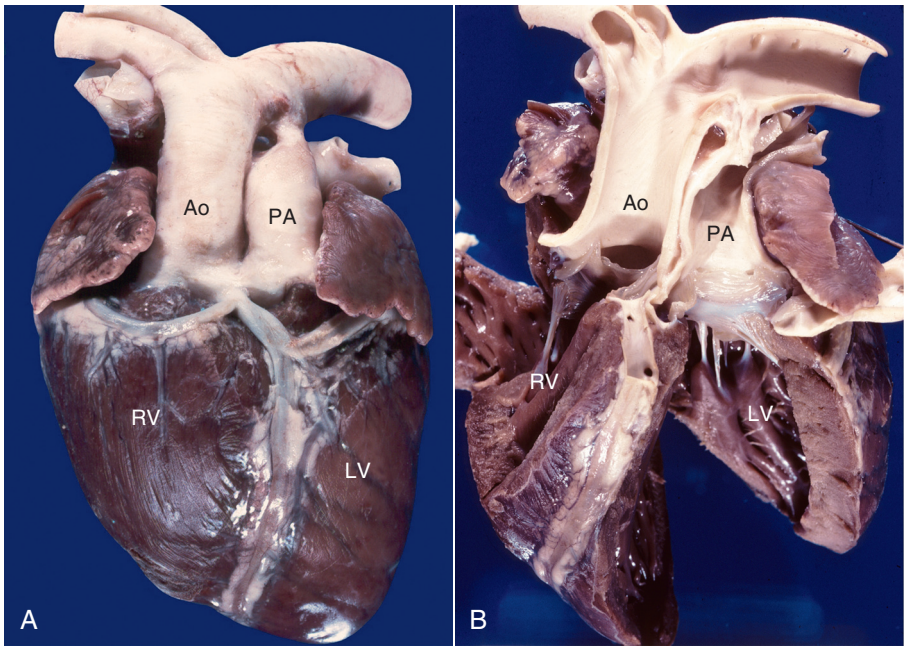

Figure 36-12 Transposition of the great vessels is shown in an affected llama, in which the aorta (*Ao*) arises from the right ventricle (*RV*) and the pulmonary artery (*PA*) arises from the left ventricle (*LV*). Note the single large coronary vessel extending down the anterior aspect of the ventricles (*A*), which clearly takes origin from the aortic root (*B*).

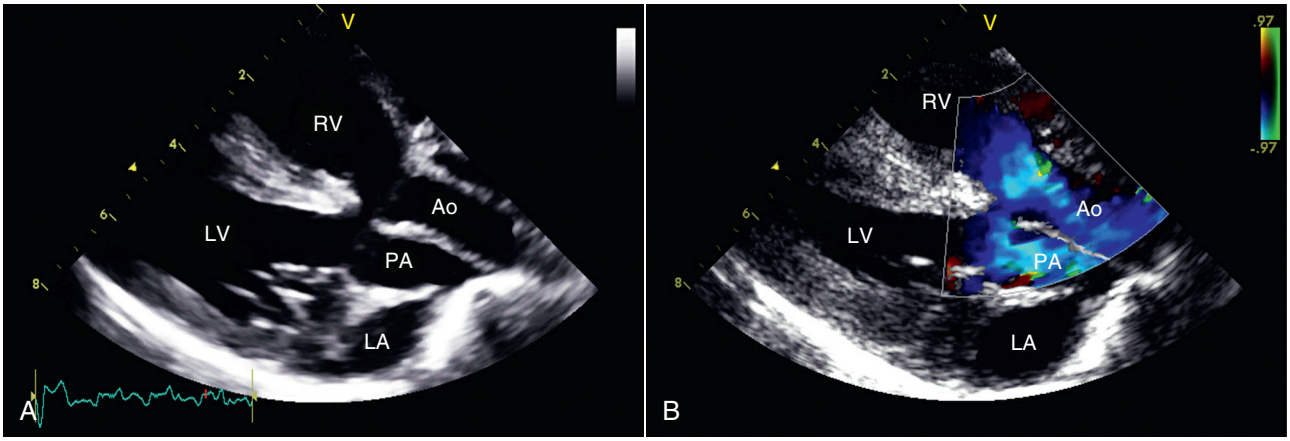

Figure 36-13 The appearance of transposition of the great vessels in an affected llama is show by two-dimensional (*A*) and color flow Doppler (*B*) echocardiography. *Ao*, Aorta; *LA*, left atrium; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RV*, right ventricle.

TGV has been documented in both llamas and alpacas on multiple occasions, yet this disorder is very uncommon in other domesticated animals. In this condition, the pulmonary artery arises from the left ventricle and the aorta arises from the right ventricle (Figures 36-12 and 36-13). This anatomic arrangement is not compatible with life unless some of the oxygenated blood returning from the lungs is able to pass from the left to the right side of the heart via an intracardiac communication or from the pulmonary artery to the aorta via a PDA. A variety of other cardiac malformations, including abnormalities of the coronary arteries, may also be identified. Affected individuals are always severely cyanotic at birth, and they usually survive only a short period. Other complex cyanosis-producing cardiac abnormalities, including hypoplasia of the left ventricle and double outlet right ventricle, have been seen in New World camelids (Figure 36-14).

Vascular Ring Anomalies

Vascular ring anomalies have been reported in both alpacas and llamas.[18,19] In contrast to other domestic species, the most common abnormality identified is a left aortic arch with either a right ligamentum arteriosum or small right PDA. This anomaly is often accompanied by aberrant origination of the right subclavian artery (Figure 36-15). The more familiar right aortic arch with constricting left ligamentum has also been observed. In those cases with a PDA, the size of the shunt was small, and a continuous murmur was only noted in one affected alpaca. Most affected animals presented at ages 3 to

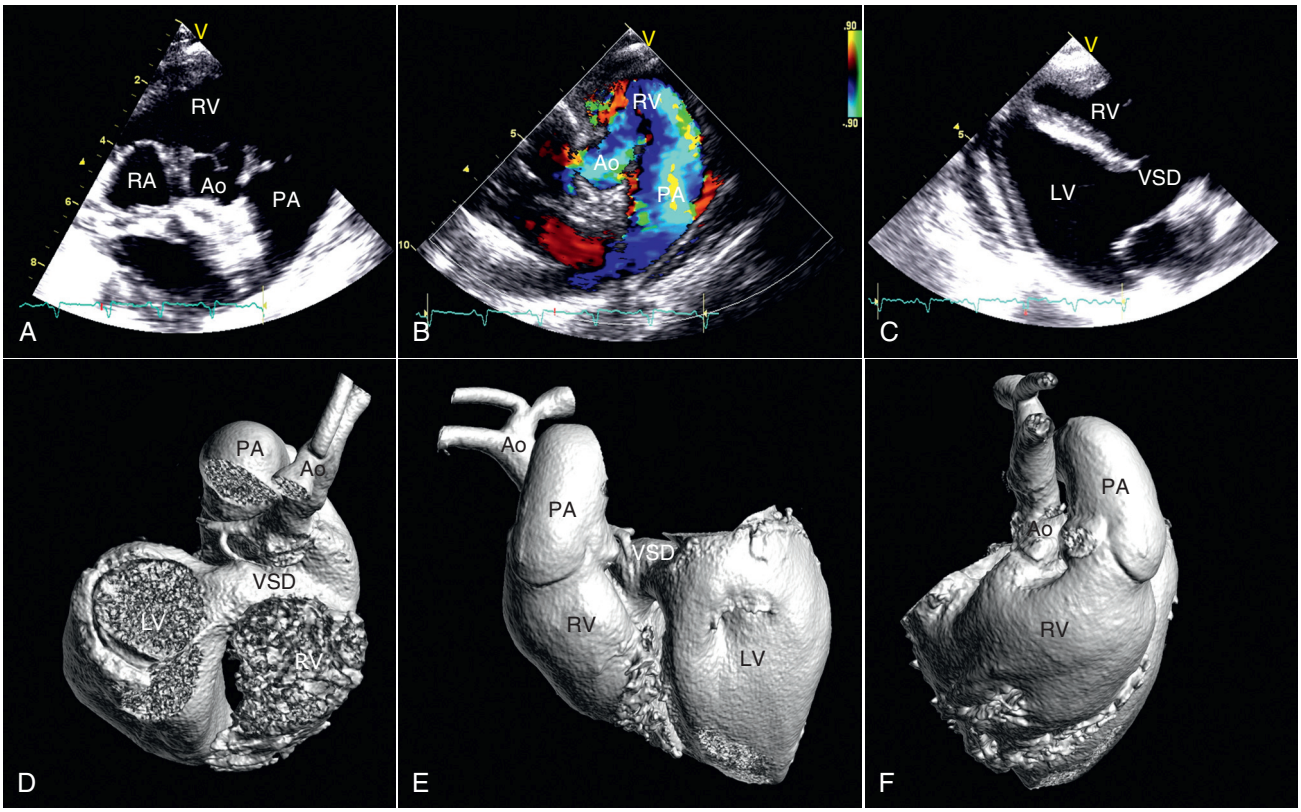

Figure 36-14 In this alpaca cria with a double-outlet right ventricle, the aorta (*Ao*) and pulmonary artery (*PA*) both arise from the right heart as shown by two-dimensional (*A*) and color flow Doppler (*B*) echocardiography. Survival is possible in the short-term because of the presence of a large ventricular septal defect (*C*). Views from three-dimensional casts of the heart of the same animal obtained via contrast-enhanced computed tomography (*D*, *E*, and *F*). *Ao*, Aorta; *LA*, left atrium; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RV*, right ventricle; *VSD*, ventricular septal defect.

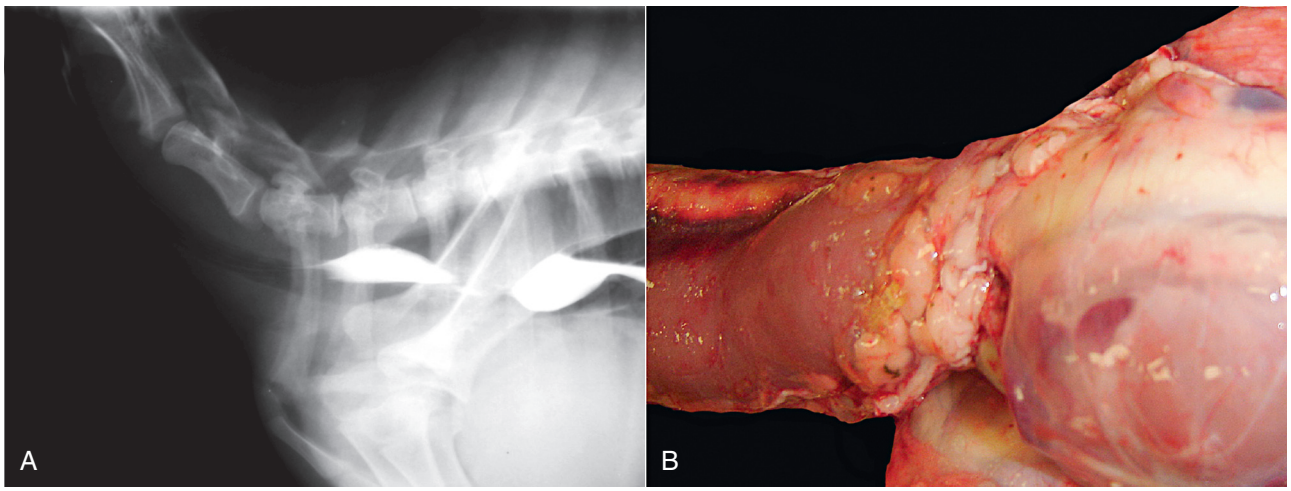

Figure 36-15 A variety of vascular ring anomalies have been reported in alpacas and llamas. Note the stricture of the esophagus in this lateral radiograph (*A*) obtained after barium administration. In the specimen shown in *B*, the vascular ring comprises a right aortic arch in combination with a left ligamentum arteriosus.

5 months, and the clinical signs were largely attributable to constriction of the esophagus. Dysphagia, abnormal regurgitation, choke, bloat, and failure to thrive are common clinical signs. Cough may also occur as a consequence of tracheobronchitis or pneumonia caused by inoculation of the airways with swallowed and regurgitated food. On occasion, the development of clinical signs may be delayed until early adulthood. Routine thoracic radiography often demonstrates a dilated esophagus both cranial and caudal to the heart base, sometimes with retained ingesta. It is sometimes possible to

identify a persistent right aortic arch on a dorsoventral thoracic radiograph, but other vascular ring malformations may easily escape detection.

Esophagoscopy, contrast esophagography, or fluoroscopy may be performed to confirm the stenotic lesion in the esophagus at the heart base (see Figure 36-15), but visualization of the vascular malformation responsible for the constriction is best accomplished by using angiography or contrast-enhanced computed tomography (CT). Inasmuch as the surgical approach to attempt repair is dependent on the precise nature of the malformation, consideration should be given to sophisticated imaging studies whenever surgical repair is contemplated. Surgical repair has been attempted, but success has been limited, partially because of concurrent aspiration pneumonia.

Other Vascular Defects

A portosystemic shunt has been reported in one juvenile alpaca with diarrhea, poor growth, and excessive tractability for its age.[20] Serum bile acid and blood ammonia concentrations were very high, and serum hepatic enzyme activities were within reference values, supportive of a diagnosis of vascular shunt. A colonic mesenteric vein portogram revealed a large extrahepatic shunt to the caudal vena cava, which was surgically ligated. The cria appeared to recover physically, behaviorally, and biochemically.

Two unrelated adult alpacas were reported to have networks of large, tortuous, anastomosing vessels in the right cranial lung lobe.[21] On the basis of the predominance of tunica media over tunica adventitia, the abnormal vessels were judged to be arterial in origin. The older alpaca had severe bilateral epistaxis and pulmonary hemorrhage linked to rupture of one of these vessels. In the younger alpaca, the vascular anomaly was considered an incidental finding, with speculation that it might have become problematic with time. In humans, such lesions are often considered congenital and usually contain arteriovenous shunts.[22] Approximately one quarter of the cases progress with time, whereas the majority remain static. Imaging studies were not performed on the alpacas but might have revealed the unusual vascularity. Vessel ligation or embolization or en bloc resection (lobectomy) have been used to treat this condition in other species.

Acquired Cardiac Diseases

Pericardial Disease

Pericardial disease is uncommon in llama and alpacas, and only a few reports of pericardial disease appear in the literature.[3,23–25] Echocardiographic identification of pericardial effusion is the most common diagnostic test (Figure 36-16). One case of pericardial effusion causing cardiac tamponade has been reported in a 2-year-old pregnant alpaca.[23] In this case, successful treatment was accomplished by pericardiocentesis and administration of antibiotics and antiinflammatory drugs. Bacteria were not cultured from the pericardial fluid in this case, and the cause of the effusion is best regarded as idiopathic. Constrictive effusive pericarditis has also been reported in a single case report of a successfully treated llama cria.[24] In another successfully treated cria, pericardial effusion led to electrical alternans on ECG.[25] An unrecognized septic event was thought to be the inciting factor. Others have identified pericardial effusion in association with a variety of disorders, including dilated cardiomyopathy, pleuropneumonia, pulmonary hypertension, and several different types of congenital heart disease. We have observed small effusions in a few llamas and alpacas with severe heart failure, which we considered an incidental secondary finding and of no great clinical significance. Mild effusion may occur with hypoproteinemia as well.

To obtain a diagnostic sample or to relieve pressure on the heart, ultrasonography-guided pericardiocentesis may be performed through the fourth intercostal space on either side, taking care to avoid hitting the heart.

Endocarditis

Endocarditis is an important but, fortunately, infrequent disorder of camelids.[26–28] In most domestic animal species, endocarditis lesions are mainly confined to the cardiac valves and mural lesions are uncommon. In camelids, mural lesions within the ventricles have been observed more often and are more dramatic than valvular lesions, at least in the population of animals evaluated at Oregon State University (Figure 36-17). In our experience, the endocardial surface of the right ventricle is more commonly affected than the left, although both ventricles are affected in half the cases. Often, the leaflets of the AV valves become embedded within the thrombotic material, with the tricuspid valve slightly more commonly affected than the mitral valve. It is usually difficult to identify a remote source of infection as the primary cause of endocarditis, although preexisting abnormalities have been identified in several reports. Bacterial organisms may sometimes be recovered either via blood culture or at necropsy, but it is often not possible to recover microorganisms before or after death.

Physical occlusion of the ventricular lumen, which causes restricted ventricular filling, and incompetence of the AV valves contribute to the development of clinical signs.

Recumbency, depression, lethargy, exercise intolerance, colic, and abdominal distention are common presentations in affected animals. Murmurs are audible if the AV valves are affected and jugular distention may be present. Distention of the abdomen may be caused by ascites and hepatomegaly, and in some cases, the enlarged liver may be palpated through the right flank. Hepatomegaly may also be detected ultrasonographically. In some cases, the liver completely fills the right paralumbar fossa. Blood work changes are variable. During quiescent periods, the complete blood cell count (CBC) and the biochemistry panel may be normal. Neutrophilia, hyperfibrinogenemia, and hyperglobulinemia may also be seen. The primary source of infection may be more instrumental in determining blood abnormalities than endocarditis. We have seen increases in liver and muscle enzymes, azotemia, and degenerative leukograms in connection with diffuse hepatic infection, hepatomegaly, and right heart failure. Abdominocentesis or other pertinent tests may also reveal information about the underlying inflammatory disorder or may just reveal copious ascites.

Definitive diagnosis is best achieved by echocardiography (see Figure 36-17). Treatment has not been rewarding, in part because of the advanced nature of the disease on detection. Antibiotics, antiinflammatory drugs, and fluids are the most common treatments.

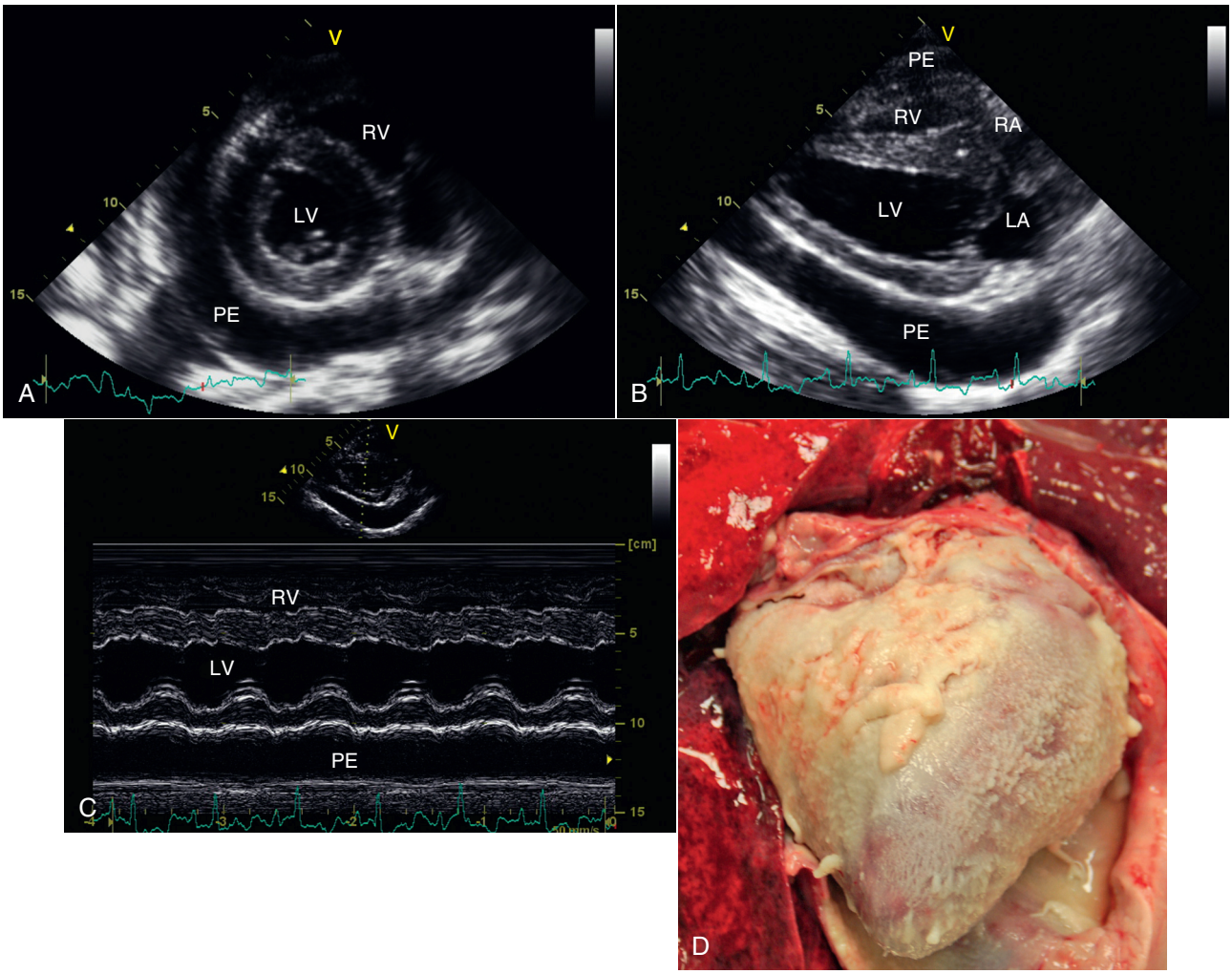

Figure 36-16 Septic pericardial effusion in this alpaca was first detected by echocardiography (*A*, *B*, and *C*) and later confirmed at necropsy (*D*). *LA*, Left atrium; *LV*, left ventricle; *PE*, pericardial effusion; *RA*, right atrium; *RV*, right ventricle.

Valvular Insufficiency

Age-related degeneration of the mitral and tricuspid valves is an uncommon finding in llamas and alpacas. As in other species, high-pressure regurgitation of blood leads to a systolic murmur over the affected valve. Echocardiography, particularly a Doppler study, is used to make the diagnosis and differentiate this from lesions associated with endocarditis (Figure 36-18).

Primary Myocardial Diseases

Primary myocardial diseases, which are conditions that predominantly affect the heart muscle, are not the result congenital or acquired valvular, pericardial, vascular, or systemic disease, and their causes are unknown or have been shown to have a heritable (genetic) basis. Myocardial diseases resulting from well-defined disease processes are referred to as *secondary myocardial diseases* or *specific heart muscle diseases*. Primary myocardial diseases are subdivided morphologically and functionally into well-characterized disorders such as dilated and hypertrophic cardiomyopathy based on the predominating anatomic and physiologic abnormalities detected clinically or at necropsy, and secondary myocardial diseases are subcategorized on the basis of specific etiology (e.g., nutritional, toxic, inflammatory, etc.).

Dilated cardiomyopathy (DCM) as well as hypertrophic cardiomyopathy (HCM) has been reported in Old and New World camelids, but neither is a commonly encountered condition.[3,29–31] In the few cases reported to date, information regarding the possibility of heritable myocardial disease in Old or New World camelids is insufficient. Of the few reported cases of DCM, echocardiography was performed to document the presence of dilated ventricles with markedly reduced systolic function, thus establishing a presumptive antemortem diagnosis. One report described a 1-week-old female llama cria with DCM in association with an umbilical infection and suspected sepsis.[3] These same authors described another case example in a 6-week-old male llama cria with ventricular tachycardia and a markedly elevated plasma cardiac troponin I concentration, indicating severe ongoing myocardial damage. The most recent reported case of DCM in a cria provided a

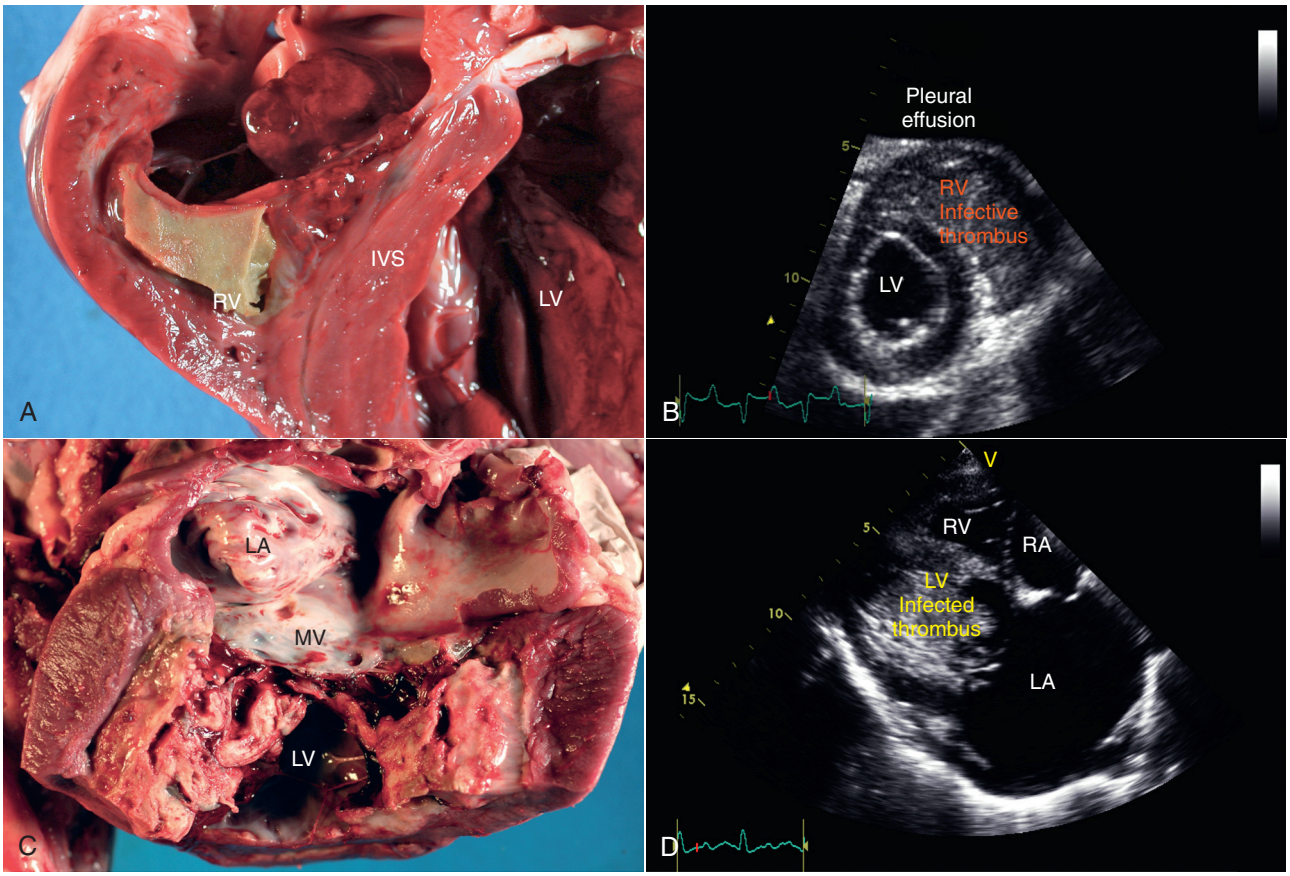

Figure 36-17 Mural endocarditis in alpacas is manifest as the deposition of infected fibrin thrombi on the walls of the right (*A* and *B*) or left ventricles (*C* and *D*), often with concurrent involvement of the ipsilateral atrioventricular valve. Note the near-obliteration of the right and left ventricular lumens noted both at necropsy (*A* and *C*) and by echocardiography (*B* and *D*).

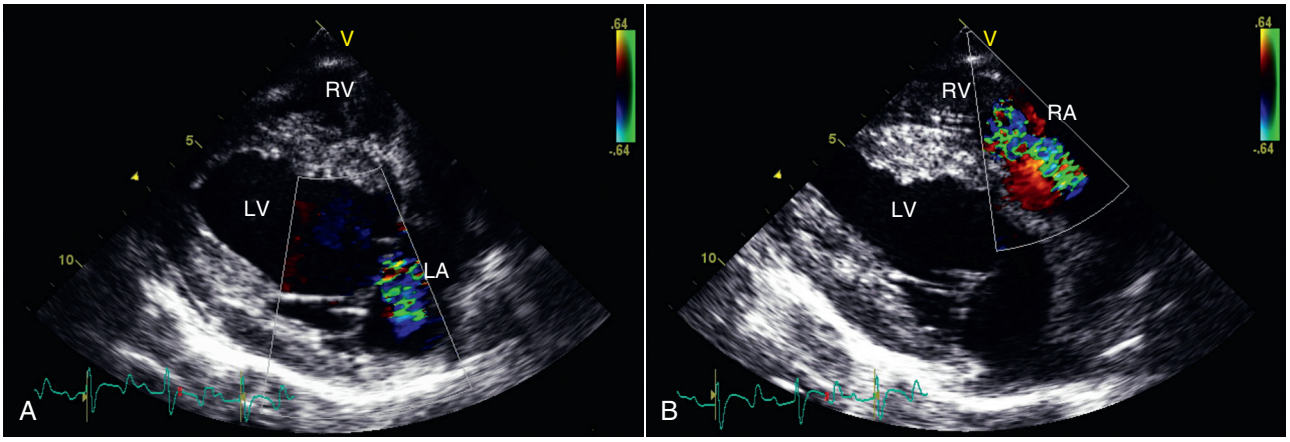

Figure 36-18 Older alpacas and llamas sometimes develop mitral (*A*) and tricuspid (*B*) regurgitation as a consequence of age-related degeneration of the atrioventricular valves as shown in these color flow Doppler echocardiograms. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

detailed description of the histology of the myocardium and noted attenuated wavy fibers that are typical of DCM in many breeds of dogs with DCM.[31]

A single case of hypertrophic cardiomyopathy has been reported in a 3-year-old male alpaca that died suddenly.[30] Hypertrophied myocardial cells and myocardial fiber disarray, typical of human HCM, were identified on sections of myocardium obtained from the interventricular septum and right ventricular free wall. Interestingly, hypertrophic cardiomyopathy has also been reported in a dromedary camel.[29]

Secondary Myocardial Diseases

Sarcocystis. New World camelids are susceptible to infection by *Sarcocystis aucheniae*.[32–35] This is a different species,

although it is biologically similar to the sarcocysts of camels or domestic ruminants. The life cycle appears to depend on a canine definitive host, which becomes infected by eating unprocessed camelid meat containing infective macrocysts. Camelids become infected by eating or drinking in areas contaminated by dog feces containing infectious sporocysts. Other carnivorous hosts have not been identified. Infected camelids develop cysts in striated muscle and cardiac Purkinje fibers. Because unprocessed camelid meat is rarely fed to dogs in North America and elsewhere, new infection is rare here.

Ingestion of large numbers of sporocysts may lead to fulminant, rapidly fatal disease 3 to 4 weeks after exposure.[35] Clinical signs include anorexia, weight loss, salivation, weakness, incoordination, fever, recumbency, pale mucous membranes, and diarrhea. Hemorrhagic diathesis and enteritis are common postmortem findings. With lower levels of exposure, disease signs are chronic and may appear years after ingestion. Signs seen include weight loss, muscle stiffness, weakness, abortion, and death.[32,35] Diagnosis of infection may be made by performing a muscle biopsy, which would reveal the cysts, areas of necrosis, and eosinophilic myositis. Treatment has not been common. Sulfa antibiotics may be of some value but must be given parenterally to camelids with relatively mature forestomach development.

Ionophore Toxicosis. Carboxylic ionophore antibiotics are frequently added to livestock feeds as coccidiostats and growth promoters. It is not known whether certain concentrations might confer health benefits to camelids, but known examples of toxicosis exist. The best publicized in New World camelids relates to salinomycin, with anecdotal reports involving monensin and lasalocid as well.[36] Salinomycin and monensin have been implicated in toxicoses of Old World camelids as well.[37–41] In general, poisoning events in camelids involve ingestion of milled feeds containing higher concentrations of the ionophore than would normally be fed to livestock, such as 60 to 90 parts per million (ppm) of salinomycin in a crumble feed, so it remains unknown whether camelids are highly susceptible or simply were overdosed.

Clinical signs of toxicosis may begin within a few days of ingestion and include weakness, recumbency, muscle tremors, dyspnea, diarrhea, and acute death. Animals that do not develop signs peracutely may develop signs of heart failure over weeks to months. Laboratory evidence includes high serum creatine kinase, alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) activities, hypocalcemia, including a decrease in ionized calcium, hyperphosphatemia, hyperglycemia, myoglobinuria, glycosuria, increases in blood troponin 1 concentrations, and hemoconcentration. Postmortem findings include necrosis of skeletal and cardiac muscles and evidence of pulmonary edema. Interestingly, in one camel, heart muscle was reported to have been spared.[41] Because the source is feed, it is common to have multiple animals on a single property affected or animals in a region that are fed the ration. Diagnosis is often presumptive and based on feeding history and clinical signs. For confirmation, feed and gastric contents may be analyzed for the presence of the ionophore.

Treatment, to date, has been mainly palliative and supportive. Positive inotropic agents are probably indicated but have seen limited use. Fluid therapy is helpful against shock but may exacerbate edema caused by heart failure.

Oleander. Until recently, the most commonly reported cardiotoxin in New World camelids was white oleander (*Nerium oleander*) and the closely related yellow oleander (*Thevetia peruviana*).[41–44] White oleander is an evergreen shrub that is native to the Mediterranean, the Middle East, western Himalayas, and Japan, but its popularity as an ornamental plant has spread it to many parts of the world. It is popular in the southern United States and along the West Coast as far north as Northern California, where it is commonly used in highway dividers. It is also found in other parts of the world with similar climates, including Australia. It prefers warm, wet climates but has deep tap roots to procure water during dry periods. Yellow oleander (*Thevetia peruviana*) is native to tropical America but has also been cultivated in a variety of locations. It is similar in many ways to white oleander, although reports of animal toxicosis are less common.

Oleander's leaves, sap, fruit, and wood are extremely toxic to humans and animals, with ingestion of as little as 0.005% of body weight in dried leaves reported to be lethal. This amount could be as little as two or three leaves for an alpaca, although more are usually ingested. The cardiotoxic principles are cardiac glycosides, principally oleandrin and neriine. *Thevetia* has similar toxins, including thevetin A and thevetin B. These glycosides are present in the highest concentrations during the plant's flowering period and are not lost during drying. They act as digitalis analogs, inhibiting the activity of the sodium–potassium pump. Intracellular potassium declines, and calcium increases. Myocardial cells lose their resting potential, pacemaker function, and eventually all electrical functions. Enterohepatic circulation of toxins leads to extended effects. Other body systems may also be affected, especially the gastrointestinal (GI) tract; other toxins such as triterpenoids may be involved in the noncardiac components of oleander poisoning.

The fresh leaf is long, thin, leathery, and glossy green, with many fine parallel secondary veins coming off at close to a right angle from the main central vein. Dried leaves are brown and easily blown in the wind. Fresh leaves or wood are reported to be caustic and extremely bitter, but dried leaves may be more palatable or mixed in with palatable feeds. The most common poisonings are from ingestion of clippings, mulch, or dried leaves, where oleander is mixed with more palatable forage. In rare cases, intoxication may result from inhaling smoke from burning oleander.

Clinical signs are thought to appear within 1 day of ingestion, possibly even within a few hours. They include anorexia, recumbency, and lethargy. Some camelids show colic signs and others develop fetid or bloody diarrhea. Close examination may reveal cyanosis, bradycardia or tachycardia, or other cardiac arrhythmias. Tremors and dyspnea are seen close to death. Sudden death is also not uncommon, and clinical disease in one camelid should lead to greater scrutiny of other camelids in that same pen or on that same farm.

Electrocardiography has revealed bradycardia, AV blocks, atrial fibrillation or flutter, depression of the ST segment, ventricular premature beats and tachycardia, and ventricular fibrillation.[44,45] Blood analysis usually reveals hyperkalemia and moderate to severe azotemia.

A diagnosis of oleander intoxication can be made by an eyewitness account or physical evidence of camelids eating or having access to the shrubs, leaves, clippings, or smoke from

burning oleander, identification of the leaves in ingesta, or two-dimensional thin-layer chromatography or liquid chromatography-mass spectroscopy of gastric (C1) contents for oleandrin. Chromatography may also be performed on urine or colonic contents, but using these samples for testing appears to be less sensitive. However, obtaining gastric contents from a severely ill camelid may have life-threatening consequences, so less invasive sample collection may ultimately be advisable. Toxin has also been detected in human blood.[46] If chromatography is unavailable, oleandrin also cross-reacts on digitalis radioimmunoassays. On physical identification of macerated leaves, it is helpful to look for the distinctive parallel secondary veins. These veins are less regular and at a more acute angle to the central vein on *Eucalyptus* leaves.

Necropsy evaluation frequently reveals relatively modest lesions. Petechiae, ecchymoses, or overt hemorrhage may be found on many tissues, particularly the heart and GI tract. Evidence of enteritis may be present. The lungs are often congested and edematous. In some cases, overt myocardial degeneration is grossly visible. Histologically, subendocardial necrosis of the left ventricle appears to be the most common lesion. Other parts of the heart could also be affected. In many cases, the major role of necropsy is to rule out other causes of death and to rapidly provide leaves or ingesta samples for analysis.

Treatment is mainly supportive. If ingestion occurred with in a few hours, gastrotomy to remove leaves should be considered. Otherwise, intravenous (IV) fluids and activated charcoal (100–300 milligrams per kilogram [mg/kg], orally [PO] or by tube, q24h for 2 to 5 days) may each have some benefit. In compromised patients, administration by oral syringe is less stressful than orogastric intubation, and sorbitol-containing charcoal compounds may be swallowed readily. Non-charcoal absorbents appear to be inferior. In humans, digoxin-specific antibody fragments to bind toxin, atropine to combat bradycardia, and lidocaine to combat ventricular arrhythmias have been used, but use of these medications has not been reported in camelids. Camelids that ate little are likely to survive, whereas any sufficiently sick to show overt clinical signs should be treated as a critical case.

Other Plant Cardiotoxins. Rhododendron, azaleas, laurel, Labrador tea, and other related plants also contain cardiac glycosides and have been associated with toxic ingestion in camelids, but camelids rarely eat enough to cause clinical cardiac disease. With laurel, for example, ingestion of 0.2% to 0.6% of body weight is required to cause cardiotoxicosis in ruminants. GI signs occur at much lower ingested amounts and are the predominant clinical problem seen in camelids. Ingestion of other plants with cardiovascular effects, including foxglove (*Digitalis purpurea*), yew (*Taxus* spp.), belladonna (*Atropa belladonna*), and false hellebore (*Veratrum* spp.) have not been reported in camelids.

Neoplasia

Lymphoma is the most common tumor found in heart tissue in camelids. The heart is involved in 25% to 40% of all camelids with lymphoma.[47,48] The myocardium, pericardium, endocardium, or epicardium may be diffusely infiltrated or peppered with discrete neoplastic foci. Signs directly referable to heart involvement are rare, except that jugular distension may occur if venous return is blocked or if epicardial or pericardial involvement results in cardiac tamponade. Heart base tumors have been seen as well but appear to be rare. These tumors are best found by using imaging techniques such as ultrasonography or cross-sectional techniques, which allow differentiation of soft tissues.

White Muscle Disease

White muscle disease in camelids is poorly described, but presumably, it can lead to a similar spectrum of conditions and signs as in other hoofstock. This includes cardiomyopathy, leading to weakness, exercise intolerance, and death. Increases in blood AST and creatine kinase (CK) activities and troponin 1 concentrations may be indicative. Measurement of blood and feed vitamin E and selenium concentrations should be confirmatory. Prevention is through proper dietary management and use of supplements, and treatment of clinical cases includes supportive care, often including IV fluids, and administration of vitamin E and selenium supplements. White muscle disease is discussed more thoroughly in Chapter 13.

The Hemolymphatic System

Anemia

The elliptical shape and small size of the camelid erythrocyte are well-known features. The shape and nature of these cells is thought to make them more resistant to osmotic stress, which may be advantageous during periods of water deprivation and subsequent rapid rehydration. Other empirical evidence for this comes from the general lack of evidence for hemolysis in spite of large, abrupt changes in blood concentrations of sodium, glucose, proteins, and other osmotically active agents in clinical cases.

The small erythrocytes, although numerous, tend to result in packed cell volume (PCV) values similar to those seen in small ruminants and generally lower than those seen in large ruminants or horses, especially in camelids at low to moderate altitudes. However, PCV values in individual cases may range from very high to very low for a variety of reasons; as in the use of serum or plasma protein concentrations, assessing hydration based on a single PCV value is problematic.

The three most common measurements of anemia in camelids are PCV, erythrocyte count, and hemoglobin concentration. Mean corpuscular volume (MCV) is not used as much as in other species because the elliptical shape of camelid erythrocytes has an inconsistent effect on automated analysis. On the basis of these indices and published reference values, anemia appears to be a common, albeit subjective, finding in New World camelids. The subjectivity comes from the fact that most published reference ranges related to red blood cell (RBC) or hemoglobin mass appear to be more generous at the upper end of the range and less so at the lower end, where the bulk of the camelids seen at my practice lie. The low end of published values for PCV are generally 27% to 30%, the higher end of the range is approximately 39% to 45%, and the midpoint is around 35%.[49–53] In contrast, 75% of our clinic population has initial PCV values between 20% and 30%, with less than half over 27%, and only 10% have PCV values above

35%. Similar results may be obtained for erythrocyte counts and hemoglobin concentrations. Thus, either a high proportion of our clinic population is anemic, or reference values inappropriately indicate that most North American camelids have values at the low end or slightly below reference values.

Most of the anemia seen is low grade, and in sick or underperforming camelids, it is by itself poorly indicative of a specific disease process. Indeed, it is rarely clinically apparent. Barring the effects of other debilitating disease processes, camelids often maintain normal activity levels until their PCV drops below 20%. This may be explained by the following apparent anomaly: A roughly linear relationship appears to exist between PCV or erythrocyte count and hemoglobin concentration in camelids except that hemoglobin concentration appears to plateau above 10 milligrams per deciliter (mg/dL) as PCV declines through the twenties and erythrocyte count declines from about 13 to 10×10^6 cells per microliter (cells/μL). The linear decline resumes after PCV drops below 20%, and erythrocyte count drops below 10×10^6 cells/μL. Thus, oxygen-carrying capacity may be maintained over the range of low-grade anemia.

On the basis of this information and clinical experience, cutoffs of PCV less than 20%, erythrocyte count less than 10×10^6 cells/μL, and hemoglobin concentration less than 10 g/dL appear to mark the border of clinical significance to anemia. Even below those values, camelids appear to be very good at hiding the effects of anemia. Camelids with PCV values in the teens may not be detected by decreased energy or activity, unless the camelid is observed carefully. In the PCV ranges from about 12% to 7%, camelids will often continue to eat and move about, although they usually lie down instead of fighting when handled or pursued and may have evidence of exercise intolerance. Mucous membrane color changes are hard to detect, even with this degree of anemia. Appetite and ability to stand wane rapidly when the PCV drops below 7%, and mucous membrane pallor finally becomes visible.

Given the lack of specific clinical signs, the clinician usually becomes aware of the presence of anemia in a patient after determination of PCV or a complete CBC. The indications for these blood tests are varied, but something usually alerts the handler or veterinarians that all is not right. Clinical evidence of weakness, lethargy, tractability, or anorexia are common but usually more reflective of a primary disease process than of anemia. In rare cases, anemia is the primary disorder, and membrane pallor may be present and noted. This means of detection is likely to become more common as color qualitative systems such as FAMACHA (Faffa Malan Chart) become more popular.

The next step is assessing severity and significance. PCV values between approximately 20% and the lower end of the reference range, or hemoglobin values greater than 10 mg/dL are so common among unthrifty or ill camelids that they are unlikely to be of any great significance or require any special diagnostics or treatment beyond a normal ill-thrift evaluation. Once these lower thresholds are surpassed, it may be worth performing a PCV-to-protein calculation. When PCV is 20% or less, if blood loss is the primary problem, the PCV should be approximately 8.7 to 10.8 times the plasma albumin concentration (in mg/dL) and 4 to 15.4 times the plasma total protein concentration (in mg/dL). Ratios less than this tend to reflect disproportionate protein loss and indicate the need for further evaluation of protein-losing processes rather than blood loss. Higher ratios are rare, especially for the albumin comparison, and may reflect hemolysis or decreased production. For the protein comparison, they may also reflect concurrent hyperglobulinemia.

Once significant anemia is detected or suspected, in the absence of overt hemorrhage, a CBC with morphologic description and reticulocyte count is indicated. The presence or absence of a regenerative response may also be difficult to discern in anemic camelids. The standard characteristics used to evaluate this in other species, including the presence of reticulocytosis, metarubricytosis, polychromasia, or anisocyotosis, may be seen in camelids with nonregenerative anemia, and even in healthy, nonanemic camelids.[54] Megalocytic or megaloblastic anemias appear to be rare and are difficult to discern because of the problems with MCV measurement. Even in the face of moderate to severe anemia, the magnitude of the regenerative response is often underwhelming. Once PCV drops below approximately 13% in clinical cases, the regenerative process often appears to be arrested altogether. In experimental trials of anemia induced experimentally through whole blood removal, metarubricytosis increases to only 20 per 100 white blood cells (WBCs; high normal = 3 per 100 WBCs), and reticulocytosis increases to only 1.5% (high normal = 0.6%).[55,56] Some individual animals on these experimental trials remained anemic for at least 3 months in spite of having no known reason for suppressed regeneration. In clinical decision making, the lack of regeneration may be confounding because the cause of anemia may no longer be present at the time of diagnostic testing.

Specific disease processes associated with decreased erythrocyte counts include internal or external bleeding, hemolysis, ectoparasitism or endoparasitism, iron deficiency, copper deficiency, neoplasms, inactive marrow, and chronic disease. In most cases, the mechanism of anemia is difficult to verify, and erythrocyte indices are within reference ranges. Blood loss may be external or internal, with internal parasites such as *Mycoplasma haemolamae*, *Eimeria*, liver flukes, and gastric nematodes the most common culprits.[57–71] The importance of *Haemonchus contortus*, in particular, has been recognized in recent years, particularly with increasing concerns of anthelmintic resistance among GI nematodes. Haemonchosis is the most common cause in our area for PCV less than 10% in camelids; GI neoplasms, and mycoplasmosis are rarer causes. External examination for wounds, lice, ticks, and lymphadenopathy, fecal examination for internal parasites, and blood film examination for mycoplasmosis should be performed in cases of unexplained anemia, and bone marrow analysis should be considered with chronic anemia. Fluorescent staining methods are used to distinguish Haemonchus from other strongyle-type egg producers (see Chapter 5). It also must be kept in mind that blood-sucking by *Haemonchus* females starts with the L4 larvae, meaning that anemia can occur during the prepatent period. Each female worm ingests approximately 0.05 ml of blood per day; every 1000 worms ingest approximately 1.4% of an adult alpaca's blood volume each day. Other internal parasites are rarely associated with anemia of this severity, but are commonly seen in camelids with PCV between around 15% and 25%. Significant non-parasitic GI bleeding has been seen with lymphoma or carcinoma, ulcerative gastritis caused by ingestion of sand or hair, and copper

poisoning. Unless compounded by one of these other factors, gastric ulceration extremely rarely leads to anemia, melena, or even a positive fecal occult blood test. Renal blood loss may occur with neoplasms or chronic nephritis. Significant bleeding may lead to overt hematuria.

Hemolytic diseases are rare. *Copper poisoning*, which is a well-known cause of hemolysis in other species, appears to cause liver necrosis and occasionally GI bleeding, but not hemolysis in camelids. A variety of poisonous plants have been associated with hemolysis in other livestock species, but of these, only *red maple toxicosis* has been described in camelids.[72] Affected alpacas showed signs of lethargy, depression, mild tachycardia, and pale mucous membranes 4 to 5 days after being fed tree clippings. Brown discoloration of the membranes and discolored urine were also observed. Laboratory analysis revealed anemia (PCV <20%), discolored plasma, anisocytosis, and Heinz body formation (seen with new methylene blue stain). Although bilirubin concentrations were high, those results were invalidated by hemolysis. PCV declined in both alpacas over the next 24 hours, and clinical signs worsened. Azotemia developed or worsened in spite of fluid administration.

Red maple (*Acer rubrum*) leaves are known to cause intravascular hemolysis, Heinz body formation, and methemoglobin in horses by an unknown mechanism, but this syndrome has not been reported in any other forestomach-fermenting herbivore other than alpacas. Potentially, these alpacas were fed a large enough dose, had better gastric absorption of the toxic principal, or had insufficient antioxidant to counteract the toxin. No specific antidote is available. In addition to transfusions to restore erythrocyte mass, fluid treatments to prevent hemoglobin-induced nephropathy are indicated.

Candidatus Mycoplasma haemolamae (formerly *Eperythrozoon*) is a well-recognized blood parasite of New World camelids. It was first identified in llamas in North America in 1988 and has since been identified in most countries where New World camelids are raised.[58,59] It has been found in llamas, alpacas, and guanacos, and vicuña are presumed to be susceptible as well.[58,59,62,68] Recent work has revealed it to be a close relation to *M. suis* of pigs and more distantly related to the hemotropic bacteria of cattle (*M. wenyonii*), and other hemotropic mycoplasma (hemoplasmas).[57] The hemoplasmas are gram-negative bacteria that lack a cell wall. They attach to the wall of erythrocytes with microfibrils, causing slight depressions at the site of adherence, but do not appear to penetrate host cells. They are presumed to cause disease through glucose consumption, activation of an inflammatory or immune response, and accelerated removal of parasitized erythrocytes by the reticuloendothelial system. Prevalence of infection in various populations has been estimated to range from approximately 10% to 20%.[62,67,68] The mode of transmission is unknown. Biting insects may play a role, and the identification of infection in presuckling neonates suggests that vertical transmission may also occur.[63]

Most infected camelids show no clinical abnormalities beyond episodic parasitemia. If one infected camelid is identified in a herd, it is likely that others are infected as well, often with varying degrees of illness, including some in apparent good health. It has been seen in camelids of all ages, including neonates less than 1 day old.[63] Those that are ill may show anything from mild signs, including progressive lethargy, recumbency, and weight loss, to acute collapse and death. Advanced clinical signs often correlate with high levels of parasitemia and anemia but also may be the result of some concurrent disorder. The interplay between mycoplasmosis and other disease is an ongoing question. Immunosuppression is thought to facilitate severe parasitemia but may also be the result of parasitemia. Camelids showing severe anemia or signs should generally be investigated for the presence of another disorder such as immunodeficiency, and treatment of that disorder should accompany any treatment for mycoplasmosis. Specific factors identified as contributing to heavy parasitemia include weather stress, heavy GI parasite loads, immune suppression or deficiency (juvenile llama immunodeficiency syndrome, corticosteroid administration, *Anaplasma phagocytophilum* infection, or debilitation caused by another disease.[60,65,69]

Diagnosis is made by identification of the parasite on blood film examination or polymerase chain reaction (PCR). The parasites are 0.5 to 1 micrometer (μm) in diameter, coccoid, rod shaped, or ring shaped and may be seen singly, in pairs, or in clumps. They tend to gather at the periphery of erythrocytes but may also be seen free in the plasma or overlying the middle of erythrocytes (where the ring-form is most common). They may be seen with Diff-Quick stain, but show up better with Giemsa stains. They must be differentiated from stain precipitate or Howell-Jolly bodies; the Howell-Jolly bodies should be within the erythrocytes. Blood smears should be made as soon as possible after the sample draw and preferably before refrigeration because the parasites fall off the erythrocytes quickly.[59] Only a few or all erythrocytes may be parasitized.

The PCR test may be used in place of blood film analysis or to detect subclinical parasitemia.[61,66] In newly infected camelids, the PCR test becomes positive 2 to 5 days before parasites are visible on blood film analysis and stays positive after visible parasitemia has resolved. PCR testing also suggests that some or even most infected camelids remain carriers, even if treated with antibiotics that eliminate visible parasitemia.[61,66] Even with a negative PCR test, future stressful or immunosuppressive influences may lead to recrudescence of parasitemia or facilitate reinfection.

Secondary signs of hemolysis such as hyperbilirubinemia, dark urine, or icterus have not been seen. In addition to anemia, *M. haemolamae* may affect camelids by stimulating a chronic immune reaction and utilizing glucose. Other blood work changes are likely to be secondary or related to another disease.

In camelids with mild anemia, the degree of anemia seems to wax and wane with the severity of the visible parasitemia. In camelids with severe anemia caused by *M. haemolamae*, evidence of a regenerative response, including reticulocytosis, high nucleated erythrocyte counts, and MCV toward the higher end of the reference range, may be seen.

Treatment of *M. haemolamae* is not always necessary. Camelids with an intact immune system may spontaneously resolve parasitemia, although recent work suggests that they may remain infected.[61] Camelids with moderate to severe anemia and parasitemia may improve after treatment, but all therapeutic plans should include provisions for decreasing environmental stress, resolving other health issues, and possibly investigating immunodeficiency. The most commonly

used treatment has been long-acting oxytetracycline (20 mg/kg, subcutaneously [SQ], q72h for 2 to 5 treatments). Oral medication has been generally less effective. Oxytetracycline decreases overt parasitemia but does not eliminate the carrier state.[61] Penicillin, florfenicol, enrofloxacin, artemisinin, and many other antibiotics appear to have no effect on hemoplasmas.[73,74] Alternative medications are currently being tested.

Nutritional disorders associated with anemia in camelids include *deficiencies in iron*, *copper*, and possibly *selenium*.[75–78] Morphologic changes consistent with iron deficiency include microcytosis (leading to anisocytosis; MCV <21 fl), hypochromasia, a decrease in mean corpuscular hemoglobin concentration (MCHC), dacryocytosis, and irregular distribution of hypochromic regions within erythrocytes. Evidence of ill-thrift, a decrease in serum iron concentration (<70 microgram per liter [mcg/L]) and clinical improvement after the administration of iron are supportive. Iron dextran (5–8 mg/kg, SQ, q7 days) appears to be an effective treatment. Adverse reactions to the injection appear to be rare, but appropriate warning of the client is warranted. Copper deficiency may be primary or secondary. Affected camelids also usually show evidence of ill-thrift and possibly neurologic signs. Hematologic changes include decreases in hemoglobin and MCHC. Demonstrating hypocupremia, inadequate dietary copper or high concentrations of antagonizing substances is confirmatory. Injectable coppers may be used with caution. With most nutritional deficiencies, anemia shows little evidence of a regenerative response, but hematocrit rebounds over several weeks after treatment.

Ulcerative conditions of the digestive tract may lead to blood loss, but these are difficult to diagnose, and the amount of blood lost is rarely significant. Therefore, they should be considered among the differentials for low-grade, undiagnosed anemia and potentially the target for specific diagnostic tests or treatments.

In most cases of anemia, no specific cause is determined. The concurrent finding of hypoproteinemia in many cases raises the suspicion of blood loss, such as blood loss from gastric ulceration, but, in fact, anemia of chronic disease (and protein catabolism) is still the most likely diagnosis. Mild to moderate anemia may require no additional treatment beyond addressing what is perceived to be the causative disorder. However, the persistence of anemia after the insult is gone is troubling and may indicate the need for some intervention. Modest interventions include dietary mineral supplements, high-quality nutrition, and an effective parasite control strategy. Iron dextran (5–8 mg/kg, SQ, q 7 to 14 days) may be administered as outlined above; injectable iron supplements are likely to be more useful than oral iron in deficient animals. Hormonal stimulation of erythrocyte production through erythropoietin supplements has not been reported. It is likely to have the same potential pitfall as with its current use in other large animal species, namely, that the available forms may stimulate an immune response that decreases endogenous erythropoietin production.

The ultimate treatment for anemia is whole blood transfusion. A conservative approach on this is common, given how little clinical disease is apparent in camelids with moderate anemia, but the increasing evidence for lack of a regenerative response is providing impetus for earlier intervention. Additionally, evidence exists that transfused cells are relatively long-lived in camelids, that is, transfusions are more than just an emergency procedure. Routinely transfusing camelids with PCV at 12% or less and occasionally transfusing when the PCV is between 13% and 16% appears to be a reasonable strategy. Chemically stabilized, purified bovine hemoglobin offers another alternative. A current commercial product has seen limited use and appears to be safe and effective.[79]

Blood transfusions in camelids are relatively easy and well tolerated. Reactions are rare, so cross-matching is frequently skipped. Most larger New World camelids such as llamas may serve as donors for other New World camelids; the use of camel donors for this purpose has not been evaluated or described. Taking up to about 1 L per 75 kg of body weight from the donor appears to be well tolerated. This represents approximately 20% of the donor's blood. A sterile catheter or bleeding needle is placed into the donor's jugular vein, which is occluded ventral to the site, and the blood is allowed to flow into bottles or bags containing 100 mL of acid citrate dextrose solution or sodium citrate solution (3.25%) per liter. When the jugular is manually held off, a 1 L bag fills in about 15 minutes or less.

Blood is administered to the donor through a filtered blood set via an IV catheter. The initial rate is a drip by gravity flow every 3 seconds for about 15 minutes; this is increased if no reaction is seen, and the entire volume is given in 1 to 2 hours. As a rule of thumb, each liter of whole blood given to an adult alpaca raises the recipient's PCV by about 5% and about half as much in a llama. Anecdotally, use of fluid pumps shortens the lifespan of some of the transfused cells.

Bone Marrow Analysis

In cases of chronic nonregenerative anemia, an inadequate regenerative response in another blood cell line, or identification of abnormal and potentially neoplastic cells on peripheral blood smear, sampling of marrow should be considered. It is relatively easy to accomplish in most domestic camelids, although it may require sedation.[80,81] Light sedation (xylazine, 0.08 to 0.1 mg/kg, IV) may be used for a standing procedure or heavier sedation (xylazine, 0.2 to 0.25 mg/kg, IV, or combinations of xylazine and injectable anesthetic agents) for lateral recumbency. Small amounts of butorphanol (0.07 mg/kg, IV or intramuscularly [IM]) may further relax the patient. The ventral midline over the sternum approximately at the level of the olecranon tuberosity, as well as a spot on the midline and approximately at the narrow midpoint of a sternebra, is clipped and aseptically prepared. A scalpel nick is made through the anesthetized skin, and an 11-gauge (alpaca) to 16-gauge (llama) bone marrow biopsy needle is introduced perpendicular or at a 45-degree angle to the sternum approximately 1 to 1.5 cm into the core of the sternebra. Several firm pulls on a 12-mL syringe are used to obtain samples, which are quickly made into smears on microscope slides. Additional sample may be collected into ethylenediaminetetraacetic acid (EDTA) tubes for later analysis. Slides are air-dried and stained with Wright-Giemsa or other stains.

RBC and WBC precursors should make up approximately 50% to 75% of the smear. They appear similar to their equivalents in other mammals except that the developing erythrocytes become progressively more elliptical as they mature. Eosinophil precursors also make up a higher percentage of the

total than in many other mammals. The nonhematopoietic cells include stromal cells and fat. The myeloid to erythroid ratio has been reported to be 0.9 to 2.9 in adult llamas and 0.47 to 1.01 in adult alpacas.[80,81] At high altitudes this ratio is usually around 0.5.[49] Stainable iron is present in moderate amounts in macrophages in the bone marrow of healthy llamas.[80]

Nitrates, Nitrites, and Cyanide

Camelid erythrocytes appear to be relatively resistant to oxidative damage. Their feeding habits also often limit their exposure to toxin-accumulating plants. *Nitrate intoxication* has been reported anecdotally in llamas exposed to water with more than 1500 ppm of nitrate and feeds with more than 7000 ppm. In cattle, 400 ppm in water is considered the toxic threshold, with acute syndromes seen at greater than 1200 ppm. Toxic feed sources usually contain at least 5000 ppm. In another putative outbreak, llamas were fed oat hay 3.2% dry matter equivalents of potassium nitrate.[82] Nitrates are reduced to nitrites by gastric microbes. Nitrites reduce hemoglobin to methemoglobin, eliminating its oxygen-carrying capacity and causing signs of hypoxemia in patients, including progressive weakness, tachycardia, cyanosis, and death within a few hours. Blood may appear dark or brown. Nitrites typically do not cause anemia or short RBC lifespan, so plasma and urine may appear normal. Analysis of gastric contents, feed sources, body fluids, particularly the aqueous humor if postmortem, may yield the diagnosis.

Cyanide toxicosis is also rarely reported.[82] In one published report, ingestion of cyanogenic plants, *Osteospermum* spp., was implicated. Death had occurred within 30 minutes. Cyanide blocks the electron transport chain, thus creating signs of hypoxemia in spite of well oxygenated, bright red blood and mucous membranes. The lethal dose of cyanide in camelids is not known. In cattle, it is approximately 2 mg/kg. Body tissues and fluids, including aqueous humor, should be collected as soon as possible postmortem for analysis.

Polycythemia or Erythrocytosis

Nonphysiologic increases in the number of circulating RBCs and amount of blood hemoglobin are extremely uncommon in camelids, especially given their strong tendency toward anemia when sick. Splenic contraction may transiently raise PCV by up to one third, which may temporarily mask the anemia or appear as erythrocytosis, but this phenomenon is much rarer in camelids than in horses. Increases in PCV associated with high altitude are also common and sustained but are more the norm for camelids than an abnormality.

Severe dehydration is a rare cause of erythrocytosis and often leads to concurrent hyperproteinemia or hyperalbuminemia (also rare in camelids), as well as azotemia, metabolic acidosis, and physical evidence of dehydration. Masses which selectively inhibit blood flow to one or both kidneys or heart or respiratory disease leading to chronic hypoxemia may contribute to erythrocytosis through greater endogenous erythropoietin production.[83] Affected camelids usually do not have concurrent hyperproteinemia or metabolic changes and may have mild leukocytosis as well because of nonspecific marrow stimulation. A thorough evaluation, including imaging studies of the kidneys or lungs, may reveal the source in these cases, and treatment would involve attempts to correct the primary disorder. If the PCV exceeds 50% in an adequately hydrated patient, some removal of blood may be indicated to prevent complications associated with high viscosity or aberrant thrombosis.

Granulocytic Anaplasmosis

Infection with *Anaplasma* (formerly *Cytoecetes* or *Ehrlichia*) *phagocytophilum* has been seen in a llama in California and a number of camelids in the northeastern United States.[65,84] This organism is considered to be closely related or identical to the pathogens of human and equine granulocytic ehrlichiosis, and camelids should be considered at risk in regions where those diseases are found. Clinical signs included decreased feed intake, lethargy, and slight ataxia. Fever and neutropenia, common signs in other species, were not noted. Fever develops early in the disease and may have subsided by the time of examination. Immunosuppression with increased susceptibility to other pathogens is another common feature in other species, and a number of infected camelids have shown evidence of co-infection with *Mycoplasma haemolamae*.[65] Presumably, anaplasmosis may facilitate other infectious conditions in camelids as well.

Presumptive diagnosis may be reached on identification of cytoplasmic inclusion bodies within neutrophils. These are usually rare, so thorough blood examination is necessary. Blood from the California llama, mentioned above, was also positive on nested PCR for the human and equine pathogens, and deoxyribonucleic acid (DNA) sequencing confirmed the close relationship, although blood from at least one alpaca with organisms seen on blood smear was negative on PCR.[84] Unfed *Ixodes pacificus* ticks from the California property were also found to be infected and were the presumptive source of the camelid infection. In other parts of the world, other ixodid ticks are the likely carriers. These ticks feed on most terrestrial vertebrates for each of their three feeding stages, enabling cross-species transmission of pathogens. Deer, rodents, and sheep are all suspected of being reservoir populations for *A. phagocytophilum*.

The infection typically responds to treatment with oxytetracycline (2 to 3 doses of long-acting oxytetracycline, 20 mg/kg, SQ, q72h, or a similar course of daily oxytetracycline). Decreasing exposure to infective ticks during their active seasons offers the best method of prevention.

Juvenile Llama Immunodeficiency Syndrome

Juvenile llama immunodeficiency syndrome (JLIDS), a syndrome of weight loss or poor growth, repeated, refractory, or chronic infections (including *M. haemolamae,* ocular infections, and juvenile tooth root abscesses), repeated or chronic parasitic infestations, depression, lethargy, nasal discharge, and a variety of generalized or organ-specific signs, was identified in llamas from 4 to 30 months of age in the Colorado area during the peak years of llama popularity in the United States (late 1980s through late 1990s).[60,85,86] Although the disease appeared to be quite common at that time and was identified throughout the United States, loss of the genetic trait, an overall reduction in llama breeding, pursuit of other

diagnoses, or decreased intensive medical management of sick llamas has led to a major reduction in confirmed cases. Individual potential cases continue to arise sporadically, as do anecdotes of a similar condition in young alpacas, but these newer cases are rarely as methodically pursued and hence remain unconfirmed.

JLIDS may be suspected in any juvenile llama (or, possibly, camelid) displaying evidence of ill-thrift or lingering infections, particularly when these conditions appear refractory to conventional treatments. Organ-specific signs may be present with localized infections, or the camelid may show evidence of chronic or advanced systemic disease. In rare cases, affected llamas die of acute sepsis prior to the development of weight loss or chronic disease. Occasionally, a herd history of similar cases exists, potentially in related camelids. The most common time for identification is at ages 10 to 12 months, with llamas as young as 2 months and as old as 3 years identified.[60,85–88] Colostral or transfused antibody may play a role in preventing disease signs over the first several months of life. Affected llamas frequently have some degree of hypoalbuminemia and normocytic, normochromic anemia, which may be exacerbated by *M. haemolamae* infection. Serum iron concentration and total iron binding capacity are low or at the low end of the normal range. WBC counts and fibrinogen may be high or low and appear to relate to whether the llama is currently fighting an infection and the nature of that infection. Lymphopenia, hypogammaglobulinemia, and lymphoid atrophy of lymph nodes appear to be common but are not always present.

The major challenge in identifying a specific immunodeficiency arises from separating the effects of the primary defect from those of complicating secondary contributors, especially in a population in which candidates are only identified once they become ill. This challenge was complicated by the lack of knowledge or tools available to investigate camelid immune function at the time of presumptive peak prevalence of JLIDS. The disease was initially defined by lack of sufficient antibody response to vaccination against *Clostridium perfringens* types C and D. Unfortunately, that test is not currently available for camelids, to our knowledge, and a major attempt to screen a large healthy llama population using this technique failed to reveal new cases. Flow cytometric studies by a different group suggested that camelids with JLIDS have extremely low circulating B-cell counts and led to the suggestion of an autosomal recessive genetic defect, but the use of flow cytometry to identify new cases prospectively has not been reported.[89] A reduced stimulation index to *Streptococcus* protein A on lymphocyte blastogenesis assay also supports the role of B-cell dysfunction.[86]

Most of the signs associated with JLIDS may also be caused by a host of other diseases, some of which may be present in llamas with JLIDS. Hence JLIDS is easy to miss, especially when diagnostic efforts cease upon identification of one of these complicating factors. The occurrence over time of compatible disease signs in related llamas, chronicity of signs, or the refractory nature of identified infectious or parasitic diseases provide evidence that an underlying immune defect may be present and justify further diagnostics.

If immunodeficiency is suspected, one of the aforementioned tests may be used to confirm it. Prior to confirmation, treatment should be directed toward identified processes such as infectious or parasitic diseases. After confirmation, in the absence of specific corrective measures, supportive treatment and treatment of opportunistic complications may be attempted. Affected animals may survive several years with treatment and conscientious management, but owners frequently elect euthanasia over treatment.

Myelodysplasia

Persistent leukopenia has been identified in a number of camelids. Most are young and have a clinical picture that resembles the JLIDS picture, but these camelids remain leukopenic even during periods of relative clinical normalcy. Bone marrow aspiration or core biopsy reveals serous atrophy of fat and a relative decrease in mature cells of both erythroid and myeloid lines and also a decrease in the myeloid to erythroid ratio (see "Bone Marrow Analysis" above). Lymph nodes and the spleen show severe depletion of lymphoid cells. In one case, fusobacterial gingivitis, stomatitis, and gastritis of C1 were present.[77]

The cause is never identified in some cases, but overdose of albendazole has been implicated as a cause of myelodysplasia resulting in persistent neutropenia.[90] The administered dose, usually given over 3 to 5 days, is often 5 to 10 times higher than the label dose for ruminants. Vitamin D deficiency was identified in another case.[77] Administration of recombinant human granulocyte colony stimulating factor (5 mcg/kg, SQ, q24h for 3 to 5 days) may promote recovery of the marrow and a gradual restoration of normal blood leukocyte counts.[81] Other treatments may include antibiotics and supportive care against opportunistic infections.

Malignant Round Cell Tumors, including Lymphoma, Neuroendocrine Tumors, and Myeloid Leukemia

Hematopoietic neoplasms and related disorders are the most commonly reported noncutaneous malignancies of New World camelids in a number of surveys world-wide.[1–5] Identified types include lymphoma, myeloid leukemia, and neuroendocrine tumors, otherwise known as *primitive malignant round cell tumors*.[47,48,77,89–104] Lymphoma and myeloid leukemia arise from members of the WBC line. Neuroendocrine tumors may arise from neural crest cells. The different types appear similar clinically and were not differentiated in camelids until the relatively recent advent of the use of immunophenotyping in llamas and alpacas. It is likely that early reports of undifferentiated tumors contain a mix of these three types and possibly others, so they will be discussed primarily together as malignant round cell tumors (MRCTs).

These tumors have been reported in camelids as young as fetuses and as old as 23 years and thus should be considered a possibility in camelids of any age. Published and personal records from 16 llamas and 19 alpacas reveal that age distribution is very similar between genders but that the median age of affected llamas is 4.5 years; the median age of affected alpacas is, however, 4.5 months, which suggests that particular scrutiny of young alpacas is warranted. A number of other reports support that juvenile alpacas have a higher prevalence of MRCTs compared with young llamas.[47,95,97]

Affected, untreated camelids often lose up to 20% of their body weight over a 4- to 6-week period and then succumb to

the effects of cachexia, neoplastic infiltration of internal organs, or secondary infections.[47,105] Altered behavior such as increased recumbency, tachypnea, decreased activity, and decreased feed intake may be noted early in the course of the disease (1–2 weeks), but specific clinical signs or laboratory abnormalities often are not noted until the disease is very advanced. Signs referable to a specific organ or system are rare. Ulcerated neoplasms of the wall of C3 or the small intestine may cause severe melena or diarrhea. Hindlimb paresis is common in camelids with spinal tumors (about 10% of total), and dyspnea and exercise intolerance are common with pulmonary infiltration.[47,102]

Hypokalemia, hypoalbuminemia, azotemia, and high counts of immature granulocytes in peripheral blood are the most common clinical pathology abnormalities, but none of these is specific to MRCT.[47,105] Neoplastic lymphocytes rarely are seen on peripheral blood examination and must be differentiated from the large reactive lymphocytes and immature granulocytes normal in camelids. Circulating transformed myeloblasts are indicative of myeloid leukemia.[104] Hypercalcemia is rare because the bound calcium fraction is often reduced from concurrent hypoalbuminemia. The blood ionized calcium fraction is often high.

Most affected camelids develop palpable external or detectable internal lymphadenopathy, and presumptive diagnosis may be made by identification of firm, discrete peripheral lymphadenopathy that does not demonstrate the characteristics of abscesses. MCRTs are among the most common causes of moderate to severe lymph node enlargement in camelids. Imaging studies may be used to identify suspicious internal lymphadenopathy or organ infiltration. Some camelids also develop pleural or peritoneal effusions that may contain neoplastic cells. Cytologic examination of bone marrow may be useful for diagnosing the neoplasm in camelids without palpable lymphadenopathy, and examination of the cerebrospinal fluid may be helpful in camelids with neurologic deficits. Definitive diagnosis is made through histopathologic examination of tissue or cytologic evaluation of a body fluid. Tru-cut biopsy samples are sufficient, whereas interpretation of fine-needle aspirates is often problematic because of poor preservation of neoplastic cells. The biopsy should be taken from a peripheral mass or, if necessary, from an internal organ. Usually, the tumors occur in multiple sites, including lymph nodes, liver, renal cortices, spleen, lungs, heart, bone marrow, gastrointestinal organs, uterus, and the spinal canal. These may be identified by imaging studies or at surgery. A small percentage of camelids have a single area of infiltration such as the thymus or gastric compartments.

Histologically, tissue infiltrates are dominated by malignant round cells. With lymphoma, these are often found in multiple, dense, coalescing aggregates that obliterate local architecture. One author suggested that neuroendocrine tumors may show more organization, with focal clumps of smaller cells arranged around capillaries, but another reported that large or small cells are possible.[56,95] Neoplastic cells appear round to pleomorphic, with one or more round or indented nucleus containing prominent nucleoli and marginated chromatin. The mitotic index may range from 0 to 9 per high-power field, with occasional bizarre mitoses present.

Immunophenotyping has revealed the different cell types responsible for these tumors.[56,94–96] B-cell lymphoma appears to be the most common (17 of 30 tested lymphomas), based on the presence of the CD79a, BLA36, and less commonly CD79b antigens. T-cell lymphoma is second (11 of 30), based on the presence of the CD3 antigen, and a small number of tumors display both CD3 and CD79a. Both B-cell and T-cell lymphoma appear to affect all ages and all areas of the body, with the exception that 80% of gastric-exclusive MRCTs were B-cell lymphoma.[48] Other MCRTs also appear to affect all areas and ages.

The clinical course is progressive, with death reported approximately 1 to 100 days after first identification of illness. One camelid with a neuroendocrine tumor appeared to have a protracted course of slow progression.[48] Chemotherapy to induce remission has been attempted, but experiences are very limited. One possible protocol is cyclophosphamide (300 mg/m^2, IV, q21 days), prednisolone (40 to 50 mg/m^2, PO, q48h), and vincristine (0.5 mg/m^2, IV, q14 to 21 days).[92] L-asparaginase (10,000 units/m^2, IM) may be added to the protocol. Concurrent antibiotic therapy is highly recommended to prevent secondary sepsis. MCRTs have been found in related camelids and sporadically in multiple camelids from the same property, but currently no evidence of a hereditary, environmental, or infectious etiology exists.

Caseous Lymphadenitis and Other Soft Tissue Abscesses

Lymph node abscesses are relatively uncommon in camelids. Major differential diagnoses include tumors (often lymphoma) or rare reactive lymph nodes, both of which have a more solid feel on palpation and appearance on ultrasonographic examination. Abscesses may be seen sporadically associated with typical abscess-forming bacteria such as *Arcanobacter pyogenes, Streptococcus equi* ssp. *zooepidemicus, Rhodococcus equi*, or *Fusobacterium necrophorum*. *Burkholderia pseudomallei* (meloidosis) is a regionally important cause of internal and external lymph node abscesses in tropical northern Australia, and *Dermatophilus congolensis* is occasionally associated with subcutaneous abscesses of the head or neck with occasionally internal masses, thought to be facilitated through penetrating bodies of plant origin.[106,107] If multiple camelids in a herd are affected, *Corynebacterium pseudotuberculosis* (caseous lymphadenitis) becomes the most likely candidate. Outbreaks of caseous lymphadenitis in alpacas have been reported in Peru and the United States, and are likely to be possible in all countries where camelids and the causative agent are present.[108,109]

C. pseudotuberculosis is a gram-positive facultative intracellular, anaerobic pathogen of the *Actinomycetes* group. It has a pleomorphic appearance ranging from coccoid to a filamentous rod. It is principally known as the cause of caseous lymphadenitis in sheep and goats and ulcerative lymphangitis in horses. Many mammalian hosts are susceptible, especially grazing species, with rare infections also identified in humans. The principal reservoir appears to be within abscesses in infected animals. The organism may contaminate but does not appear to invade intact skin. Contamination may occur directly from draining wounds or contaminated exhalations or milk, from the environment, where the organism may persist a year or more, or potentially through fly spread in a contaminated environment. Skin breaks during shearing are

thought to be an important means of initiating infection in small ruminants and are likely to promote spread from infected small ruminants to camelids or within an infected herd of camelids as well, but the disease has been found in young camelids that have never been shorn.[108,109] Other skin wounds, such as ear tag or microchip sites or traumatic injuries, may facilitate infection as well. Ingestion of contaminated feeds or infected milk may be another route of interspecies transmission.[110]

After initial inoculation, camelids may be febrile, lethargic, and anorexic for a week or more.[111] They have an acute local reaction, which may be obscured by fleece, and neutrophilic leukocytosis. The malaise, fever, and leukocytosis are often gone by the time of clinical identification, and the acute local reaction is replaced by subcutaneous swelling, possibly draining pus out of a fistula.[109] With time, ill-thrift might develop; with mammary infection, poor growth of offspring might be noted. The most common sites for externally palpable abscesses are around the head, associated with major lymph nodes, and in the mammary gland. External abscesses may break open and drain intermittently. In South America, internal abscesses appear to be common as well, primarily affecting the perirenal lymph nodes and occasionally the liver or lung.[108] Internal abscesses may be less common in North America.[109] Compared with small ruminants, the infrequency of lung lesions and frequency of mammary lesions suggest that milk-borne transmission may be more important than respiratory transmission in camelids.

A presumptive diagnosis may be made on feel and appearance, particularly when multiple camelids are affected. Unlike in sheep, abscess contents are relatively liquid and drain readily. Because of the herd implications of identifying this specific infection, more specific diagnostics are usually warranted. Bacteriologic cultures on discharges or aspirates from lesions may be performed to grow and identify the organism, but open lesions are often contaminated, and *C. pseudotuberculosis* does not grow readily from all lesions. The PCR test may enhance speed and sensitivity but is not widely available. A number of serologic tests have been examined in small ruminants as well, but most have issues with sensitivity, specificity, or both. Hemolysis inhibition testing and enzyme-linked immunosorbent assay (ELISA) against cell wall components have been reported in alpacas.[109,111]

In small ruminants, culling is usually the treatment of choice, based on the refractory nature of this disease to treatment, the high rate of internal abscesses, and the likelihood that infected animals are worsening environmental contamination. In camelids, individual animal treatments are more common. Affected camelids should be isolated, especially if they have open wounds or a draining mammary abscess. When possible, subcutaneous abscesses should be removed en bloc. It this is not possible, they may be opened and cleaned frequently with disinfectants. On the basis of South American data, ultrasonographic or cross-sectional imaging of the perirenal lymph node area should be considered, as these tests would have the highest likelihood of finding an internal mass. The mammary gland should also be examined closely in female camelids. Antibiotics should be considered, particularly those of the penicillin class. However, although *C. pseudotuberculosis* may appear sensitive to many antibiotics in the laboratory, clinical response is often poor. Intracellular or intrabscess reservoirs and growth in biofilms appear to afford protection. Over the time of treatment, which may last several weeks in an individual, additional abscesses may arise on affected animals or herdmates, so they should be monitored carefully. If no new abscesses have arisen for at least 3 months, additional masses appear unlikely in North American herds. If animals have no internal masses, they are likely to thrive after resolution; if internal lesions are present, unthriftiness may continue or develop. The role of serologic testing in diagnosing either internal or preabscess infection is still under review.

Prevention aims at avoiding introduction of the organism into a herd and avoidance of transmission within the herd. Camelids should be kept a healthy distance from infected sheep or goats, and should preferably avoid premises occupied by contaminated animals for at least a year. Unpasteurized milk or colostrum from infected animals (chiefly cattle or goats) may be another source of infection but has not been proven in camelids; these products are preferably obtained from caseous lymphadenitis-free dairies. A whole-cell bacterin toxoid is available for sheep in the United States. Its safety and efficacy in camelids have not been established. Vaccination with *C. pseudotuberculosis* culture supernatant containing high concentrations of active toxins appeared to provide superior protection in alpacas than use of either lower toxin concentrations or cell wall components, although all types off vaccine appeared to decrease acute signs.[112]

Adult Sepsis

Generalized infections are a relatively common ailment in sick camelids, with disease signs potentially reflecting multisystemic involvement, but more commonly not directing the clinician toward any particular organ system. These infections may be caused by aggressive agents such as *Salmonella*, *Listeria*, *Streptococcus equi* ssp. *zooepidemicus*, or more commonly, by opportunistic organisms taking advantage of a weakened immune system or compromised skin or mucosal boundary.[113–121] *Streptococcus* appears to be the most common primary pathogen, and *Escherichia coli* and *Clostridium* are the most common opportunists. The role of the opportunist is important to recognize for two reasons: (1) Camelids with generalized sepsis may have an underlying condition requiring specific diagnostic tests and treatment, and (2) the development of sepsis in a camelid with another disorder often leads to a worsening of signs and prognosis and usually requires aggressive specific treatment for sepsis.

The onset of sepsis is often marked by a worsening of the animal's attitude and strength. Weakness, lethargy, anorexia, and decreased responsiveness to external stimuli are the main behavioral signs. Cold extremities, poor pulse quality, poor mucous membrane color and capillary refill, tachycardia, and fever or hypothermia are common physical abnormalities. Almost any organ-specific sign is possible as well, particularly when the infection came through that specific system. Regardless of any underlying disease, it is often this marked worsening in the animal's demeanor that alerts the owner to illness in the first place. Thus, sepsis should be considered a possibility in most sick camelids.

The most commonly reported portal for infection is through compromised GI mucosa. Coccidia, stomach worms,

whipworms, and coronavirus are the most common causes, with *Salmonella*, forestomach acidosis, gastric ulcers, and tumors representing other important causes.[47,48,70,122–127] The blood culture was positive in roughly one third of camelids with coccidiosis tested at our clinic. Affected animals may have overt GI signs such as diarrhea or colic but frequently do not. If present, the GI-specific signs are often transient and far milder than expected, given the severe clinical condition.

Non-GI disorders are less common. A small number of camelids have respiratory tract infections that become disseminated, particularly with *S. zooepidemicus*, or urogenital infections, particularly with *E. coli* or *Pseudomonas*. *Listeria monocytogenes* infection is frequently disseminated in camelids, although the original route of entry is seldom known.[116–118] Although *Listeria* may cause neurologic disease, it may result in generalized sepsis as well. Liver flukes are another important parasitic cause of sepsis and have been linked to both clostridial hepatitis and bacterial endocarditis in camelids. Chronic infections such as tooth root abscesses occasionally lead to sepsis.[27,128] Poor immune function may be caused by a specific immune defect, as with JLIDS, or develop in relation to the effects of infectious agents, cachexia, or hypoproteinemia.[85] In crias, failure of passive transfer is a major factor. Cria sepsis is covered in Chapter 42.

In general, sepsis should be suspected whenever a camelid's clinical condition appears worse than any identified disease process can account for. Given the vague nature of many camelid diseases and that this vagueness often delays the recognition of illness before the disease becomes advanced, this is likely to be a more frequent situation than with many other domestic species. Other times to be especially alert include when a camelid with a known disease or immunodeficiency suffers an acute setback.

A wide variety of clinical pathology or imaging abnormalities are possible with sepsis. Common, nonspecific evidence of advancing disease includes azotemia, metabolic acidosis, and increases in liver enzyme activities. Other changes may point toward involvement of a particular organ system, for example, electrolyte loss with either GI or renal disease and hypoxemia with respiratory disease. A very low serum iron concentration is a fairly specific indicator of acute sepsis, but iron is not part of many standard chemistry panels. Hematologic abnormalities are also variable. High peripheral blood counts of immature neutrophils or those with toxic changes are relatively specific to sepsis. Neutropenia is also a fairly good indicator (for an exception, see "Myelodysplasia" earlier in this chapter), with the understanding that it may be masked initially by the animal's stress response. To avoid missing neutropenia in these camelids, a 24-hour, follow-up CBC should be considered. Some camelids with sepsis, particularly when caused by a gram-positive organism, may have true neutrophilia and potentially monocytosis.

Definitive diagnosis involves identifying a microbe in one or more body fluid. Collection of blood, abdominal fluid, thoracic fluid, or cerebrospinal fluid may be indicated either by specific signs or a thorough general workup. Culture of the organism allows for sensitivity analysis. Sometimes, the organisms are seen on cytologic examination but do not grow in culture. Antibiotic selection in such cases becomes a matter of educated guesswork. With all types of bacteria implicated in sepsis, initial antibiotic choice should provide broad-spectrum coverage, including anaerobes. Combinations of a penicillin-class drug and an aminoglycoside are the most popular protocol, once the camelid is adequately hydrated. Other treatments may include general supportive care, fluids, nonsteroidal antiinflammatory medications, or endotoxin binders, as needed, as well as appropriate treatment for organ specific signs or underlying diseases. Prognosis is better if sepsis is acute, the camelid still appears principally fit, and any underlying process is temporary. It is worse with drawn out diseases, weak or recumbent camelids, or those showing major dysfunction of any particular organ system. Most of the organisms of sepsis are opportunists, so preventing the predisposing diseases and recognizing and treating them early are the best defenses.

Bovine Viral Diarrhea Virus Infection

Since the earliest days of camelid popularity in the United States, camelid owners have been concerned about transmission of bovine viral diarrhea virus (BVDV) from cattle to their animals. These concerns were originally based on evidence of seroconversion in camelids in South America and the occurrence of vague illnesses, including apparent immunodeficiency, in North America.[129,130] Of further concern was the increasing knowledge that nonruminant hosts such as the white-tailed deer could serve as BVDV vectors and reservoirs.[131] BVDV was isolated on rare occasions from llamas and alpacas with upper respiratory infections, diarrhea, or ill-thrift, and linked through maternal or fetal titers to reproductive failures.[131–133] These infections appeared to be transient, leading to short-term seroconversion and viral shedding. Experimental efforts to model the disease through intranasal infections with various strains of BVDV including type 1a, type 1b, and type 2, consistently revealed that adult camelids developed viremia and nasal shedding after infection but that these were transient, lasting less than 10 to 13 days, and accompanied by minimal to no clinical signs.[134,135] Concerns about persistence of infection in camelid herds, particularly in association with reproductive failures, and supported by the 2002 report of isolation of BVDV type 1b from a fetus, could not be substantiated using BVD Type 1a.[134,136] On the basis of these findings, each incident of natural infection was presumed to arise from a new cross-over event from a ruminant or other noncamelid host.

A few years later, evidence began to emerge for herd outbreaks of illness, abortion and stillbirth, and persistent infection in camelids in Canada and the United States.[137–139] Similar evidence came later from England.[140–142] All typed isolates from these outbreaks are type 1, with the majority further defined as type 1b. Marked genetic homogeneity is seen among most of the U.S. isolates, as well as evidence for some distinct strains, but no link between North American and British outbreaks.[143] Experimental inoculation of pregnant llamas with bovine-origin type 1b and type 2 strains and an alpaca-origin type 1b strain also appeared to create persistently infected crias with either type 1b strain.[144] These data suggest that persistent infections arise predominantly (or perhaps, exclusively) from type 1b strains and that these infections may persist within camelid herds or arise from interspecies transmission.

The transiently ill adults and some of the crias identified over the years probably represent acute infections, but a high proportion of the affected camelids in these recent outbreaks are crias showing characteristics of persistent infection. Persistent infection to BVDV develops in the bovine fetus when its dam has viremia at some point between approximately day 40 and day 125 of pregnancy. A similar exposure window is postulated for camelids, with presumptive infection occurring around 65 to 70 days of pregnancy in some reports, around 70 to 80 days in one experimental trial, and between 64 and 114 days during one outbreak.[137,138,144,145] Infections before that period may lead to embryonic death and infection after that period may lead to abortion, stillbirth, or premature underweight birth, and it is possible that the window for development of persistent infection is wider than has been confirmed experimentally. If the fetus is infected during the appropriate window, it also develops viremia and widespread tissue distribution of the virus but does not develop an antibody titer. It remains infected lifelong, potentially suffering illness and also serving as a source of infection for herdmates. To date, over 60 crias in the United States are thought to have been born persistently infected. In one study, 25% of the tested U.S. alpaca herds had at least one seropositive cria, and 6% had at least one persistently infected cria, indicating that exposure to BVDV is relatively common and that the risk for developing persistently infected crias is real.[146]

Clinical signs described in the recent outbreaks include transient bouts of lethargy and anorexia in adults, followed weeks to months later by abortions or stillbirths. Crias born during or after outbreaks may be born early and underweight, or appear normal.[145] A small percentage may have abnormally thin, coarse ("Suri-like") fleece or congenital neurologic deficits (circling, hyperesthesia), and some rapidly develop poor growth and evidence of infectious disease, including chronic ocular or nasal discharge, pneumonia, or diarrhea. Others remain healthy for several months or longer before showing signs. Clinicopathologic examination of persistently infected crias may reveal mild anemia, monocytosis, and hypoferremia. Sixty-four percent of persistently infected crias do not survive beyond 1 year.

Identification of persistently infected crias also allowed identification of crias with prolonged viremia indicative of chronic or recurrent infections.[145] These crias not only maintained evidence of infection for 2 or more months (maximum = 251 days) but also developed a measureable antibody response. They displayed other clinical characteristics of persistent infection, but these abnormalities normalized with resolution of viremia. As such, these individuals may be difficult to distinguish acutely from camelids with true persistent infections and may also serve as a source for intraspecies transmission during their period of viral shedding.

In individual cases, BVD may be suspected, but is unlikely, in any case of ill-thrift, particularly when ocular or nasal discharge exists. The case becomes stronger with known exposure to cattle or other potential hosts, if illness coincides with episodes of early or late reproductive failure, and if multiple animals are affected. Diagnosing acute infections may be difficult. For a short time, usually no more than 10 to 14 days, virus isolation or PCR on whole blood or nasal secretions may be successful. These same tests plus immunohistochemistry may be used on tissues from a dead animal or aborted fetus, including the placenta. A rise in antibody titer or the presence of a positive titer in an unvaccinated camelid may also be used as evidence of exposure; titers usually persist longer than the viremia required for PCR or virus isolation. Identifying infected or exposed camelids in a herd is of greater importance if pregnant dams are present because abortion or the birth of persistently infected crias may follow, or if exposure to ruminants or cervids is not known because it suggests the presence of a persistently or chronically infected shedder in the herd.

In outbreaks or with disease in crias, the likelihood of a persistently or chronically infected camelid becomes more likely. These may be the source of the infection or its result. The unintentional introduction of persistently infected animals into a herd has been surmised to be the cause of several outbreaks.[137,140,145] Virus isolation or PCR on whole blood are the most common tests, with PCR usually preferable because of faster turn-around times and less danger of sample mishandling. False-negative results on these tests have arisen from true neonates, in which maternal antibody is thought to interfere for up to 12 weeks, particularly with virus isolation. Serologic tests often yield negative results from persistently infected animals but are often positive in herdmates, especially the dam and other contact animals. Some crias with seropositivity may be chronically infected and thus may serve as a source of infection for herdmates.[145] Serologic testing of representative animals is a good initial screening test for whether a herd has been exposed or not. Ear-notch immunohistochemistry is positive in some cases. Postmortem tests are the same as in acutely infected animals except that the virus is usually more widespread. The conventional definition of persistent infection includes two positive PCR or virus isolation tests taken at least 3 weeks apart and without evidence of a serologic response (barring that caused by colostral antibody), but chronically infected crias complicate that definition.

Upon identification of any camelid that is positive on PCR or virus isolation, it is imperative to separate it from any camelids involved in the breeding program for a minimum of 12 weeks. Over this time, at least one more PCR or virus isolation test should be performed at least 21 days, preferably at least after 56 days, after the first. Lengthening the interval or repeating the test more times increases specificity for persistent infection over simple chronic viremia. All crias born over the next 10 to 12 months should be considered suspect and tested immediately after birth and again after 3 months of age before being cleared.

If BVDV is found, no specific treatment is available. Persistent infection is a lifelong state, and affected animals act as the main source of continued reinfection in a herd. Suspect and confirmed persistently infected animals should be quarantined or removed from the herd altogether. With acute or chronic infection, supportive care may be necessary, particularly if the animal has fever, diarrhea, or anorexia. Although the precise effects of BVDV in immunocompetent camelids have not been described, some immunosuppression and facilitation of opportunistic infections is likely, especially in crias.

To screen a healthy herd for BVD risk, serologic tests are usually adequate. Vaccination is discouraged, so titers in unvaccinated animals usually reflect exposure. Follow-up testing (blood PCR or virus isolation, or skin immunohistochemistry) in positive herds may be used to try to identify

internal (persistently infected camelid) or external (ruminant, cervid) sources.

Preventing BVDV infection has several facets. Reports suggest that acute infections may be caused by a variety of types of BVD virus, but that all persistent infections stem from type 1b infections.[140,143,147] Possibly, only BVD type 1b is able to cross the camelid placenta. Some transmission may occur between camelids, but infections by distinct strains in North America and apparently independent development of infections in England stress the likelihood that novel cross-over events are likely to continue wherever camelids are in contact with ruminants or possibly cervids.

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