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4

Respiratory Diseases

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Diseases of the Upper Airway

These disorders are characterized by inspiratory dyspnea. The increased resistance to airflow caused by upper airway obstructions often creates audible inspiratory noise and results in referred airway sounds through the tracheobronchial apparatus. Sounds that have been "referred" to the lower airway from an upper airway obstruction may be misinterpreted as lower airway in origin in such cases unless the upper airway is examined and the trachea auscultated. If the respiratory sounds can be heard without a stethoscope, they are most likely originating from the upper respiratory tract. The upper airway examination should include detection of airflow from both nostrils, close examination of soft tissues of the head, and oral examination if necessary. Severe upper airway obstruction can cause open-mouth breathing and head extension as the affected cow tries to decrease the resistance to airflow (Fig. 4.1).

Mechanical or Obstructive Diseases

Congenital

Etiology and Signs

Congenital disorders, including pharyngeal cysts of respiratory epithelial origin, nasal cysts, cystic nasal conchae, skull anomalies, laryngeal malformations, and branchial cysts, have been observed in calves and adult cows. Inspiratory dyspnea with audible snoring sounds or stertorous breathing is a sign common to most of these problems. The condition may be present at birth or is most often observed within the first few months of life. The degree of dyspnea associated with these abnormalities tends to be progressive as a result of either enlargement of the lesion (cyst) or worsening upper airway edema and swelling from the mechanical overwork associated with respiratory efforts to move air through an airway narrowed by a malformation. Environmental conditions of high heat and humidity may markedly exacerbate the dyspnea.

Diagnosis

Specific diagnosis requires physical examination, including visual inspection of the nares and oral cavity, endoscopy, and skull radiography (Fig. 4.2). In addition, aspiration for cytology and cultures may be indicated for cystic lesions. Most cystic lesions become secondarily infected.

Treatment

The method of treatment depends on the specific lesions found. Cystic conditions may be the most treatable because surgical removal offers some hope of being curative. Simple drainage or drainage with cautery of cystic lesions is not likely to be successful. Therefore referral of such cases to veterinary surgeons experienced in upper airway surgery is recommended so that complete excision of the secretory epithelium can be completed. Other conditions such as laryngeal malformations and skull anomalies have a poor prognosis.

Regardless of the cause, symptomatic or supportive treatment may be necessary before diagnostic procedures are performed in calves with severe dyspnea, lest the stress of examination or endoscopy induce anoxia. A tracheostomy should be considered to allow safe diagnostic manipulation. Misinterpreting anoxic patient-struggling as wildness requiring additional physical restraint is a frequent, and potentially fatal, error in judgment made by inexperienced clinicians. When a dyspneic animal struggles during examination, usually it is anoxic, frightened, and extremely anxious. All restraint of the head and neck should be relaxed, and the animal should be allowed to "get its breath." Continued restraint during these situations may result in asphyxiation of the animal.

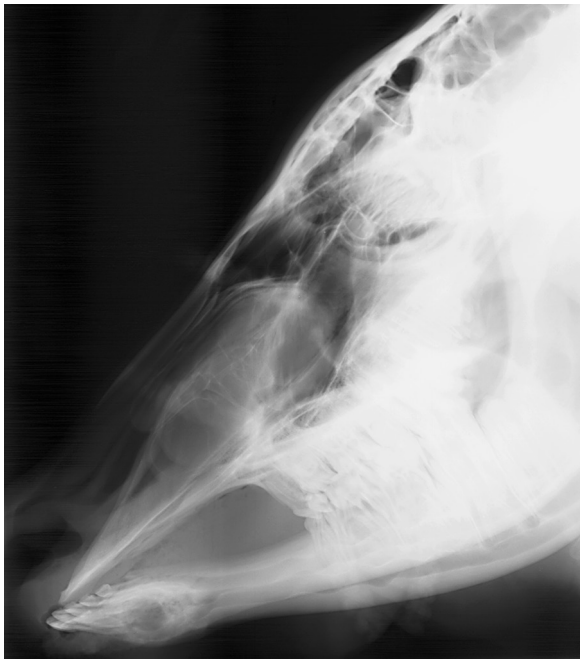
Although the prognosis for congenital lesions varies with the specific diagnosis, generally it is guarded to poor.

Acquired

Etiology and Signs

Acquired mechanical or obstructive lesions of the upper airway may occur in calves or adult cattle. Most of the lesions represent enlargement or inflammation of tissues and structures external to the airway itself. Impingement into the upper airway by soft tissue masses such as pharyngeal abscesses, laryngeal or pharyngeal branchial cysts, retropharyngeal cellulitis, necrotic laryngitis, pyogranulomatous swellings (e.g., wooden tongue), enlarged lymph nodes, neoplasms, foreign bodies, or enlarged maxillary sinuses comprise the majority of lesions. Pharyngeal abscesses and necrotic laryngitis are probably the most common acquired causes of obstruction. Pharyngeal abscesses and retropharyngeal cellulitis may occur after traumatic injury to the mouth when an animal is treated with oral medication requiring the use of a balling

• **Fig. 4.1** Open-mouth breathing and neck extension in adult Holstein with retropharyngeal abscessation, upper airway obstruction and pain associated with iatrogenic trauma.



• **Fig. 4.2** Radiograph of a conchal cyst in a 6-month-old heifer.

gun, speculum, or other device in either adults or calves (Fig. 4.3). These lesions may also arise in calves with no history of iatrogenic pharyngeal trauma or oral medication.

Regardless of the cause, progressive inspiratory dyspnea is the primary sign observed in affected cattle. Fever may be present with pharyngeal abscesses, cellulitis, or chronic maxillary sinusitis. Unilateral nasal discharge or reduced airflow from one nostril may be present with maxillary sinusitis or unilateral neoplasms of the nasal pharynx or maxillary sinus. Lymphadenopathy may be present as a primary sign in neoplastic conditions, such as juvenile lymphosarcoma and adult lymphosarcoma (Figs. 4.4 and 4.5), or as a secondary sign in cases of soft tissue infections. Unilateral Horner's syndrome and progressive exophthalmos have been observed in slow-growing adenocarcinomas of respiratory epithelial origin in the nasopharynx (Fig. 4.6). Cattle with unilateral nasal obstruction often show more obvious respiratory signs during hot weather. One cow with Horner's syndrome would demonstrate open-mouth breathing only on hot days because of the nasal mucosal vasodilation and edema (Fig. 4.7).

A fetid odor may exist on the breath caused by chronic inflammation or tumor necrosis in some cattle. The owner may report a progressive course of stertorous breathing eventually leading to open-mouth breathing. Inflammatory lesions often have a more acute course than neoplasms, but this is a generality rather than a rule. Obvious external swelling may be present in certain conditions such as chronic maxillary sinusitis, pharyngeal or retropharyngeal abscesses, and lymphosarcoma.

Diagnosis

A complete physical examination followed by manual and visual inspection of the oral cavity is the first diagnostic procedure. Relative equality of airflow and the odor of the breath should be evaluated at the nostrils. If chronic maxillary sinusitis is suspected, the upper premolar and molar teeth should be examined closely for abnormalities.

Endoscopy should be performed in an effort to identify a specific lesion or the anatomic region of impingement of tissue into the airway. When performing endoscopy in a calf or cow with severe upper airway dyspnea, most of the mucosal surfaces (e.g., soft palate, larynx, and respiratory pharynx) will be edematous from exertional or labored respiratory efforts. This edema should not be misinterpreted as the causative lesion (see Video Clip 4.1).

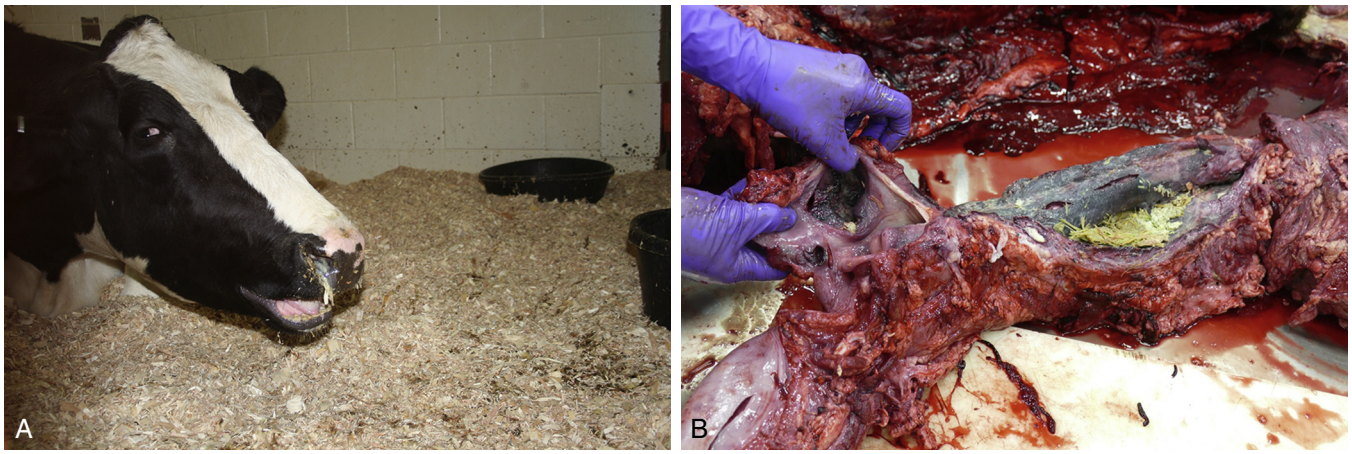
Skull radiographs may be necessary if physical examination and endoscopy fail to identify a lesion. Radiographs are helpful for definitive diagnosis of sinusitis or nasal or sinus cysts and for identifying the location of soft tissue masses such as abscesses or tumors. In addition, radiographs help to identify metallic foreign bodies and abscessed tooth roots in cases of chronic maxillary sinusitis.

Diagnostic ultrasonography, if available, may help in the assessment of soft tissue swellings and laryngeal cartilage abnormalities. This technique also has been used to locate retropharyngeal abscesses and nonmetallic foreign bodies so that external drainage may be performed safely.

In the case of obvious or palpable swellings of the head or pharynx, aspirates for cytology and culture are indicated. Similarly, biopsies for histopathology are indicated for solid masses or enlarged lymph nodes where neoplasia is suspected.

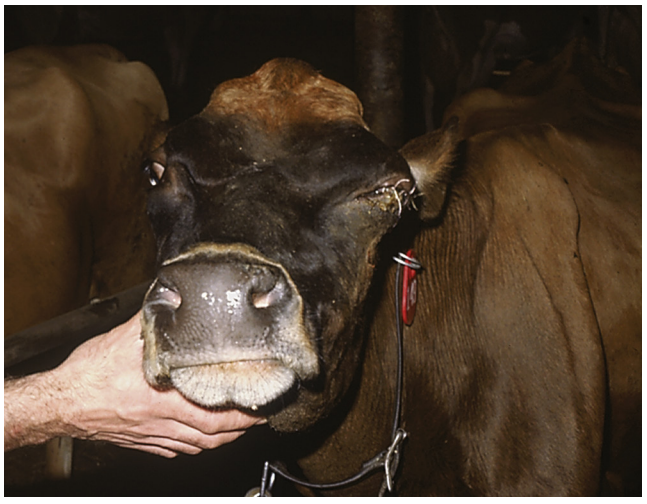
Treatment and Prognosis

Treatment is most successful when external compression of the upper airway can be cured through treatment of an inflammatory lesion. Pharyngeal or retropharyngeal abscesses should be drained either by manual pressure during oral examination or externally under ultrasound guidance with liberal incisions that avoid vital structures. Internal drainage is preferred unless the abscess is close to the skin surface. External drainage is technically difficult for deep pharyngeal abscesses located more than a few centimeters below the skin surface. Vagus nerve damage,



• **Fig. 4.3** **A,** Adult Holstein open-mouth breathing with an extended neck and upper airway stridor associated with pharyngeal laceration. **B,** Post mortem image of the same animal demonstrating laceration in pharynx (held by gloved left hand) and feed material that accumulated outside the cervical esophagus coincident with severe gangrenous cellulitis.

• **Fig. 4.4** Juvenile lymphosarcoma in a 4-month-old Milking Shorthorn calf presented because of inspiratory dyspnea.



• **Fig. 4.6** Aged Jersey cow with an adenocarcinoma of respiratory epithelial origin. The mass caused reduced airflow through the left nasal passage, left-sided Horner's syndrome, and exophthalmos. The eyelids have been sutured together to protect the eye.

• **Fig. 4.5** Adult Holstein with a lymphosarcoma mass in the pharyngeal area that caused inspiratory dyspnea.

• **Fig. 4.7** Open-mouth breathing in a 5-year-old cow with unilateral Horner's disease (etiology unknown). The cow had no respiratory difficulties during the winter months.

vascular injury, salivary duct laceration, and acute cellulitis are potential complications associated with opening abscesses. The salivary duct was severed in one calf we treated, and saliva flowed from the incision for a couple of days after which the salivary flow stopped and the calf had a complete recovery. If drainage is not liberal, abscesses tend to recur. If recurrence is obvious, culture and sensitivity coupled with drainage through multiple sites are indicated. Daily flushing of the drainage sites is important. Systemic antibiotics should be administered for 1 to 2 weeks after drainage; *Trueperella pyogenes* and *Fusobacterium* spp. are the most common organisms cultured, so β-lactams are the most commonly used antibiotic class.

Chronic maxillary sinusitis should be treated by trephination of the sinus, removal of any teeth that have infected roots, daily flushing of the sinus with dilute disinfectants or sterile saline, and appropriate systemic antibiotics for 1 to 2 weeks.

In general, neoplasms have a hopeless prognosis, and the animal should not be treated. Juvenile lymphosarcoma often causes upper airway dyspnea via enlarged pharyngeal lymph nodes. Occasional adult-form lymphosarcoma cases have one or more very large (10–20 cm diameter) pharyngeal or mediastinal lymph nodes that will cause dyspnea. Lymphosarcoma usually results in death within 1 to 6 months of diagnosis. Adenocarcinomas originating in the respiratory epithelium in older cattle (i.e., more than 8 years of age) may have an insidious but progressive course over months to years. Therefore, unlike cattle with lymphosarcoma, these animals may be allowed to survive for some time to deliver another calf or to undergo superovulation and embryo transfer. Only if the animal stops eating, develops severe respiratory distress, or is suffering from exposure damage from an exophthalmic eye will euthanasia be necessary. Cattle affected with primary squamous cell carcinoma, metastatic squamous cell carcinoma, or osteosarcoma originating in a sinus, bone, or periocular location occasionally may have enough tumor mass or lymph node metastases to develop inspiratory dyspnea. Cattle with squamous cell carcinomas frequently have a fetid breath odor from the primary tumor and should not be made to suffer unduly.

Inflammatory Diseases

Allergic Rhinitis

Also called summer snuffles, allergic rhinitis occurs primarily in yearling or adult cattle turned out on pasture in the spring and summer. This condition also has been described as a familial problem in a group of Holstein-Angus cattle. Affected cows do not act ill but have a bilateral thick nasal discharge (Fig. 4.8, *A*) and nasal pruritus with variable but often progressive degrees of nasal stertor and increased respiratory rate and effort. Affected cattle may rub their noses so frequently that foreign bodies may become trapped in the nasal cavity, and significant self-induced trauma may ensue. Diagnosis is based on clinical signs; endoscopic examination of the nasal and nasopharyngeal cavity (Fig. 4.8, *B* and *C*); and when indicated, cytology of nasal mucus, tracheal aspirates or nasal biopsy, all of which contain large numbers of mononuclear cells and eosinophils (Fig. 4.8, *D*). Treatments generally include removing the affected animals from the pasture, or if that is not possible, the administration of corticosteroids to nonpregnant heifers. Improvement in clinical signs is generally noted within 5 to 7 days after removal from pasture.

Granulomatous Rhinitis

Diffuse nasal granulomas are uncommon in dairy cattle in the northern United States. *Rhinosporidium* is the most common cause of granulomas that are observed. The granulomas develop on the nasal mucosa through the turbinate region, and as they enlarge, the nasal airway is progressively compromised. Therefore signs include a progressive inspiratory dyspnea, nasal discharge, and nasal pruritus.

Frequently, epistaxis is reported by the owner. Inspection at the nares with the aid of a focal light source allows observation of tan or brown granulomatous masses in the nasal region. Endoscopy further defines the lesion. Biopsy for tissue culture and histopathology is indicated to determine the exact cause of the nasal granulomas.

Treatment consists of sodium iodide solution intravenously (IV; 30 g/450 kg once or twice at 24-hour intervals) followed by 30 g of organic iodide powder orally each day until signs of iodism occur. Although permitted in some countries such as Canada, parenteral sodium iodide is not approved for use in lactating dairy cattle in the United States.

Granulomas Caused by Actinobacillus lignieresii or Actinomyces bovis

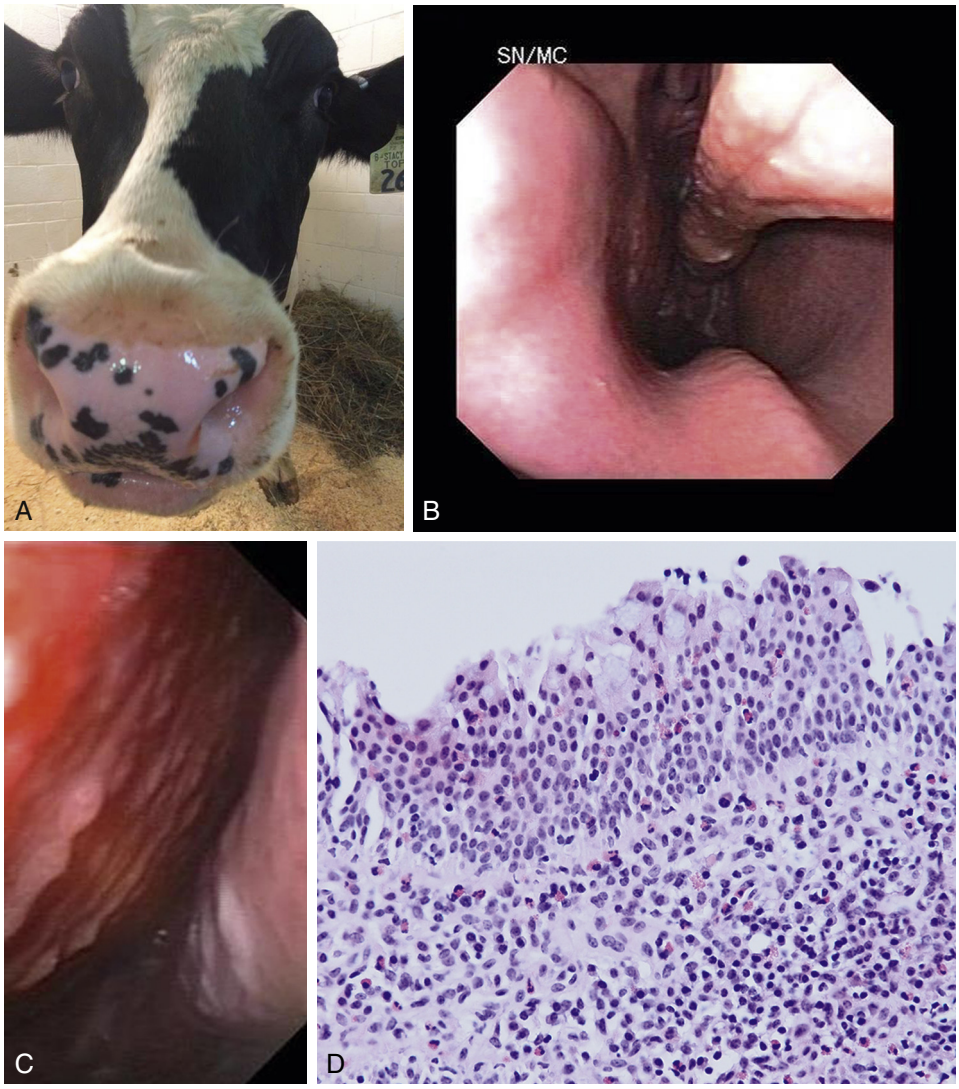
Etiology and Signs

Actinobacillus lignieresii granulomas within the nasal cavity usually are unilateral masses within the external nares and appear as red, raised, fleshy masses that bleed easily and look very similar to *Rhinosporidium* granulomas (Fig. 4.9). Signs include a progressively enlarging mass in one nostril, progressive decrease in airflow, and inspiratory dyspnea as the lesion enlarges to occlude the nostril completely. These granulomas may originate at the site of nose-lead lesions of the mucosa near the nasal septum or at other mucosal sites of soft tissue injury from restraint, foreign bodies, or fibrous feed.

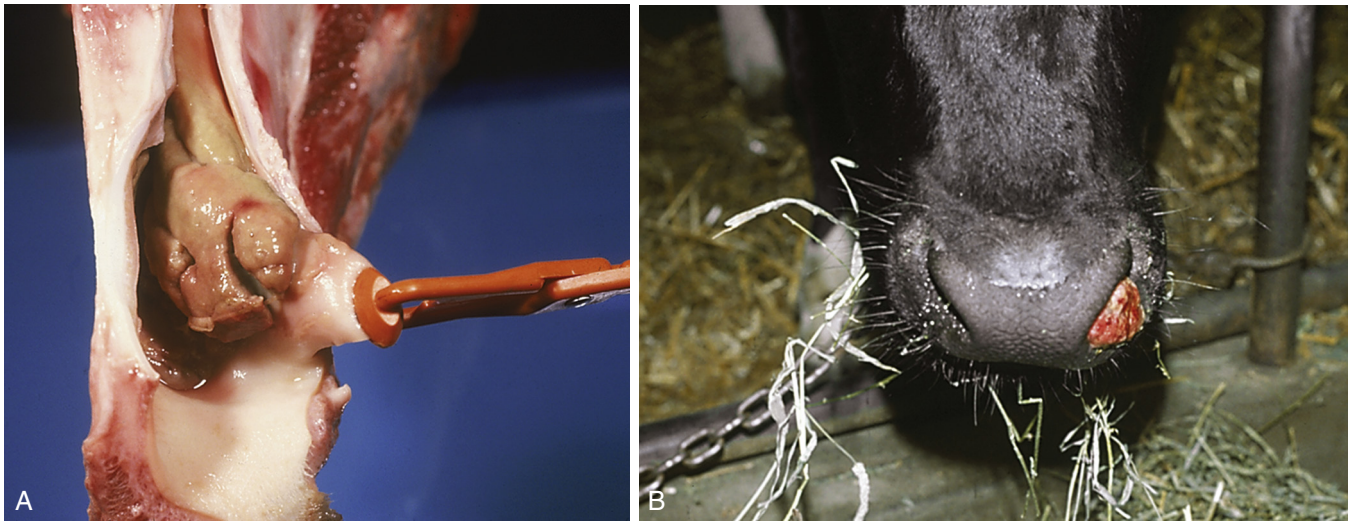
Progressive inspiratory dyspnea and nasal discharge are found in patients having granulomas deeper in the nasal cavity, larynx, pharynx, or trachea. *Actinomyces bovis* was responsible for multiple tracheal granulomas in a cow treated at the New York State College of Veterinary Medicine.

Diagnosis

Granulomas can be confused with tumors on gross inspection. Therefore diagnosis requires biopsy for histopathology and tissue culture. Sulfur granules may be observed grossly on cut surface and suggest the diagnosis. Although usually found near the external nares, granulomas caused by *A. lignieresii* or *A. bovis* could occur anywhere in the upper airway or trachea because these opportunists reside in the oral cavity and pharynx. When soft tissue infection occurs after injury to the mucosa, both organisms produce similarly appearing granulomas. Endoscopy and radiographs are necessary to identify deeper granulomas at locations other than the external nares.



• **Fig. 4.8** **A,** Nasal discharge in a pastured 17-month-old Holstein heifer with a 3-week history of progressive nasal stertor and discharge caused by allergic rhinitis. **B,** Endoscopic examination of the heifer's nasal cavity showing multiple nodular lesions in the nasal mucosa. **C,** Close-up photo of the nodular lesions seen in the nasal mucosa via endoscopy. **D,** Histopathology of a biopsy taken from the nasal mucosa of the same heifer showing a pronounced mononuclear–eosinophilic reaction.



• **Fig. 4.9** **A,** Necropsy specimen of nasal turbinate region showing *Rhinosporidium* granulomas. **B,** *Actinobacillus* nasal granuloma in a Holstein cow.

Treatment

Treatment for granulomas caused by *A. lignieresii* consists of excisional biopsy to debulk the mass to the level of nasal mucosa and sodium iodide therapy until iodism is observed. Usually this requires IV sodium iodide (30 g/450 kg) initially and at 2- to 3-day intervals for several treatments or oral organic iodide (30 g/450 kg) daily after the initial IV dose. Cryosurgery has been used successfully on these granulomas after debulking. In severe or recurrent cases, antibiotic therapy may be necessary in addition to sodium iodide. Penicillin and ampicillin have been used to treat infection caused by *A. lignieresii*. Whenever possible, an antibiotic should be selected based on organism culture and sensitivity results. Usually the prognosis is good.

Granulomas caused by *A. bovis* are much more difficult to treat because this organism is poorly responsive to sodium iodide therapy. Treatment with penicillin (22,000 U/kg intramuscularly [IM] once a day), in conjunction with sodium iodide, may be effective. Surgical debulking of soft tissue granulomas also is indicated. The prognosis for lesions caused by *A. bovis* is guarded because of the limited clinical knowledge regarding treatment of this organism, and the fact that many owners may not treat for a sufficient time.

Frontal and Maxillary Sinusitis

Etiology and Signs

Frontal sinusitis in calves and adult cattle may be acute or chronic. Acute frontal sinusitis is more common and usually follows sharp dehorning techniques. Older calves and mature cattle dehorned by laypeople are most at risk because of nonsterile equipment and techniques. Signs of acute sinusitis include fever (103.0° to 106.0°F [39.4° to 41.1°C]), unilateral or bilateral mucopurulent nasal discharge, depression, and headache type pain characterized by partially closed eyes, an extended head and neck, head pressing or resting the muzzle on support structures (interestingly, cattle with severe skeletal or mild to moderate visceral pain can also often be found pressing their muzzles against an object, which suggests this must be a pain relief point), and sensitivity to palpation on percussion of the sinus. When acute sinusitis follows recent dehorning, purulent drainage or heavy scabs may be observed at the wound in the cornual portion of the sinus. A multitude of bacteria such as *T. pyogenes, Pasteurella multocida, Escherichia coli,* and anaerobes may contribute to acute frontal sinus infection. Tetanus is another possible complication of acute frontal sinusitis if wound debris or scabs occlude the cornual opening to allow an anaerobic environment.

Maxillary sinusitis is rare in cattle, especially compared with horses, but as in the equine species, it can be a spontaneous primary condition or occur secondary to diseased teeth roots. Secondary maxillary sinusitis related to dental disease is only likely to become more unusual in dairy cattle as the average age of dairy animals becomes younger. Occasional secondary cases may also present in association with osteomyelitic conditions of the skull such as lumpy jaw (Dr. Mike Livesey, University of Wisconsin, 2017, personal communication). Extension of frontal sinusitis associated with dehorning into the more rostral maxillary sinus is also possible. The most common presenting signs are chronic, purulent, unilateral nasal discharge; it is very rare to see facial asymmetry, but affected cattle may sometimes show resentment and sensitivity during percussion of the skull over the maxillary sinus region on the relevant side. As mentioned in the previous section, they may also have mild upper airway noise caused by a reduction in air flow on the affected side.

• **Fig. 4.10** Chronic frontal sinusitis in a mature bull. The bull died from septic meningitis caused by the sinusitis.

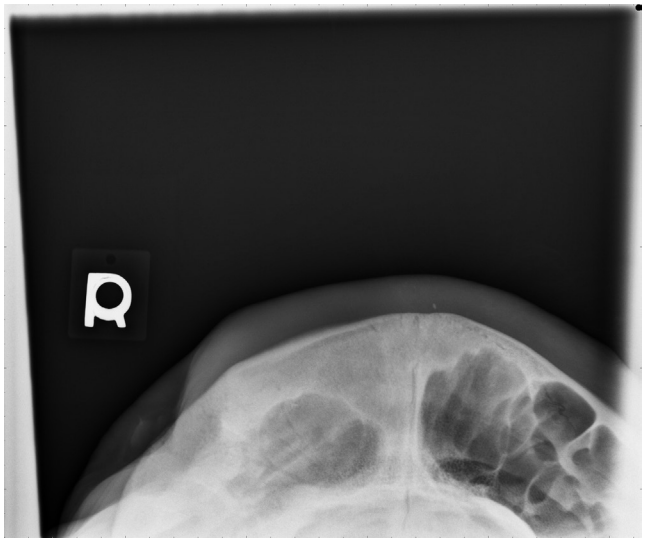
Chronic frontal sinusitis does not develop until months to years after dehorning and may be completely unassociated with dehorning because it occasionally occurs in animals dehorned by noninvasive techniques, polled animals, or animals with horns. Ascending respiratory tract infections, as in other species, are a cause of chronic frontal sinusitis and usually are caused by *P. multocida*. Chronic frontal sinusitis associated with old dehorning complications such as low-grade infection, bony skull fragments, or sequestra typically is associated with infection by *T. pyogenes* or mixed infections that may include *T. pyogenes*, *P. multocida*, anaerobes, or miscellaneous gram-negative organisms. Signs of chronic frontal sinusitis include gradual loss of condition and production that may be persistent or intermittent. Unilateral nasal discharge usually is observed, again as a persistent or intermittent complaint. Additional signs include head pressing, an extended head and neck, partially closed eyes, or resting of the muzzle on inanimate objects, all of which signal headache or pain. Intermittent or persistent fever is present. Bony expansions of the sinus may occur, causing asymmetric facial distortion, especially in cattle that do not have significant nasal discharge because of occlusion or obstruction of the opening of the ethmoidal meatus into the nasal cavity. In fact, some cattle have intermittent bony swelling of the sinus that becomes less apparent during times of sinus drainage and subsequent nasal discharge. Palpation or percussion of the frontal bone overlying the affected sinus causes pain, and the patient may be extremely apprehensive when the examiner approaches the head. Bony expansion of the sinus may result in ipsilateral exophthalmos and decreased air movement through the ipsilateral nasal passage (Fig. 4.10). Neurologic complications, including septic meningitis, dural abscesses, and pituitary abscesses, are possible in neglected cases as a result of erosion through the bony sinus. Tetanus is another

potential complication. Occasionally, cattle with chronic frontal sinusitis have developed orbital cellulitis, pathologic exophthalmos, or facial abscesses from infectious destruction of the postorbital diverticula of the sinus, allowing soft tissue infection of the orbit (Fig. 4.11).

Diagnosis

In acute cases, diagnosis is based on signs, history, and palpation and percussion of the sinus. Ancillary data include bacterial culture and susceptibility testing to ensure proper antibiotic selection. Radiographic imaging (Fig. 4.12) and computed tomography (CT) provide helpful information regarding the extent of the lesion; severity of any accompanying osteomyelitis; and in the case of CT, greater detail regarding the possible involvement of deeper soft tissues of the head. Diagnostic imaging studies are also of great value in the evaluation of chronic nasal discharge associated with maxillary sinus infection (Fig. 4.13).

• **Fig. 4.11** Orbital cellulitis, exophthalmos, and facial abscesses secondary to extension of chronic frontal sinusitis into the orbital soft tissue.



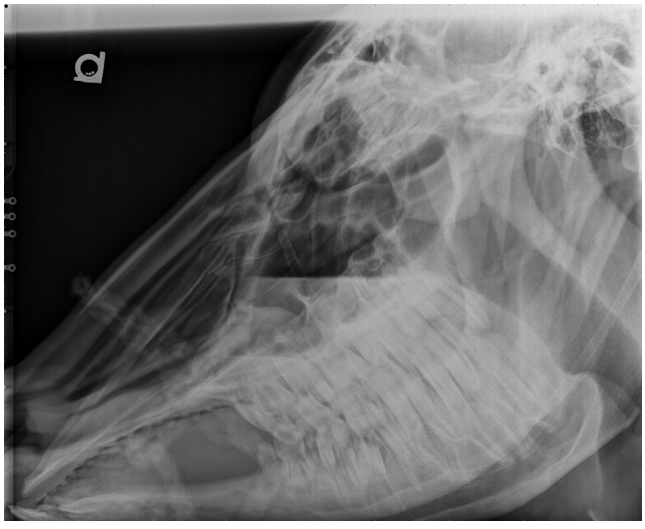
• **Fig. 4.12** Oblique, "skyline" radiograph of frontal region of a yearling Holstein bull that had purulent discharge from dehorning scar (performed at 6 months of age). Note the periosteal reaction and soft tissue opacity in the affected (R) sinus.

The diagnosis of chronic cases may be possible based purely on clinical signs coupled with palpation and percussion of the sinus. As with acute sinusitis, imaging can be very helpful in the evaluation of highly suspect cases prior to surgical intervention. When mature animals are affected, however, it is important to rule out neoplasia and other differentials. Drilling into the frontal sinus with a Steinmann's pin and collection of purulent material for cytology and bacterial cultures will confirm the diagnosis (Fig. 4.14). Sedation and local anesthesia allow this procedure to be performed with minimal patient discomfort.

Treatment

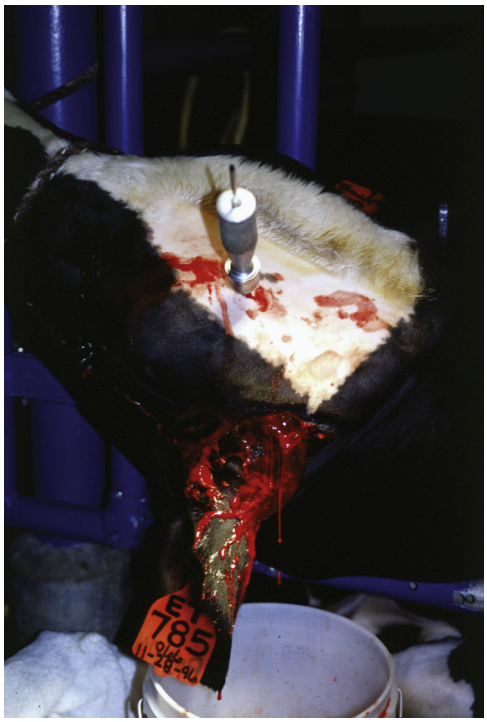
In individuals with acute frontal sinusitis, treatment requires cleansing of cornual wounds, lavage of the sinus with saline, or saline and mild disinfectant solutions, and appropriate systemic antibiotics for 7 to 14 days. Penicillin usually suffices, but selection of a systemic antibiotic is better based on culture and susceptibility testing. Tilting the patient's head to allow the sinus to fill and then twisting the head to empty the sinus facilitate lavage and drainage. Systemic analgesics such as aspirin or flunixin meglumine greatly aid patient comfort. The prognosis is good.

Treatment of chronic frontal sinusitis requires trephination of the sinus at two sites to allow lavage and drainage. One site is at the cornual portion of the sinus, and the second is located over the affected sinus approximately 4.0 cm from midline and on a transverse line connecting the caudal bony orbits (Fig. 4.15). A third site caudodorsal to the rim of orbit and medial to the temporal ridge has been recommended, but we have found this site to be dangerous because it occasionally results in orbital soft tissue infection as compromised softened bone is penetrated. Further caution regarding trephination of the sinus should be practiced in animals younger than 2 years of age because the rostral and medial rostral portions of the sinus may not be developed in younger animals. Attempts to establish rostral-medial drainage in these



• **Fig. 4.13** Lateral skull radiograph of 5-year-old Jersey bull with chronic unilateral nasal discharge. Note the horizontal fluid line within the maxillary sinus.

animals may risk invasion of the calvarium. Drains may be placed to maintain communication between the two trephine sites and prevent premature closure of the wounds. Trephine holes should be at least 2.0 to 2.5 cm in diameter or they will close prematurely. Liquid pus is a positive prognostic sign, and pyogranulomatous or solid tissue in the sinus is a grave prognostic sign. Antibiotic selection must be based on culture and susceptibility testing and should be continued for 2 to 4 weeks. Analgesics such as oral aspirin are used to improve the patient's comfort. Trephination and lavage are also the preferred treatments for primary or secondary maxillary sinusitis, although one will also need to attend to the inciting causes such as diseased tooth roots or maxillary osteomyelitis in secondary cases. It can be anatomically challenging in cattle to adequately access and drain all the somewhat convoluted pockets of the maxillary sinus cavity in affected cattle.

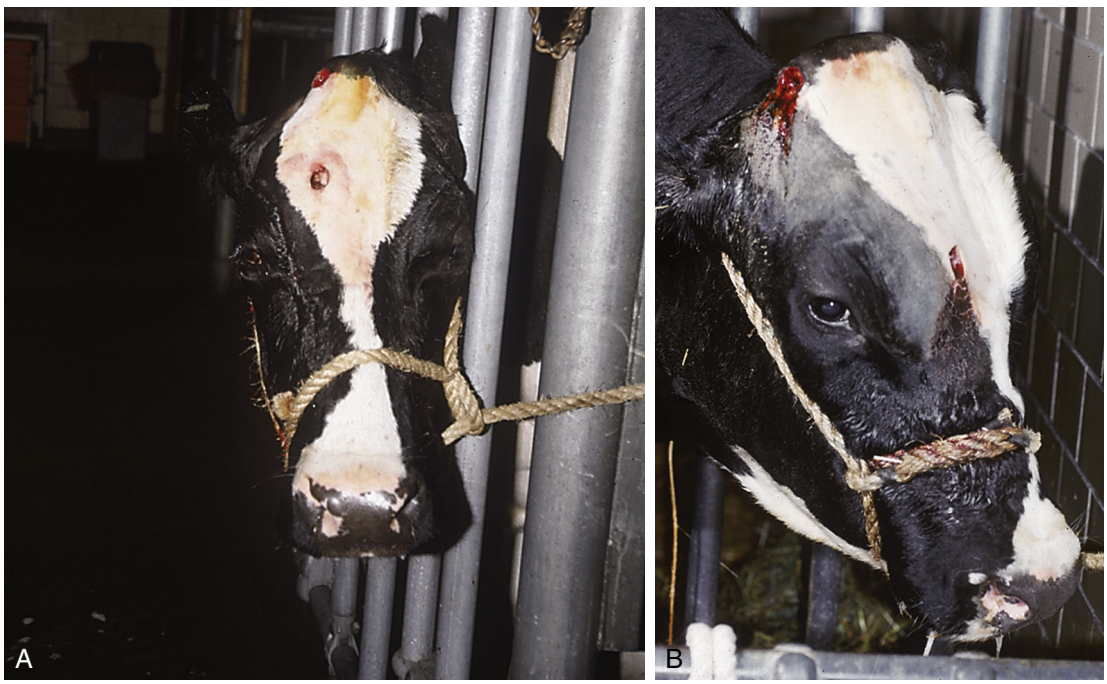


• **Fig. 4.14** Sinus trephination with a Steinmann pin to facilitate sample collection in a bull with chronic sinusitis. Note the caudal trephination flap that has already been made in the dehorning site to facilitate sinus lavage.

The prognosis is fair to good with appropriate therapy as described earlier unless neurologic signs have been observed. Neurologic signs and orbital cellulitis constitute severe and usually fatal complications of chronic frontal sinusitis. On several occasions, especially in animals younger than 18 months of age, Dr. Rebhun performed enucleation successfully to allow orbital drainage necessitated by severe orbital cellulitis and ocular proptosis in addition to trephination of the affected sinus. Long-term wound care, antibiotics, and nursing are essential if treatment is elected for such complicated cases.

Laryngeal Edema

Laryngeal edema secondary to bracken fern intoxication has been described in calves. Termed the "laryngitic" form, this idiosyncratic response leads to progressive dyspnea without obvious signs of hemorrhage as expected in older animals affected with bracken fern toxicity. Laryngeal edema has also occurred after vaccination of cattle, presumably as part of an adverse immune response. Cattle with persistent upper airway obstruction and dyspnea caused by conditions associated with the soft tissues of the retropharynx or larynx may develop laryngeal edema as a secondary complication. In cases of acute laryngeal edema associated with immune reaction or anaphylaxis, specific therapy with antihistamines, epinephrine (1–5 mL of 1:1000 epinephrine IV or 4–8 mL subcutaneously [SC] or IM) and



• **Fig. 4.15** **A,** Trephination sites surgically created to treat chronic frontal sinusitis in a 4-year-old Holstein cow. **B,** Trephination sites surgically created to treat chronic frontal sinusitis in a 3-year-old Holstein bull.

corticosteroids (mindful of pregnancy status of the animal) (40 mg of dexamethasone or 100–500 mg of methylprednisolone sodium succinate) should be instituted immediately. Almost as quickly as the clinician administers these drugs, a decision as to whether or not a tracheostomy is necessary should be made, but one should not prevaricate for many minutes if the emergency drug treatment does not alleviate the upper airway dyspnea almost immediately. Diuretic therapy is indicated if fulminant pulmonary edema is occurring with anaphylaxis, evidence of which is usually provided when the tracheostomy is placed because individuals with "wet lungs" will remain distressed and tachypneic despite the patent upper airway that has been established. The bovine larynx appears to be rather less dynamically forgiving than the equivalent structure in horses. One of the authors (SP) has treated several cattle with laryngeal edema from anaphylaxis, trauma from intubation, or associated with soft tissue or cartilaginous infections (mainly calves with necrotic laryngitis) that have seemingly recovered from the initial swelling or infectious lesion only to be left chronically with severely diminished arytenoid function. This acquired lack of normal arytenoid abduction has led to repeated bouts of dyspnea and upper airway noise during hot and humid weather, exertion, or even just in response to mild tachypnea. Consequently, this has led to repeated emergency tracheostomy or discussion with the owners regarding the placement of a permanent tracheotomy or a tracheolaryngotomy for long-term resolution. A similar situation sometimes arises with calves that are left with deformed arytenoids after apparent recovery from necrotic laryngitis or laryngeal chondritis.

Necrotic Laryngitis (Calf Diphtheria)

Etiology and Signs

Necrotic laryngitis represents an atypical site of infection by the anaerobe *Fusobacterium necrophorum*, the organism responsible for calf diphtheria. Calf diphtheria is an infection of the soft tissue in the oral cavity after mucosal injury caused by sharp teeth in calves of 1 to 4 months of age. Calves affected with calf diphtheria usually have abscesses in the cheek region and mild salivation and may refuse solid feed (Fig. 4.16). The infection spreads among calves fed from common utensils or feeders or those in such close group contact that they may lick one another. When the larynx becomes infected in the atypical form of this disease, the affected calf develops a progressive inspiratory dyspnea. Low-grade fever (103.0° to 104.5°F [39.44° to 40.28°C]) may be present along with a painful short cough that is observed when the calf attempts to drink or eat. As the condition worsens over several days, both inspiratory and expiratory dyspnea may be apparent, but the inspiratory component always will be worse. A necrotic odor may be present on the breath.

Audible inspiratory efforts are heard externally. Harsh sounds of airway turbulence are heard when a stethoscope is placed over the larynx; these sounds are also referred down the tracheobronchial tree to confuse auscultation of the lower airway.

Diagnosis

Endoscopy is helpful in confirming the diagnosis. In some calves, the lesions can be seen by using an oral speculum, but endoscopy is much easier and less stressful for the patient. If the calf is in extreme dyspnea or is anoxic or cyanotic, a tracheostomy should be performed before endoscopy (Fig. 4.17). The larynx will be found to be uniformly swollen and may appear to have cartilaginous deformities in chronic cases (Fig. 4.18). The laryngeal opening always is narrowed, and mucosal necrosis will be present in acute cases. Chronic cases may have laryngeal deformity and airway narrowing, but the necrotic, infected cartilage may be covered by normal mucosa (see Video Clips 4.2 and 4.3). If the mucosa appears normal on endoscopic examination performed via the nose and the tracheostomy opening, ultrasound examination of the larynx can be very helpful in detecting the severity of cartilage necrosis (Fig. 4.19). It should be noted that adult cattle may also develop bacterial infections in and around the arytenoid cartilages causing either cartilage necrosis or soft tissue abscess formation (see Video Clips 4.4 and 4.5). Branchial cysts may also occur in cattle and have an appearance similar to laryngeal abscess (see Video Clip 4.6).

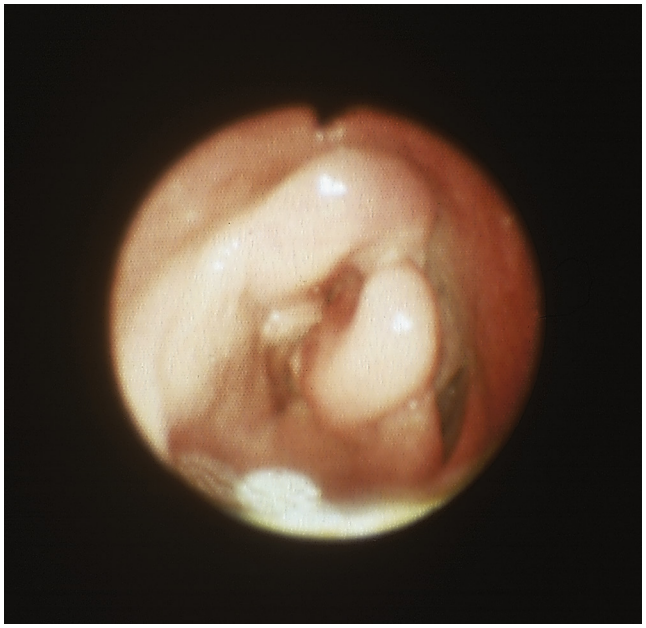
Treatment

Long-term therapy is required because infection of cartilaginous structures usually exists. Acute cases should be treated with penicillin (22,000 U/kg IM twice daily). A tracheostomy is essential for treatment of calves that have severe dyspnea (Fig. 4.20; see Video Clips 4.7A and B). This provides a patent airway

• **Fig. 4.16** Typical cheek abscess observed in calf diphtheria.

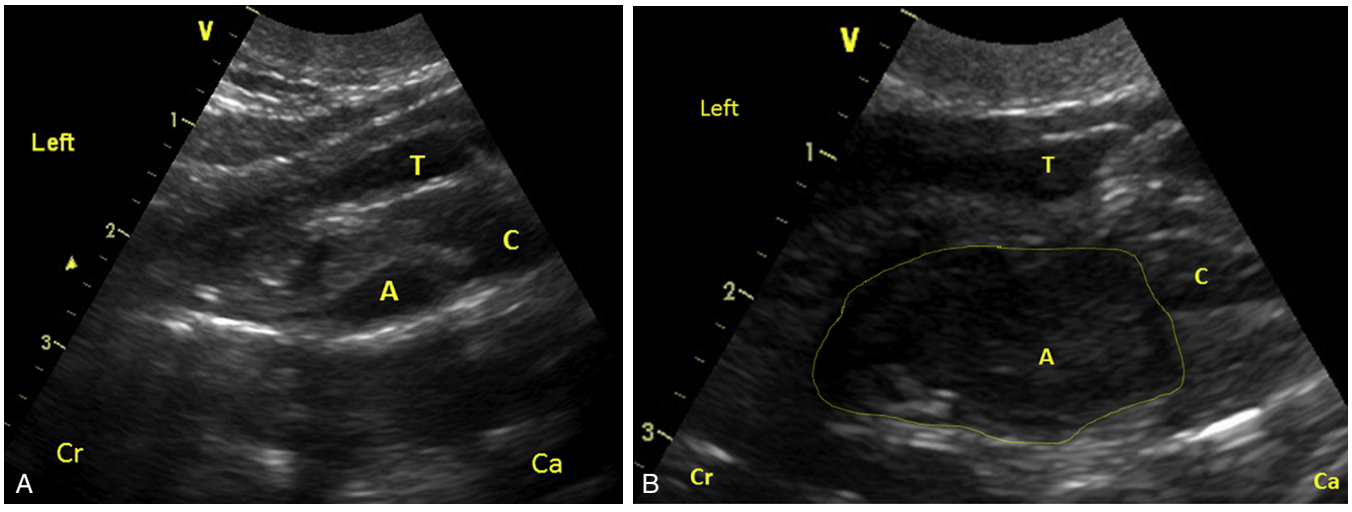
• **Fig. 4.17** A 4-week-old Holstein calf with progressive respiratory noise and cough that presented in respiratory distress. A temporary tracheostomy had to be performed because of the severity of the respiratory obstruction and distress.

and rests the inflamed larynx from further exertional irritation while the infection is controlled. Affected animals can improve from severe respiratory distress and being almost moribund to eupnea in minutes after placement of the tracheostomy. It also allows for easier evaluation of the lower airway; the degree to which bronchopneumonia is worsening the animal's condition is much easier to evaluate by auscultation, if imaging modalities (radiographs or ultrasound) are not available, when one does not have to try to filter out the considerable referred upper airway noise that is typically present before the tracheostomy is placed. The prognosis for acute cases is fair; the goal is to be able to allow the temporary tracheostomy to heal by second intention after it is apparent that normal air flow and eupnea are possible when the temporary tracheostomy is "test" occluded. The temporary tracheostomy, although usually placed under emergency-type conditions, should be located in the proximal third of the neck, close to the larynx. Daily wound care and changing of the tracheostomy tube are critical because the site is usually very "exudative" and prone to purulent discharges that can occlude the airway or become inhaled and travel distally. It is advisable to remove a semicircular part of the adjacent tracheal rings immediately dorsal and ventral to the initial skin incision when placing the tracheostomy tube even if this is performed after a smaller diameter tube has been initially placed for emergency relief. Radiographs can be helpful not only diagnostically but also to give an idea of the diameter of tracheostomy tube that the patient's upper airway can accommodate, although the diameter of the stoma is the usual limiting factor. Radiographs or ultrasonography of the lungs are also helpful to assess the amount of pneumonia (aspiration is common in these cases). Concurrent, severe bronchopneumonia worsens the prognosis markedly and is often suggested by only mild improvement in tachypnea when a tracheostomy is placed.



• **Fig. 4.18** Endoscopic view of laryngeal deformity and profoundly narrow laryngeal airway in a 3-month-old Holstein calf that had necrotic laryngitis and chronic laryngeal cartilage infection caused by *Fusobacterium necrophorum*.

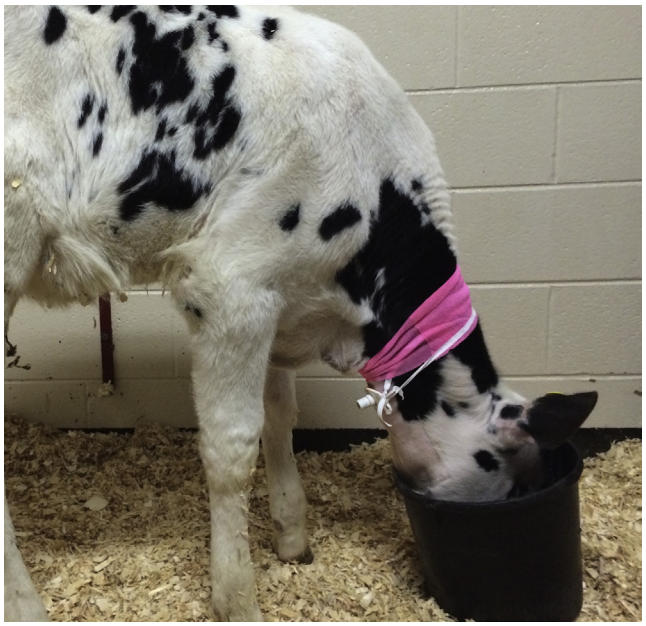
Chronic cases have a poor prognosis because laryngeal deformity and cartilaginous necrosis have often already occurred or abscesses within the laryngeal cartilage already have developed (Fig. 4.21). Treatment is similar to that described for acute cases but should be extended to 14 to 30 days in patients valuable enough to warrant treatment, or the necrotic cartilage should be surgically removed or debrided. A tracheostomy may be necessary for the reasons listed earlier, and some clinicians recommend concurrent treatment with sodium iodide in the hope of penetrating the deep-seated cartilaginous infection. *T. pyogenes* frequently contributes to, or replaces, *F. necrophorum* as the causative organism in chronic infections because these two organisms are synergistic. For valuable cattle with the chronic form, referral to an expert surgeon familiar with performing a permanent



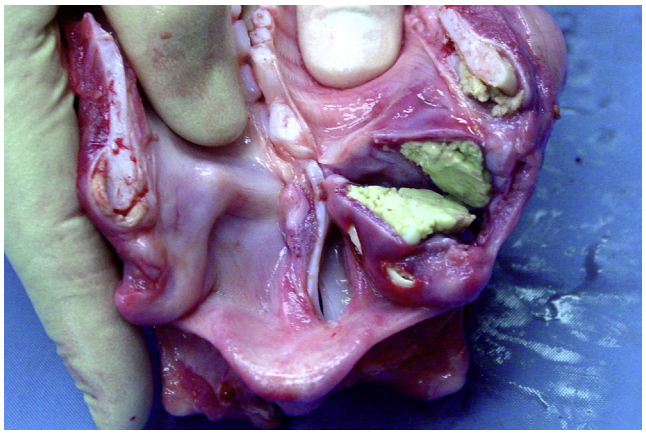
• **Fig. 4.19** Comparative ultrasound images of a normal calf larynx (**A**) with the larynx of the calf (**B**) in Fig 4.17 demonstrating necrosis of the cartilage. An abscess associated with the arytenoid cartilage is identified by the yellow outline. An endoscopic examination performed via the nose and tracheotomy site had not shown any appearance of necrosis, only swelling. A laryngotomy and partial arytenoidectomy were performed, and the calf recovered completely. Ultrasound image key: (T) Thyroid cartilage, (C) Cricoid cartilage, (A) Abscess in arytenoid cartilage, (Cr) cranial, (Ca) caudal (V) ventral. Image courtesy of Dr. M. Cercone.

tracheotomy, the tracheolaryngotomy technique as described by Gasthuys, or a subtotal arytenoidectomy via laryngotomy is recommended. Surgical details are described in the Farm Animal Surgery text, edited by Drs. Fubini and Ducharme.

Anatomic differences in skin redundancy and strap musculature between horses and cattle, even in calves, make surgery more challenging. By removal of the caudal part of the cricoid cartilage and two to three proximal tracheal rings, a permanent tracheolaryngotomy can be established as a long-term solution, and cattle can still thrive after this procedure (Figs. 4.22 and 4.23) but are, of course, susceptible to blockage of, or aspiration into, the stoma. Recently, Nichols and Anderson have described an additional surgical option of partial or subtotal arytenoidectomy via laryngotomy for the long-term management of such calves. Calves can grow and survive to adulthood. It has been convention to say that these animals cannot calve without assistance because of their inability to forcibly abdominally contract against a closed airway (Valsalva maneuver); that has not been our experience! In dairy calves, the prognosis for animals that undergo such permanent upper airway surgeries must always be guarded, and the treatment goal should preferably be resolution of the condition medically, often with the combined use of a temporary tracheostomy, during the acute stages of the disease.



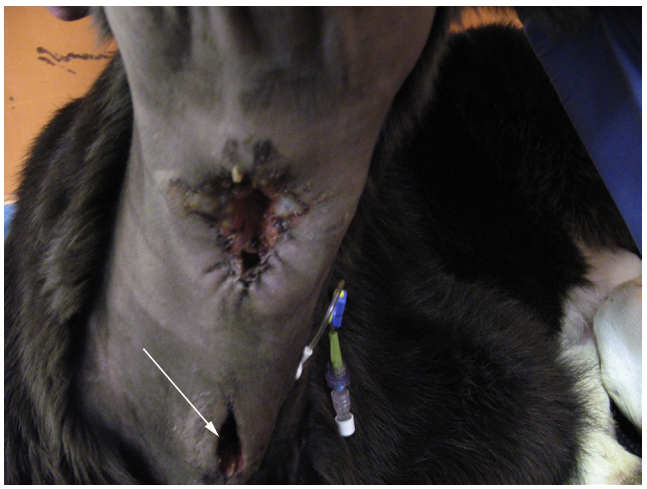
• **Fig. 4.20** Weanling-age Holstein heifer with temporary tracheostomy in place for treatment of severe necrotic laryngitis with chondritis. Immediate relief and desire to eat were associated with tube placement. (Courtesy of Rachel Borchardt.)



• **Fig. 4.21** Postmortem image of the larynx from a 6-week-old Holstein calf with severe necrotic laryngitis with abscess formation involving the left arytenoid and perilaryngeal tissues. Epiglottis is positioned at the bottom of the image, and fingers are within the proximal trachea.

Tracheal Obstruction

Tracheal obstruction is not common but may occur from either intraluminal obstruction with exudative debris as occurs with infectious bovine rhinotracheitis (IBR) infection or from



• **Fig. 4.22** Permanent tracheolaryngotomy in 2-month-old calf as a treatment for chronic necrotic laryngitis (ventral view). The image was taken 2 days postoperatively. The more distal stoma *(arrow)* represents site of previous emergency tracheostomy. Note the exudative discharge from the permanent stoma, which will persist for a prolonged period and require wound care.

• **Fig. 4.23** Holstein heifer from Fig. 4.20 as a yearling. A permanent tracheolaryngotomy had been created for long-term management 7 months previously. (Courtesy of Rachel Borchardt.)

extraluminal obstruction caused by abscess or lymphosarcoma or as a result of proliferative callus on the first ribs in calves (Figs. 4.24 to 4.26). Congenital tracheal stenosis independent of rib injury has also been reported to occur within the cervical or thoracic portions of the trachea (Fig. 4.27).

The diagnosis is generally easy if endoscopy and radiography can be used to support the clinical examination. Most calves with tracheal obstruction resulting from proliferative rib calluses are several weeks of age when respiratory signs develop and affected calves often have a history of dystocia at birth.

Treatment for intraluminal inflammatory obstruction includes nebulization with acetylcysteine, inhalational antibiotic, and an appropriate bronchodilator (ipratropium inhaler or aminophylline or atropine systemically). Prosthetic repair of tracheal compression caused by proliferative callus formation has been described, but the procedure is technically difficult, and because of the young age of the patient, the prosthesis eventually needs to be removed to permit normal growth of the trachea.

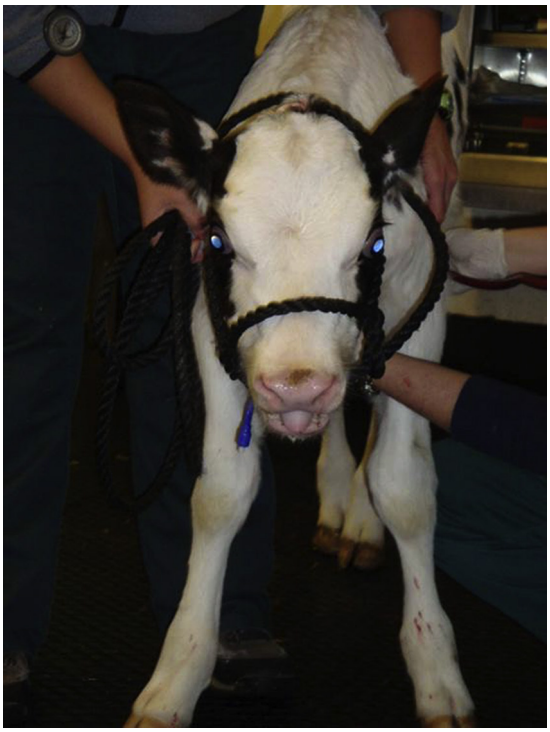
Diseases of the Lower Airway

Bacterial Bronchopneumonia

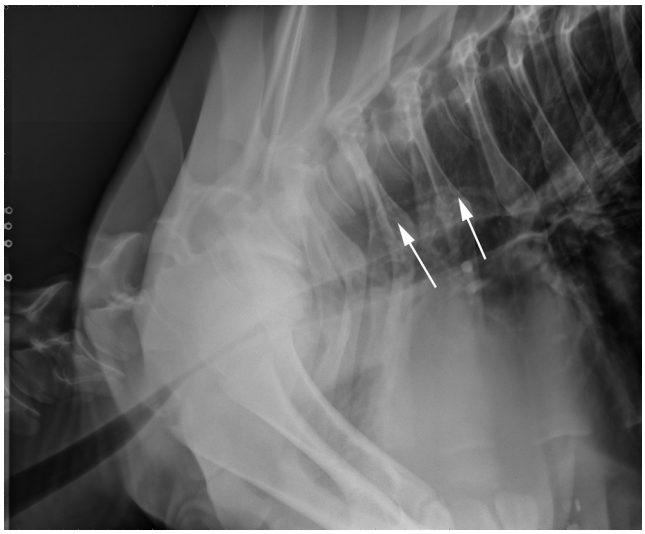
This remains the most important cause of morbidity and mortality from respiratory disease in dairy calves and adult cattle. Virulent strains of *Mannheimia haemolytica* and *Histophilus somni* are primary pathogens capable of causing acute infections of the lower airway and lung parenchyma. These organisms do not always require the help of environmental and management stressors or other infectious agents to cause life-threatening or fatal pneumonia. Chronic lower airway infections by *P. multocida* and *T. pyogenes* may cause pneumonia in calves either previously infected or co-infected with primary bacterial pathogens (*Mannheimia* and *Histophilus* spp.) or viral or *Mycoplasma* pathogens of the respiratory tract or in animals stressed by shipment, poor management, or ventilation insufficiencies.

Chronic suppurative bronchopneumonia in adult cattle and calves may also be the result of previous aspiration; combinations of *P. multocida*, *T. pyogenes*, *Fusobacterium* spp., and *Mycoplasma* spp. are frequently cultured. Aspiration pneumonia associated with these same pathogens may also be observed in calves with white muscle disease, calves fed via an inappropriately large opening on the nipple of milk feeding bottles, premature calves with inadequately developed protective reflexes of the glottis, and calves with retropharyngeal diseases that interfere with normal upper airway reflexes. Milk-fed calves who are tachypneic or dyspneic because of either upper or lower airway disease, whatever the etiopathogenesis, may also aspirate as a secondary problem as they struggle to swallow properly at very high respiratory rates. Head and neck position during feeding can play a role in increasing or decreasing the likelihood of this occurring, to the extent that hospitalized sick and weak calves that are being fed from a bottle at our institution are routinely encouraged to nurse with the head and neck along a more parallel axis to the ground than is their natural tendency. In general, feeding from a bucket lessens the chances of aspiration.

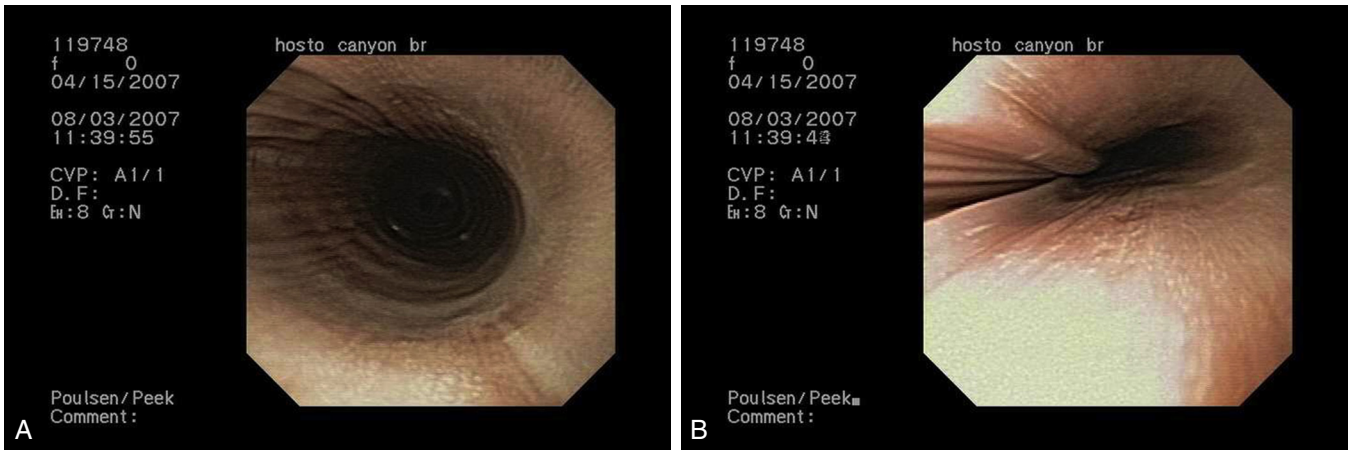
It is imperative for bovine practitioners to understand the causes, predisposing factors, treatment, control, and prevention of the pathogens associated with bacterial bronchopneumonia, such is the prevalence and impact of the disease. It is by far the most common and significant cause of respiratory disease in dairy calves. When investigating outbreaks of bacterial bronchopneumonia of dairy calves during the first few



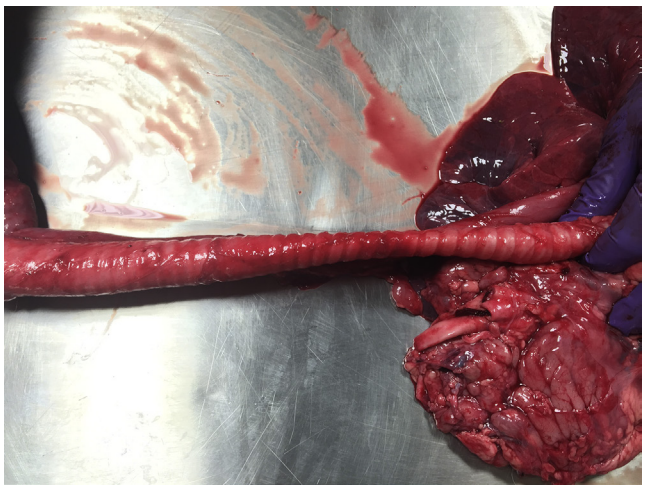
• **Fig. 4.24** A 5-week-old Holstein calf with respiratory distress and a loud honking sound during breathing. This was caused by tracheal compression resulting from a large callus associated with healed rib fractures. The fracture of the ribs had likely occurred during delivery.



• **Fig. 4.25** Thoracic radiograph of 6-week-old Holstein calf with tracheal compression associated with callus formation over multiple proximal rib fractures *(arrows)* associated with dystocia. The calf had been noted to be persistently tachypneic and exercise intolerant since shortly after birth.



• **Fig. 4.26** Endoscopic images of trachea from calf in Fig. 4.25, proximal to (**A**) and at the level of (**B**) the stenotic segment.



• **Fig. 4.27** Postmortem specimen from a 5-day-old Brown Swiss calf with congenital stenosis affecting the cervical trachea.

weeks of life, it is also critical to incorporate an evaluation of adequacy of passive transfer. There is compelling evidence that adequate transfer of immunoglobulin during the immediate neonatal period is a pivotal determinant of susceptibility to respiratory disease. Greater morbidity and mortality are anticipated with all infectious diseases to include bacterial bronchopneumonia when colostral transfer is suboptimal. When testing total protein by refractometry in calves between 1 day and 7 days of age, the goal is for individuals to be at 5.5 g/dL or higher; on a herd basis, when fewer than 75% of all calves in this age group meet this criterion, then the herd is deemed to have a problem with passive transfer.

In addition, it must be emphasized that the only way to diagnose and control contagious respiratory disease in cattle is to know the exact identity of the pathogens and predisposing causes. This can be accomplished only by careful history, thorough physical examination, collection of appropriate samples, and collaboration with a diagnostic laboratory capable of identifying all known bovine respiratory pathogens. The five major bacterial pathogens of the bovine lower airways currently are *M. haemolytica*, *P. multocida*, *Mycoplasma* spp., *H. somni*, and *T. pyogenes*. They will be discussed separately. Although other organisms may be involved, they seldom cause herd problems and will not be discussed in detail.

Mannheimia haemolytica

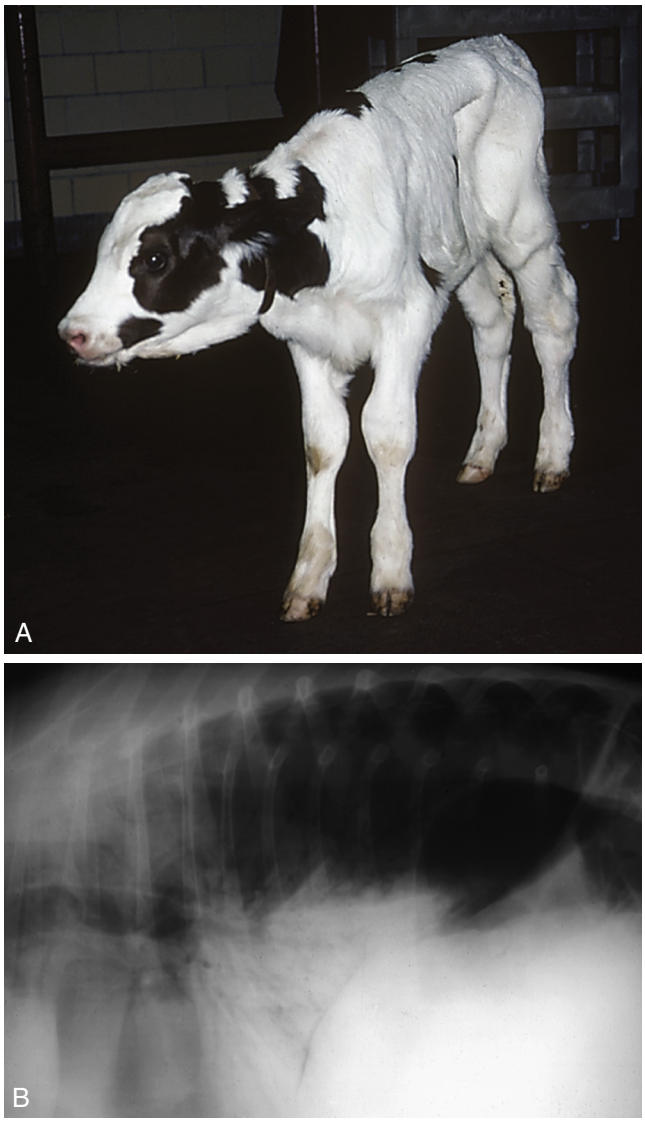
Etiology and Signs

M. haemolytica is a gram-negative rod that may be a normal inhabitant of the upper airway but is not cultured from the upper airway of normal cattle as frequently as *P. multocida*. Several properties of *M. haemolytica* contribute to its pathogenicity. These include a capsule that provides defense against phagocytosis; production of an exotoxin (leukotoxin) lethal to alveolar macrophages, monocytes, and neutrophils; cell wall–derived endotoxin that helps to initiate complement and coagulation cascades; and the ability to reside in the upper airway among other nonpathogenic serotypes and then convert/or overgrow under stressful stimuli to a pathogenic serotype, A1, that is more virulent. The cytotoxicity of the leukotoxin is associated with its ability to bind and interact with β2 integrin leukocyte function–associated antigen 1. Currently, *M. haemolytica* is a leading cause of death as a result of respiratory infection in dairy cattle and calves in most areas of the United States. This organism is a primary pathogen not always needing assistance from other viral or *Mycoplasma* agents to establish lower airway infection, although it is well demonstrated that bovine herpesvirus 1 (BHV1) infection can activate genes that will increase leukotoxin binding, cytotoxicity to bovine mononuclear cells, and the severity of *M. haemolytica* infection. When a virus such as IBR, bovine respiratory syncytial virus (BRSV), or bovine viral diarrhea virus (BVDV) does infect a herd, mortality will be greatly increased if *M. haemolytica* bronchopneumonia is superimposed. In this situation, the bacteria may cause death because the viral infection compromises mechanical and cellular defense mechanisms. Similarly, compromise of the mucociliary clearance apparatus alongside depression of other components of airway defense can be consequences of poor air quality under conditions of poor ventilation, inadequate fresh air changes, and increased partial pressures of inspired noxious gases such as ammonia from soiled bedding. This is true in broad terms for all of the infectious causes of lower airway disease, whether

commensal or true pathogen, and serves to emphasize the importance of air quality and ventilation in the prevention and control of pneumonia. The mortality rate may approach 30% to 50% when a virulent *M. haemolytica* infection is superimposed on a preexisting viral infection (e.g., BHV1 or BVDV) in a herd. Cattle that are stressed are at great risk of *M. haemolytica* pneumonia because stress triggers activation of the organism to a more virulent form, permits greater colonization of the virulent strain, and compromises the host defense mechanisms. Corticosteroids, either endogenous or exogenous, impair endotoxin-induced expression of antimicrobial peptides in the upper airway of cattle which would normally be an important part of the host defense response to gram-negative organisms such as *Mannheimia* and *Histophilus* spp. A similar negative effect is noted via endogenous corticosteroid release upon lactotransferrin production, which is another important antimicrobial determinant within the airways. Social group disruption, weaning, and transportation are all established paths to corticosteroid release in calves in particular and are therefore important risks to be aware of when troubleshooting husbandry factors that may be contributing to death losses caused by infection with *M. haemolytica*. Thus, *M. haemolytica* is frequently isolated as the cause of "shipping fever pneumonia" associated with shipment of cattle, transport of cattle to shows, or recent purchase of replacement animals. Classic signs of pneumonia generally develop 1 to 2 weeks after any of these stresses. The morbidity and mortality percentages tend to be much greater for *M. haemolytica* pneumonia outbreaks than if *P. multocida* is found as the cause of "shipping fever".

A great deal of variation in pathogenicity and antibiotic resistance exists amongst isolates of *M. haemolytica*. Therefore, the veterinarian must accept the fact that signs produced by these types may vary from mild to severe. Mild infections or less pathogenic *M. haemolytica* may mimic *P. multocida* with respect to clinical signs and response to therapy, but severe infections may be so drastic as to cause death within hours of the first clinical signs. In rare instances, the death can be so peracute that a toxicity is suspected. A less pathogenic form has been seen causing high fever in recently fresh cows, all of which had a remarkably quick recovery after treatment with ceftiofur.

Signs of acute *M. haemolytica* pneumonia include fever, depression, anorexia, markedly decreased milk production, salivation, nasal discharge, moist painful cough, and rapid respirations (Fig. 4.28). The fever may be as high as 108.0°F (42.22°C) but usually ranges between 104.0° and 107.0°F (40.0° and 41.67°C). Auscultation of the lungs reveals moist or dry rales in the anterior ventral lung fields bilaterally. Bronchial tones indicative of consolidation in the ventral lung fields are observed much more frequently than with acute *P. multocida* infections. Pleuritic friction sounds may be auscultated in some cases because of stretching or compression of fibrinous adhesions between the parietal and visceral pleura. The dorsal lung fields may sound normal on auscultation of animals with mild to moderate *M. haemolytica* pneumonia. In more severe cases, however, the dorsal lung may be forced to overwork because of the ventral lung consolidation. This



• **Fig. 4.28** **A,** Calf affected with *Mannheimia haemolytica* pneumonia showing an anxious expression, an extended head and neck to minimize upper airway resistance, and ventral edema caused by both albumin loss into the severely infected lungs and gravitational edema. **B,** Thoracic radiographs of the calf. Caudoventral consolidation is highlighted by air bronchograms. Consolidated lesions with air bronchograms give rise to the bronchial tones heard on auscultation.

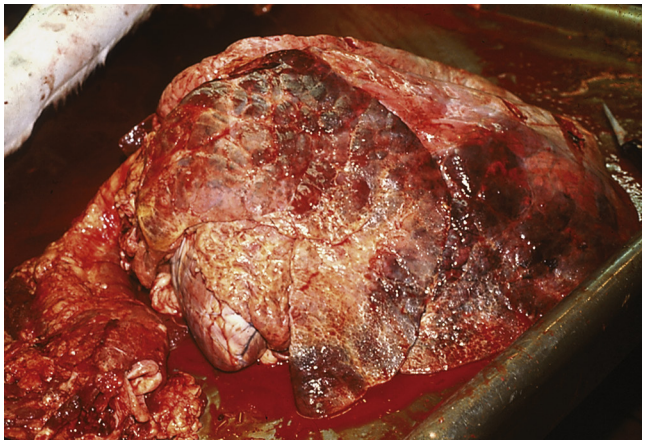
overwork creates interstitial edema or bullous emphysema on occasion, and these pathologic changes cause the dorsal lung to be abnormally quiet on auscultation. Auscultation of the trachea will reveal coarse rattling or bubbling sounds caused by the inflammatory exudate free in the trachea. Palpation of the intercostal regions over the pneumonic lung causes the animal pain. Occasional cases have an accumulation of transudative or exudative pleural fluid in the ventral thorax unilaterally or bilaterally that causes a total absence of sounds when auscultation is performed.

More severe or neglected cases may show open-mouth breathing (Fig. 4.29), anxious expression, and SC emphysema secondary to tracking of air from bullae rupture in the dorsal lung field and have harsh bronchial tones ventrally with inaudible lung sounds dorsally. Respiratory dyspnea is

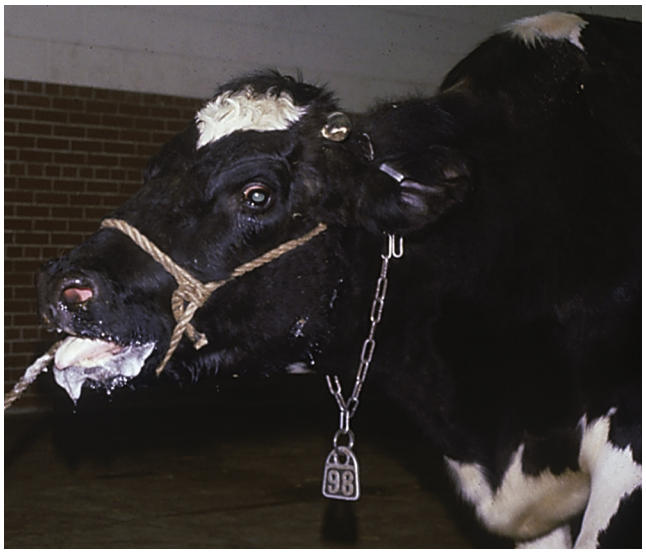
marked in such cases and affects both inspiratory and expiratory components, with the expiratory component being the most obvious. An audible grunt or groan may accompany each expiratory effort, and the animals are reluctant to move because of hypoxia and painful pleuritis.

A peracute rapidly consolidating form of *M. haemolytica* bronchopneumonia occasionally has been observed in the northern United States and has resulted in high morbidity and mortality within affected herds. The causative *M. haemolytica* has proven extremely resistant to antibiotics. In some instances, it is resistant to all antibiotics approved for use in dairy cows. Signs in acutely affected cattle include high fever (106.0° to 108.0°F [41.11° to 42.22°C]), marked depression, salivation, increased respiratory rate (60–120 breaths/min), complete anorexia and milk cessation, reluctance to move, and an absence of rales when the ventral lungs are auscultated. Profound bronchial tones may be audible bilaterally that indicate consolidation of 25% to 75% of the ventral pulmonary parenchyma (Fig. 4.30), alongside quiet or inaudible sounds in the dorsal lungs where the remaining pulmonary tissue has been subjected to extreme mechanical and physiologic stress to maintain gas exchange. SC emphysema and pulmonary edema are common sequelae in these cattle. Ventral abdominal pain can be elicited in the cranial abdomen as a result of the fibrinous pleuritis present. This pain and absence of rumen activity coupled with the other signs have caused many veterinarians to initially confuse this rapidly consolidating pneumonia with peritonitis caused by hardware or a perforating abomasal ulcer. The major reason for this error is the absence of rales with this form of *M. haemolytica*. Therefore we have had to "retrain" our ears to auscultate carefully for bronchial tones versus normal or harsh bronchovesicular sounds. Careless auscultation of air sounds in the ventral lung field may not discriminate between bronchial tones and vesicular sounds. Acute infection with this form of *M. haemolytica* results in progressive dyspnea and death in 12 to 48 hours unless the veterinarian is fortunate enough to choose as the first treatment an antibiotic to which the organism is susceptible.

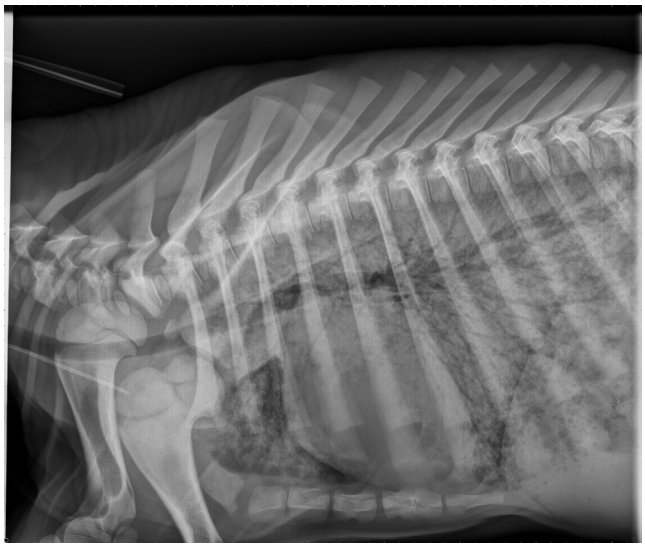
We have also seen this rapidly consolidating form of bacterial bronchopneumonia sporadically in hospitalized cattle, especially calves, in the 1 to 2 days after intubation and ventilation for general anesthesia, when presumably the animal is unfortunate to have a subclinical, preexistent infection that becomes diffusely disseminated during anesthesia (Fig. 4.31). Microbiologic investigation of these cases postmortem have typically yielded pure growths or combinations of *M. haemolytica* or *P. multocida*, but the antimicrobial resistance patterns of the isolates obtained have not typically been very intimidating. The combined stressors of hospitalization, anesthesia, and surgery presumably contribute significantly, but the progression and deterioration have been relentless and the patient's demise inevitable.



• **Fig. 4.30** Necropsy view of lungs affected by peracute rapidly consolidating *Mannheimia haemolytica* pneumonia. Consolidation exists in over 80% to 90% of the lung parenchyma, and fibrin is obvious on the visceral pleura. The clinical course of the disease was 36 hours.



• **Fig. 4.29** Cow affected with severe *Mannheimia haemolytica* pneumonia showing open-mouth breathing, pulmonary edema froth at muzzle, an anxious expression, dehydration, and an extended head and neck to maintain a "straight line" upper airway.



• **Fig. 4.31** Radiograph of a neonatal Holstein calf that underwent general anesthesia and laparotomy at 7 days of age. Radiography was obtained 36 hours after anesthesia and demonstrates marked, diffuse consolidating bronchopneumonia that was ultimately fatal by 48 hours after surgery.

Diagnosis

As with *P. multocida* pneumonia, accurate diagnosis of *M. haemolytica* bronchopneumonia requires culture of the organisms from tracheal wash specimens or bronchoalveolar lavage (BAL) fluid collected from acute, untreated cattle (Figs. 4.32 and 4.33), or postmortem cultures of lung and lymph node specimens. Because mortality is greater for *M. haemolytica* than *P. multocida*, necropsy specimens will often be the source of diagnostic material.

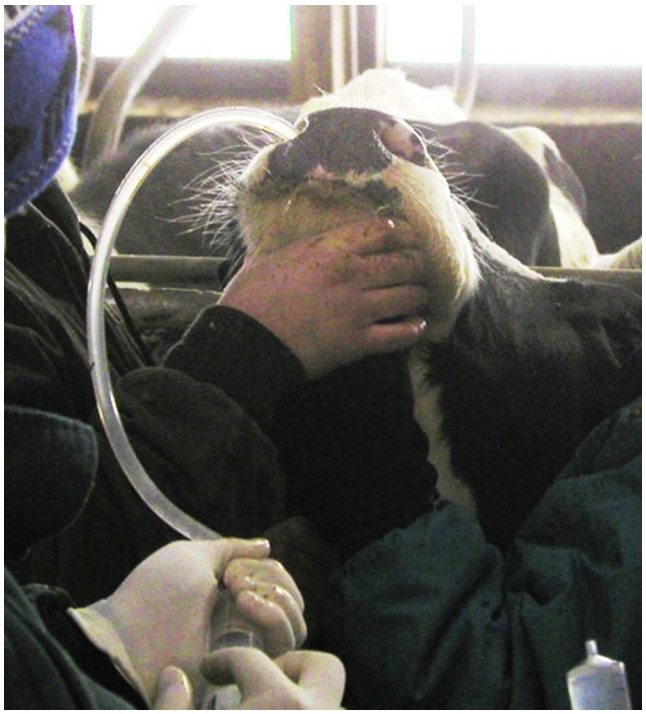
When it is apparent that the disease is epidemic in the herd, the veterinarian should obtain appropriate cultures via diagnostic fluid samples or fresh lung tissue at necropsy from several animals so that the delay in accurate diagnosis and receiving information regarding bacterial susceptibility to antibiotics is as short as possible. Tracheal wash; nasopharyngeal swab; BAL fluid; or necropsy specimens also should be cultured, submitted for polymerase chain reaction (PCR), or antigen tested for viral pathogens, *H. somni*, and *Mycoplasma* spp. Serum for viral titers should be collected from several acute cases so that it may be compared with convalescent serum titers in the future if the animals survive. In this way, some viral agents that are difficult to isolate, such as BRSV, may be identified as primary or contributing causes of the respiratory outbreak. Having collected these samples for culture, PCR, antigen testing, and evidence of seroconversion, the veterinarian will now have a basis, albeit retrospective, to identify the pathogens involved and attribute the disease to *M. haemolytica* alone or in combination with other pathogens. This will be of importance for future preventive measures.

Gross pathology specimens show a bilateral fibrinous bronchopneumonia with 25% to 75% or more of the lungs involved. The distribution is anterior/ventral in all cases, and the affected lung is firm, meaty, friable, and discolored. Usually fibrin is present on both the visceral and parietal pleura. Increased amounts of yellow or yellow-red pleural fluid are found frequently. In acute cases with advanced pulmonary parenchymal consolidation or in chronic cases, the dorsal lung may have bullous emphysema or interstitial edema present.

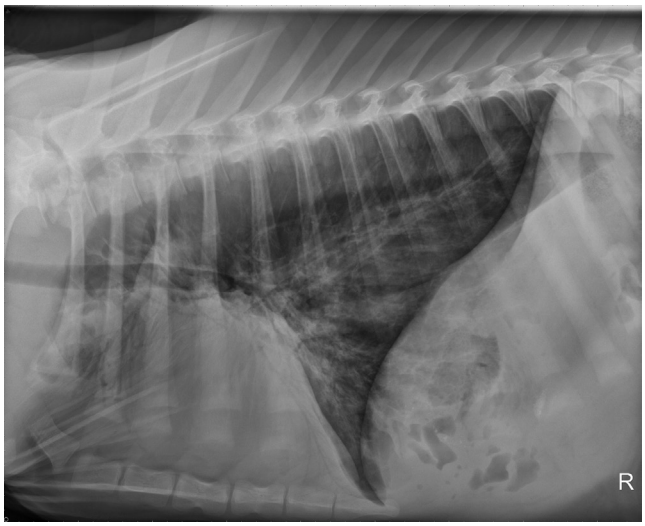
A complete blood count (CBC) from acutely infected cattle usually will show leukopenia characterized by a neutropenia with a left shift as neutrophils move to the site of severe infection. Fibrinogen values are elevated.

Diagnostic imaging has been historically of greatest value for prognosing an individual valuable calf or cow. An estimation of the degree of pulmonary consolidation and any abscess formation may be aided by either radiography (Fig. 4.34) or

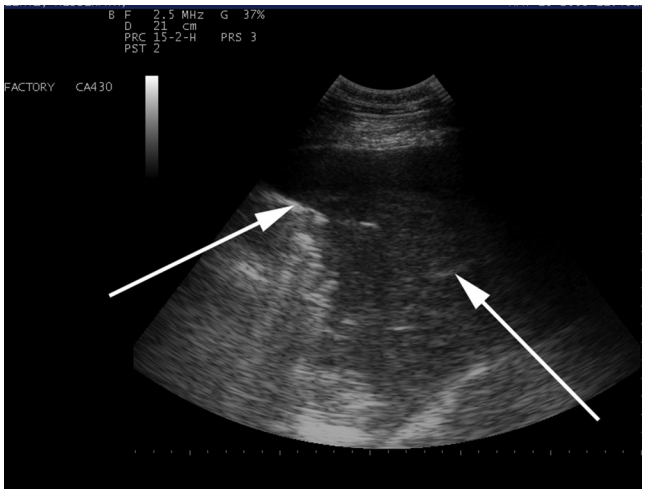
• **Fig. 4.32** A cow being restrained with two halters in preparation for a transtracheal wash. This method of restraint helps keep the head and neck straight during the procedure.



• **Fig. 4.33** Adult cow being restrained for a bronchoalveolar lavage (BAL) procedure. The neck is held in extension during passage of the BAL tube; the presence of the tube in the airway is easily detected by the paroxysmal coughing that is incited as the tube is passed distally from the trachea to the bronchi. (Courtesy of Dr. Sheila McGuirk.)



• **Fig. 4.34** Thoracic radiograph of 5-week-old Holstein calf recovering from mild bronchopneumonia associated with *Mannheimia haemolytica* infection. Moderate anteroventral consolidation is present as evidenced by air bronchograms cranial to cardiac silhouette. The calf made a complete recovery.



• **Fig. 4.35** Transthoracic ultrasound appearance of severe fibrinous pleuropneumonia associated with *Mannheimia haemolytica* infection. There is a large volume of variably echogenic free pleural fluid *(right arrow)* separating the ventral lung tip *(left arrow)* from the diaphragm and chest wall.

ultrasonography. Although ultrasonographic findings of lobular or lobar pneumonia and anteroventral consolidation can be seen with *M. haemolytica* infection, these are by no means specific to this organism and are seen in association with a number of other etiologic agents, especially other bacteria and *Mycoplasma*. However, if thoracic ultrasonography demonstrates significant pleural fluid and fibrinous pleuropneumonia in cattle with acute, highly febrile disease, then one's index of suspicion should be much higher for *M. haemolytica* (Fig. 4.35). Although less common in dairy than in beef animals, *H. somni* can also give a similar ultrasonographic appearance with fibrinous pleuropneumonia and free pleural fluid, as can severe *P. multocida* pneumonia.

Treatment

Broad-spectrum antibiotics constitute the major therapeutic approach to *M. haemolytica* pneumonia. Again, the veterinarian is forced to use "best guess" judgment when selecting an initial antibiotic in most cases. After collection of appropriate diagnostic samples, antibiotic therapy should commence immediately. Because life-threatening signs usually appear in at least some of the affected cattle, the veterinarian is more likely to select broad-spectrum antibiotics immediately. The currently available antibiotics for dairy cows and calves in the United States are shown in Table 4.1. Even when the causative bacterial organism is known, antibiotic therapy may be unable to cure the patient for a variety of reasons, such as the chosen antibiotic does not reach adequate tissue levels in the lung; the organism is resistant to the antibiotic; the organism is sensitive in vitro but in vitro inhibitory concentrations do not occur in the patient as a result of the dose, frequency of dosage, or other pharmacologic considerations; the drug may not be able to penetrate consolidated lung or work in purulent tissue; and in vitro susceptibility tests may not reflect in vivo success of an antibiotic against a specific organism. Consequently, the Kirby-Bauer disc assay has been criticized as too crude a test compared with mean inhibitory concentration (MIC) or bactericidal concentration tests that can give a concentration of drug that inhibits or kills an organism. This MIC value then can be compared with known achievable blood and tissue levels of the antibiotic in the patient to determine likelihood of successful treatment. In a recent pharmacokinetic study in six calves, plasma, interstitial fluid (ISF) and pulmonary epithelial lining fluid (PELF) concentrations of ceftiofur (using the ceftiofur crystalline-free acid formulation), enrofloxacin, tulathromycin, and florfenicol were measured in 6-month-old calves to determine the plasma pharmacokinetics of each drug and the likelihood that the drugs would attain levels in bronchial fluid or lung that are above the MIC for common bovine pneumonia pathogens. Based solely on the pharmacokinetic data and previously reported MICs for bovine respiratory pathogens, it was found that drugs such as florfenicol and ceftiofur with high PELF concentrations were expected to be effective in the control of respiratory disease, but those with high ISF concentrations, including enrofloxacin and florfenicol, may be more effective in treatment of active respiratory infections. It was hypothesized that the often reported clinical efficacy of tulathromycin could be related to its antiinflammatory properties. Textbook charts that quote percentages of isolates sensitive to various antibiotics are seldom helpful because both geographic differences in strains and temporal resistance patterns occur. In some instances failure of antimicrobial treatment may also be attributed to the fact that the pulmonary pathology is irreversible or viral, or that *Mycoplasma* spp. or *T. pyogenes* pathogens may coexist to complicate the treatment response. Appropriate withdrawal times for any antibiotic selected for milk and slaughter residues must be known and observed and may shape decisions by the producer as to which antibiotic is chosen so that an immediate slaughter option is maintained.

The industry continues to seek the "silver bullet"—a magic antibiotic that will cure all cases of *Mannheimia* and other bacterial pneumonias. This silver bullet would take away the need for diagnostic work or preventive medicine; excuse management techniques that predispose to pneumonia; and, of course, would only be available through veterinarians. As a profession, we persist in overuse of every new antibiotic that becomes available. We ask these antibiotics to do things that cannot be done while ignoring older time-tested antibiotics and corrective management advice. The silver bullet does not, and will not, exist.

A clinical improvement in response to appropriate antibiotic therapy will appear as better attitude and appetite and a decreasing fever within 24 hours. A decrease of 2°F (1.1°C) or more should be considered clinically indicative of improvement. The body temperature continues to decrease into the normal range over 48 to 72 hours in most cases that have been treated with appropriate antibiotics. Depending on which antibiotic is used, a minimum of 3 days of antibiotic coverage is often required, and more often 5 to 7 days of continuous therapy is necessary and less likely to result in recurrence.

Antiinflammatory medications are used by many veterinarians in conjunction with antibiotic therapy, as discussed in a subsequent section on *P. multocida* pneumonia.

TABLE 4.1 Dosages and Frequencies of Selected Antibiotics for Treatment of Respiratory Disease in Dairy Cattle

Antibiotic	Dose	Frequency	Age
Ceftiofur (as Naxcel)*	1.1–2.2 mg/kg IM or SC	Once daily for 3 days; additional treatments on days 4 and 5 are permitted if response is incomplete	Adult cattle and replacement heifers
Ceftiofur (as Excenel RTU EZ)*	1.1–2.2 mg/kg IM or SC	Once daily for 3 days; additional treatments on days 4 and 5 are permitted if response is incomplete	Adult cattle and replacement heifers
Ceftiofur (as Excenel RTU EZ)*	2.2 mg/kg IM or SC	Every other day for two treatments (48 h apart)	Adult cattle and replacement heifers
Ceftiofur (as Excede)*	6.6 mg/kg in posterior of ear	Once; can be repeated in contralateral ear in 72 h	Adult cattle and replacement heifers
Oxytetracycline HCl alone or in combination with sulfadimethoxine	11 mg/kg IV	Twice daily; use only in well-hydrated cattle	Adult cattle and replacement heifers
Florfenicol (as Nufluor)	20 mg/kg IM (neck only)	Repeated after 48 h	Replacement heifers; not in animals >20 months of age
Florfenicol (as Nufluor or Nufluor Gold)	40 mg/kg SC (neck only)	Single treatment or for control in high-risk cattle	Replacement heifers; not in animals >20 months of age
Florfenicol with flunixin (as Resflor Gold)	40 mg/kg SC (neck only)	Single treatment	Replacement heifers; not in animals >20 months of age
Ampicillin	5–11 mg/kg IM (often used at up to twice this dose in an extralabel manner)	Once daily for up to 7 days	Adult cattle and replacement heifers
Enrofloxacin	7.5–12.5 mg/kg SC	Single treatment	Replacement heifers; not in animals >20 months of age
Enrofloxacin	2.5–5 mg/kg SC	Once daily for 3 days; may repeat on days 4 and 5 if response is incomplete	Replacement heifers; not in animals >20 months of age
Tilmicosin	10–20 mg/kg SC	Single treatment or for control in high-risk cattle	Replacement heifers; not in animals >20 months of age
Tulathromycin	2.5 mg/kg SC in neck	Single treatment	Replacement heifers; not in animals >20 months of age
Gamithromycin	6 mg/kg SC in the neck	Single treatment	Replacement heifers, not in animals >20 months of age and not in dairy veal calves

*All ceftiofur use in the United States must conform strictly to the product license label; no extralabel use is permitted.
IM, Intramuscular; IV, intravenous; SC, subcutaneous.

If corticosteroids are used as part of initial therapy, we believe that 20 mg of dexamethasone or a comparable dose of prednisone for an adult cow is the maximum. This should not be used more than once, and it should not be used at all in pregnant cattle. Currently in our clinics, we do not use any corticosteroids in the treatment of *M. haemolytica* pneumonia. Flunixin meglumine or other nonsteroidal antiinflammatory drugs (NSAIDs) are sound therapeutic agents for use in *M. haemolytica* pneumonia for the first 1 to 3 days of therapy. Excessive doses of NSAIDs or prolonged treatment with these agents should be avoided. Again, aspirin is the safest drug for this purpose (at a dosage of 240–480 grains orally twice daily for an adult cow or 25 grains/100 lb body weight twice daily for calves). Flunixin meglumine at 0.5 to 1.1 mg/kg is the most commonly recommended and only approved NSAID for treating bovine pneumonia and has been documented to improve clinical outcomes when combined with antibiotics compared with antibiotic treatment alone. We do not routinely use the high end of the labeled dose for flunixin (2.2 mg/kg) because of concerns over gastrointestinal (GI) side effects; however, other colleagues feel differently and are prepared to administer it at least once at this dose in the treatment of a critically ill patient.

Antihistamines such as tripelennamine (1 mg/kg twice or thrice daily) are less commonly used these days but are still

used by many experienced clinicians as supportive therapy. Atropine may be a useful adjunct in advanced cases showing marked dyspnea, open-mouth breathing, or pulmonary edema. Atropine is used at 2.2 mg/45 kg body weight IM or SC twice daily to decrease bronchial secretions and to act as a mild bronchodilator.

In severe cases, dehydration may be a complication because of toxemia and fever causing depression of appetite and water consumption. In addition, some cattle are so dyspneic that they are unable to take time to drink, lest they become more hypoxic. Any IV fluid therapy that excessively expands the intravascular volume may cause or worsen existing pulmonary edema, consequently the fluid volume administered must be appropriate. Administering fluids through a stomach tube is safer regarding pulmonary edema, but the procedure is very stressful to an already hypoxic and dyspneic animal. Clinical judgment is required for these decisions, and in most cases, it is best to hope that antibiotic therapy will improve the animal within 24 to 48 hours so that the cow or calf may hydrate itself through adequate water consumption. Adequate water and salt, and small amounts of fresh feeds should be used to promote appetite.

Any management or ventilation deficiencies should be remedied immediately, and fresh air is of the utmost importance. It is better that the animals be in the cold fresh air than in a poorly ventilated or drafty but warm enclosure. The worst environmental effects occur when cattle develop *M. haemolytica* pneumonia during hot, humid weather because the additional respiratory effort to encourage heat loss complicates existing hyperpnea. Intranasal oxygen is beneficial for affected cattle being treated in a hospital.

The prognosis always is guarded until signs of clinical improvement are obvious. Cattle improving within 24 to 72 hours have a good prognosis, but those that take more than 72 hours have a greater risk of chronic lung damage or subsequent abscessation.

After endemic *Mannheimia* or *Pasteurella* infection in groups of calves, Drs. King and Rebhun observed occasional calves that developed peracute respiratory distress and dyspnea as a result of proliferative pneumonia 2 to 4 weeks after recovering from confirmed *Mannheimia* or *Pasteurella* pneumonia. At necropsy, resolving anterior ventral pneumonia from the previous *Mannheimia* or *Pasteurella* infection was observed in anterior ventral lung fields, and the remainder of the lung was diffusely firm, heavy, and wet. Histopathology in such cases confirms proliferative pneumonia. Viral cultures, fluorescent antibody (FA) procedures, and serology have been negative for other pathogens, including BRSV, which also may cause a delayed-effect hypersensitivity pneumonia but with different lesions. After observation of a number of these secondary proliferative pneumonia cases in the necropsy room, they were able to clinically recognize and treat several calves with this problem. The calves had a history of being part of a pneumonia outbreak 2 to 4 weeks previously and then apparently recovering. A sudden onset of extreme dyspnea in one recovered calf typifies the clinical situation. Signs include mild fever, open-mouth breathing, and diffusely quiet lungs. The cause of this disorder is unproven, although increased exposure of the dorsal lung field to inhaled rumen gases after ventral consolidation has been proposed. Treatment consists of atropine (2.2 mg/45 kg twice daily), furosemide (25 mg/45 kg once or twice daily), broad-spectrum antibiotics, and box stall rest in a well-ventilated area. Response to therapy is slow, but survivors gradually improve over 7 to 10 days.

Vaccination of dairy cattle against *M. haemolytica* is performed in many dairy herds, although proof of efficacy is not always agreed upon. A leukotoxin bacterin is most commonly used and will result in serum antibodies against one of the *Mannheimia* leukotoxins. One recent study in calves demonstrated efficacy of a modified live virus (MLV) vaccine combined with the *Mannheimia* leukotoxin antigen in protecting calves challenged with *Bibersteinia trehalosi*, a gram-negative pathogen similar to *Mannheimia* spp. that also has a leukotoxin gene.

Pasteurella multocida

Etiology and Signs

P. multocida is a gram-negative normal inhabitant of the upper airway of cattle and calves. The normal defense mechanisms of the lower airway prevent colonization of the lung by *P. multocida* via physical, cellular, and secretory defenses in the healthy state. *P. multocida* is, however, a likely opportunist any time lower airway defense mechanisms are compromised. Chemical damage to mucociliary clearance, such as is caused by ammonia fumes in poorly ventilated barns, may allow *P. multocida* the opportunity to colonize the lower airway. *P. multocida* also is found in mixed infections of the lung along with *M. haemolytica*, *H. somni*, *T. pyogenes*, *Mycoplasma* spp., and various respiratory viruses of cattle. *Fusobacterium* and other anaerobic organisms may also be concurrently present in chronic suppurative pneumonia of adult cattle. As a general rule, the more chronic the pneumonia in cattle, the more likely *T. pyogenes* is involved.

The strains of *P. multocida* isolated from the lungs of cattle or calves frequently are sensitive to many antibiotics, including penicillin. This is in definite contrast to *M. haemolytica*, in which antibiotic resistance is much more probable. This difference is important regarding treatment and prevention of *P. multocida* pneumonia.

The signs of acute *P. multocida* pneumonia include fever, depression, mild to severe anorexia, a moist cough, increased rate and depth of respiration, and a decrease in milk production commensurate with the degree of anorexia. The fever ranges from 103.5° to 105.5°F (39.72° to 40.83°C) in most cases. Moist and dry rales will be auscultated in the anterior ventral lung field bilaterally and are classical findings in acute cases. Usually the dorsal lung fields are normal. Nasal discharge may be serous or mucopurulent in nature and is more apparent in calves than adult cows. The acute disease may occur in cattle of any age but tends to be more common in weaned calves and other grouped animals. When seen in younger animals, the acute disease usually is indicative of poor ventilation, excessive ammonia fumes, failure of passive transfer of immunoglobulins, or part of a

diarrhea–pneumonia complex. All of these predisposing factors are common in dairy calves placed in veal operations or other indoor group housing facilities. *P. multocida* has been found as the cause of neonatal septicemia in calves receiving inadequate colostrum. These septicemic calves may show signs of meningitis, septic uveitis, septic arthritis, septic pericarditis, septic myocarditis and mucopurulent nasal and ocular discharge (Fig. 4.36) in addition to the typical signs of acute *P. multocida* pneumonia.

Acute *P. multocida* pneumonia tends to occur as either an infectious epidemic or endemic disease in groups of housed calves or adult cattle and may affect 10% to 50% of the animals within a group. It is one of the causes of "enzootic pneumonia" in calves, but this is not the preferred term because it gives little information as to the exact cause of the pneumonia. During an acute outbreak, the degree of apparent illness and auscultatable degree of pneumonia will vary greatly among affected cattle or calves. If only one animal in a group is infected, predisposing causes or stress unique to that animal should be sought when establishing a history (e.g., recent purchase, recent calving, possibility of BVDV-persistent infection [Fig. 4.37], transport to a show, sale, or poor ventilatory management).

Chronic pneumonia resulting from *P. multocida* causes signs similar to the acute disease, but bronchial tones indicative of consolidation are frequently limited to the anterior ventral lung fields. The abnormal area may be missed unless the stethoscope is pushed under the shoulder and the calf or cow forced to take a deep breath. In calves this can be accomplished most easily by holding the mouth and nose shut for a short period (Fig. 4.38). Transthoracic ultrasound can also be extremely helpful in the identification of consolidated bronchopneumonic lung lesions (Fig. 4.39; see Video Clip 4.8). Animals affected with chronic pneumonia may have marked exacerbation of dyspnea and an increased respiratory rate (≥60 breaths/min) if housed in poorly ventilated areas or where the environmental temperature exceeds 70.0°F (21.1°C). *T. pyogenes* is a common secondary invader in lungs chronically infected with *P. multocida*.

Diagnosis

P. multocida pneumonia may be suspected after obtaining the appropriate history from the owner and finding typical signs complete with anterior ventral pneumonia and bilateral auscultatable rales. However, confirmation requires culture of *P. multocida* from tracheal wash samples, BAL fluid, or necropsy specimens of acute, untreated affected animals. Neutrophils predominate the white blood cell components of the tracheal wash or BAL fluid, and gram-negative rods may be observed intracellularly in acute cases. The hemogram may show a degenerative left shift typical of acute infection in cattle or may be normal in mild cases. Chronic cases (≥2 weeks) may have neutrophilia, and adult cattle may show hyperglobulinemia in the serum. Many of these more chronic bronchopneumonia cases, especially adult cows with chronic suppurative pneumonia, may have

• **Fig. 4.37** This 3-year-old Jersey bull at a stud facility developed *Pasteurella multocida* pneumonia without any environmental stress factors. The bull was later proven to be persistently infected with bovine viral diarrhea virus, which likely resulted in immunosuppression.

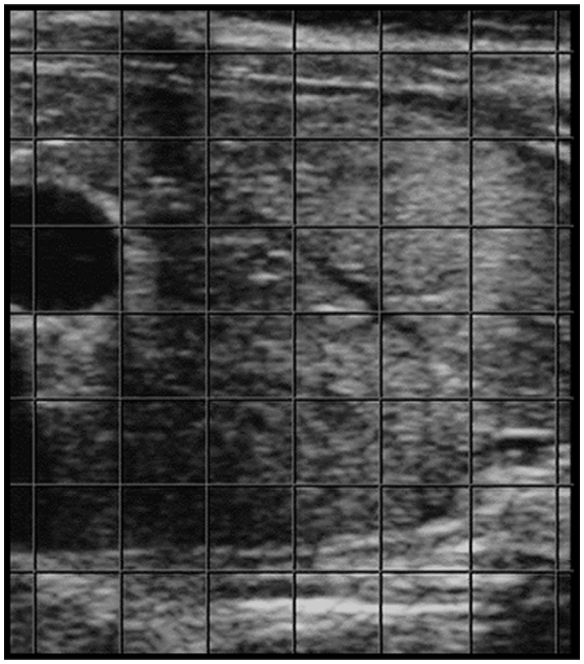
• **Fig. 4.36** Neonatal calf with *Pasteurella multocida* septicemia. In addition to pneumonia, signs included fever, hypopyon, and mucopurulent nasal and ocular discharges.

• **Fig. 4.38** An easy method of properly auscultating the lungs in calves. To make the calf breathe deeply, the calf is backed into a corner and one hand is placed over the mouth and nose until the calf struggles, at which time the calf is allowed to breathe. Alternatively, in adult cows, a plastic garbage bag can be used over the cow's nose and mouth to force deep breathing.

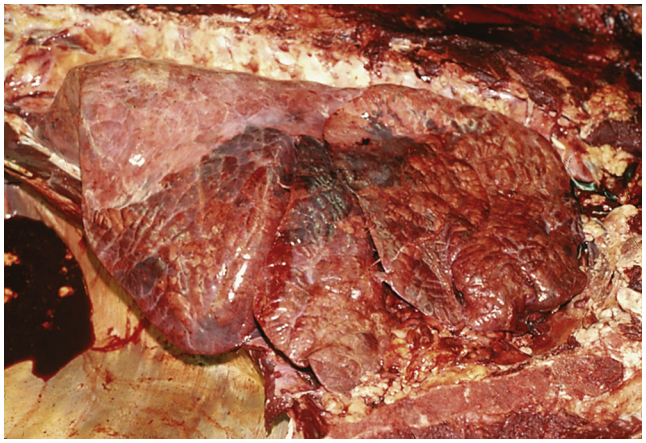
mixed infections etiologically with both *T. pyogenes* and *Mycoplasma* spp. commonly co-isolated or demonstrated by PCR.

Gross pathology of fatal acute cases includes bilateral anterior ventral pneumonia with the affected portion of lung being firm and discolored red or blue (Fig. 4.40). Palpation of the firm affected lung is the key to gross pathologic diagnosis. Fibrin may coat the surface of the parietal or visceral pleura but tends to be less than that observed with *M. haemolytica*. Chronic cases show similar firm, pneumonic lung parenchyma but often have bronchiectasis and pulmonary abscesses.

Radiographs seldom are necessary but may be helpful for individual, chronically infected calves or mature cattle to identify abscesses and the degree of consolidation for prognostic purposes. Ultrasound examination helps define the severity of lung involvement and can be used to monitor response to therapy.



• **Fig. 4.39** Ultrasound image of severe consolidating bronchopneumonia in a calf. Note that tissue has a solid "hepatized" appearance rather than the normal pleural reverberations seen with a healthy aerated lung.



• **Fig. 4.40** Necropsy findings in a calf that was affected with severe cranioventral pneumonia caused by *Pasteurella multocida*.

Treatment

Antimicrobials and changes in husbandry or management constitute the integral components of effective therapy for *P. multocida* pneumonia. Many antibiotics have been used, including penicillin, ampicillin, erythromycin, and tetracycline. Sulfa drugs (trimethoprim–sulfa has been used in calves because it can be individually mixed with milk to bypass the forestomachs) also have been effective when administered either alone or in combination with antibiotics such as penicillin or tetracycline. Ceftiofur, a broad-spectrum third generation cephalosporin approved for use in *Pasteurella* pneumonia in cattle, can be effective when the isolate is susceptible, which is frequently the case with *P. multocida,* and often the case with *M. haemolytica,* and *H. somni*. However, the increasing prevalence of *Mycoplasma* spp. co-infection in calves with bovine respiratory disease (BRD), for which the cephalosporin group is ineffective (along with other β-lactams such as penicillin and ampicillin), means that ceftiofur has become less relevant as a first-line antimicrobial choice. Macrolides (tulathromycin, tilimicosin, tildipirosin, gamithromycin), enrofloxacin, and florfenicol have become the most common first-line antibiotics for the treatment of undifferentiated BRD in dairy calves. The practicing veterinarian must often start antibiotic therapy without knowing results of cultures and antibiotic sensitivity tests. Therefore initial treatment is based on previous experience, geographic differences in antibiotic sensitivity, and economic factors. Animals that are febrile, anorectic, and dyspneic require treatment. Other animals that have mild fever and depression but continue to eat and do not act very ill may not require treatment. Individual or small groups of sick animals may be treated empirically if fatalities are not anticipated. However, if an epidemic situation is apparent, it always is best to do transtracheal washes from several animals before any treatment. Having done this, the veterinarian may start empiric therapy cognizant that definitive antibiotic sensitivity results will be forthcoming in about 3 days. It should be mentioned here that although transtracheal washes are recommended as part of a good diagnostic "workup," clinical response to antibiotics does not always correlate with in vitro susceptibility tests. For example, we have attended several calves with severe chronic pneumonia that had been treated with macrolides, β-lactams, and fluoroquinolones with no response but when treated with IV tetracycline and intramuscular penicillin and housed in a well ventilated hospital environment responded remarkably well, often despite in vitro resistance of the pathogen to these drugs (see Video Clips 4.9A and B). The macrolides, fluoroquinolones, and florfenicol all have a spectrum of activity in lung tissue that includes gram-negative organisms such as *P. multocida*, *M. haemolytica,* and *H. somni* as well as efficacy against *Mycoplasma* spp., and hence they represent sound empiric choices

until individual isolate sensitivities are known. Thus, if the animals fail to respond to the initial choice of antibiotic, an alternative, specific antibiotic may be selected based on the sensitivity results as soon as these are available. Strict attention to responsible antimicrobial use, and adherence to federal regulations regarding not only drug withdrawals but also the requirements of the American Medicinal Drug Use Clarification Act (AMDUCA) are critical duties of the veterinarian. Within the United States, veterinarians and producers must be particularly aware of the defined dose, route, and duration restrictions for cephalosporin use in all dairy cattle, alongside the categoric requirement that enrofloxacin only be administered to calves younger than 20 months of age with respiratory disease. The necessity for intravenous administration when using flunixin in lactating cattle is another emphatic requirement in the United States; unfortunately, flunixin has become one of the most common violative tissue residues in cull dairy cows at many slaughter plants because of on-farm perivascular and non-intravenous parenteral administration.

There is, however, a combination injection containing flunixin and florfenicol that is available and labeled for SC administration in nonlactating cattle younger than 20 months of age, but a stand-alone injection of flunixin must always be given IV. Dosages and frequency of administration of the commonly used antimicrobials used to treat pneumonia in cattle are listed in Table 4.1. Regardless of the antibiotic selected, all treated cattle should have temperature and attitudes recorded daily so that 24- and 48-hour evaluations can be assessed. A trend of decreasing temperature into the normal range should proceed at 1° to 2°F per day when an effective antibiotic is used; the attitude, appetite, and degree of dyspnea should improve along with the return to normal body temperature. There has been extensive work done in feedlot cattle examining the efficacies and economics of various antibiotics in pneumonia outbreaks and although this can provide valuable information, dairy practitioners must remember that geographic variations in bacterial serotypes and antibiotic susceptibility exist and that antibiotic resistance is likely to increase in the years to come. Individual treatment generally is easier for dairy animals than for beef animals.

Treatment decisions and the process by which antimicrobial selections are made necessarily differ between adult cattle and calves, especially on larger facilities. Increasingly in calves, on-farm protocols such as the Wisconsin and California clinical scoring systems are used as health screening tools (see later section) that operators can use to identify individuals with an aggregate of physical examination findings that may justify treatment. The specificity of these clinical scoring systems is high, but sensitivity is much lower for individual calf pneumonia detection. These are commonly used for periodic assessments of large groups of calves and have been principally developed with the goal of improving early identification of disease and reflect efforts to diminish the impact of BRD on preweaning heifer morbidity and mortality. Hopefully, individual or groups of adult cattle with either acute or chronic bronchopneumonia caused by *P. multocida* would not escape diagnosis because of their clinical signs. Such oversight would be even less likely with *M. haemolytica* because of the greater clinical severity typically seen with this agent. However, timely diagnosis is a ubiquitous and omnipresent challenge in adults as well as calves with milder clinical illness. In adult dairy cattle, the increased observation and daily examination often afforded to recently postparturient cows means that nasal discharge, cough, fever, and tachypnea are all likely to be picked up quite promptly. Indeed, one must be careful not to attribute a diagnosis of pneumonia too frequently merely on the basis of fever and tachypnea, as is quite common. Unfortunately, pneumonia can become a default diagnosis in febrile adult cattle that are breathing faster than normal when the latter is only a physiologic response to true fever of any cause or indeed hyperthermia that may be environmental in origin during hot weather. Identification of mild respiratory disease in dairy cattle beyond the fresh pen can be a challenge. Observation of feeding behavior and monitoring daily milk weight deviations become the tools by which cows beyond early lactation can be identified for further examination, but dry cattle are most easily overlooked on large dairies. We have been involved in several herd investigations of chronic bronchopneumonia in cattle in early lactation when it was highly probable that the onset of respiratory disease in many individuals occurred late in the previous lactation or during the dry period but was missed during the initial stages because of lesser oversight of cattle at these times. It is also worth emphasizing that such chronic bronchopneumonia "outbreaks" in adult cattle are rarely as simple as a single infectious agent that is a new pathogen to the farm; inevitably, the outbreak is multifactorial with components of overstocking, poor ventilation, and nutritional stressors during the transition period often contributing. There has never been, nor will there likely ever be, a replacement for experienced and devoted husbandry that invests time and watchful observation of the individual or groups of cattle for the identification of disease.

Many practitioners use antiinflammatory agents in conjunction with antimicrobial therapy. The goals of antiinflammatory medications are to reduce fever, block specific parts or mediators of the inflammatory cycle, and counteract endotoxins released by the cell wall of causative gram-negative organisms, to result in symptomatic improvement through better appetite and attitude. The two general groups of drugs include corticosteroids and NSAIDs such as aspirin and flunixin meglumine. Corticosteroids have a marked antiinflammatory and antipyretic activity that often leads to a "steroid euphoria" with resultant improved attitude and appetite within 24 hours. Although corticosteroids have these positive effects and also block several parts of the inflammatory cycle, they are dangerous if used repeatedly or in high dosages. Corticosteroids tend to stabilize small vessels and may reduce some of the chemotactic factors and lysosomal enzymes that cause a vicious cycle of increasing inflammation in the lung. However, they also partially or completely inhibit macrophage activation and antimicrobial

peptide expression, which are serious detriments to the defense mechanisms of the lower airway. If the veterinarian elects to use corticosteroids, one treatment of low-dose (10–20 mg/450 kg) dexamethasone may be given as part of the initial therapy and should not be used thereafter. This treatment cannot be used in pregnant cows because of the abortifacient qualities of dexamethasone. Corticosteroids have potent antipyretic properties, and this may lead to a false sense of security because the veterinarian may assume that the proper antibiotic has been used based on a decreasing fever 24 hours after treatment when in fact the antibiotic has not been effective, and fever will return 24 to 48 hours later. We do not recommend the use of corticosteroids for bacterial pneumonia.

Nonsteroidal antiinflammatory drugs are safer than corticosteroids in the treatment of bacterial bronchopneumonia in cattle but are not without some disadvantages. Advantages include blockage of some prostaglandin-mediated inflammation within the lung, antiendotoxin effects, and antipyretic activity. Disadvantages include inability to gauge response to specific antibiotics based on body temperature alone as a result of the artificial decrease in fever caused by NSAIDs and the possibility of toxicity manifested by abomasal ulceration or renal damage if treatment is excessive in frequency, dosage, or duration. Aspirin may be the safest of the commonly used NSAIDs in cattle and is given at 240 to 480 grains orally twice daily for an adult animal, but flunixin meglumine at 0.5 to 1.0 mg/kg IV once daily may be the most effective. Aspirin and flunixin meglumine have caused abomasal ulceration when administered for a prolonged time to sick cattle, especially if the animal remains inappetent and has diminished water intake for the duration of treatment. Renal toxicity also is a risk, especially in a dehydrated animal in which the cytoprotective and vascular effects of prostaglandins are essential during reduced renal perfusion. We prefer flunixin when NSAID therapy is selected, but these drugs are adjuncts, not essentials, for the treatment of bronchopneumonia caused by *P. multocida*.

Bronchodilators such as aminophylline have been used in cattle with pneumonia but do not appear to be beneficial clinically except when given by constant infusion (CRI) to calves with respiratory distress. Aminophylline at 5 mg/kg IV over 60 minutes repeated twice daily or 10 mg/kg as a 24-hour CRI can be of considerable benefit in the treatment of severely dyspneic calves with bronchopneumonia. Occasionally, we have used higher doses than this but they can be associated with excitement and agitation, which are obviously undesirable, so it may be helpful to start at this dose and incrementally increase according to tolerance and a demonstrated need by virtue of insufficient clinical response or unimproved blood gases. Aminophylline is well absorbed when given orally to cattle, but we have not had a consistent clinical response when it is given by this route. Atropine given parenterally or ipratropium by inhalation may also be effective bronchodilators. If albuterol could be used in cattle, it might be beneficial because this drug has been shown in other species to act not only as a bronchodilator but also to improve mucociliary clearance. Parasympatholytic bronchodilators have been shown to be more effective in calves than sympathomimetic drugs.

Antihistamines are used as adjunctive therapy in bovine bronchopneumonia by many practitioners. Drugs such as tripelennamine hydrochloride (1 mg/kg IM or SC twice or thrice daily) are believed to improve the animal's attitude and appetite. These symptomatic observations may be valid, but because histamine has not been shown to be one of the major inflammatory mediators in *Pasteurella* pneumonia, no scientific evidence exists to justify the use of these drugs.

The recognition and correction of management problems or ventilation deficiencies may be as important, if not more so, than any of the previous pharmaceuticals when treating endemic *P. multocida* pneumonia. Because the organism primarily is an opportunist that gains access to the lower airway after insults to the physical, cellular, or secretory defense mechanisms, predisposing causes should be sought and corrected. In calves, poor ventilation, crowding, and poor husbandry relating to excessive ammonia fumes may be sufficient to allow *P. multocida* to descend from its normal habitat of the upper airway and colonize the lungs. Examples include changeable temperature and humidity when calves are grouped during the indoor housing season (especially fall, spring, and during winter thaws), broken fans, failure to clean large pens when calves have been in groups for weeks to months, lungworms, and drafts that the confined calves cannot escape. Fresh air is vital to recovery and should be provided even if it means allowing the animals access to outside air in inclement weather.

In adult cattle, all of these factors apply, but ventilation deficiencies predominate. In modern free-stall facilities, transition cow management practices that add greater stress to an already changeable and stressful period appear to greatly impact the acquisition of acute pneumonia and progression to chronic disease. Frequent pen moves, overstocking, poor ventilation, and concurrent metabolic disease alongside some of the treatments and therapeutic practices used by producers all substantially increase the chances for postpartum respiratory disease to become a herd problem. Bronchopneumonia caused by *P. multocida* alone usually is a management problem. Although it certainly is recognized that previous viral infection or mixed infections (e.g., *Mycoplasma* spp.) can and do predispose to *P. multocida* pneumonia in calves and adult cattle, it must be emphasized that management factors are very important. Secondary *P. multocida* pneumonia, such as that following viral respiratory infection, will be discussed in conjunction with viral diseases. Failure of cattle affected with *P. multocida* pneumonia to respond to appropriate antibiotic therapy based on culture and susceptibility results should alert the veterinarian to the fact that; (1) *P. multocida* is not the only agent involved in the epidemic (i.e., a virus or *Mycoplasma* spp. also may be present or was present, so viral isolation, PCR, paired serology, and so forth are indicated), (2) the predisposing management or ventilation problems have not been corrected, and (3) lungworms should be ruled out.

Vaccination involving *P. multocida* is discussed later in the prevention section within this chapter.

• **Fig. 4.41** A 4-month-old heifer with *Histophilus somni* pneumonia. This heifer was one of several group-housed heifers of similar age with an acute onset fever, cough, and labored breathing. *H. somni* was the only pathogen identified on a tracheal wash sample. All of the heifers had clinical recovery after ceftiofur treatment. Clinical findings would be indistinguishable from those of *Pasteurella multocida* or mild *Mannheimia haemolytica* infection.

Histophilus somni

Etiology and Signs

H. somni has been identified as a pathogen of the lower airway in dairy cattle with increasing frequency. It is occasionally identified as the cause of herd outbreaks of pneumonia in dairy cattle or calves in the northern United States. *H. somni* may be the only pathogen isolated or may be found in conjunction with *Mycoplasma* spp. or *Pasteurella multocida* in diagnostic samples. Although *H. somni* occasionally is isolated from the upper airway of normal cattle as a commensal, this gram-negative organism can occasionally be isolated from the lungs or tracheal wash fluid of clinical pneumonia patients too. A shift in the normal upper airway bacterial flora, stress activation of latent *H. somni* in the upper airway, and factors that negatively impact upper and lower airway defense mechanisms may all contribute to lower airway infection.

The pathogenicity of both *H. somni* and *Mannheimia haemolytica* can be attributed to several shared characteristics: (1) An endotoxin derived from the cell wall lipopolysaccharides; (2) Exotoxins that are lethal or damaging to alveolar macrophages, neutrophils, and vascular endothelium; and (3) Chemotactic factors and possible hemolysins common to *H. somni* and other bacteria that act as inflammatory mediators. Vasculitis is a predominant feature of *H. somni* pathology. *H. somni*–stimulated platelets have been shown to contribute to endothelial cell damage, which may play a role in the pathogenesis of the vasculitis and thrombosis. In addition, *H. somni* has a propensity to cause disease in the heart muscle and sometimes the central nervous system. Involvement of the latter two organ systems appears to be considerably more common in beef cattle than in dairy.

The signs of *H. somni* bronchopneumonia in calves (Fig. 4.41) and adult cattle are indistinguishable from moderate to severe *P. multocida* pneumonia or mild to moderate *M. haemolytica* pneumonia. Affected animals have fever (103.5° to 106.6°F [39.72° to 41.44°C]), an increased respiratory rate (40–80 breaths/min), depression, nasal discharge, occasional hypersalivation, painful cough, and decreased milk production proportional to the degree of anorexia observed. Dyspnea may be marked in some cases, and these cattle will show anxiety and reluctance to move. Neurologic signs or septicemia caused by *H. somni*, as observed in feedlot animals, is less common in dairy cattle and calves. One reason for this may be that most pneumonia in dairy calves occurs within the first 3 months of life and the neurologic form of *H. somni* only affects cattle older than 4 months of age. If, however, any cattle develop neurologic signs during an outbreak of bronchopneumonia in a herd or group of calves, *H. somni* should be strongly suspected as the cause of the illness.

Auscultation of the lungs typically identifies bilateral anterior ventral pneumonia characterized by moist and dry rales, and bronchial tones indicative of ventral consolidation can be found in up to 50% of cases. Tracheal rales may be auscultated as a result of the heavy mucopurulent exudate found in the trachea. Palpation of the intercostal spaces (ICSs) overlying the pneumonic regions may be painful to the animal.

Diagnosis

Because the signs usually are similar to those of *Pasteurella* and *Mannheimia* pneumonia, the veterinarian should collect appropriate samples (tracheal washes for bacterial culture and antimicrobial sensitivities, or necropsy cultures from lung and lymph nodes) and institute therapy. A failure of response to standard broad-spectrum antibacterial therapy typifies *H. somni* pneumonia. Usually an exact diagnosis as to etiology has to await culture and sensitivity results from diagnostic samples. CBCs are variable and nonspecific, with either a degenerative or regenerative left shift observed and elevated fibrinogen levels. Acute and convalescent serum may be helpful retrospectively if the diagnostic laboratory used for testing has the capability to establish *H. somni* titers.

Postmortem specimens will show firm anteroventral areas of pneumonia bilaterally. Fibrin may be apparent in the visceral and parietal pleura overlying the areas of pneumonia. In some cases, red blotches or hemorrhage are apparent. White microabscesses may be observed also.

Treatment

Although *H. somni* apparently is sensitive in vitro to many antibiotics, including penicillin, clinical results in vivo have been discouraging. Ampicillin and ceftiofur have been commonly used for *H. somni* pneumonia in calves and adult cattle. Ampicillin is used at 11 to 22 mg/kg twice daily by injection for 3 to 7 days in most cases. Just as with *P. multocida*, the increasing likelihood of *Mycoplasma bovis,* or other *Mycoplasma* spp. being involved in undifferentiated BRD and the lack of β-lactam efficacy against this group of organisms may mean that veterinarians preferably select a different first choice antibiotic, such as a macrolide, enrofloxacin, or florfenicol, depending on signalment. Enrofloxacin reportedly has good efficacy against *Histophilus* spp. but currently is not approved for use in lactating dairy cattle in the United States; however, it can be used in calves less than 20 months of age. There are no reports of arthropathy in young calves treated with enrofloxacin. In a recent *H. somni* experimental inoculation metaphylactic study, tildipirosin was superior to tulathromycin.

Response to effective antibiotics will be manifested by a progressive decrease in body temperature to the normal range over 24 to 72 hours. For this reason, the treating veterinarian may find it best not to use NSAIDs or corticosteroids in patients with *H. somni* pneumonia because these drugs decrease the temperature artificially through antipyretic effects and interfere with interpretation of appropriate antibiotic selection.

Just as in *Pasteurella* bronchopneumonia, ventilation or management factors that predispose to altered lower airway defense mechanisms should be corrected immediately. The prognosis is fair to good unless severe pneumonia and marked dyspnea are present.

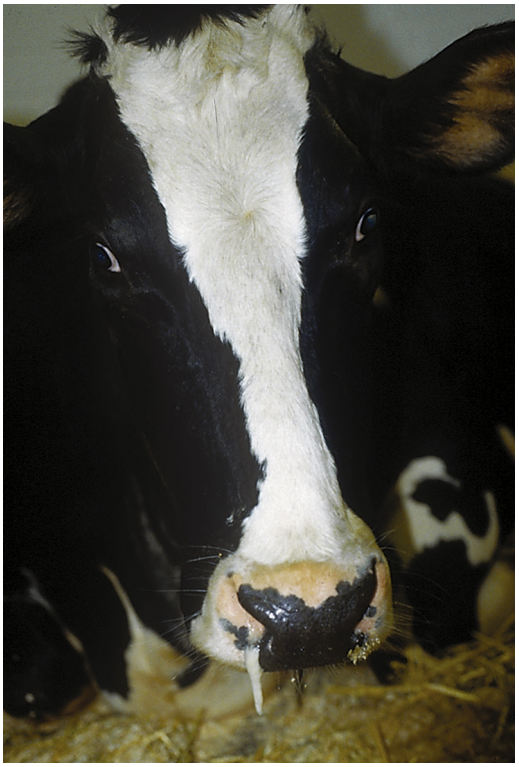
Trueperella pyogenes: Chronic Suppurative Pneumonia

Etiology and Signs

T. pyogenes is a gram-positive coccobacillus that acts as a ubiquitous opportunist capable of establishing chronic pyogenic infections virtually anywhere in the bovine body. In the lung, it is a secondary invader that usually only establishes infection after suppression of host physical, cellular, or secretory defense mechanisms or as an opportunist that colonizes areas of necrosis such as can occur in the lung after infection with any one of several other infectious agents. Physical factors such as inhalation pneumonia also may allow *T. pyogenes* to infect the lung, and viral, bacterial, or *Mycoplasma* agents may precede infection with *T. pyogenes*. Immunosuppression caused by acute or persistent infection with BVDV has been followed by *T. pyogenes* pneumonia in calves and adult cows. Similarly, calves affected with bovine leukocyte adhesion deficiency (BLAD) frequently have *T. pyogenes* pneumonia. Pulmonary infection is aided by the proteases and hemolysins that the organism produces. These factors contribute to tissue necrosis and inflammatory events that perpetuate the organism's existence. *Fusobacterium* and other pathogenic anaerobic organisms may also be found concurrently with *T. pyogenes, P. multocida,* and *Mycoplasma* spp.

Signs are indicative of chronic or recurrent infection, the hallmark of *T. pyogenes* pneumonia. The history usually indicates illness of at least 1 week's duration or recurrent episodes of pneumonia over weeks to months. There may only be one (usually adult cattle) or a few animals (usually calves) affected out of a group or herd. In adult dairy cattle, it seems particularly common for clinical signs to develop after freshening (Fig. 4.42). In some cases, there may be severe SC emphysema over the dorsum, suggesting a rupture of diseased alveoli associated with calving as a cause of pneumomediastinum, SC emphysema, and sometimes pneumothorax. Although chronic suppurative pneumonia should be considered in cattle with dorsal emphysema after calving, similar emphysema may be found sometimes in apparently healthy cattle after calving and, of course, in cattle with interstitial pneumonia. Bullous emphysema and pneumothorax are most commonly associated with BRSV infection of both adults and calves in the United States, but severe, chronic bronchopneumonia with involvement of *T. pyogenes* and extensive ventral consolidation is another common cause of these signs in adults. Affected animals may show low-grade fever (103.0° to 105.0°F [39.44° to 40.56°C]), rapid respiratory rate (40–100 breaths/min), dyspnea characterized by exaggerated inspiratory and especially expiratory efforts (particularly when stressed), head and neck extension when lying down, cough, nasal discharge (Fig. 4.43), rough hair coat, poor body condition (Fig. 4.44), depression, inappetence, or decreased milk production. Some cattle maintain normal respiratory rates but exhibit the other signs. Chronic

• **Fig. 4.42** A 5-year-old cow with cough and respiratory distress after calving 5 days earlier. The cow had chronic suppurative pneumonia with an acute onset of respiratory signs associated with the stress of calving.



• **Fig. 4.43** This mature Holstein cow presented to the hospital for poor production and weight loss. Although the respiratory rate was within normal limits, the cow coughed after rising; had slight head and neck extension when lying down; and, as seen in this photo, had small and intermittent purulent nasal discharge. *Pasteurella multocida*, *Trueperella pyogenes*, and *Mycoplasma* spp. were cultured from a tracheal wash. The cow improved dramatically after tetracycline therapy.

• **Fig. 4.44** **A,** Poor hair coat, hunched back, and ill-thriven appearance of a 3-year old Holstein cow with chronic suppurative pneumonia. **B,** Postmortem image of the thoracic cavity from the same animal showing marked consolidation ventrally (left side of the image) and adhesions to the chest wall.

suppurative pneumonia should always be considered a differential for the "poor doing" cow.

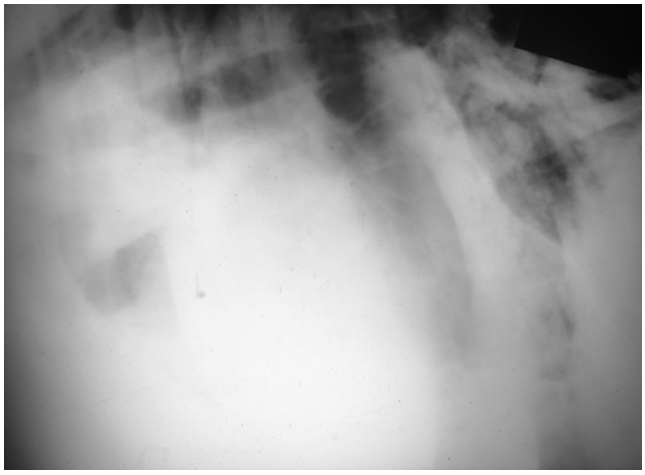
Auscultation of the lungs reveals moist and dry rales in the ventral 25% to 50% of both lungs in calves and one or both lungs in adult cattle, bronchial tones indicative of consolidation in the ventral lung fields, and coarse tracheal rales caused by a thick mucopurulent airway exudate. High environmental temperatures, high humidity, and poor ventilation exacerbate the clinical signs. A fetid smell may be present after a cough if anaerobic bacteria are present. Auscultation during rebreathing, paying close attention to the cranioventral lung fields under the triceps musculature for the presence of bronchial tones indicative of consolidation, is important when investigating possible cases of mild to moderate chronic suppurative bronchopneumonia.

Diagnosis

History and physical signs are very suggestive of *T. pyogenes* pneumonia, but specific diagnosis requires culture of the organism from tracheal wash samples or lung tissue. There may only be one or a few animals affected with signs of chronic pneumonia after a preceding herd endemic of pneumonia caused by other organisms. Chronic or recurrent cases are referred to as "lungers" by some farmers.

Radiography or ultrasonography of the thorax is helpful in establishing a prognosis because lung abscesses, bronchiectasis, and consolidation (sometimes remarkably severe in a single lobe) (Fig. 4.45) are common in the affected lung (see Video Clip 4.8). Because of its diagnostic utility in identifying consolidation and peripheral abscessation, thoracic ultrasonography can be of great value in the diagnosis of these lesions (see Video Clip 4.10). Attention should be directed toward the ventral and cranial ICSs of both hemithoraces.

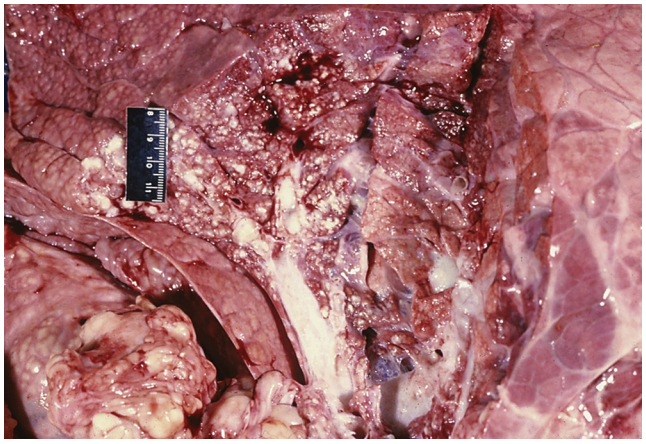
A CBC may show neutrophilia or be normal. Serum globulin often is in the high range of normal or elevated (>5.0 g/dL), especially in adult cattle. The animal should be screened for persistent infection with BVDV via buffy coat viral isolation or whole blood PCR particularly if only a single cow or calf in the herd is diseased. Gross necropsy of fatal cases reveals anterior ventral consolidation with areas of purulent bronchiectasis and multiple pulmonary abscesses (Figs. 4.46 and 4.47).



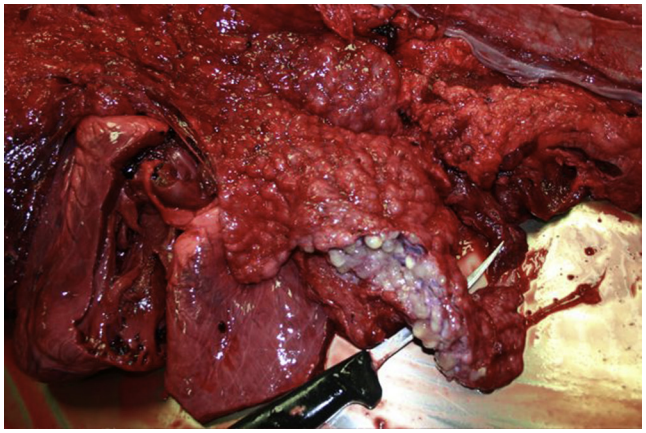
• **Fig. 4.45** Radiograph of a cow with chronic suppurative pneumonia and a dramatic lobar consolidation.

Treatment

Treatment is frustrating, and the prognosis is poor for patients with pneumonia caused by *T. pyogenes*. Other causative organisms such as *P. multocida, M. haemolytica, Mycoplasma* spp., or *Fusobacterium* also may be cultured from the tracheal wash sample. Specific to the involvement of *T. pyogenes,* penicillin is the drug of choice and should be given at 22,000 U/kg twice daily for 7 to 30 days. Although penicillin is effective against *T. pyogenes* in vitro, the in vivo pulmonary infection should be likened to an abscess because of the heavy accumulation of *T. pyogenes* pus in areas of bronchiectasis or encapsulated lung abscesses. If another pathogen, in addition to *T. pyogenes*, is isolated from the tracheal wash sample, appropriate antibiotic therapy should be selected for this organism as well.



• **Fig. 4.46** Necropsy view of cut section from the cranioventral lung region of a calf showing bronchiectasis and pulmonary abscesses typical of chronic *Trueperella pyogenes* pneumonia.



• **Fig. 4.47** Severe, chronic suppurative pneumonia with multiple, nodular *Trueperella pyogenes* abscesses throughout the right ventral lung from a mature Holstein cow with a history of chronic cough, recurrent fever and weight loss.

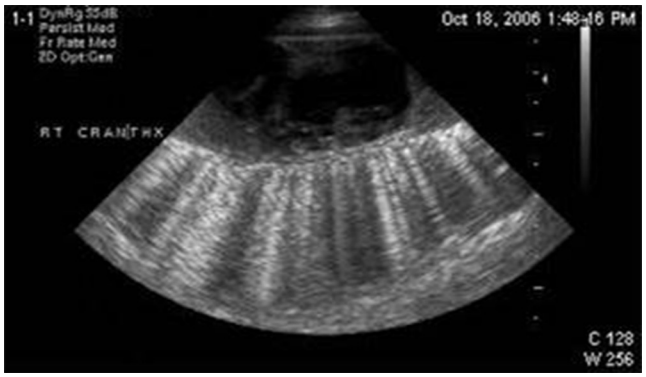
Ceftiofur, ampicillin, and tetracyclines are other commonly used therapies. Clinical treatment frequently results in short-term improvement followed by relapse, sometimes as distant as 1 year later, when the animal is stressed or subjected to high environmental temperatures, humidity, or poor ventilation. Signs of improvement will be indicated by a consistently normal rectal temperature, improved respiratory function, and improvement in overall body condition and attitude. Many affected animals eventually succumb to the infection or are culled because of poor condition and production.

Mycoplasma Pneumonia

Etiology and Signs

Several species of *Mycoplasma*, including *Mycoplasma dispar, M. bovis, Mycoplasma bovirhinis,* and others, have been isolated from the lungs of calves and cattle with pneumonia. In addition, *Ureaplasma* organisms and occasional isolates of *Mycoplasma bovigenitalium* have been found from lower airway infections in cattle. *M. dispar* and *M. bovis* probably are the two major types identified. These organisms may be normal inhabitants of the upper airway in some cattle. Experimentally, *Mycoplasma* spp. have caused pneumonia in calves when introduced either into the lower airway or via nasal inoculation. This pneumonia is characterized by peribronchiolar and peribronchial lymphoid hyperplasia and purulent bronchiolitis. Lesions usually are limited to the anterior ventral tips of the lung lobes, and the associated clinical signs are mild. Gross inspection at necropsy reveals ventral areas of lung lobes that are red-blue and firm, appearing almost as atelectatic areas, and that ooze purulent material from the airways on cut sections. *Mycoplasma* pneumonia has been described as a "cuffing pneumonia" because lymphoid hyperplasia appears around the airways and expands with chronicity. *Mycoplasma* organisms have several properties that contribute to their pathogenicity, including inhibition of the mucociliary transport mechanism (at least in humans). In addition, they cause some degree of humoral and cell-mediated immunosuppression in calves and they avoid phagocytosis by attaching to ciliated epithelium above the level of alveolar macrophages.

In our clinics, *Mycoplasma* frequently is isolated from acute and chronic calf pneumonia outbreaks and may be involved in up to 50% of chronic calf pneumonia endemics that we investigate. However, *Mycoplasma* spp. seldom is the only pathogen isolated in these outbreaks, and one or more of *H. somni, P. multocida,* and *M. haemolytica* usually are isolated as well. Because *Mycoplasma* appears ubiquitous on many farms, we wonder whether the *Mycoplasma* infection has been present in the calves' lungs for a long time and contributes to impaired host defense against bacterial and viral pathogens or whether the *Mycoplasma* infection is acute along with the other pathogens. It is also increasingly co-identified with *T. pyogenes* in cases of chronic suppurative bronchopneumonia. In herds with active *Mycoplasma* pneumonia, *Mycoplasma* frequently can be isolated via nasopharyngeal swab from the majority of cows and calves, most of which appear healthy. Therefore the ubiquitous nature of the organism makes it nearly impossible for calves on these farms not to become infected. The subsequent low-grade pneumonia and defense mechanism compromise caused by the *Mycoplasma* infection may precede the onset of clinical pneumonia associated with other bacterial and viral pathogens. How significant *Mycoplasma* spp. is to the entire problem is difficult to determine, but we believe it increases the risk of calfhood pneumonia. In addition to pneumonia, *M. bovis* may also cause otitis media, mastitis, and arthritis once it becomes established in a herd. The spread of *Mycoplasma* spp. can be significantly increased by the feeding of unpasteurized, infected waste milk. Effective control measures for *Mycoplasma* when it is ubiquitous on a premise are challenging and made more so because effective vaccines are not available. In endemic herds, the feeding of unpasteurized waste milk is a known risk factor for transmission of the organism to calves, and this practice should be actively discouraged. Pasteurization removes the risk of *Mycoplasma* spread by this means but only makes economic sense on larger dairies or heifer-rearing operations. When pasteurization is used, periodic quality control assessments by culture are very important to confirm continued equipment efficacy at removing viable *Mycoplasma* spp. from the milk being fed to the calves. Producers should never assume



• **Fig. 4.48** Ultrasound findings in the cranial thorax of a 4-month-old Holstein calf with a 2-week history of pneumonic signs and lameness of the left rear leg and marked swelling of the left rear stifle. The calf was euthanized because of a poor prognosis, and *Mycoplasma* spp. were cultured from the pleural fluid (seen above on ultrasonography) and the stifle joint.

that these pieces of equipment remain effective over long periods without checking.

Signs of pure *Mycoplasma* pneumonia may be very mild. In several calf and heifer outbreaks of pure *Mycoplasma* pneumonia, the only signs observed were coughing induced by stress or movement of the animals, a slight increase in the respiratory rate (40–60 breaths/min), and low-grade fever (103.5° to 105.0°F [39.72° to 40.56°C]). Most affected animals continued to eat and experienced only mild depression. Owners reported observing a slight mucopurulent nasal discharge in the animals in the mornings that disappeared after the animals became active, ate, and licked their noses clean. Tracheal washes grew pure cultures of *Mycoplasma*, and no other pathogens were identified by bacterial cultures, viral isolation, PCR, or retrospective paired serology. However, pure *Mycoplasma* is the exception rather than the rule because, in our clinics, *Mycoplasma* usually is isolated in conjunction with other pathogens in the majority of pneumonia outbreaks in which it is involved. Signs of pneumonia in these instances are identical to those described for the other specific bacterial or viral agents isolated. The *Mycoplasma* component does not have any unique clinical features except for its association with otitis media and arthritis in young cattle and perhaps that affected animals sometimes respond poorly to specific antibiotic therapy directed against the bacterial pathogen, especially when the selected antimicrobials have poor efficacy against *Mycoplasma* organisms. When this occurs, a contributory viral or *Mycoplasma* infection should always be suspected. Undoubtedly the association between *Mycoplasma* infection of the lower airways and involvement of this organism with otitis cases in heifer replacement calves preweaning is an increasingly strong one on many farms. It is currently much more common to see comorbid pneumonia and otitis than it is to see the arthritic form in this age of calf. The arthritic form seems to be more common in older, weaned heifers and bulls but can also coexist with the pneumonic form (Fig. 4.48).

Diagnosis

This is totally dependent on demonstration of the organism in diagnostic airway fluid or necropsy samples. The diagnostic emphasis in many laboratories has switched from culture of the organism to identification by PCR. Typically, the primers used are specific to *M. bovis,* but increasingly diagnostic laboratories use additional primer sets for non–*M. bovis* species, too. In pure *Mycoplasma* pneumonia, fatalities are rare, but typical gross lesions of *Mycoplasma* pneumonia appear as red-blue firm areas in the anterior ventral lung. These areas resemble atelectatic areas but are firm, and pus may be expressed from the airways within these firm areas on a cut section. Histopathology demonstrates the "cuffing pneumonia" previously described.

In most instances in which *Mycoplasma* is merely one component of infection, gross necropsy lesions are typical of the other pathogens—usually anterior ventral consolidating bronchopneumonia typical of *Mannheimia, Pasteurella,* or *Histophilus* infection or abscessation caused by *T. pyogenes*. Occasionally, *Mycoplasma* is obtained from lungs showing typical lesions of BRSV, BVDV, or other viral infections.

Treatment

Treatment for *Mycoplasma* pneumonia may be unnecessary in some pure *Mycoplasma* infections because the cattle do not appear extremely ill. In pure infections, oxytetracycline hydrochloride (11 mg/kg once or twice daily) was historically the "go to" antimicrobial, but there is increasing concern over resistance and a lack of clinical response with this antibiotic. Subsequently, other antimicrobial choices such as tulathromycin (2.5 mg/kg SC), florfenicol (20 mg/kg IM in the neck), erythromycin (5.5 mg/kg twice daily), and tilmicosin (10 mg/kg SC) or other macrolides may provide effective therapy in many cases. Enrofloxacin or other fluoroquinolones are reported to be the most effective antibiotic against *Mycoplasma*, but these are not approved for use in lactating dairy cattle in the United States. In vitro antimicrobial testing for *Mycoplasma* spp. is rarely performed or available. As a consequence, antibiotic selection is empiric but should be done mindful of the fact the β-lactams will not work.

When *Mycoplasma* is isolated along with *P. multocida*, *M. haemolytica*, *T. pyogenes*, *Fusobacterium* spp., or *H. somni*, antibacterial therapy should also address the other bacterial pathogens. If the *Pasteurella* or *Histophilus* isolate is sensitive to tetracycline or erythromycin, choosing one of these drugs may provide efficacy against both the bacteria and *Mycoplasma*. Fortunately, if treatment is directed against the bacterial pathogens and ventilation or management factors are corrected, the calves often recover and the *Mycoplasma* infection may not require specific therapy.

At our clinic, we have investigated several chronic heifer and postweaning calf pneumonia problems in which *Mycoplasma* and *P. multocida* or *Mycoplasma* and *H. somni* have coexisted. These problems have been very difficult to solve. In these herds, the *Mycoplasma* infection seems to be ubiquitous and seems to infect calves very early in life. Calf hutches and individual rearing of calves may not be effective in preventing *Mycoplasma* infection in some of these herds, but calf hutches do seem to prevent bacterial infection in the calves pre-weaning. Therefore, as soon as the calves are grouped after

weaning, a pneumonia outbreak is caused by both bacterial and *Mycoplasma* components. Every new group seems to be affected, and attempts at prevention appear futile. Isolation of calves to a separate farm after immediate removal from their dams may be the only solution. Other recommendations for prevention of *Mycoplasma* infection in calves include avoiding feeding *M. bovis*–infected milk, using separate feed buckets and bottles for every calf, housing with good ventilation, and preventing calves from direct contact with other cattle.

Bibersteinia trehalosi

In recent years, there has been increased attention given to this organism worldwide, more particularly for its role as a pathogen of small ruminants, especially sheep. Taxonomic reclassification of the organism from its previous allocation as a *Pasteurella* organism within the past decade has been followed by increased reports of the organism being cultured from diagnostic specimens obtained either ante- or postmortem from cases of BRD in dairy calves and adults in the United States. At the current point in time, its role as a primary pathogen is uncertain. Although it can undoubtedly be obtained from the lungs and lower airways of diseased dairy cattle, attempts to reproduce clinical respiratory disease experimentally via direct inoculation have usually been unsuccessful. Whether it can predictably behave as an opportunistic infectious agent of the lower airway, in a manner comparable to *P. multocida*, and clarification of its role in BRD, await further research.

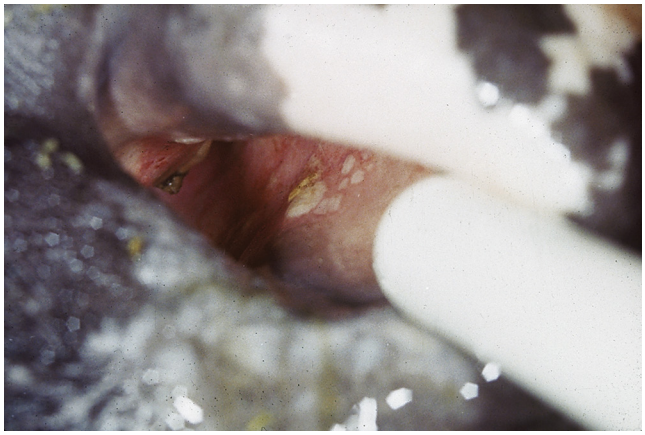
Viral Diseases of the Respiratory Tract

Infectious Bovine Rhinotracheitis

Etiology and Signs

Infectious bovine rhinotracheitis (also known as IBR, BHV1, or "red nose") is an infection of the upper airway and trachea caused by BHV1. Infection may assume many forms in cattle, including respiratory, conjunctival, or infectious pustular vulvovaginitis affecting the caudal reproductive tract; infectious balanoposthitis of the male external genitalia; endemic abortions; and the neonatal septicemic form characterized by encephalitis and focal plaque necrosis of the tongue. Bovine herpesvirus 5 (BoHV5) may also cause outbreaks of encephalitis in young stock. The respiratory form of BHV1 is the most common and may occur alone or coupled with the conjunctival form. DNA variants of BHV1 initially described correlated to specific system disease, but recent genomic mapping has found no basis for these divisions. Abortions may occur in association with any of the forms of the disease, either during the acute disease or in the ensuing weeks after an outbreak. Each infected herd seems to have one predominant clinical form of the disease, but occasional animals may also show signs of other forms during an endemic. Recent work suggests that genetic factors may play a role in the relative resistance of cattle to IBR virus and that this resistance may be mediated by type 1 interferon genotypes.

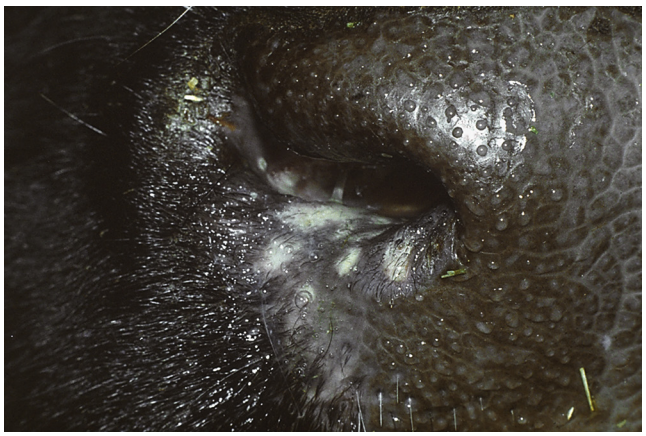
Similar to many other herpes viruses, BHV-1 virus is capable of recrudescence when previously infected cattle harboring latent virus infection are stressed by infectious diseases, shipment, or corticosteroids. Immunity from natural infection or vaccination is short lived and probably does not exceed 6 to 12 months. Respiratory disease caused purely by IBR is associated with high morbidity but low mortality in susceptible animals. Fatalities seldom result from primary or recurrent IBR infections unless secondary bacterial bronchopneumonia, especially *M. haemolytica*, or concurrent viral infection with BVDV or BRSV occurs. (These viruses are discussed further in this section.) The IBR virus compromises the physical and cellular components of the lower airway defense mechanism by damaging mucociliary transport and the mucus layer and directly infecting alveolar macrophages. Therefore combination infections may result in high mortality rates because of multiple agents compromising lower airway host defense mechanisms and possible immunosuppression, especially with concurrent BVDV infection. As stated previously, BHV1 infection upregulates genes that activate receptors for the leukotoxin of *M. haemolytica* and contribute to the severity of that disease.



• **Fig. 4.49** Classical infectious bovine rhinotracheitis plaques on the mucosa overlying the nasal septum of a Holstein cow. The view is through the right nares, and a penlight is present in the right lower corner of the image.

Because most dairy cattle and calves currently are vaccinated for IBR, owners and veterinarians sometimes overlook or fail to consider the possibility of IBR infection during acute respiratory outbreaks or herd abortions. However, the confusing array of bovine vaccines available to laypeople, use of outdated or mishandled vaccines, and inadvertent failure to vaccinate individual groups or herds of cattle still predispose to occasional acute outbreaks of IBR.

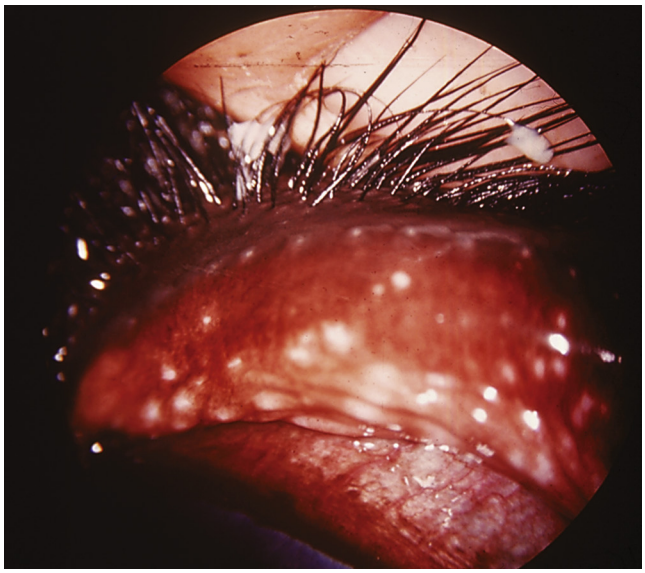
The clinical signs of the IBR-respiratory form include a high fever of 105.0° to 108.0°F (40.56° to 42.22°C); depression; anorexia; rapid respiration (40–80 breaths/min); heavy serous nasal discharge that becomes a thick mucopurulent discharge during the first 72 hours of infection; a painful cough; a dried necrotic crusting of the muzzle; white plaques visible on the nasal mucosa, mucosa of the nasal septum (Fig. 4.49), and sometimes on the external nares and muzzle (Fig. 4.50); occasional mucosal ulceration of the muzzle and oral mucosa; coarse tracheal rales caused by mucopurulent exudate or diphtheritic membranes in the larynx and trachea; and referred sounds and rales from the upper airway heard over both lung fields (especially in the area of the major bronchi). This fulminant form of clinical IBR has fortunately become quite uncommon in dairy cattle, as vaccine technology and



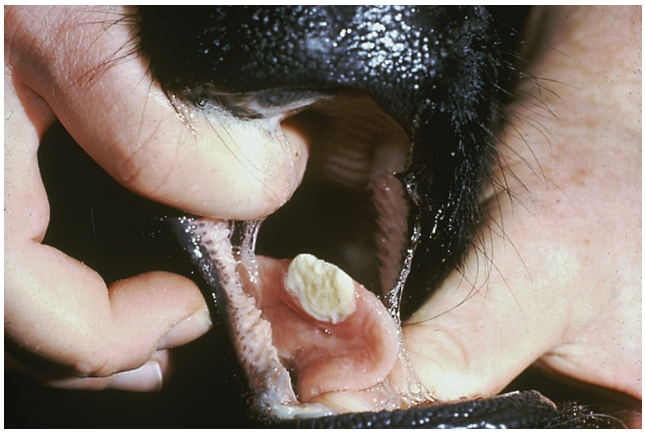
• **Fig. 4.50** Plaques from infectious bovine rhinotracheitis on the mucosa and mucocutaneous junction of the right nares region in a Holstein cow.

widespread and effective vaccination programs have combined to reduce cases of natural disease. Although bronchitis and bronchiolitis occasionally have been observed, most cases do not have pulmonary pathology unless secondary bacterial bronchopneumonia occurs. Bacterial bronchopneumonia usually occurs within 7 to 10 days after acute IBR infection when bacteria complicate the viral illness. Devastating mortality rates may occur in stressed, recently transported or purchased animals that develop IBR infection concurrent with BVDV infection, BRSV infection, or virulent strains of *M. haemolytica* bronchopneumonia. In outbreaks in adult herds, the disease seems to cause the most severe signs in first-calf heifers and may severely affect their future milk production during the remainder of the first lactation.

Affected animals show signs for 7 to 14 days and recover after this time unless secondary infection occurs. Abortions may occur during the acute infection or in the subsequent 4 to 8 weeks. Although fetal death can occur at any stage of gestation, most abortions occur in cows in the second or third trimester of pregnancy. Direct fetal infection or stress and high fever may contribute to the reproductive losses. The conjunctival form sometimes coexists with the respiratory form and is characterized by unilateral or bilateral severely inflamed conjunctivae and serous ocular discharge that becomes mucopurulent within 2 to 4 days. In addition, multifocal white plaques composed of lymphocytes and plasma cells appear grossly on the palpebral conjunctiva (Fig. 4.51). Some cattle also have corneal edema in the peripheral cornea, but ulcerations do not occur (also see Chapter 14). BHV1 has a similar synergistic (increased pathogenicity) role with *Moraxella bovis* in the eye as with *M. haemolytica* in the lung. Calves with the encephalitic form of IBR may demonstrate necrotic plaques on the ventral surface of the tongue or proximal GI tract at necropsy (Fig. 4.52).



• **Fig. 4.51** Multifocal white plaques on the palpebral conjunctiva of a Holstein cow affected with the conjunctival form of infectious bovine rhinotracheitis.



• **Fig. 4.52** White plaque on the tongue of a neonatal calf infected with infectious bovine rhinotracheitis.

Diagnosis

Usually the diagnosis of IBR is based on physical examination when characteristic signs and pathognomonic nasal mucosal plaques are present. Laboratory confirmation is possible by FA techniques during the acute stage (lesions <7 days are best). Scrapings of mucosal lesions and the white plaques in the nasal mucosa should be positive in almost all acute cases. In addition, viral isolation is possible during this time. Undoubtedly, the emphasis for diagnosis in most commercial and state veterinary diagnostic laboratories now rests with PCR, as indeed it does for the majority of viral infections of economic significance in cattle. Amplification of viral DNA using highly specific and sensitive primers for BHV1 can be performed on airway fluid samples, nasopharyngeal swabs, and fresh tissue. This greatly facilitates the accurate and timely diagnosis of BHV1 infection. However, there is one note of caution regarding PCR tests for the diagnosis of BHV1 in that one must obtain an accurate vaccine history when submitting samples or interpreting test results. It is evident (Dr. Keith Poulsen, Wisconsin State Diagnostic Laboratory, personal communication) that recent modified live virus administration can give a false-positive PCR result because of vaccinal virus, on some occasions for up to 14 days after administration. Additional testing using sequencing would be necessary for distinguishing vaccine from field strains. Positive PCR results after IBR vaccination appear to be a more pronounced phenomenon with intranasal

products compared with parenterally administered vaccines. We have performed PCR diagnostics on a number of respiratory disease cases when it was only on later questioning that the recent vaccination event was discovered; frequently, vaccination was performed in the face of clinical disease in a sick patient, possibly serving to prolong shedding. Unfortunately, with BHV1, there is also the possibility of latent viral recrudescence from nervous tissue in a sick animal whose primary disease has suppressed its immune system. Individual sick cows with septic mastitis, septic metritis, bacterial pneumonia, and so forth may show typical IBR plaques as a result of recrudescence of latent virus of natural or live vaccine origin during their illness. A diagnosis of primary IBR should not be made in these cattle. Although the plaque represents the only manifestation of BHV1 disease seen in such immunocompromised animals, importantly, they may be a contagious risk for in-contact and naive animals. There are consequently a number of factors to consider when interpreting the significance of a positive PCR result for BHV1, especially in an animal with only limited clinical signs. Paired serum (acute and then convalescent, 14–21 days later) samples provide another means of positive diagnosis.

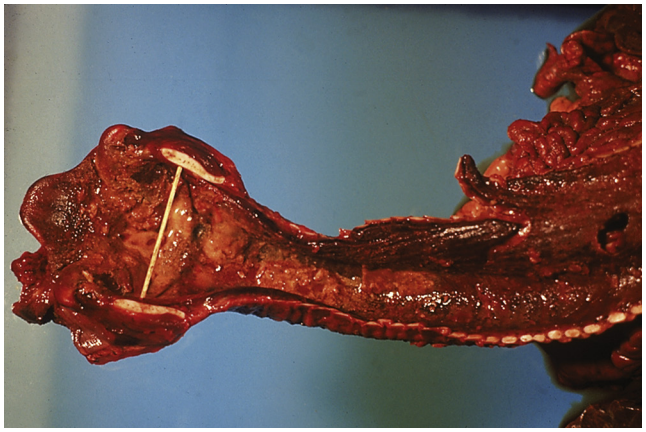
Necropsy of fatal IBR cases will show diffuse inflammation, necrosis, ulceration, and diphtheritic membranes throughout the nasal passages, larynx, and trachea (Fig. 4.53). Characteristic white plaques will be visible in the inflamed nasal mucosa and sometimes in other areas of the nasopharynx or trachea. Oral mucosal ulceration sometimes occurs. Secondary bacterial bronchopneumonia or superimposed viral infections may mask some IBR lesions.

Bovine Respiratory Syncytial Virus

Etiology and Signs

Bovine respiratory syncytial virus has become one of the most important respiratory pathogens in dairy calves and adult cattle in the past 25 years. The virus certainly may have been present for much longer, but new diagnostic procedures, improved technology in virology, and recognition of the virus and its pathophysiology have heightened awareness of this disease. The virus is a pneumovirus within the paramyxovirus family and is distinctly different from the bovine syncytial virus (BSV), which is a spumavirus in the retrovirus family. There is no current evidence that the BSV is a pathogen in cattle. Respiratory disease caused by BRSV was first reported in Europe during the 1970s and has been recognized throughout the United States since the 1980s in endemic form in beef and dairy cattle. Observations from both experimental and natural disease have been reported, and it is now accepted that BRSV was likely the cause of many poorly defined epidemics heretofore diagnosed as "atypical interstitial pneumonia" (AIP) in calves and adult cattle. It also is likely that BRSV infection has preceded, and predisposed cattle to, severe bacterial bronchopneumonia but gone undiagnosed because of overwhelming bacterial lesions.

The virus produces a humoral antibody response, which is helpful both for diagnosis and epidemiologic surveys. Based on surveys completed in several regions of the United States, BRSV infection appears common in cattle because more than 50% of adult cattle surveyed have titers to BRSV. More recent work suggests that up to 70% of calves have now been exposed to BRSV by breeding age. The virus has caused sporadic clinical disease in dairy cattle and calves and probably has gone undiagnosed frequently. Outbreaks of BRSV may be limited to calves, affect only adult cows, or can involve all animals in a herd. Morbidity is high, but mortality as a result of BRSV infection is much lower unless secondary bacterial bronchopneumonia ensues. The virus apparently does not infect alveolar macrophages but may damage physical defense mechanisms of the lower airway, such as mucociliary transport, and may lead to antigen–antibody complexes that subsequently engage complement and result in damage to the lower airway. Although experimental reproduction of the clinical disease has not been consistently successful in challenge studies, recent studies have helped further explain the pathogenesis of the disease. Two- to 6-month-old calves have been successfully infected and have marked production of inflammatory cytokines (tumor necrosis factor, interleukins 6 and 8, and interferon); these are thought to help promote viral clearance but may also have a pathogenic role in causing airway obstruction. Previous work suggests that BRSV alters macrophage function sufficiently to short cycle and depress responsiveness of lymphocytes. In any event, interstitial pneumonia, secondary bacterial pneumonia, airway obstruction, and pneumothorax are very common after BRSV infection. Many unexplained facets of BRSV infection persist despite the proliferation of research on the virus. For example, BRSV infection often arises in herds that appear to have excellent management and have not purchased new cattle, shipped and returned existing cattle, or stressed animals in any apparent way. Where did the infection come from in these herds? Was it latent in a recovered animal, or was it introduced by regular visitors to the farm? Cattle are thought to be the reservoir, but it has not yet been shown how or why the virus activates,

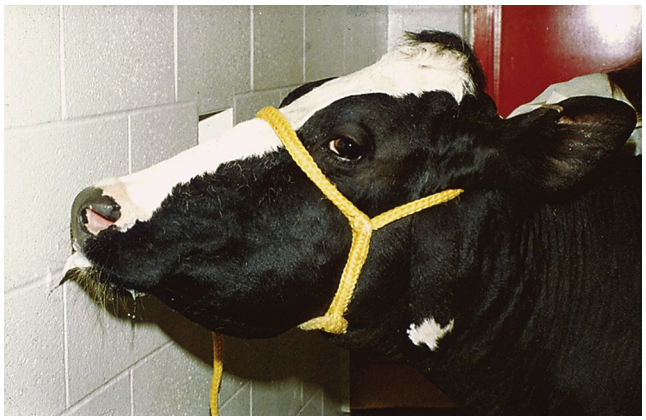


• **Fig. 4.53** Severe mucosal necrosis involving larynx and trachea of a cow that died from infectious bovine rhinotracheitis (IBR). Although fatal cases of pure IBR are rare, the pathology presented highlights the damage to the physical defense mechanisms of the lower airway that predisposes to secondary bacterial pneumonia. (Courtesy of Dr. John M. King.)

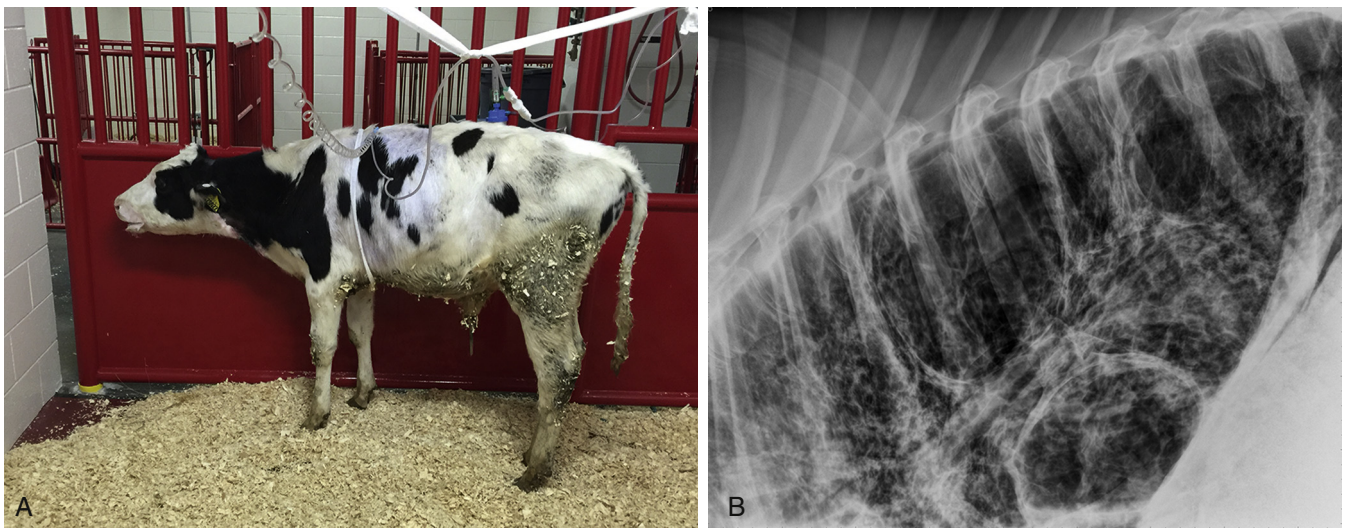
replicates, and spreads to cause all clinical epidemics. In closed herds that experience recurrent infections, there appears to be a high degree of sequence variation among BRSV isolates associated with clinical disease, suggesting that BRSV populations may be heterogeneous and relatively diverse, challenging control and prevention even in well-managed herds.

Fortunately, because of increased awareness of BRSV in cattle, bovine practitioners are beginning to suspect the disease based on clinical signs and routinely seek virus identification, histopathologic confirmation of the virus, or serologic confirmation when acute epidemics of respiratory disease occur in cattle.

The signs of acute BRSV range from inapparent to fulminant. In most outbreaks, acute BRSV infection causes high morbidity in the affected group within several days to 1 week. Clinical signs include high fever (104.0° to 108.0°F [40.0° to 42.22°C]); depression, anorexia, decreased milk production, salivation and serous or mucoid nasal discharge. The degree of dyspnea varies from a merely increased respiratory rate (40–100 breaths/min) to open-mouth breathing. Also, in all but the mildest outbreaks, a percentage of the affected cattle will have SC emphysema palpable under the skin of the dorsum, especially near the withers (Fig. 4.54). Auscultation of the lungs in acute cases may reveal a wide range of sounds. Increased bronchovesicular sounds, bronchial tones, fine crepitation caused by emphysema, and rales (usually as a result of secondary bacterial bronchopneumonia) have been described. Practitioners have found that the lungs may auscultate as diffusely very quiet or almost inaudible in acutely affected cattle in some outbreaks. This has been a very important sign and initially appears in contrast to the outward signs of dyspnea displayed by these cattle. However, the relative deficit of airway sounds fits the existing pathology because pneumothorax or diffuse interstitial pulmonary edema and emphysema compress the small airways and cause the lungs to be quieter than one would expect (Fig. 4.55). This is the same phenomenon that occurs in proliferative pneumonia in which the alveoli and small airways are obliterated or reduced in size. If secondary bacterial pneumonia occurs, bronchial tones or rales are heard in the anterior ventral lung region, and the dorsal and caudal lungs become quieter because of mechanical overwork, increasing the degree of edema and emphysema. Dyspnea is severe in such cases, and affected animals usually show open-mouth breathing and an audible grunt or groan with each expiration (see Video Clip 4.11). This dyspnea is more obvious if affected animals are stressed by handling or being made to move. Despite the high fevers and respiratory distress, affected cattle frequently do not look septic (e.g., severe depression, scleral injection) as with acute overwhelming bacterial pneumonia. There does appear to be some seasonality to outbreaks in the northern United States, with most occurring in the fall or winter.



• **Fig. 4.54** A mature cow representative of a herd outbreak with BRSV infection. This cow had respiratory distress and severe subcutaneous emphysema over the chest, back, and face (notice indentation of the halter on the face).



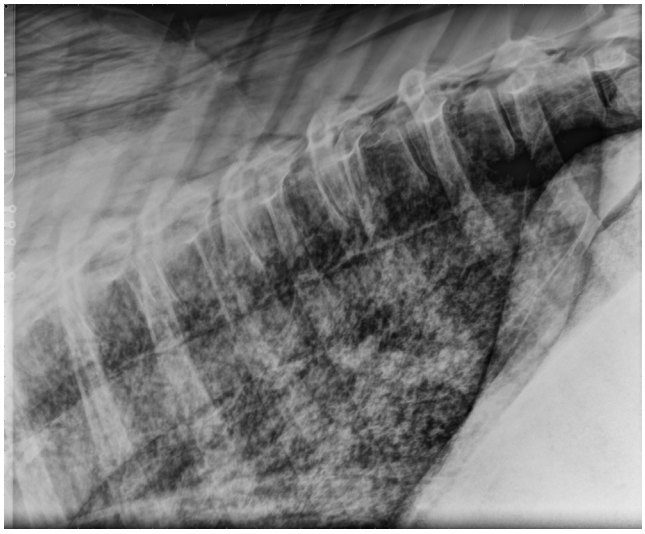
• **Fig. 4.55** A 4-month-old Holstein bull with acute bovine respiratory syncytial virus pneumonia. **A,** Note the open-mouth breathing. **B,** Radiographs of the same bull showing severe diffuse interstitial pneumonia with bullae formation.

A biphasic disease progression may occur in some cattle with BRSV infection. The first stage or phase of the disease is characterized by mild or more serious signs as described earlier. The affected animals apparently improve over the next few days only to develop peracute severe respiratory distress several days to several weeks after their initial improvement. Because these animals initially appeared to have mild disease and responded to treatment, this secondary phase is entirely unexpected. Secondary acute dyspnea is thought to reflect an immune-mediated disease caused by hypersensitivity or a severe T helper 2 response in the lower airway and lung parenchyma and is frequently fatal.

Diagnosis

The signs of BRSV infection in calves or adult cattle may be suggestive of the diagnosis, especially when acute onset, high fever, and SC emphysema are found in several affected animals. These signs are rarely seen in calves younger than 6 weeks, but calves aged 2 to 6 months seem to be most commonly affected. Auscultation of the lungs in acute cases may be helpful if the lungs sound diffusely quiet despite obvious severe dyspnea. The veterinarian must be cautious in diagnosing BRSV based only on the finding of SC emphysema or pneumothorax in some animals. Any severe pneumonia (especially other interstitial pneumonias or severe consolidating bronchopneumonia) can also cause SC emphysema because the only remaining normal lung tissue (dorsal or caudal lung fields) is overworked to the point at which emphysema and interstitial edema are likely. Therefore, SC emphysema may be suggestive of, but not pathognomonic for, BRSV. Thoracic radiographs will commonly reveal findings suggestive of diffuse interstitial pneumonia (Fig. 4.56). As with most of the diseases discussed thus far, laboratory confirmation is the only definitive means to confirm a diagnosis of BRSV. Virus isolation from tracheal wash fluid or necropsy specimens has been used but is often unrewarding because BRSV is quickly cleared, or a rapidly developing secretory antibody neutralizes the virus within the respiratory tract. FA techniques may be used for tracheal wash samples, nasopharyngeal swabs, and necropsy specimens of infected lung. The advent of PCR has made a significant and positive impact on our ability to accurately diagnose BRSV. Both conventional reverse transcription polymerase chain reaction (RT-PCR) assays for the viral genome and real-time RT-PCR for BRSV detection are markedly superior in terms of sensitivity to either immunofluorescence or virus isolation. Diagnostic, multiplex RT-PCR kits that also detect parainfluenza-3 (PI3) and BHV1 are often used but as discussed under the section on BHV1, one has to be careful of false-positive PCR tests when modified live viral vaccines have been recently (<14 days) administered. Serology can be helpful in establishing a diagnosis of BRSV because a marked humoral antibody titer occurs in response to the infection. Baker and Frey emphasize that antibody titers may increase early after acute infection and often peak before 2 weeks postinfection. Therefore, collection of serum on day 1 and day 14 would be important when evaluating seroconversion to BRSV. The same authors state that young calves may have titers derived from colostrum. These titers, indicative of passive immunity, are only partially protective against BRSV infection but can interfere with vaccinal responses in young calves. Thus, older calves, heifers, or adult animals are better populations to sample.

Gross postmortem findings and necropsy specimens may be very helpful in establishing a diagnosis. This is especially true if death has been acute and secondary bacterial pneumonia has not yet developed to somewhat mask the pulmonary lesions caused by BRSV. Both experimental and natural infection with BRSV produce similar gross lesions consisting of atelectic, consolidated pneumonia with deep red to purple lesions that are "rubbery" on palpation. There is often extensive lobular or lobar consolidation affecting the cranial, middle, and accessory lobes surrounded by lobules of more normal, pink, overinflated lung. The caudodorsal lungs typically fail to collapse and are distended by interlobular, interlobar, and subpleural emphysema and edema (Figs. 4.57 and 4.58). If secondary bacterial bronchopneumonia coexists with BRSV,



• **Fig. 4.56** Thoracic radiograph of 2-year-old Holstein heifer with diffuse interstitial pneumonia caused by acute bovine respiratory syncytial virus infection.

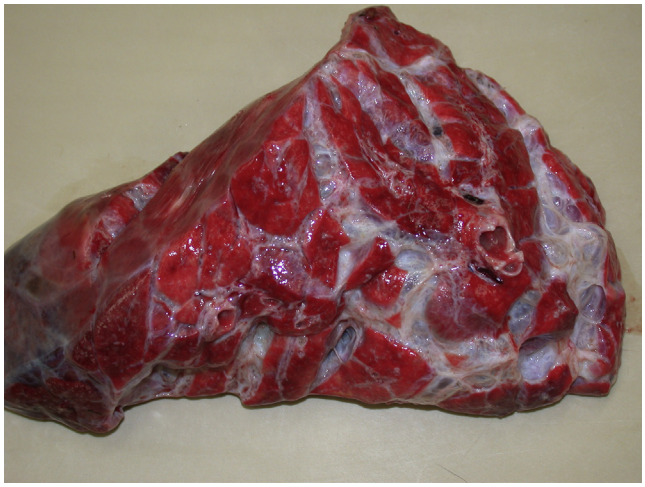
• **Fig. 4.57** Cut section of lung at necropsy of a fatal case of bovine respiratory syncytial virus pneumonia. Interstitial edema and emphysema are apparent. (Courtesy of Dr. John M. King.)

the heavily consolidated anterior ventral lung fields usually are more uniformly dark colored, firm, and fibrin covered (Fig. 4.59). In this instance, typical BRSV lesions of emphysema, edema, and scattered palpably firm areas will still be found in the lung caudal and dorsal to the consolidated areas.

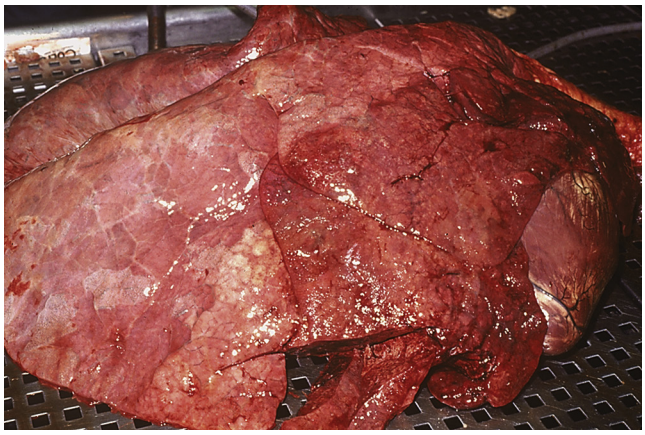
Several times at our clinic, we have obtained *Pasteurella* or *Mannheimia* isolates from tracheal wash specimens that have complicated the course of a BRSV outbreak. Unsurprisingly, cattle in these herd outbreaks failed to respond, or responded unusually slowly, when placed on antibiotics chosen for their specific *Pasteurella* or *Mannheimia* isolate. This poor clinical response can be a signal that another pathogen is contributing to the herd problem.

Treatment

Therapy for acute BRSV infection is symptomatic and supportive. Broad-spectrum antibiotics are indicated to counteract or discourage secondary bacterial bronchopneumonia and should be initiated after collection of diagnostic samples from acutely infected calves or mature cattle. After cultures are completed, specific antimicrobial therapy may be instituted if bacterial pathogens or *Mycoplasma* spp. are isolated.



• **Fig. 4.58** Marked lobular separation caused by emphysema and interstitial edema in a cut section of dorsal lung field from a mature bull that had died from acute bovine respiratory syncytial virus infection.



• **Fig. 4.59** Necropsy view of lungs from a fatal case of bovine respiratory syncytial virus combined with secondary *Mannheimia haemolytica*. This combination of pathogens killed 30 of the 55 heifers in the group within 10 days during inclement winter weather.

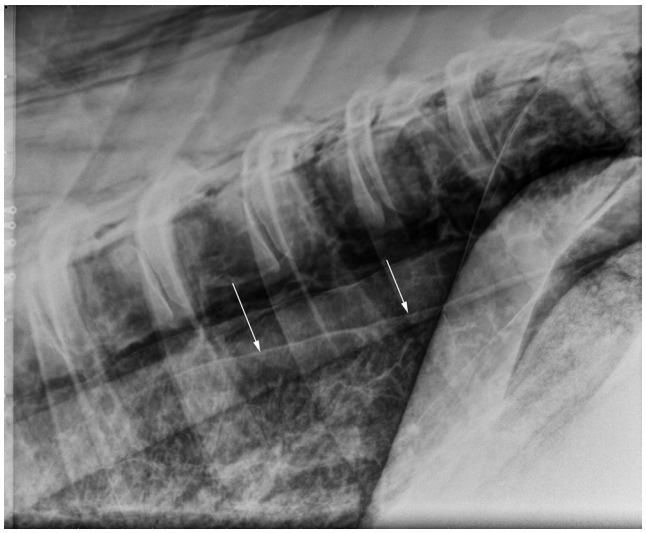
Nonsteroidal antiinflammatory drugs may be helpful in acute BRSV infections. Aspirin or flunixin may be used at the same dosages mentioned previously. Corticosteroids have been recommended for treatment of BRSV infections in calves. Calves or nonpregnant cattle with respiratory distress but minimal evidence of sepsis may receive some benefit from these drugs in diminishing the pulmonary pathology created by BRSV and, in a few cases, a dramatic improvement in clinical signs can be observed. Corticosteroids can predispose to secondary infections and abortions, and their use should be selective. Antihistamines also have been recommended for treatment of BRSV and may be used (tripelennamine hydrochloride at a dosage of 1 mg/kg IM twice daily).

Any cattle that develop the second phase or stage of BRSV infection, which appears as a hypersensitivity reaction, should receive antiinflammatory medication in addition to broad-spectrum antibiotics. The peracute onset and extreme dyspnea exhibited by these animals is usually fatal; therefore heroic therapeutic measures are indicated. Several drugs may be indicated, and clinical judgment will determine which therapeutic agents will be used. For an adult cow with this form of the disease, drugs that may be considered and their dosages can be found below:

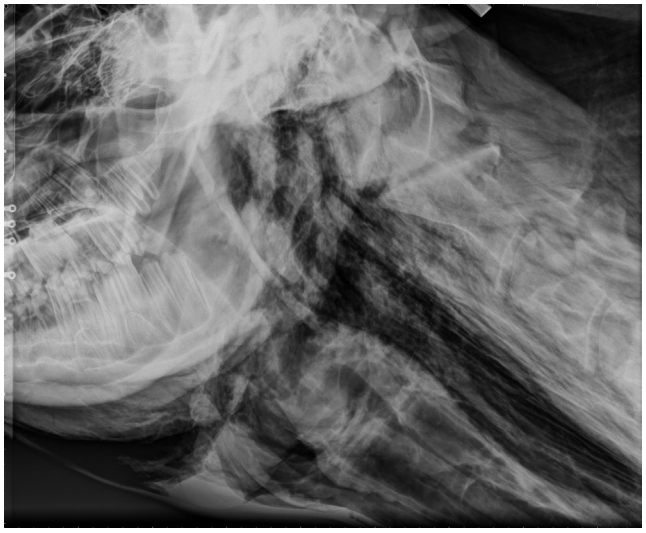
1. Broad-spectrum antibiotics; based upon previous tracheal wash or lung culture results
2. Dexamethasone; 10-20 mg once daily IM or IV (not in pregnant cattle)
3. Antihistamine; tripelennamine hydrochloride 1 mg/kg IM twice daily
4. Atropine; 0.048 mg/kg IM or SC twice daily
5. NSAID; flunixin 1 mg/kg IV every 12 or 24 hours, aspirin 240–480 grains twice daily
6. Furosemide; 250 mg once or twice daily (if severe pulmonary edema is present)

Intranasal oxygen (10–15 L/min) is often used in our hospitals for acute BRSV infection and will frequently decrease the respiratory rate and effort. Nebulization with corticosteroids and antibiotics can be helpful, but a bronchodilator should be administered either before beginning the nebulization or at the same time. Systemic atropine, aminophylline (10 mg/kg as a CRI over a 24-hour period) or inhaled ipratropium can be used for bronchodilation. In animals that develop pneumothorax, evacuation of free air from the pleural space can offer significant improvement. The complete mediastinum of cattle often confines pneumothorax to one hemithorax, but bilateral disease or severe unilateral lung collapse caused by pneumothorax may necessitate evacuation. Details regarding specific treatment of pneumothorax are given later in this chapter.

In summary, the veterinarian must allow for a wide range of severity in BRSV outbreaks. In some mild outbreaks, no animals will require treatment. On the other hand, severe outbreaks complicated by pneumothorax (Fig. 4.60), severe emphysema (Fig. 4.61), or bacterial pathogens may result in 10% to 30% mortality rates despite heroic treatment efforts.



• **Fig. 4.60** Thoracic radiograph of an adult Holstein cow with pneumothorax and lung collapse associated with peracute bovine respiratory syncytial virus infection. *Arrows* indicate the dorsal edge of the collapsed lung. The animal was presented in severe respiratory distress but survived with evacuation of air by chest tube placement and aggressive supportive medical therapy.



• **Fig. 4.61** Radiograph of 4-year-old Holstein bull with acute bovine respiratory syncytial virus infection, pneumothorax, and massive subcutaneous emphysema. Note the dramatic dissection of air throughout cervical region that had tracked from the thoracic inlet.

Vaccination will be discussed later, but the literature on BRSV vaccination is confusing, with some articles showing protection conferred by inactivated or modified live vaccines, others demonstrating no protection when inactivated vaccines are used, and a few suggesting an adverse immune response on subsequent exposure to the virus in previously vaccinated cattle. Most recently, protection from challenge infection has been demonstrated to be good after the intranasal administration of a MLV vaccine marketed for parenteral administration.

Parainfluenza-3

Etiology and Signs

Experimentally, PI3 virus is capable of infecting the bovine respiratory tract and predisposing infected animals to more severe pneumonia when subsequently exposed to bacterial pathogens such as *M. haemolytica*. After experimental inoculation, the virus infects the upper and lower airways of calves with subsequent damage to ciliated epithelial cells, mucus layer, and mucociliary transport alongside infection of alveolar macrophages. As bronchitis and bronchiolitis ensue, purulent exudate fills some small airways. Despite this pathology, PI3 infection is a mild disease unless complicated by secondary bacterial agents. Based on serologic surveys, most cattle probably have been exposed to PI3 infection as calves. We seldom identify PI3 in bovine respiratory outbreaks in dairy calves or cows in the northern United States. One might argue that this can be explained by virtue of the fact that most dairy animals are vaccinated against this virus, but it seems unlikely that this virus is an important contributor to BRD in the United States.

The signs of PI3 infection include fever (104.0° to 107.0°F [40.00° to 41.67°C]), depression, anorexia, nasal and ocular serous discharge, increased respiratory rate (40–80 breaths/min), tracheal rales, and occasional rales in the lower lung fields. Fatalities are uncommon, and recovery should occur over 7 days.

The signs of PI3 complicated by bacterial pneumonia are simply those of a moderate to severe bacterial bronchopneumonia as previously described under the various bacterial pathogens. Response to specific treatment for the bacterial bronchopneumonia, however, would be less prompt and complete than anticipated for bacterial infection alone.

Diagnosis

The clinical signs of PI3 infection in calves or cattle are not specific enough to allow definitive diagnosis. Therefore, virus isolation or PCR amplification from acutely infected individuals via tracheal wash, nasopharyngeal swabs, or necropsy specimens are necessary to definitively identify the infection. Paired serum samples also are helpful because humoral antibody production is anticipated after infection. Virus isolation attempts may be fruitless if samples are not collected early in the course of the disease, further emphasizing the value of PCR diagnostically.

Fatal cases usually are complicated by secondary bacterial pneumonia, especially *M. haemolytica* or *P. multocida*. Therefore, gross pathology lesions suggest bacterial bronchopneumonia, and a diagnosis of PI3 is easily missed unless the veterinarian requests viral diagnostics or obtains paired serum samples from surviving animals.

Treatment

Treatment must address the frequent secondary bacterial pneumonia. There are no characteristic clinical signs to allow veterinarians to diagnose PI3 specifically.

Bovine Viral Diarrhea Virus

Bovine viral diarrhea virus is one of the major pathogens of dairy cattle and may cause a wide range of lesions or clinical syndromes. This pestivirus from the Flaviviridae family causes fever, mucosal erosions, diarrhea, abortions or reproductive failure, congenital anomalies, persistent infection of fetuses infected between 40 and 120 days of

gestation, and many other signs. The disease is discussed fully in Chapter 6. However, BVDV has been incriminated as a "respiratory virus" in cattle, and some strains can certainly be isolated from the lower airway and alveolar macrophages of infected cattle. Some BVDV strains (genotypes 1a and 1b of the non-cytopathogenic biotype) are more commonly found in the lungs of cattle and are frequently associated with respiratory disease outbreaks. All strains of BVDV are immunosuppressive and predispose infected cattle to bacterial or other viral pneumonia. Naive cattle exposed to a type 2 strain may develop severe interstitial pneumonia, thrombocytopenia, bone marrow necrosis, diarrhea, and acute death, sometimes without having mucosal erosions. Additionally, a persistently infected calf or cow may suddenly develop bacterial pneumonia without other predisposing factors, and this scenario should be considered as a possible reason for a single case of bacterial pneumonia in a herd.

During acute BVDV infection, high fevers occur in affected cattle early in the course of the disease. These cattle may show no other signs—no diarrhea, no mucosal lesions—and merely appear depressed and febrile at 106.0° to 108.0°F (41.11° to 42.22°C). Because the high fever necessitates increased physiologic heat loss, some cows have mild increases in their respiratory rate (40–60 breaths/min), but the lungs are normal on auscultation or may have slightly increased bronchovesicular sounds. These cattle are merely in the early stages of acute BVDV infection, and unless a superimposed bacterial infection develops, true clinical pneumonia may not occur. If the animal seroconverts and responds to the BVDV in a normal fashion, no other signs may develop. Some cattle will progress from this early stage of fever with no other overt signs to blatant mucosal lesions and diarrhea 7 to 14 days after the original onset of fever. This situation has been observed in natural outbreaks and with experimental BVDV infection with certain strains of BVDV in naive cattle. Most cattle with BVDV have mild pulmonary lesions or normal lungs grossly and histologically, unless an opportunistic bacterial pneumonia has developed. Naive cattle infected with the type 2 strain, however, may die with severe interstitial pneumonia.

Acute BVDV infection causes profound immunosuppression in affected animals for 7 to 14 days or until they recover. Research documents the negative effects that BVDV infection has on neutrophil, macrophage, and lymphocyte function. Humoral and cell-mediated immune functions are depressed during acute BVDV infection. Furthermore, leukopenia in the peripheral blood is a well-known feature of acute BVDV infection in cattle. Although naive or susceptible cattle fully recover immune function after the development of adequate humoral antibody against BVDV, they are very susceptible to secondary infection during the acute BVDV infection and associated immunosuppression. Alveolar macrophages are frequently infected with BVDV, which would be expected to have a direct negative effect on lung protection against invading bacteria. Therefore, the results can be devastating if a cow or a group of cattle acutely infected with BVDV has the bad fortune to become infected with *P. multocida*, *M. haemolytica*, or *H. somni* at the same time. Bacterial bronchopneumonia may progress rapidly because host defense mechanisms are negligible. In addition, cattle may die so quickly from severe pneumonia that necropsy identifies bacterial pneumonia as the sole cause of death. The existence of BVDV infection will only be confirmed if specific PCR, viral isolation, antigen detection, or immunohistochemistry is performed. Some affected cows develop signs of mucosal disease, or some fatalities demonstrate typical BVDV lesions as well as bacterial pneumonia at necropsy. Other management-related stresses, transportation, pen reorganization, poor ventilation, and so on, may also contribute to the development of bacterial pneumonia during concurrent BVDV infection.

In summary, BVDV by itself rarely causes major respiratory disease except for type 2 infections in naive cattle, which may cause interstitial pneumonia and acute death, sometimes without the typical upper GI tract lesions. Type 1 strains are commonly isolated from the lower airway and pulmonary macrophages in BVDV outbreaks and play a potentially important role in the BRD complex. Acute BVDV infection (any strain) may result in transient immunosuppression that predisposes to severe respiratory infections in cattle concurrently exposed to other respiratory pathogens. This immunosuppressive effect is not limited to the respiratory tract and certainly would also contribute to drastic illness if a cow acutely infected with BVDV experienced septic mastitis, metritis, or salmonellosis.

Bovine Respiratory Coronavirus

The role coronavirus plays in the BRD complex is not clear. There is rather more emphasis placed on it in the literature as it relates to BRD in feedlot cattle than in dairy cattle. Even in feedlot cattle, there is conflicting evidence as to its economic significance as well as its role in clinical disease. Coronavirus is commonly found in outbreaks, either acute or endemic, but can also be commonly found in healthy animals. Experimentally, all of Koch's postulates have been fulfilled with respect to causing respiratory disease in neonatal calves; as such, it may be important, particularly if the farmer describes a "pneumonia–enteritis" complex in 1- to 8-week-old calves. Unfortunately, the frequency with which many diagnostic laboratories can identify bovine coronavirus from diagnostic samples taken from the airways or lungs of both healthy and diseased dairy calves adds further confusion to the issue. Typically, the PCR primers used to identify bovine coronavirus from diagnostic samples do not differentiate between enteric and respiratory strains, so close are they that it requires full sequencing to distinguish them.

Other Viruses

In addition to bovine respiratory coronavirus several other viruses, including adenoviruses (types 3 and 7) and rhinoviruses (bovine rhinitis virus A and B), have been shown experimentally to be potential pathogens of the bovine respiratory tract. Clinically, there are no pathognomonic features of these viruses. Except for coronaviruses, diagnostic

laboratories seldom identify these viruses in outbreaks of infectious respiratory disease in cattle or calves.

Control and Prevention of Infectious Respiratory Diseases in Dairy Cattle: General

The control of acute or chronic endemic respiratory disease within groups of calves or adult cattle broadly consists of four components:

1. Definitive diagnosis of the causative agent(s)
2. Specific medical therapy
3. Correction of management, environmental, or ventilation deficiencies that contribute to, or perpetuate, the respiratory disease
4. Preventive medicine, including management techniques and vaccination

Most of these points have been addressed in the discussion of treatment for each of the infectious agents in this section. Field outbreaks of respiratory disease may be limited to individual groups, such as weaned calves, breeding age heifers, milking cows, and dry cows, or may involve all animals on the premises. When only one group is affected, the veterinarian should try to determine what management, environmental, or ventilation conditions might have predisposed this group to the development of clinical disease. It also is necessary to elicit information from the owner regarding vaccination history, previous outbreaks of respiratory disease, recent purchase of animals, recent movement of resident animals to shows, and other facts that may help to explain how the respiratory infection may have become established in a group of animals or the entire herd.

Respiratory viruses, bacteria, and *Mycoplasma* spp. may be involved separately or in combination in these outbreaks. Although severe outbreaks of pure BRSV or Mannheimiosis do continue to occur, the majority of respiratory disease cases in dairy calves and adult cattle that we encounter belong in the category of chronic bacterial bronchopneumonia, often compounded by the presence of *Mycoplasma* spp. In calves, one should also be cognizant of the role that *Salmonella* Dublin can play in respiratory disease outbreaks, especially toward the end of the preweaning period and into group housing! Because many of the bacterial agents discussed in this chapter can be considered ubiquitous in cattle populations one has to consider what stressors or triggers have compromised affected individuals or groups to tip the scales in favor of disease occurrence.

There is no doubting the increasing prominence of *Mycoplasma* infection on many modern dairies, not just as a respiratory pathogen but also as a cause of mastitis and synovitis–arthritis. Many *M. bovis* infections that become chronic and lifelong are acquired in calfhood, and the major manifestations of illness in milk-fed calves are pneumonia and otitis. Feeding of contaminated colostrum or waste milk is thought to be the primary means of transmitting *Mycoplasma* to young calves. Aerosol spread or transmission by direct contact may subsequently occur to calves housed with, or very near, infected cohorts. Use of colostrum replacer, milk replacer, and pasteurization of waste milk and colostrum are all strategies to reduce exposure of young calves. Heat treating colostrum to less than standard milk pasteurization temperatures is effective in killing important calf pathogens without damaging the immunoglobulins. As colostrum pasteurization becomes more commonplace, it is probable that many dairies will turn to this technique as a means of reducing the pathogen burden that calves are exposed to in the immediate postnatal period. Standard pasteurization procedures are already commonly used to successfully treat waste milk before feeding it to calves. There are no effective vaccines currently available for the prevention of *Mycoplasma* spp. infection in cattle.

Cattle housed in tie stall barns are predisposed to infectious pneumonia when marked environmental temperature and humidity fluctuations occur during the indoor housing season. Late fall and early spring, as well as winter thaws, are the times most likely to vary widely in temperature and humidity. Increased humidity and ammonia accumulation both occur in areas with inadequate ventilation. Ammonia dissolves in the suspended water vapor and is an irritant to the respiratory epithelium. Exhaled bacteria and viruses are included in microscopic droplets of moisture. Prevention of respiratory infections in these settings requires improvement in the ventilation to dilute the pathogens and remove the irritants. If the walls or ceiling accumulate condensation or the odor of ammonia in the barn is noticeable, there is inadequate ventilation. Normally, the inside temperature in these barns in winter should not exceed 50°F (10°C). All modern free-stall barns in cold climates are now curtain sided and these can be adjusted according to weather conditions in the winter to allow adequate fresh air entry for removal of humidity and ammonia. A temperature gradient of only a few degrees between inside and outside is frequently adequate to drive the necessary air exchanges for maintaining air quality inside the barn. A useful resource for facilities design for housing of dairy cattle is provided by the University of Wisconsin through partnerships with private industry; https://thedairylandinitiative.vetmed.wisc.edu

Whenever possible, prevention of infectious respiratory disease in dairy cattle is more desirable than treatment and control measures. Prevention consists both of effective vaccination programs and management designed to reduce the probability of infectious respiratory disease. Currently, highly effective vaccines are available for IBR, PI3, and BVDV. Strong, enduring vaccinal protection against BRSV infection is probably the most sought after advance in the immunoprophylaxis of viral BRD because outbreaks continue to occur in vaccinated herds. More recent MLV products administered intranasally offer the best opportunity for improved prevention and should be incorporated into all herd programs. Vaccines against *H. somni* and *P. multocida*, although available, have equivocal evidence-based literature in terms of disease prevention and economic benefit. The relevance of vaccines for protection against disease caused by opportunistic colonization of lower airways by these commensal pharyngeal organisms will likely always remain

contentious. Newer vaccines against *M. haemolytica* that are based on leukotoxins of this bacterium have been proven beneficial in reducing morbidity and mortality rates in cattle. Such commercial products are often combined with antigens of *P. multocida*.

Vaccination strategies for herds should be individually determined and include the assessment of risk for all age groups. Closed herds in isolated settings have a much lower risk of contagious pathogen acquisition than herds that continuously purchase animals or exhibit cattle. However, mortality rates in heifer calves are frequently high enough that many dairies continue to purchase replacement animals merely in order to maintain herd numbers. This need to purchase cattle is only accentuated if the dairy is attempting to expand in size. Regardless, primary immunization requires two doses of vaccine and is best done at an early age. Optimal response to viral vaccines occurs after the waning of colostrally derived antibodies. Thus, current general recommendations are to begin the primary series at about 3 months of age with the second dose administered 2 to 4 weeks later. Recent research indicates the greatest response to immunization against IBR and BVDV occurs if the first two doses are a killed product and the subsequent booster is a modified live vaccine. All major vaccine producers offer combination products with options for killed or modified live virus that provide the four major viral components in a single injection. The *M. haemolytica* leukotoxoids are a distinct product but may be combined with *P. multocida*. Subsequent boosters are administered at frequencies that correspond to the perceived risk and usually at times or ages that offer some convenience to management. The duration of immunity after proper vaccination is mostly not known for each of the components of the routinely used products. Thus, recommendations for low-risk herds may be annual revaccination of the entire herd, but high-risk herds may be given boosters two or three times per year. Alternatively, in many large herds, adults are vaccinated in conjunction with the lactation cycle. For example, a modified live booster is given at 30 days in milk, and killed boosters are given at 120 and 240 days of gestation. When boosters are given at specific points in the lactation cycle, one must be aware of the negative influence that poor reproductive performance or management decisions such as use for embryo transfer or oocyte donation will have on the efficiency of the program. We have seen a number of situations when either on a herd level or for individually valuable cattle, the decision to booster for example at dry-off has meant a 5- to 6-month delay between the booster and the onset of the next lactation, or an early lactation vaccine booster has been separated by over 6 months from the average time of early gestation in the next pregnancy. These circumstances can also contrive to lessen the value of colostrum as a means of adequacy of passive transfer.

Efforts will no doubt continue to develop new immunization products with greater safety, efficacy, and efficiency. Veterinarians are encouraged to remain abreast of these new developments because new knowledge and technologies may make our current practices obsolete.

Control and Prevention of Infectious Respiratory Disease Specific to Dairy Calves

Bovine respiratory disease, particularly in dairy calves, is a multifactorial disease in which a combination of host, agent, and environmental factors contribute to infection of the upper and lower airways by viral and bacterial pathogens. Viruses commonly isolated from calves with respiratory signs and which may cause primary disease include BRSV, BHV1, and PI3. Infection by bovine viral diarrhea virus increases the susceptibility of the calf to disease but is not usually a primary cause of disease. Coronavirus is commonly isolated from the nasopharynx; however, the role of this pathogen in BRD is still under debate. Interestingly, the increasing research use of metagenomics and deep sequencing during the investigation of BRD is serving to rapidly and markedly increase the number of bovine viruses that can be detected in clinical cases. These types of investigations are not yet "routine" for the workup of field cases, but there is undoubtedly a plethora of new viruses (bovine rhinitis A and B, bovine adenovirus, bovine influenza D, and others) in addition to bovine coronavirus that have been previously uncharacterized but that can be found in clinically pneumonic cattle but only rarely in healthy case control animals. The relevance of these agents, as stated with coronavirus, is uncertain from a causal perspective but should be an active area of research in the near future. Viral infection with pathogens often causes destruction of the respiratory epithelium, resulting in impaired mucociliary function and secondary bacterial infection from pathogens normally residing in the nasopharynx. Bacterial respiratory pathogens include *Pasteurella multocida*, *M. haemolytica, T. pyogenes,* and less commonly, *H. somni* and possibly *Bibersteinia trehalosi*. *Mycoplasma bovis* is also of increasing relevance in endemic respiratory disease problems in calves. Neutrophilic infiltrates in the bronchial, bronchiolar, and alveolar compartments of the lung are the main pathological changes associated with bacterial bronchitis, bronchiolitis, and bronchopneumonia. Specifics regarding most of these pathogens have been discussed previously.

Clinical cases of BRD typically suffer from some combination of cough, fever, and nasal and ocular discharge. Changes in respiratory pattern and depression can be present in either severe, acute or end-stage, chronic cases. Droopy ears and head tilt occur when calves are comorbid with otitis media or interna. Poor body condition and small stature develop with chronic disease (Fig. 4.62). In general, inappetence is a poor proxy for predicting respiratory disease in calves. Subclinical respiratory disease, or more specifically subclinical pneumonia, is present in dairy calf populations and presents an additional challenge for management.

Respiratory disease affects approximately 12% to 16% of preweaned calves. However, on any given farm, prevalence of BRD can vary markedly from none to nearly all of the calves. This means that BRD is much more of a problem for certain herds. At least 20% to 30% of calves affected by BRD require multiple antimicrobial treatments, and interestingly, compared with veterinarians, producers are twice as

• **Fig. 4.62** Two 5-week-old Holstein calves from a commercial dairy. The calf on the left demonstrates the impact of chronic pneumonia on growth. The calf on the right is a healthy penmate.

• **Fig. 4.63** Indoor group housing with supplemental air provided through positive-pressure ventilation. The *black triangle* indicates the positive-pressure tube.

likely to retreat. In the United States, 22% of all preweaned calf deaths are the result of BRD, with case fatality rates ranging from 2% to 9%.

Studies have documented reductions in body weight associated with both clinical and subclinical BRD. Calves experiencing BRD are older when they deliver their first calf, are less likely to enter the milking string, and have greater odds of not completing their first lactation. The short-term costs associated with managing BRD are approximately $10 to $16 per calf. Long-term effects increase such estimates by reducing postweaning growth rates, longevity, and future production.

Many risk factors must be managed properly in order to prevent disease. Overcrowding and poor air quality have long been understood to contribute to BRD. Drafts, high ammonia levels, housing with older animals, large herd size, diarrhea, prolonged time to dam separation, and BRSV vaccination have all been reported as risk factors. In enclosed barns, low air bacterial counts within calf pens, solid barriers between calves, and the ability of the calves to nest in deep straw protects preweaned calves from BRD during the winter months in the northern United States. Separating previously sick calves from healthy calves in group housing has also been associated with a lower risk of BRD in the healthy calves. Based on clinical experience, an age difference within a preweaning group pen of less than 7 to 10 days is associated with a lower risk for disease.

When calves are housed in individual hutches outdoors, ventilation is much less of a concern if the calves can freely move in and out of the hutch and bedding is regularly added. However, with the increased prominence of indoor housing, ventilation must be a priority. Most barns are naturally ventilated and rely on prevailing winds to create air exchanges. In the northern United States, the goal should be approximately four changes per hour in the winter and up to 45 to 60 changes in the summer. Unfortunately, wind is not always present; therefore, these barns require fresh air exchange systems that are supplemented by mechanical ventilation. This is particularly important in the winter when curtains are closed to regulate the barn temperature. Negative pressure, or tunnel ventilation, is not commonly used in calf barns because of problems associated with proper distribution of air within the calf pens, particularly in the winter. Occasionally, "neutral-pressure" ventilation is used by which clean air is pushed in and old air is forced out by mechanical means. The most common method of supplementing fresh air is through positive-pressure ventilation (PPV). In PPV, a fan directs small amounts of clean, fresh air through a distribution tube fitted with strategically sized holes (Fig. 4.63). Old, stagnant air passively leaves the barn through an open ridge, simultaneously removing pathogens and noxious chemicals. Whichever system is used, thorough documentation of the efficacy in achieving the appropriate air exchanges without creating drafts on the calves is essential. Air speed can be quantitatively assessed using anemometers, and air movement can be qualitatively assessed using an insect fogger. These tools help identify drafts as well as areas of dead air. Air sampling units can also be used to culture the pen air at the level of the calf. High-quality pen air should have bacterial counts of less than 30,000 CFU/m^3 on blood agar plates. Pen air exceeding 100,000 CFU/m^3

has been associated with respiratory disease. If an improvement in calf health is not noted after installation, the tubes and associated fans should be reassessed for proper design and installation, and any other possible deficits in management should be investigated, including passive transfer status of the calves, nutritional status, health and biosecurity of new arrivals, vaccination status, commingling, screening methods, treatment protocols, and stocking density. Stocking density has the greatest impact on air quality, and simply increasing ventilation 10-fold does not ameliorate the impact of doubling stocking density. In group pens, preweaned calves should be provided approximately 35 sq ft of bedded space per calf.

In addition to housing and ventilation, the potential association between failure of passive transfer (FPT) and the development of BRD must not be overlooked. This is often an early bottleneck to achieving acceptable levels of BRD in a herd. Although not every calf with FPT will develop BRD, several studies have documented an increased risk in calves with insufficient absorption of maternal immunoglobulins. Passive transfer can quickly be assessed at the herd level by refractometry. Brix refractometry and total protein (TP) refractometry can both be used. Ideally, at least 80% of calves should have evidence of adequacy of passive transfer when tested between 1 and 7 days of age (serum Brix ≥8.4% and serum TP ≥5.5 g/dL).

Maternal antibody levels peak within the calf approximately 24 to 48 hours after ingestion of colostrum and are at significantly lower levels by approximately 3 weeks of age. Often indoor-housed dairy calves are initially treated for BRD around this time. Although maternal transfer of antibody to the newborn calf provides many great benefits, high levels of maternal antibodies are associated with a delayed antigen responsiveness and antibody production by the neonate, as well as selective inhibition of lymphocyte responses. Several studies have shown that administration of a parenteral vaccine in a seropositive calf will not achieve the same immunologic response as that from a seronegative or colostrum-deprived calf.

This potential for maternally derived blockade has been one of the issues causing concern regarding the practice of vaccinating calves during the first few months of life to prevent BRD. However, this should never be used as justification on farm for poor colostral management or timeliness of colostrum delivery nor as a potential "upside" to FPT or partial passive transfer. In general terms, it is also a very weak argument for precocious vaccination protocols in preweaned heifer replacements. That being said, it is worth pointing out that mucosal vaccination via the intranasal rather than by the parenteral route may provide an option to bypass this problem for some infectious agents.

Intranasal vaccination between 3 and 8 days of age with a trivalent viral vaccine against BRSV, BHV1, and PI3 has been shown to be protective against BRSV challenge 9 weeks after vaccination but not at 14 weeks after vaccination, suggesting that the duration of immunity to BRSV is short lived. One of the authors (TO) has also demonstrated that this same viral vaccine can reduce the probability of developing ultrasonographic lung lesions. Recently, an intranasal vaccine against *Pasteurella multocida* and *M. haemolytica* has also become available commercially in the United States, although peer-reviewed literature regarding its efficacy is lacking. In general, vaccination protocols for young calves should be designed keeping in mind the specific infectious pressures for the individual farm, and should never serve as a replacement for good management. Multiple doses of a parenteral, modified live viral vaccine before and/or just after weaning are costly, time consuming, and may negatively impact feed intakes.

There have been recommendations in the face of endemic respiratory disease in calves to hyperimmunize young calves against viral and bacterial diseases by repeated vaccination at 2-week intervals. To date, there is no evidence that this strategy has any merit. Rather, the environmental and management ideas discussed earlier are more likely to provide health and economic returns to the herd. Another widely used strategy for undifferentiated respiratory disease of recently weaned calves is metaphylaxis of the at-risk group. Current practice in many dairies is to wean a group of calves and move them within 1 week or so to group housing. This change, particularly when more than 10 calves in a group are moved at one time, seems to be a trigger for respiratory disease. Control has been achieved in many herds with mass medication at the time of a move with a single injection of a long-acting antibiotic such as oxytetracycline, tilmicosin, tulathromycin, or florfenicol, or by feeding chlortetracycline and sulfamethazine pellets for 5 to 7 days. Herds that practice a more gradual assembly of large groups of calves or that simply have fewer calves seem to be at much lower risk for this problem.

Besides managing the previously mentioned risk factors, there are at least five additional on-farm requirements for effective control of BRD; (1) competent and dedicated personnel, (2) defined screening examinations and diagnostic criteria, (3) consistent and clear treatment and vaccination protocols, (4) a dedicated and permanent place for record keeping in which treatments are always documented, and (5) oversight of records. Increasingly, the majority, if not all, of these are the day-to-day responsibility of farm personnel, not veterinarians. However, there is a pivotal and essential role for veterinarians in the establishment and oversight of each of the first four of the listed items. Periodic reassessment and quality control of each facet of BRD control must involve the veterinarian, and for the veterinarian's input to be most effective and respected, he or she needs to be consistently on farm and up to date. Furthermore, veterinarians have an equally important role to play with respect to responsible use of medications on farm, observance of withdrawal times, and adherence to regulatory specifications regarding legal and illegal drug use.

Personnel responsible for BRD screening should be competent and dedicated. Appropriate training ensures competence and helps the screener understand the purpose of his or her role. As herd size allows, ideally, screeners should not

work with adult cattle. This may not be possible in smaller herds, where one person works in multiple management areas. In such situations, precautions, including working with younger animals first, hand washing, use of gloves, and changing coveralls and boots, will help avoid transmission of disease from older cattle to the younger calves. Treatment and vaccination protocols should be based on data gathered from deep nasopharyngeal swabs, tracheal wash, or BAL fluid analysis. Posting these protocols helps ensure consistency, which can only be monitored when records are maintained and oversight is implemented.

Systematic screening can improve early detection rates and initiate treatment decisions, which should reduce the impact of BRD on calf health and welfare and the cost of raising replacement animals. Clearly defining the screening exam and its required frequency ensures regular and consistent examination of all calves at risk of developing respiratory disease. The most widely used system, the Wisconsin Calf Scoring Chart (WCSC), divides the response to respiratory disease into five categories; body temperature, nasal discharge, cough, ocular discharge, and ear position. Each category is assigned 0 to 3 points corresponding to the subjective level of abnormality (0 = normal, 1 = mild, 2 = moderate, and 3 = severely abnormal), and the total number of points is summed to arrive at an overall respiratory score. Calves with two abnormal categories are considered sick, and treatment is recommended. Mortality rates have been shown to immediately decrease, and morbidity rates decrease within 1 to 2 months after implementation of twice-weekly respiratory scoring by producers.

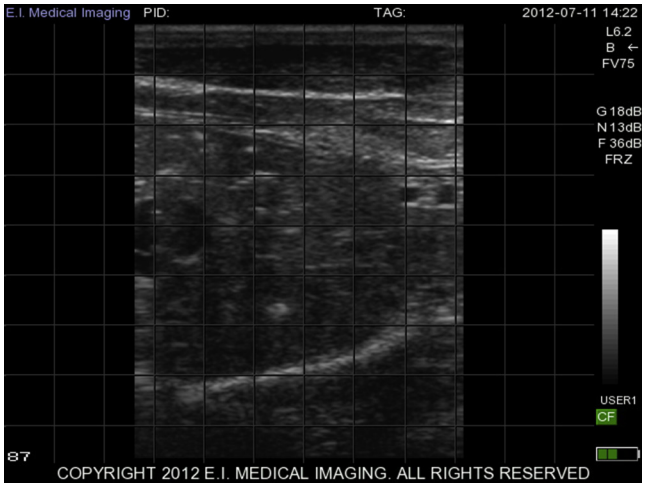
Clinical scoring typically ranks the severity of clinical signs in a subjective manner. More recently, three novel scoring systems have been developed, offering alternatives to the WCSC, using statistical methods instead of subjective judgments to assign weights to describe the severity of the abnormality within each category (e.g., nasal discharge). Each of these systems correctly classified approximately 90% of the animals and required less handling than the WCSC. Although these scoring systems are not intended to act as gold standards for the diagnosis of BRD, they can serve as a useful means of identifying a large proportion of clinically affected calves under some conditions, particularly when one considers that any on-farm scoring technique must be practically useful, repeatable, and consistent in the hands of non-veterinarians. At the very least, such periodic assessments increase observation of calves by attentive individuals who are invested, possibly both personally and financially, in improving calf health. The DART (depression, appetite, respiratory, and temperature) system is another type of screening system that relies on the presence of depression, inappetence, abnormal respiratory pattern, and fever, to indicate when treatment is necessary. Unfortunately, these signs are not consistent in ill calves, and systematic cutpoints have not been well established. However, examination is warranted if a calf does demonstrate these signs. Calves that are standing for excessive periods after feeding when herdmates are resting (or vice versa) should also be evaluated.

The increased utilization of on-farm clinical scoring by non-veterinarians for the timely identification of respiratory disease in calves undoubtedly represents a compromise in terms of precision and accuracy compared with an experienced clinician, particularly if that individual has access to diagnostic imaging. In significant part, clinical scoring is a response to the reality of increased intensification with regard to dairy calf rearing, serving to increase the risk of BRD alongside an increasing awareness and relevancy of the economic impact of respiratory disease in the first 2 months of life. It has coincided with a change in veterinary involvement on many farms from the day-to-day diagnosis and treatment of individual animals to a more population-based approach dictated by the value of individual grade cattle. However, in addition to physical diagnostics, there is substantial benefit to imaging of lung lesions, whether it is via radiography, CT, or ultrasonography.

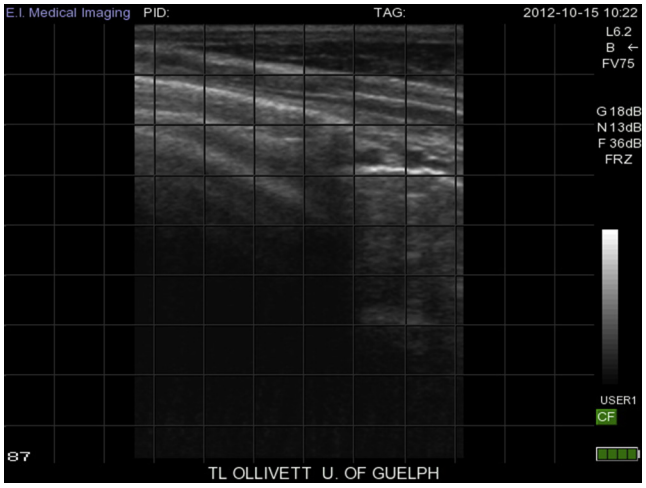
Unfortunately, radiography and CT are not practical in all but individually valuable calves, so despite their diagnostic utility, it is difficult to envisage any widespread role for these in the near future. However, ultrasonography can be performed using portable, readily available machines without the fear of radiation exposure. Furthermore, ultrasonography provides diagnostic advantages in terms of accuracy over clinical scoring. Recently, the WCSC, thoracic auscultation, and treatment records of 106 calves from 13 Canadian dairy farms were compared with the results of thoracic ultrasonography in a cross-sectional study. Using an ultrasonography cutoff of 1 cm, and lung consolidation as a case definition; the sensitivity and specificity of the WCSC were 55% and 58%, respectively; and the sensitivity of thoracic auscultation compared with ultrasonography ranged from 3% to 17%. This provides strong evidence that both clinical scoring and auscultation underestimate the prevalence of lung lesions in dairy calves compared with thoracic ultrasonography. Importantly, thoracic ultrasonography is no longer the province of referral clinics and university teaching hospitals, and it is increasingly common for it to be used by practitioners on farm for reasons of diminishing equipment cost as well as the fact that medium frequency linear probes that double up for reproductive use are excellent for thoracic ultrasonography.

As long ago as the early 1990s, research began on the diagnostic utility of ultrasonography for BRD. The pathology associated with BRD includes cellular infiltration into the airways, which along with cellular debris, effectively displace air from the lung tissue, resulting in nonaerated or consolidated lung lesions that are easily detectable by ultrasonography. These lesions appear homogeneous and hypoechoic (Figs. 4.39 and 4.64 and Video Clips 4.8 and 4.12). This is in stark contrast to the hyperechoic echogenicity of normal lung, which also displays reverberation artifact (Fig. 4.65 and Video Clip 4.13). Such changes allow for the ultrasonographic detection of lung lesions regardless of the clinical state of the animal. These lung lesions typically have a cranioventral distribution, starting in the cranial aspect of the right cranial lobe or right middle lung lobe and proceeding caudally.

Evidence confirming the accuracy and diagnostic utility of ultrasonography has been forthcoming from several prospective field studies in recent years. An initial small study showed that ultrasonography was a reliable method of confirming clinical bronchopneumonia in 18 Holstein calves up to 5 months of age. In a separate study conducted at the University of Montreal, three observers with varying levels of experience imaged 10 dairy calves (healthy, $n = 4$; treated for BRD, $n = 6$). The inter-observer agreement varied from moderate to almost perfect (kappa = 0.6–1.0) depending on the experience level of the observer. Another study assessing lung lesions post mortem previously identified by ultrasonography after experimental bacterial infection documented excellent agreement between the postmortem examination and ultrasound distribution of lesions. In calves with subclinical lung lesions, the sensitivity and specificity of ultrasonography were an impressive 94% and 100%, respectively. Experimental challenge studies have demonstrated that pathologic changes within the parenchyma of the lung occur as early as 2 hours and peak 6 hours after experimental bacterial challenge and that these changes can already be detected by that time with thoracic ultrasonography.



• **Fig. 4.64** Consolidated lung imaged as homogeneous, hypoechoic structure. Note the step in the pleura (top right of image) as the lung deviates around the internal thoracic artery and vein (seen in cross-section in the ventral aspect of the image), which defines this as the cranial aspect of the right cranial lung lobe. This is a lobar pneumonia because the entire lung lobe is consolidated.



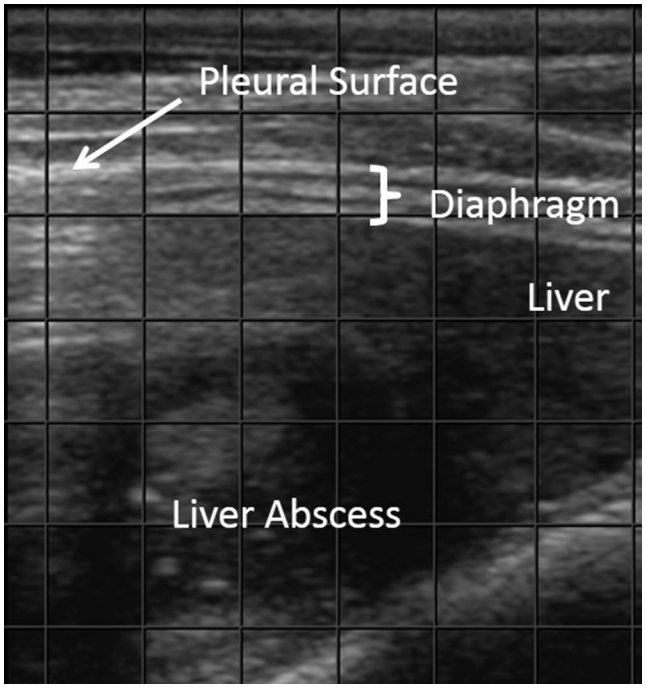
• **Fig. 4.65** Normal gas-filled lung imaged as a hyperechoic line, representing the pleural interface, with reverberation artifact deep to the interface. Interpretations of the lung parenchyma deep to the pleural interface cannot be made when reverberation artifact is present. Note the step in the pleura as the lung deviates around the internal thoracic artery and vein (seen in cross-section in the ventral aspect of the image), which defines this lung lobe as the cranial aspect of the right cranial lung lobe.

It is possible to use many different types of ultrasound probes for the identification of lung lesions associated with respiratory disease in dairy calves. In the literature, probe frequency and probe design has ranged from 3.5 MHz sector, 3.5 to 13 MHz linear, 7.5 MHz, and 5 MHz sector. Fortunately, transrectal probes intended for pregnancy diagnosis are slimmer and permit better access to the axillary region and cranial thorax of young dairy calves. These probes, with frequencies varying between 3.5 and 8 MHz, are widely used by bovine practitioners for reproductive purposes, making them preferred for practical, field-based use of ultrasonography in dairy calves, often without the need for added investment in new equipment.

The operator must have a good understanding of bovine lung anatomy and the typical locations of lung lesions in order to perform an accurate ultrasound examination. A systematic approach based on the identification of specific ultrasonographic landmarks will also help prevent detection errors. In general, the recommended ultrasonographic examination extends from the 10th ICS toward the 1st ICS by moving the probe ventrally along the grain of the hair in a dorsal to ventral fashion. The probe should be moved in a slightly caudal direction, staying within one ICS to avoid imaging the rib. Very slight adjustments can move the ultrasound beam onto or off the rib surface or enhance visualization of a lung lesion. The preferred transducing agent is 70% isopropyl alcohol, applied directly to the hair coat with a spray or squirt bottle. The hair does not need to be clipped despite the common recommendations to do so in existing literature.

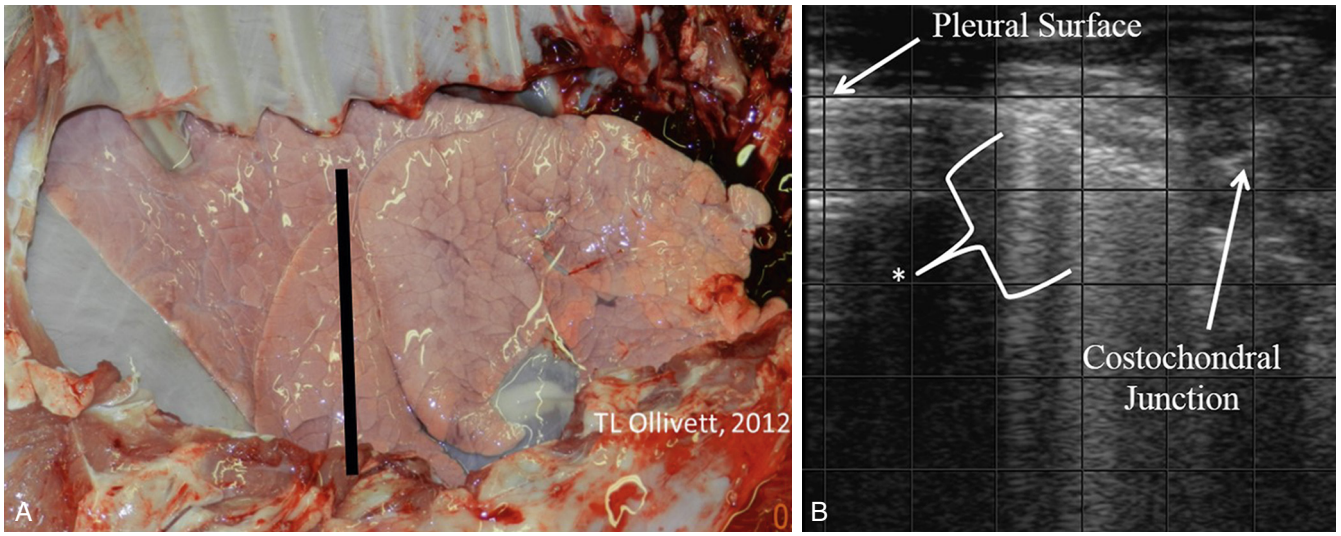
When scanning the right and left caudal lung lobes from the 10th to the 6th ICS, the diaphragm will mark the ventral border of the lung (Fig. 4.66). The liver can be seen deep to the diaphragm on the right, and the spleen is imaged deep to the diaphragm on the left. The right middle lung lobe is imaged from the right 5th ICS, and the caudal aspect of the left cranial lung lobe can be imaged between the left 4th and 5th ICSs. In both lobes, the ventral image landmark includes a pleural interface that dives deep within the image, as the costochondral junction appears ventrally (Fig. 4.67). The elbow roughly approximates the location of the 5th ICS. The caudal aspect of the right cranial lung lobe is imaged from the right 4th and 3rd ICSs. The heart is the ventral image landmark in both of these locations (Fig. 4.68). The cranial aspect of the right cranial lung lobe is imaged from the right 2nd and 1st ICSs (see Figs. 4.64 and 4.65). These two locations image similarly having an obvious

step in the pleural interface as the lung moves around the internal thoracic artery and vein. The pleural step and these two vessels serve as the ventral image landmark on the right side. On the left thorax, the cranial aspect of the left cranial lung is imaged mainly from the 3rd to the 2nd ICSs where the heart is the ventral image landmark. It is noteworthy that the cranial aspect of the right cranial lung lobe can be imaged from the left 2nd ICS as it crosses the thorax in front of the heart (Fig. 4.69). Occasionally, when just the tip is consolidated, it can be imaged only from here.

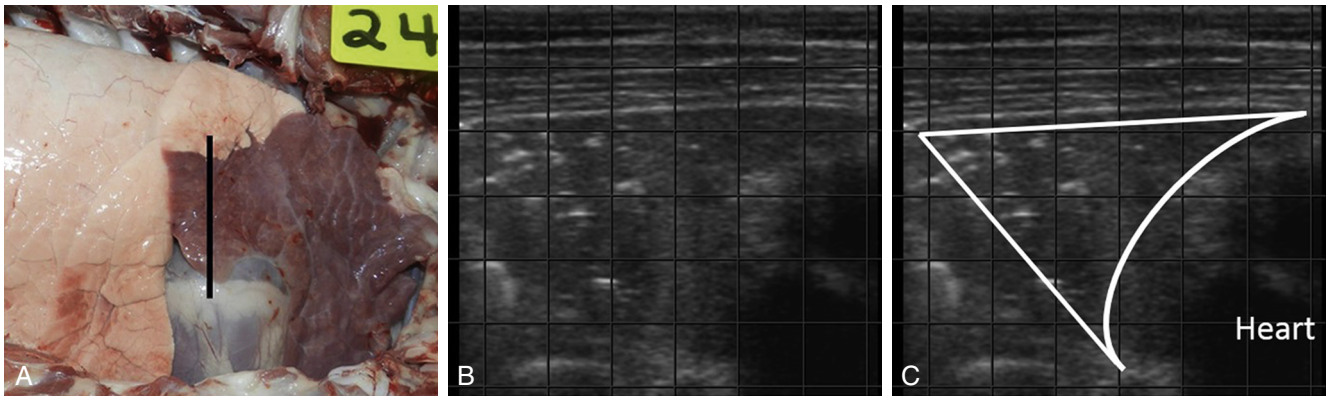


• **Fig. 4.66** The caudal lung lobes are imaged from the 6th to 10th intercostal spaces (ICSs) on either side of the thorax. The diaphragm represents the ventral image landmark within each ICS. On the right, the liver is imaged deep to the diaphragm. On the left, the spleen (not shown) can be imaged deep to the diaphragm.

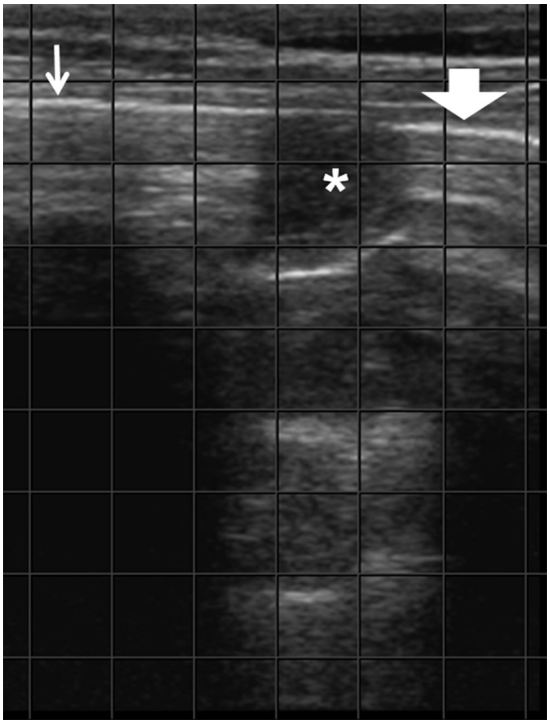
The cranial aspect of the right cranial lung, the right middle lung lobe, and the caudal aspect of the left cranial lung are most commonly affected by bronchopneumonia. Because bacterial bronchopneumonia rarely affects the caudal lung lobe, the ultrasound examination can be modified to exclude this portion of the lung when the goal is simply to screen calves for this disease. Individual, poor-doing calves should have a complete diagnostic examination performed. Prognosis is worse for individual calves with caudal lung lobe involvement, abscessation, or poor body condition identified during the ultrasound examination. Several studies have reported on the measured depth of the ultrasonographic consolidation over several locations on the thorax. It has been determined that the maximum depth of consolidation is well correlated to the number of locations with consolidation. Categorical scoring systems, however, are easier and more practical for assessing the severity and type of lung lesions versus measuring the amount of consolidation. An easy-to-use, 6-point scoring system is outlined in Table 4.2. Based on comparative histopathology, calves with ultrasound scores of 3 to 5 have lobar bacterial bronchopneumonia. Score 2 lesions are typically viral in nature when the lesions are smaller than 1 cm in diameter. Calves scoring 0 or 1 are typically normal. Lobular lesions (score 2) represent discrete areas of consolidation within otherwise aerated lung (Fig. 4.70 and see Video Clip 4.12). In other words, the normal hyperechoic pleural interface with reverberation artifact can be seen dorsal and ventral to the lung lesion. Lobar lesions indicate that there is full-thickness consolidation of the lung lobe (see Fig. 4.64 and see Video Clip 4.8). In this instance, normal lung cannot be imaged at any point ventral to the start of the lesion. Ultrasound scoring of calves assists the veterinarian



• **Fig. 4.67** The right middle lung lobe (**A**) is imaged from the right 5th intercostal space (ICS), and the caudal aspect of the left cranial lung lobe can be imaged between the left fourth and fifth ICSs. In both lobes, the ventral image landmark includes a pleural interface that dives deep within the image, as the costochondral junction appears ventrally (**B**). The *asterisk* indicates pleural roughening or comet-tail artifacts. The *black bar* indicates the image location.



• **Fig. 4.68** Gross specimen (**A**) and ultrasonographic images (**B** and **C**) of the caudal aspect of the right cranial lobe with lobar consolidation in the right fourth intercostal space. Ultrasonographic features of consolidation with homogeneous, non-aerated lung with occasional hyperechoic foci and an absence of normal pleural reverberation artifact can be seen in **B**. Note the liver-like, wedge-shaped appearance of the hypoechoic, consolidated lung dorsal to the heart (*white outline* in **C**). For images B and C, dorsal is to the left side of the image, ventral is to the right side of image, superficial is at the top of the image, and deep is at the bottom of the image. The *black bar* indicates the image location.



• **Fig. 4.69** The cranial aspect of the right cranial lung can be imaged from the left second intercostal space as it crosses the thorax in front of the heart. Occasionally, when just the tip is consolidated, it can be imaged only from here. The *thin arrow* indicates the left lung, the *thick arrow* indicates the right lung, and the *asterisk* indicates the thymus.

not only with diagnosis and staging severity but also permits assessment of response to therapy and resolution of pneumonia in individual calves. At the farm level, besides determining the prevalence of respiratory tract disease, clinical pneumonia, and subclinical pneumonia, ultrasound scoring can be used to determine if timely diagnosis by cow-side personnel is occurring and whether or not the farm treatment protocols are effective. Thoracic ultrasonography can also improve purchasing and culling decisions.

TABLE 4.2 Description of Categorical Scoring System Used for Rapid Detection of Lung Lesions in Dairy Calves

Ultrasonographic Score	Description
0	Very few or no comet-tail artifacts; no hypoechoic consolidation
1	Diffuse comet-tail artifacts; no hypoechoic consolidation
2	Lobular pneumonia with singular or multifocal patchy consolidation
3	Lobar pneumonia with only one lobe entirely consolidated
4	Lobar pneumonia with two lobes entirely consolidated
5	Lobar pneumonia with three or more lobes entirely consolidated

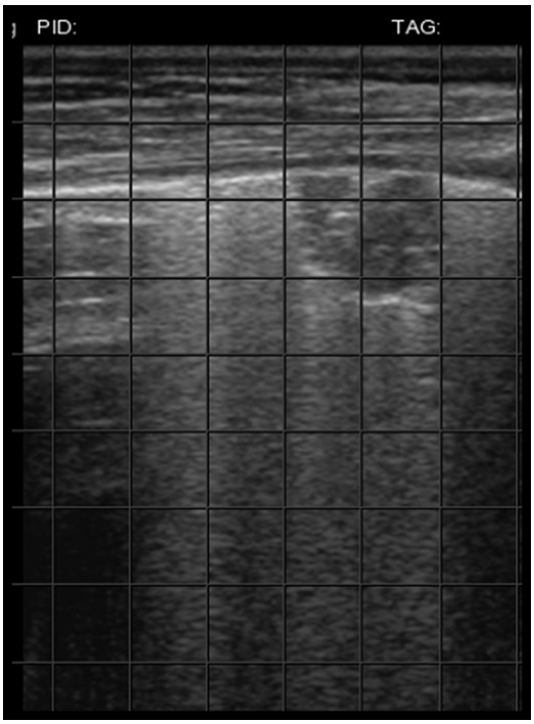
Parasitic Pneumonia

Dictyocaulus viviparus

Etiology and Signs

Dictyocaulus viviparus is the lungworm of cattle and causes parasitic pneumonia and bronchiolitis in calves and adult cattle. This parasite has a direct life cycle, so infection merely requires management factors that allow a buildup of the parasite in the environment and ingestion of the infective larvae by naive cattle.

Adult lungworms reside in the trachea and bronchi. Eggs produced by female adults hatch either in the trachea or before being passed in the feces. The progression to the infective third stage larvae requires only 5 days, and the larvae are then ingested during consumption of contaminated grass in a



• **Fig. 4.70** Lobular lesions (score 2) are discreet areas of consolidation within otherwise aerated lung. In other words, the normal hyperechoic pleural interface with reverberation artifact can be seen dorsal and ventral to the lung lesion.

pasture or bedding in heavily contaminated box stalls. Ingested larvae traverse the intestinal wall to reside in mesenteric lymph nodes, moult to the fourth stage, and within 1 week migrate to the lungs through lymphatics or blood vessels. The final fifth stage is reached after the larvae arrive in the bronchioles. The prepatent period is approximately 4 weeks because this period is required for the larvae to mature to egg-laying adults.

Signs of primary infection include varying degrees of dyspnea, a characteristic deep and moist cough, and moist rales or crackles heard over the entire lung field. Coughing is more severe and prominent than with most other bovine pneumonias. Diffuse rales rather than rales limited to the anterior ventral lung fields are an important sign that differentiates lungworm from bacterial pneumonias. Severely affected calves or cows will show "heave"-like breathing with visible expiratory and inspiratory effort. In some cases, emphysema is present when heavy airway exudate results in extreme mechanical respiratory efforts. Fever (103.0° to 106.0°F [39.44° to 41.11°C]) may be present in some cases as opportunistic bacteria such as *P. multocida* invade the damaged lower airway and establish a secondary bacterial bronchopneumonia. Fever also may be present simply from exertion involved in breathing during warm weather or in poorly ventilated barns. Usually several animals in a group or the entire herd will show signs, but mortality rates tend to be very low. Affected cattle continue to eat unless severe dyspnea or coughing interferes with their ability to ingest feed. In cases with severe dyspnea, frequent coughing, marked expiratory effort, and open-mouth breathing are noted.

In addition to the signs of primary infection, veterinarians should be aware of the reinfection or acute larval migration syndrome that occurs in adult cattle previously exposed to the parasite on farms with endemic *D. viviparus*. Although age-related immunity to *D. viviparus* exists in adult cattle in endemic areas, this immunity may be incomplete or may not be able to overcome heavy challenge. Although most ingested larvae are killed or fail to mature in previously infected cattle, heavy exposure apparently allows large numbers of larvae to simultaneously reach the lungs and cause respiratory signs through either an immune-mediated mechanism or from migration of large numbers of larvae into the lung. Signs usually develop 14 to 16 days after exposure to contaminated pastures. Coughing that is frequent and deep, as well as an increased respiratory rate, characterizes the syndrome. Milk production decreases acutely in affected cattle. Rales may not be present. Fecal examinations are usually negative for *Dictyocaulus* with this form because the disease is a result of the L4 migration into the lung.

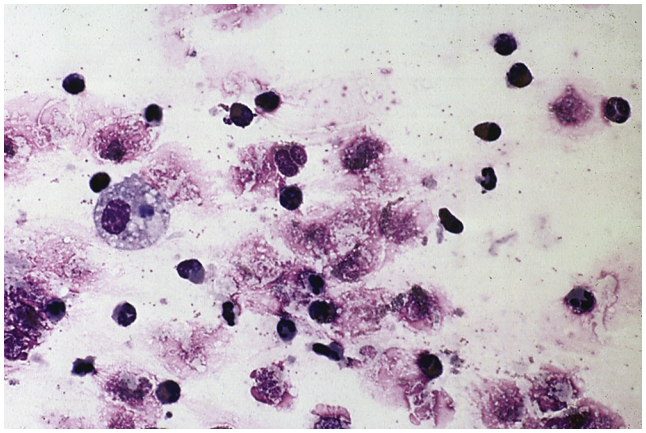
Diagnosis

In primary infections, the diagnosis is aided by history, physical examination findings, laboratory or postmortem confirmation, and knowledge of the life cycle of the parasite.

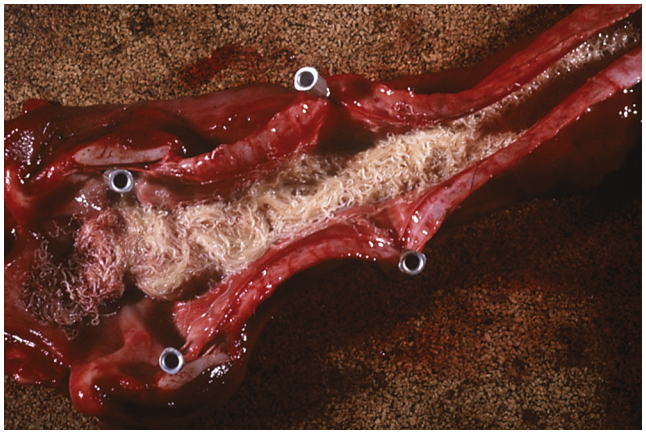
The characteristic deep, moist cough and moist rales auscultated throughout the entire lung are the most significant clinical signs, especially if found in a majority of the cattle within a group. As with any parasitic disease, some affected animals ("weak sisters") display more blatant signs than others, but most within the group are affected. History may be very helpful if animals have been placed on pasture recently or confined by group housing (heifers) to pens having a base consisting of several months of manure accumulation.

Baermann's technique performed on fresh manure is indicated for specific diagnosis but is of limited value in prepatent and postpatent infections. Therefore, both Baermann's technique and tracheal washes should be performed on several animals. If larvae are found using Baermann's technique, the diagnosis is confirmed as a patent infection. In prepatent infections, tracheal wash samples may identify parasites, rule out other causes of pneumonia, and allow cytologic confirmation of eosinophilic inflammation typical of parasitic bronchitis and pneumonia. In postpatent infections, tracheal wash cytology also indicates eosinophilic inflammation and may suggest chronic inflammation. Eosinophilic tracheal wash cytology should be highly suggestive of parasitic pneumonia (Fig. 4.71). In temperate areas of the world where the disease is more commonly endemic, milk and serum enzyme-linked immunosorbent assay (ELISA) tests based on a recombinant major sperm antigen of *D. viviparus* are used to identify infection in individuals and groups of lactating cows.

Necropsy findings in fatal cases vary with the stage of infection. In early prepatent infections, microscopic examination of bronchial exudate may be necessary to identify larvae, but in later prepatent infections, the larvae are obvious if the airways are properly opened and inspected. Eosinophilic bronchitis may be confirmed by histopathology. Patent infections are obvious because large numbers of mature parasites up to 8.0 cm in length are found in the airways (Fig. 4.72). Secondary anterior ventral bacterial



• **Fig. 4.71** Wright-Giemsa stain of tracheal wash from a cow representative of a herd problem of chronic cough and decreased production. Lungworms (*Dictyocaulus viviparus*) were found to be the cause of the disease. The large number of eosinophils on this 40X slide is highly suggestive of lungworm infection.



• **Fig. 4.72** Necropsy specimen of trachea from fatal lungworm infection in a calf showing hundreds of *Dictyocaulus viviparus* lungworms. (Courtesy of Dr. John Perdrizet.)

bronchopneumonia may be present, and interstitial emphysema is observed in occasional severe cases. In postpatent infections, chronic bronchitis, bronchiectasis, and secondary bronchiolitis obliterans may be observed.

The reinfection syndrome is characterized by clinical signs of severe coughing in the majority of cattle after their introduction to infected pastures. Tracheal wash samples will reveal eosinophilic inflammation. It is important to note that Baermann's technique will yield negative results. Necropsy lesions in the reinfection syndrome consist of small greenish-gray subpleural nodules, green exudate occluding small airways, and occasional green tinting of the interlobular septa. Histologically, eosinophils predominate, but lymphocytes, plasma cells, macrophages, and giant cells may be observed within the airways.

Treatment

Treatment of primary *D. viviparus* infection consists of an anthelmintic to destroy the parasite and, when necessary, antibiotic therapy to control secondary bacterial infection of the lower airway.

Levamisole phosphate (8 mg/kg body weight, SC or orally), fenbendazole (5 mg/kg orally), albendazole (10 mg/kg orally), and ivermectin (0.2 mg/kg SC) all have been recommended as treatments for primary *D. viviparus* infection in the past. Moxidectin (0.5 mg/kg) and eprinomectin (1 mL/10 kg) as pour-on preparations should also be effective and are currently approved for dairy cattle in the United States. Levamisole has been very effective in our clinics but is no longer approved for use in dairy cattle. Affected cattle should not be allowed back on infected pastures, and confined cattle should be removed from infected manure packs until the pens can be cleaned completely of manure and bedding. Anthelmintic resistance among nematodes in ruminant populations is of increasing concern worldwide, particularly in the more temperate areas where lungworms are more of a consistent problem in pastured dairy cattle. When we have encountered lungworm as a clinical entity in the northern United States, resistance to either the avermectins or benzimidazoles has not appeared to be a significant problem.

Because the most common secondary bacterial invader is *P. multocida*, patients with bacterial bronchopneumonia may be treated with tetracycline, ceftiofur, ampicillin, or penicillin. Secondary bacterial pneumonia may mask the presence of lungworms in calves or heifers. Such animals frequently appear to improve temporarily while on antibiotic therapy but then quickly relapse when antibiotics are withdrawn. Antibiotic therapy in these instances may cause resolution of fever and improved attitude but will not alleviate coughing or severe dyspnea. Only when further diagnostics are pursued in live patients or necropsies are performed in fatal cases will the true diagnosis be obtained and effective treatment instituted.

Although the reinfection syndrome appears to be an immune-mediated disorder, affected cattle appear to respond rapidly to levamisole injections, according to Breeze. Without treatment, continued coughing and production losses persist in the affected animals for weeks.

Control

Control of *D. viviparus* infections requires management decisions regarding contaminated pastures. Because infective larvae have been shown to survive winter conditions, pastures should not be grazed in the early spring. Before being pastured, yearling heifers should be treated with anthelmintics effective against *D. viviparus*, and all animals should be treated routinely with anthelmintics at monthly intervals if the animals are to be placed on contaminated pastures. Targeted strategic anthelminthic treatments are sometimes used in endemic areas in efforts to reduce the development of anthelminthic resistance rather than automatic, repeated deworming based on a calendar date. This approach would also be of benefit from the perspective of diminishing drug resistance among conventional GI nematodes such as *Ostertagia* because on most occasions, deworming treatments during the grazing season try to control multiple nematode populations. Moisture promotes survival and activity of infective larvae. Highlighting this fact, clinical lungworm infections in the northern United States are observed primarily during wet summers. We have seen it as a

herd problem in grazing herds, especially when pasture burdens build up during the late summer months from infected heifers and adult cows become reinfected when grazing those same pastures. Similarly, we have observed outbreaks in the lactating herd when they were allowed to graze pasture that had been fertilized with manure from replacement heifers. Whenever possible, extreme care and additional anthelmintic treatment are indicated during wet summers and when animals are pastured in swampy, low-level endemic areas. The use of an irradiated live *D. viviparus* vaccine has been an integral part of lungworm control in other areas of the world for many years but does not form part of the routine vaccination program for dairy cattle in the United States. Increased confinement of cattle in the U.S. dairy industry will likely make this disease less and less common in future years.

Ascaris lumbricoides

Etiology and Signs

Although reported rarely, *Ascaris lumbricoides*, the swine ascarid, has been identified as a natural and experimental cause of pneumonia in cattle. Exposure of susceptible cattle to large numbers of larvae occurs when the cattle are placed in bedded pens, corrals, or poor-quality pastures previously used by pigs.

Clinical signs consisting of elevated temperature, elevated respiratory and heart rates, marked dyspnea, coughing, and an expiratory grunt develop 7 to 14 days after the cattle are exposed to ascarid ova. Auscultation of the lungs may reflect interstitial changes of pulmonary edema and emphysema. Therefore initial increased bronchovesicular sounds may be replaced by decreased sounds as further interstitial pathology and emphysema ensue. The clinical course lasts 10 to 14 days in most cases and occasionally may be fatal.

One experimental study suggested that initial exposure to ascarid larvae resulted in very mild signs, but reexposure resulted in pronounced signs. This may imply an immune-mediated cause or component to the severe interstitial pneumonia.

Diagnosis

Diagnosis of this disease is difficult unless historical information leads to suspicion of exposure to *A. lumbricoides* ova. A tracheal wash sample may demonstrate an eosinophilic inflammatory pattern. Definitive diagnosis requires identification of the parasite or histopathology to reveal the larvae and associated interstitial pneumonia.

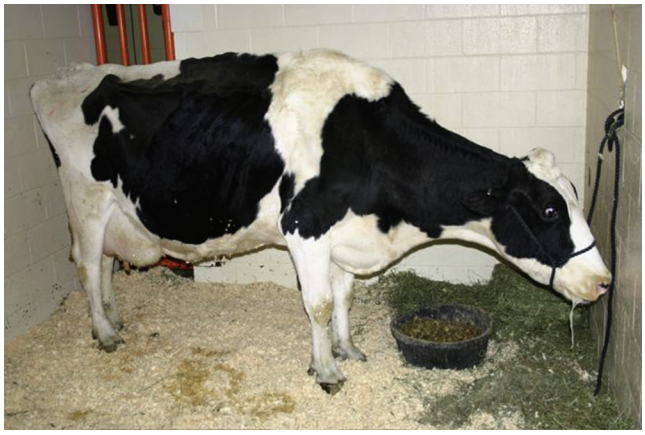
Treatment

Treatment is nonspecific and supportive in the hope that the normal life cycle of the parasite will eliminate the larvae. Prevention involves avoidance of environments used by swine.

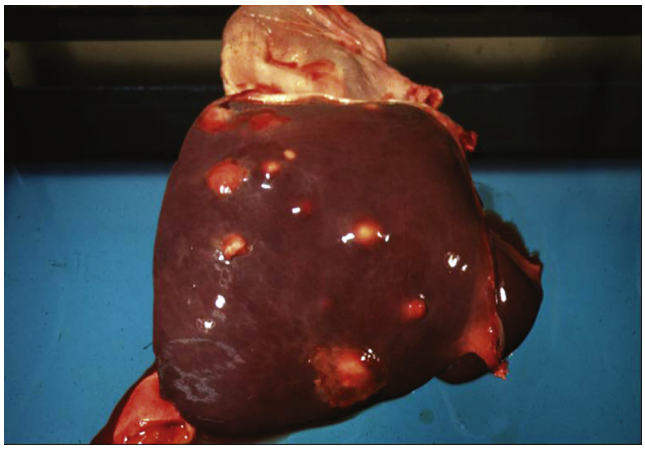
Caudal Vena Caval Thrombosis and Respiratory Diseases Related to Liver Abscessation

Etiology and Signs

Caudal vena caval thrombosis (CVCT) results in a variety of clinical respiratory syndromes in cattle. The origin is most commonly septic thromboemboli originating from an abscess



• **Fig. 4.73** A 5-year-old Holstein cow with caudal vena caval thrombosis syndrome associated with a large, nonhepatic, abdominal abscess. The cow presented with open-mouth breathing in respiratory distress.



• **Fig. 4.74** Multiple hepatic abscesses that were an incidental finding at postmortem in an adult dairy cow. Abscesses, although multiple, were small and located well away from the hilus. No evidence of embolic showering to other sites was evident at postmortem.

at the hilus of the liver showering the caudal vena cava, right heart, and pulmonary arterial circulation. Potentially, other septic foci that are nonhepatic in origin, such as abdominal abscesses caused by hardware (Fig. 4.73) and deep digital sepsis, can also be the source of the thromboembolic showering. Although most cattle do not show signs of illness when the shower occurs, some cattle experience acute death from massive pulmonary infarction or have an acute onset of profound respiratory distress at the time of a thromboembolic episode. Cattle that have inapparent seeding of the pulmonary arteries or survive an acute respiratory distress episode caused by thromboemboli may eventually develop dyspnea, hemoptysis, and anemia. Epistaxis is the most common clinical sign observed in those cows with hemoptysis.

The classic pathogenesis of CVCT starts in the forestomach or abomasum and involves inflammatory or ulcerative mucosal lesions that allow bacterial seeding of the portal circulation with subsequent formation of liver abscesses. Therefore rumenitis, ruminal acidosis, abomasal ulcers, and similar disorders predispose to the condition. This same pathogenesis is responsible for "sawdust livers" in feedlot beef animals, but in dairy cattle, the abscesses usually are larger and fewer in number. Many dairy

cattle have only one abscess. The location is much more important than the number of abscesses, however, because only those at the hilus of the liver or adjacent to the post cava represent significant risk (Fig. 4.74). *F. necrophorum* and *T. pyogenes* are the most common organisms isolated from liver abscesses in dairy cattle. Most cattle with liver abscesses show no clinical signs of illness unless an abscess erodes into the vena cava or multiple large abscesses develop. This disease occurs sporadically in heifers and adult cattle but is rare in calves. This may be the result of calves being fed less intensive diets than heifers or lactating animals.

In CVCT, erosion of a liver abscess into the vena cava with formation of a septic venous thrombosis instigates the clinical disease, and the affected cow may show one of the following syndromes.

Sudden Death Syndrome

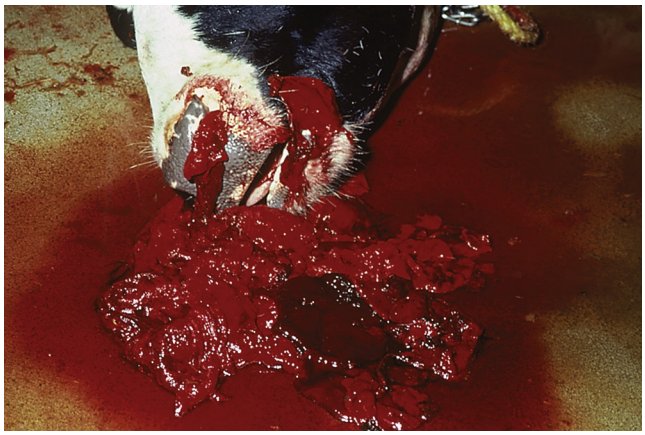
Acute rupture of a liver abscess into the caudal vena cava may result in massive release of thromboemboli to the right heart and subsequent pulmonary artery thrombosis, pulmonary infarction, exotoxemia or endotoxemia, and anoxia. Sudden death may result, and this syndrome represents one of the more common causes of acute death in adult dairy cattle. The possibility that this is a potential cause of death with few to no premonitory signs should be kept in mind when performing a field necropsy on an adult cow that has unexpectedly died. Close attention to the perihilar area of the liver and the caudal vena cava should always be part of a thorough gross pathological examination in such cases. This sudden death may represent a hypersensitivity reaction after a previous clinically inapparent thromboembolic episode; however, sudden rupture of a large hilar abscess into the caudal vena cava or embolic movement of an existing large septic thrombus may cause enough direct pulmonary infarction to cause death without the need for a previous sensitizing episode. *F. necrophorum* toxins have also been shown to aggregate cattle platelets, and this may play some role in the development of thrombosis in this condition.

Acute Respiratory Distress Syndrome

This syndrome appears in one animal within a group or herd. The affected cow has peracute onset of respiratory distress, fever, labored breathing, and increased respiratory and heart rates. Pulmonary edema, SC emphysema, and open-mouth breathing also may be observed. Auscultation of the thorax generally reveals reduced airway sounds resulting from pulmonary edema, pulmonary infarction, and bullous emphysema brought on by exertional respiratory efforts. Rales may be auscultated in some instances, but in general, the lungs are quieter than expected given the obviously labored respirations. The key to diagnosis is the fact that only one animal is affected with severe lower airway disease, and to the owner's knowledge, the cow has had no unique stress or previous problems.

Hemoptysis, Epistaxis, Chronic Pneumonia, Anemia Syndrome

This classic syndrome is associated with CVCT in cattle and results from singular or multiple episodes of thromboembolism from the hilar liver abscess and subsequent septic thrombosis originating in the caudal vena cava. Septic thromboemboli create pulmonary abscesses at their endpoint in pulmonary arteries, and aneurysms develop proximal to each of these abscesses within the affected pulmonary arteries. Because the pulmonary arterial branches in cattle course close to bronchi, eventual enlargement of the abscesses predisposes to their rupture into airways. Sudden discharge of purulent material into the airway creates septic bronchopneumonia followed immediately by minor or major hemorrhage from the arterial aneurysm now communicating directly into the airway. This hemorrhage may be sufficient to result in hemoptysis and subsequent epistaxis. Affected cattle are unthrifty and frequently have been treated for recurrent bronchopneumonia characterized by fever (103.0° to 106.0°F [39.44° to 41.11°C]), increased respiratory rate, as well as auscultable rales, crackles, or wheezes within localized areas of the lung. Some affected cattle develop endocarditis caused by the septic thrombus in the caudal vena cava persisting as a source of chronic bacteremia through the right heart and pulmonary arteries.



• **Fig. 4.75** Massive pulmonary hemorrhage and acute death in a 3-year-old Holstein cow with hepatic-pulmonary abscesses. The cow was calving when the hemorrhage occurred.

Epistaxis or hemoptysis may be slight and intermittent or may be profound and acute and result in sudden death (Fig. 4.75). Curiously, it seems quite often the case that the appearance of the blood at the nares and mouth in such cases is a vivid, arterial red—a paradoxical finding given that the described pathophysiology involves aneurysmal damage to the pulmonary arterial circulation, which is, of course, the only arterial part of the circulation with a low oxygen tension. Perhaps the close anatomic proximity of the bronchial arteries to the pulmonary circulation or potential extension of pulmonary abscesses into the venous side of the pulmonary capillary network explains the apparent arterial blood loss. Epistaxis associated with coughing and chronic bronchopneumonia in dairy cattle indicates an extremely guarded prognosis because of the irreversible nature of the pathology in CVCT. Other signs such as ascites, generalized visceral edema, and diarrhea are possible if the thrombosis occludes the caudal vena cava and results in portal hypertension. Right heart failure and chronic passive congestion of the liver may also develop in some chronic cases.

Diagnosis of Sudden Death Syndrome

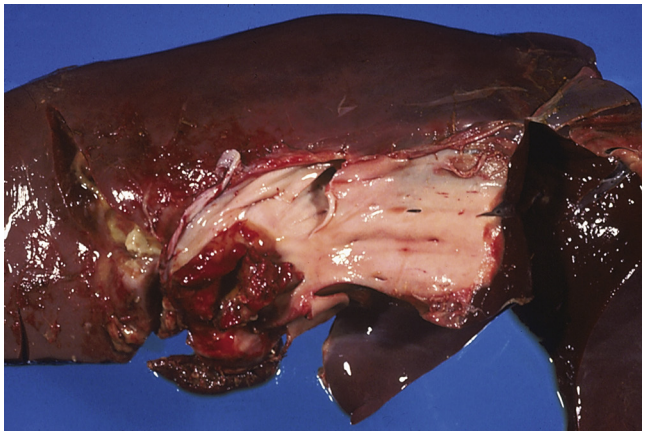
The diagnosis of CVCT requires careful necropsy when sudden death results. In general, affected animals have appeared completely healthy before death. Only one animal is affected in the herd, and the suddenness of death precludes physical examination or ancillary laboratory data. Necropsy will typically reveal a hilar liver abscess with rupture into the caudal vena cava (Figs. 4.76 and 4.77). The lungs may show bullous emphysema, pulmonary edema, pulmonary infarction, and pulmonary arterial thrombosis.

Diagnosis of Acute Respiratory Distress Syndrome

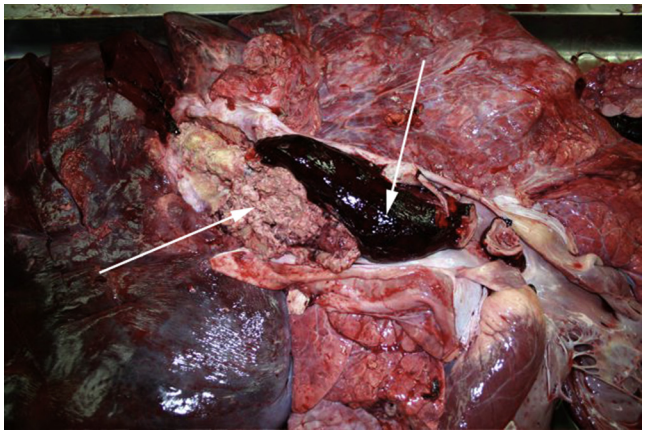
Sudden onset of respiratory distress in a single cow within a herd raises an index of suspicion of acute CVCT. History and physical examination findings should be used to exclude other causes of severe lower airway disease and acute respiratory distress, although this can be challenging. An elevated serum globulin level (>5.0 g/dL) further raises the index of suspicion but cannot confirm the diagnosis. Thoracic radiography, although not widely available in practice, is very helpful to the diagnosis because it usually demonstrates focal or multifocal pulmonary infarction and densities resulting from septic emboli, diffuse pulmonary edema, and bullous emphysema. An enlargement of the thoracic vena cava between the cardiac silhouette and the diaphragm may also be detected radiographically. In field situations, the affected cow is treated symptomatically and gradually may improve over 5 to 10 days. Subsequently, however, these animals usually develop hemoptysis, epistaxis, anemia, and chronic pneumonia typical of the classic signs associated with CVCT. The average lag phase between improvement from the acute syndrome and the onset of epistaxis is 3 to 6 weeks.

Diagnosis of Classical Caudal Vena Caval Thrombosis with Epistaxis, Hemoptysis, Anemia, and Chronic Bronchopneumonia

This form remains the most common clinical syndrome of CVCT. Elevated heart rate, increased respiratory rate, auscultatable rales, persistent or recurrent fever, anemia, and hemoptysis are frequent signs. The owner may have observed epistaxis on several occasions or only once (Figs. 4.78 and 4.79). Some affected cattle bleed out acutely with few premonitory signs. A heart murmur caused by anemia or endocarditis may be present. On rare occasions, generalized edema of the hind parts, ventrum, and udder, as well as ascites may be present in some animals. If edema is generalized, diarrhea caused by GI edema is often also observed. Frequently, serum globulin (>5.0 g/dL) and fibrinogen (>600 mg/dL) are elevated, and a neutrophilic leukocytosis may be present in the hemogram. Thoracic radiography or ultrasonography is helpful in identifying distinct pulmonary abscesses. Transabdominal ultrasonography of the right 8th through 12th ICSs can be useful to identify liver abscesses and allows visualization of the hilus and abdominal caudal vena cava close to the hilus. The causative thrombus may be lodged



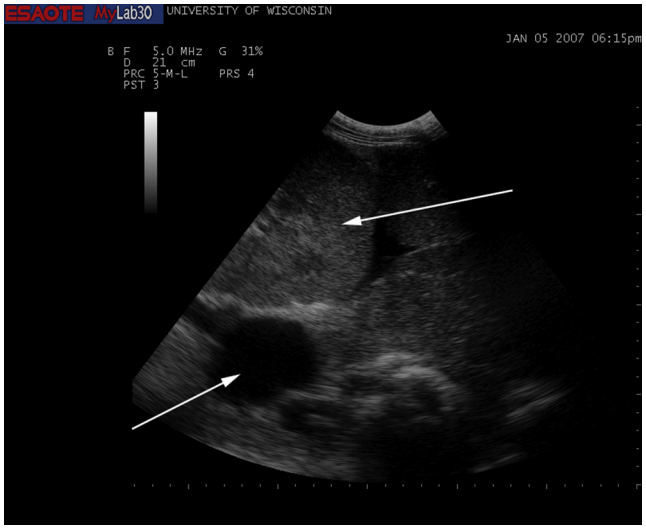
• **Fig. 4.76** Necropsy specimen from a cow that died from rupture of a hilar liver abscess into the postcava. The site of rupture into the postcava is apparent as a rough-edged crater highlighted against the intima of the vein. The purulent remnants of the abscess appear to the left of the crater. (Courtesy of Dr. John M. King.)



• **Fig. 4.77** Necropsy of a 6-year-old Holstein cow euthanized for severe epistaxis, weight loss, and poor production. Note the large friable abscess *(left arrow)* between the liver and extending through the diaphragm alongside a massive, adherent thrombus *(right arrow)* within the caudal vena cava.

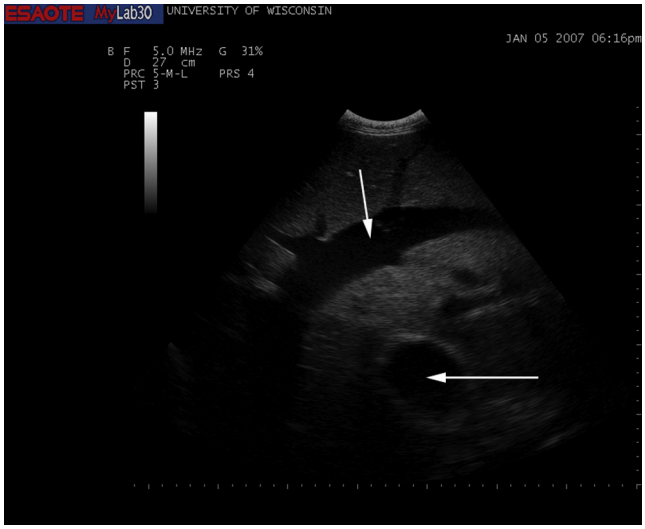
• **Fig. 4.78** Slight epistaxis that was intermittently observed in a cow with caudal vena caval thrombosis.

• **Fig. 4.79** Severe epistasis and hemoptysis in a Holstein with caudal vena caval thrombosis (CVCT) that survived for 3 months after initial diagnosis.



• **Fig. 4.80** Transabdominal ultrasound image of 4-year-old Holstein cow with caudal vena caval thrombosis syndrome. Note the large hepatic abscess *(upper arrow)* and prominent, enlarged caudal vena cava *(lower arrow)* measuring approximately 7 cm in diameter at its widest.

in the caudal vena cava and may also sometimes be visualized ultrasonographically or else its presence inferred by significant intrahepatic vessel enlargement on ultrasonography alongside an increase in the diameter of the perihilar vena cava (normal diameter, 2–5 cm) (Figs. 4.80 and 4.81 and see Video Clip 4.14). Thoracic radiography assists in identifying the severity of pulmonary pathology and may also identify an enlargement of the thoracic vena cava close to the diaphragm in cases of CVCT (Fig. 4.82). Endoscopy will help confirm the origin of hemorrhage in the lower airway and will allow collection of tracheal wash material for cytology and culture if desired.



• **Fig. 4.81** Transabdominal ultrasound image of the same cow as in Fig. 4.80 demonstrating prominent, distended intrahepatic vasculature *(upper arrow)* and vena cava *(lower arrow)* caused by a thrombus that was obstructing the caudal vena cava.

Treatment

Therapy for CVCT causing acute respiratory distress is symptomatic and includes:

- Broad-spectrum antibiotics such as oxytetracycline, ceftiofur, or penicillin to control septic thromboemboli. *F. necrophorum* and *T. pyogenes* are the primary organisms found in these abscesses
- Furosemide (250–500 mg IM twice daily per adult animal) if pulmonary edema is present
- Atropine (2.2 mg/45 kg body weight SC twice daily) as a supportive bronchodilator and to dry bronchial secretions
- Aspirin or another NSAID in standard dosages as an anti-inflammatory drug. Initially, flunixin meglumine may be used (250–500 mg/450 kg body weight) to counteract possible endotoxemia.

If improvement is observed, the animal should be maintained on long-term antibiotics in the hope that the septic thromboemboli may be sterilized. Rifampin may be added to improve antibiotic penetration, but this represents extralabel drug use and is expensive. Currently, in the United States, the use of rifampin also requires the client to guarantee that neither milk nor meat from that individual will be sold for human consumption, making its use very rare. The prognosis is poor because a large thrombus tends to persist in the caudal vena cava, and constant or intermittent embolic showering is likely to continue. Few cattle have survived long term.

Treatment of CVCT with classic signs of pneumonia, epistaxis, hemoptysis, and anemia seldom is worthwhile because of the extensive pathology that exists. Valuable cattle may be treated with long-term penicillin (22,000 U/kg IM twice daily) and aspirin (240–480 grains/450 kg body weight orally twice daily). Aspirin therapy would be contraindicated in cattle that have already exhibited epistaxis. Penicillin is the antibiotic of choice, given the causative organisms, and aspirin may be safe for long-term use in an effort to discourage

• **Fig. 4.82** Mature Red and White Holstein bull with caudal vena caval thrombosis syndrome presented with marked epistaxis (**A**) and with very enlarged thoracic vena cava on thoracic radiographs (vessel is outlined by *arrows*) (**B**).

further platelet aggregation and thrombosis. When epistaxis has been observed and confirmed to originate from the lower airway, the prognosis is extremely guarded. Attempted therapy may be worthwhile in extremely valuable cattle in the hope that only a few pulmonary arterial abscesses have developed, giving the cow a chance to survive. However, it is rare for a cow with well-defined signs of CVCT to survive. Cattle with CVCT and hemoptysis/epistaxis generally do not survive more than 3 weeks once bleeding is noted.

Control

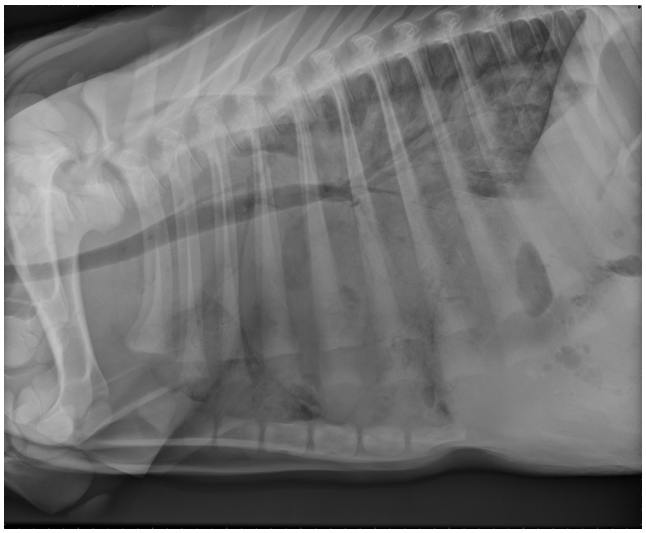
Prevention or control of CVCT in cattle involves nutritional changes. Highly acidic diets that predispose to clinical or subclinical rumenitis and abomasal ulceration have to be tempered by buffers, prefeeding hay before high-energy grains such as high moisture corn, or most commonly by feeding total mixed rations. Dairy rations should not be fed to yearling or bred heifers. High production herds are most at risk for rumenitis and abomasal ulceration secondary to intensive feeding of high-energy, acidic diets. Most cattle with liver abscesses are asymptomatic, and those having hilar abscesses that go on to develop CVCT probably suffered initiation of the pathophysiology months to years before the onset of clinical signs. When more than an occasional case of CVCT appears in a herd, immediate evaluation of the herd's nutritional program is in order. One cow in a herd with CVCT is unfortunate but a common clinical problem. More than one cow in the same herd with CVCT, however, signals a potential serious economic loss and requires changes in the feeding program. Evaluation of the herd for subacute rumen acidosis is indicated under these circumstances and is described in Chapter 5.

Inhalation Pneumonia

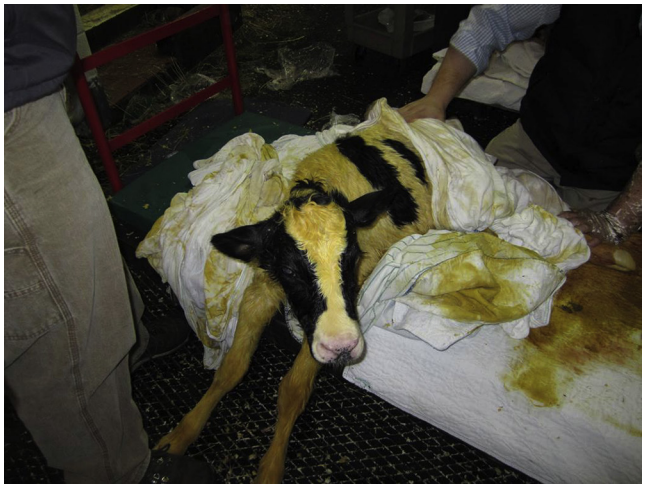
Etiology and Signs

Inhalation pneumonia occurs when feed materials, milk, or medications enter the trachea; the animal fails to clear the airways of the material; and septic bronchopneumonia ensues. In calves, white muscle disease and iatrogenic inhalation pneumonia are the two most common causes. White muscle disease caused by selenium or vitamin E deficiency may affect the tongue, muscles of mastication, or muscles involved in swallowing and predispose to inhalation of milk or milk replacer as the affected calf tries to drink. White muscle disease may on rare occasion cause similar problems in adult cattle. Iatrogenic inhalation pneumonia in calves follows inadvertent intubation of the trachea with stomach tubes or esophageal feeders or, more commonly, from use of abnormally large holes on the end of nipple bottles that overwhelm the calf's ability to swallow and "flood" the airway. Nipple bottles used to feed calves should only drip milk when the bottle is turned upside down! Prematurity or dysmaturity may also predispose to inhalation pneumonia as a result of incompletely developed laryngeal protective reflexes (Fig. 4.83). Bottle feeding weak calves while recumbent is another common cause of aspiration pneumonia. Inhalation pneumonia may also occur from oral dosing of large volumes of medication (e.g., Pepto-Bismol, mineral oil) with the head held in an elevated position. Inhalation pneumonia also may follow pharyngeal trauma by stomach tubes, esophageal feeders, or balling guns, resulting in dysphagia or neurogenic swallowing deficits. Crude or neophytic use of stomach tubes, feeders, and balling guns by laypeople causes most iatrogenic inhalation pneumonia. Inhalation pneumonia may also occur from aspiration of meconium often associated with a prolonged dystocia (Fig. 4.84).

In adult cattle, milk fever (parturient hypocalcemia) is the most common cause of inhalation pneumonia. A severely hypocalcemic cow not only is recumbent but also may lie in lateral recumbency and thus become bloated. Regurgitation of rumen ingesta may lead to inhalation because the cow's



• **Fig. 4.83** Severe aspiration and inhalation pneumonia in a 4-day-old neonatal Brown Swiss calf that had been delivered after protracted dystocia. Thoracic radiographs show severe ventral, consolidating bronchopneumonia consistent with aspiration. The calf had been unable to stand since birth, was tube fed 2 L of colostrum in lateral recumbency, and was then allowed to nurse in recumbency for the next four feedings. It had become progressively more dyspneic but had coughed very little.



• **Fig. 4.84** Aspiration of meconium caused pneumonia in this calf that was delivered after a prolonged dystocia. Clinical signs of pneumonia began on day 2.

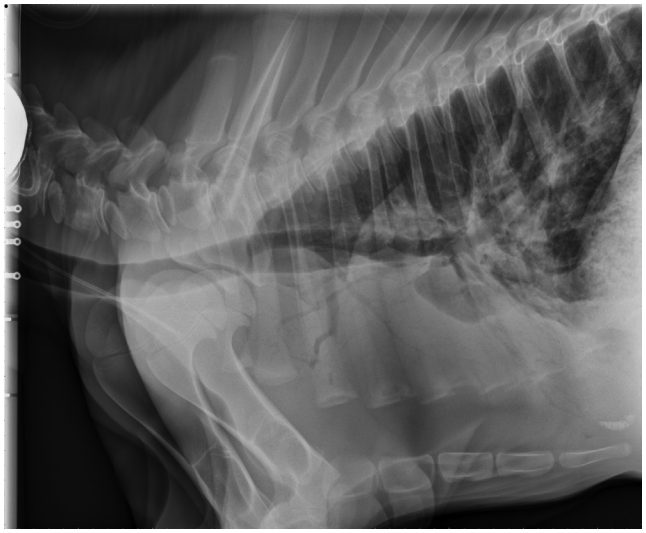
semicomatose state prevents her from clearing the regurgitated ingesta from her pharynx and airway.

Pharyngeal trauma caused by stomach tubes, magnet retrievers, and balling guns may injure vagal nerve branches traversing the pharynx. This neurogenic injury may lead to dysphagia and to defective eructation and regurgitation and may predispose to inhalation pneumonia. Inadvertent intubation of the trachea during attempts at stomach tubing by an unskilled person creates a significant risk of inhalation in adult cattle as in calves. Choke, although rare in dairy cattle today, certainly represents a significant predisposing cause of inhalation pneumonia as well. Cattle that have choked on vegetables or other feedstuffs should be assessed carefully for early signs of inhalation pneumonia. Occasionally, cattle in dorsal recumbency for surgery, whether under sedation or general anesthesia, may regurgitate and inhale feed material into the trachea and lower airways. Consideration of this potential outcome when deciding on a surgical approach in a high-risk patient makes obvious sense. For general anesthesia, the selection of an endotracheal tube with the correct diameter can help preserve and protect the airway, and holding the cow off feed for at least 24 hours before performing elective surgery in dorsal recumbency may also diminish the risk of aspiration.

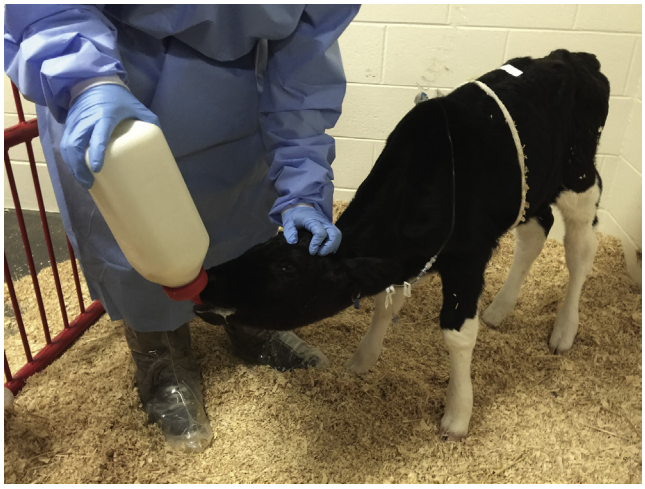
Neurologic disease constitutes another potential cause of inhalation pneumonia in cattle. Listeriosis and other diseases that affect the cranial nerves involved in deglutition, mastication, and swallowing food predispose to inhalation pneumonia, although our experience is that aspiration pneumonia associated with listeriosis has rarely caused a clinical problem. Botulism represents an intoxication that may lead to inhalation pneumonia secondary to dysphagia.

Signs of inhalation vary with the relative volume and content of the inhaled material. For example, inadvertent administration of a large volume of fluid into the trachea results in immediate signs of dyspnea, respiratory distress, cyanosis, and repeated coughing. The affected calf or cow will often expel some of the material from the nose or mouth as a frothy liquid before dying within minutes to hours. Smaller volumes of milk (calves with white muscle disease) or feed inhaled into the lower airway cause a septic bronchopneumonia as the microorganisms contained in the causative material proliferate. In this instance, signs are progressive in nature and consist of a fever poorly responsive to antibiotics, dyspnea, rapid respirations, and rales or bronchial tones in both anterior ventral lung fields (unless the animal was in lateral recumbency at the time of inhalation, in which case the major portion of the pathology may occur in only one lung). Rather than groups of animals being affected, as is typical with contagious pneumonia, only an individual animal tends to be affected with inhalation pneumonia. However, when groups of calves are affected with white muscle disease, several calves may be affected with inhalation pneumonia simultaneously. Individual cattle with inhalation of rumen ingesta secondary to milk fever or other problems develop a progressive gangrenous pneumonia with fever, dyspnea, and toxemia. Rapid consolidation of affected lung tissue occurs, and bronchial tones and rales may be auscultated, usually in the cranioventral lung fields.

Radiography, if available, will often demonstrate a classic ventral distribution to the consolidating bronchopneumonia due to inhalation, both cranial and caudal to the cardiac silhouette (Fig. 4.85). In the severest cases, the radiographic lesions may be more diffuse and severe (see Fig. 4.83). Broad-spectrum antibiotic therapy is effective only if the amount of ingesta inhaled was relatively small. In most instances, the course is one of progressive deterioration over several days, ending in death. Sometimes inhalation of saliva or small amounts of water or feed as a result of dysphagia is treatable with broad-spectrum antibiotic therapy. We have



• **Fig. 4.85** Moderate aspiration and inhalation pneumonia in a 9-day-old Holstein calf presented for diarrhea. Radiographs demonstrate consolidating bronchopneumonia cranial and caudal to the cardiac silhouette.



• **Fig. 4.86** Correct posture for a sick, hospitalized calf during nursing. Note the pressure on the calf's poll region to maintain orientation of the head and neck parallel to the ground. Many calves resist this as they recover, wanting to orient the head more perpendicularly, consistent with the orientation of the bottle.

had the best results with cattle that develop some degree of inhalation pneumonia secondary to dysphagia induced by pharyngeal trauma. Because the amount of inhaled material usually is unknown, treatment is indicated unless the animal shows profound dyspnea and cyanosis in which case euthanasia should be elected.

Treatment

Therapy for inhalation pneumonia involves broad-spectrum antibiotics directed against the microbes normally present in the material inhaled. NSAIDs also would be indicated for supportive therapy. Antibiotic therapy should be continued for at least 2 weeks if symptomatic improvement occurs. Persistent fever, depression, dyspnea, and toxemia are negative signs and generally signal a fatal outcome. Cattle with any form of dysphagia should be fed off the ground to lessen the risk of aspiration. In the event of meconium aspiration in a neonate, a single dose of dexamethasone (5 mg/50 kg calf) may be given alongside antimicrobial and other supportive therapy (eg; oxygen if available).

Prevention

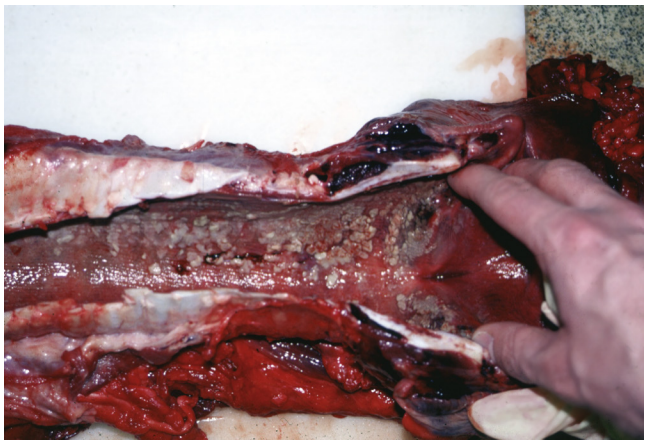
Inhalation of certain necrotizing or nonabsorbable chemicals (e.g., mineral oil) is uniformly fatal, and treatment is not indicated. Prevention of inhalation pneumonia can be practiced only when the problem is anticipated and is largely a matter of common sense. Therefore, withdrawing feed from animals with choke, dysphagia, and other known problems may be helpful. Prompt treatment of milk fever or other diseases that may prevent an adult cow from maintaining sternal recumbency is important in preventing aspiration pneumonia. Management practices such as routine or therapeutic drenching of postparturient cattle should only be performed by laypeople who have been properly trained and provided with appropriate equipment. The feeding of milk to weak, recumbent, premature, or dysmature calves should also be predicated on common sense and an awareness that normal protective airway reflexes may be overcome by impatient feeding practices (e.g., enlarging holes in nipples) or by allowing these calves to nurse with the head and neck hyperextended or dorsiflexed, as appears to be their instinctive habit. Feeding from buckets or a bottle with the head and neck in a neutral position parallel to the ground can lessen the risk of inhalation (Fig. 4.86).

Thermal and Chemical Damage to the Lower Airway

Etiology and Signs

Barn fires and occasionally grass fires in pastures are responsible for thermal and smoke injury to the respiratory tract in cattle. Chemical damage may be mild, as a result of common gases such as ammonia, or severe, as in accidental exposure to anhydrous ammonia.

Thermal damage resulting from excessive heat and smoke inhalation has been well described for comparative species. The pathophysiology involves heat-induced edema and necrosis of the mucosal lining; pulmonary edema and congestion; destruction of the mucociliary apparatus; hyaline membrane formation; and filling of the small airways with proteinaceous fluid, sloughing tissue in the form of diphtheritic membranes, hyaline membranes, and inflammatory cell debris (Fig. 4.87). Pathology tends to be progressive with increasing dyspnea as small airway occlusion develops hours to days after the original thermal and smoke insult. Therefore it is difficult to estimate the severity of the lesions immediately after the fire. Dyspnea characterized by an increased respiratory rate may be the only sign. Cattle with obvious facial burns, muzzle burns, or diphtheritic crusts in the nasal



• **Fig. 4.87** Postmortem specimen of trachea from a cow that had died from smoke inhalation during a barn fire. Note the severe tracheal mucosal erosions and diphtheritic damage.

cavity should be suspected of having sustained significant smoke inhalation. Pulmonary edema is an early sign of severe thermal damage and suggests that subsequent pathology with hyaline membrane formation will follow. Other signs in severely affected animals include cough, tachypnea, wheezing, cyanosis, and stridor. In severe cases, respiratory distress will develop 1 to 24 hours after the initial injury, and bacterial bronchopneumonia may develop within 1 to 4 days in cattle that survive the initial thermal injury. Carbon monoxide poisoning is a common cause of death for animals at the time of the fire or shortly thereafter.

Chemical damage resulting from high environmental concentrations of ammonia largely reflects poor management or inadequate ventilation within an enclosure. Excessive buildup of manure and urine without adequate ventilation will allow ammonia fumes to damage the physical defense mechanisms of the lower airway. Secondary bacterial pneumonias are the most common sequelae to this problem. The relevance of ventilation to the prevalence of calf pneumonia in housed calves during the winter months in the northern United States is increasingly evident. The aerial microenvironment and air quality does not have to deteriorate to the level at which the human nose or eyes are irritated for there to be a significant and detrimental impact on the amount and severity of respiratory disease, especially in preweaned calves. During many investigations of calfhood pneumonia over the past decade, the issues of air quality and inadequate passive transfer have proven consistently to be the two most important drivers of respiratory disease in the first 8 weeks of life (see earlier section).

We have also observed a progressive increase in respiratory rate in some hospitalized cattle that have their bedding changed frequently and are kept in deeply bedded stalls for 2 weeks or more. This has occurred in all seasons of the year and does not seem to be simply temperature related. There is no coughing, and tracheal washes have not revealed a cause for the tachypnea. If the cows are put outside, the respiratory rates return to normal in 1 to 3 days.

Anhydrous ammonia is an extremely dangerous chemical that is widely used in agriculture today. It is used as a source of nonprotein nitrogen for forages and fertilization of various crops. The chemical seeks out water when it comes in contact with vegetable matter or tissue. Accidental exposure to anhydrous ammonia can be lethal to animals or humans who come in contact with the material. Because of the intense water affinity of the chemical, anhydrous ammonia seeks moist tissues such as the eye and respiratory tract. As a result of this contact, moist tissue rapidly desiccates followed by necrosis as the chemical dehydrates the tissue. Corneal edema, epithelial necrosis, and corneal stromal burns immediately develop in the eyes. The mucosa of the respiratory tract is burned, and after dehydration, sloughs and diphtheritic membranes fill the airways, leading to hypoxia or suffocation. Pulmonary edema develops rapidly, and death may occur peracutely or be delayed by hours or a few days. Secondary bacterial pneumonias are possible if the animal survives the initial chemical injury.

Insecticides that are fogged into barns for fly control occasionally may induce chemical damage or sensitivity within the lower airway. The exact mechanism of action is not fully understood, but tachypnea, coughing, and mild dyspnea may be observed.

Diagnosis

The diagnosis of thermal or chemical injury is made by the history and physical examination findings. Ancillary information seldom is necessary. Endoscopy and thoracic radiography may provide prognostic information for valuable animals but seldom are used in practice.

Treatment

Major treatment considerations for acute thermal injury of the airway include improved oxygenation and establishment of an adequate airway. If laryngeal edema is so severe as to result in respiratory distress, a tracheostomy may be necessary. A tracheostomy should not be performed unless severe upper respiratory distress is present because the procedure further predisposes to secondary bacterial bronchopneumonia in burn patients. Oxygen administration is indicated if acute dyspnea suggests possible carbon monoxide poisoning.

Judicious dosages of furosemide (25–50 mg/45 kg body weight) may be necessary if pulmonary edema is present. Use of corticosteroids for acute pulmonary distress caused by thermal injury is controversial. Steroids have been proposed as initial therapy to "short cycle" parts of the vicious cycle of inflammation because they decrease mediators of inflammation, stabilize inflamed vasculature, and decrease edema of the upper and lower airway. If steroids are used, they should be given immediately rather than waiting for the subsequent pathology and respiratory distress that will follow thermal injury over the next 24 hours. A single,

one-time "shock" dose of 0.1 to 1.0 mg/lb dexamethasone or 200 to 500 mg of prednisolone sodium succinate can be given. Abortifacient properties of dexamethasone need to be considered before it is used in pregnant animals, and a significant risk associated with the use of steroids in the form of possible secondary bronchopneumonia also must be considered. Dr. Rebhun commented that he had treated some barn fire victims with dexamethasone but that the results were hard to interpret.

In one valuable yearling bull, a high dose of corticosteroids was used initially without deleterious consequences, but the bull developed a left displacement of the abomasum within 24 hours of treatment. A cause-and-effect relationship for the exogenous corticosteroids on the displacement never was confirmed but certainly was suspicious. NSAIDs may be used at regular dosages without the additional specific risks presented by corticosteroids. However, NSAIDs probably do not block the ongoing pathophysiology of lower airway disease as effectively as corticosteroids. Prophylactic systemic antibiotics are reported not to influence the subsequent development of bacterial bronchopneumonia. Some literature regarding treatment of thermal and chemical injury to the respiratory tract in humans discourages the use of prophylactic antibiotics for fear of allowing resistant strains of bacteria to emerge in the lower airway. In cattle, especially valuable ones, broad-spectrum antibiotics usually are used on a prophylactic basis, although no controlled data support their use. Tetracyclines may help decrease inflammation via their inhibitory effect on metalloproteinases. Disadvantages of tetracyclines are that they are bacteriostatic, and many commensal organisms may be resistant to the drug. If used, practitioners should be aware of their potential to cause nephrotoxicity, particularly in hemodynamically challenged patients.

If tracheostomies or tracheal washes are performed, extreme care should be taken to minimize iatrogenic introduction of pathogens into the respiratory tract. As in thermal skin injury, *Pseudomonas* spp. and other opportunists are the major bacteria to invade damaged tissue.

Nebulization with antibiotics, bronchodilators, corticosteroids, acetylcysteine, or surfactant has also been used in affected cattle. Acetylcysteine has anticollagenase and antioxidant effects via its glutathione-promoting properties.

In chemical injury resulting from anhydrous ammonia, exposed animals and the entire environment should be sprayed with water to destroy residual fumes. Emergency personnel and fire companies should be summoned immediately so that gas masks and protective clothing are available for people spraying water in the area and repairing the leak. All humans in the area should move upwind and leave the area until the leak and fumes have been controlled. Cattle exposed but still alive should not be stressed and should be allowed immediate access to as much fresh air as possible. No specific treatment is possible. Symptomatic treatment may include furosemide, prophylactic antibiotics, or oxygen therapy. Animals with chemically injured eyes should have topical antibiotic and atropine ointments applied to the eyes several times daily.

Mycotic Pneumonia

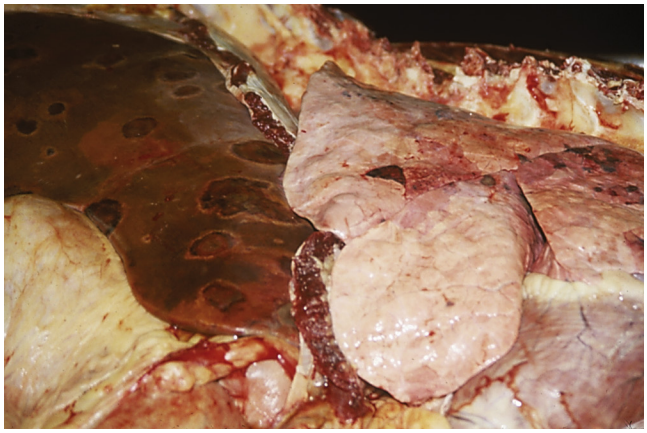
Etiology and Signs

Mycotic or fungal pneumonia usually results from embolic dissemination of fungal organisms from other infected organs such as the rumen, liver, abomasum, or mammary gland. Immunosuppression and immunosuppressive drugs (corticosteroids) predispose to fungal infection, as does intensive antibiotic therapy, which may deplete normal bacterial flora and promote fungal growth. Lactic acid indigestion (toxic rumenitis) remains one of the leading causes of mycotic pneumonia. Pathophysiology evolves from chemical rumenitis through bacterial rumenitis to subsequent mycotic rumenitis, especially if the affected cow has been treated with antibiotics. Embolic infection of the lungs ensues as a result of seeding of the portal circulation and liver from the primary ruminal infection. Similarly, fungal pneumonia has been observed as a sequela to severe septic mastitis in dairy cattle. Intensive antibiotic therapy and overzealous use of corticosteroids predisposed these animals to mycotic infections that became septicemic from the udder and then involved the lungs. Although *Aspergillus* spp. are the most common fungal organisms identified, theoretically any yeast or fungus could be causative.

Signs are nonspecific but consist of persistent fever that is unresponsive to antibiotics (104.0° to 108.0°F [40.0° to 42.2°C]), increased respiratory rate, and variable abnormal lung sounds in one or both lungs. The marked and persistent, often cyclical, fever and the lack of response to antimicrobials are key features of mycotic disease. Rales and increased or decreased bronchovesicular sounds may be heard in individual cases. A primary site of severe infection such as the mammary gland, forestomach, or uterus usually is apparent, or evident from the history, and the respiratory signs may be disregarded or difficult to identify consistently. Multiple organ failure and neurologic signs frequently coexist or develop because of the fungal septicemia. Occasional cases of disseminated fungal disease with fungal pneumonia can be seen in septicemic calves or calves with severe enteritis that have received extensive antibiotic or corticosteroid treatment; similar to adults, affected calves also tend to present with substantial fevers that have been persistent in the face of aggressive antimicrobial therapy.

Diagnosis

The diagnosis is difficult and at best may only be suspected before the death of the individual. Tracheal washings may identify the organisms during cytology or following culture procedures but also may be initially and erroneously disregarded as evidence of environmental upper airway contamination of the tracheal wash sample. However, as



• **Fig. 4.88** Necropsy specimen showing mycotic hepatitis *(left)* and pneumonia *(right)* secondary to lactic acid indigestion. Mycotic lesions appear similar to "targets" with red centers and pale peripheries.

a generality, it is worth pointing out that cytologic demonstration of fungal elements on tracheal wash fluid is more commonly caused by sample contamination than true mycotic pneumonia.

Gross and histologic pathology confirms the diagnosis. Discolored multifocal areas of pneumonia are present grossly (Fig. 4.88), and hyphae are identified by histopathology.

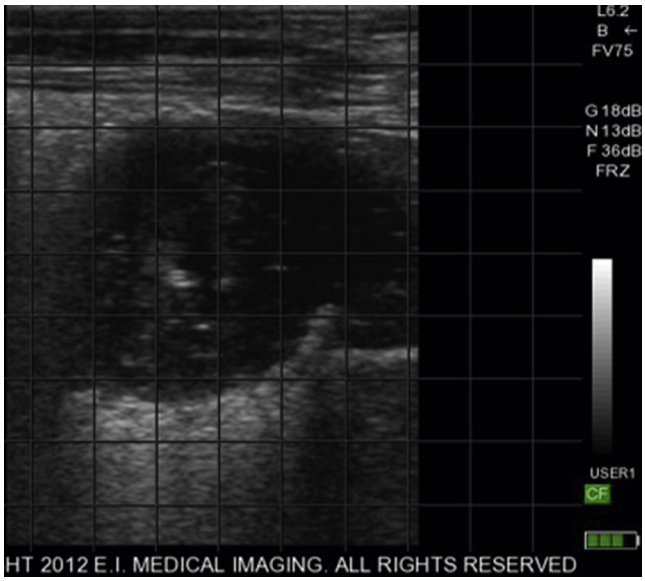
Treatment

No successful treatment has been described for mycotic pneumonia in cattle, and the primary infection coupled with mycotic pneumonia or mycotic septicemia usually is fatal.

Prevention

Although intensive antibiotic therapy is necessary for certain infections in dairy cattle, practitioners should be aware that chronic localized infections in the udder, uterus, or GI tract that are treated with long-term antibiotics may predispose to yeast or fungal overgrowth and potential embolic spread. Repeated IV therapy by practitioners or laypeople using drugs from contaminated multidose vials also may lead to direct mycotic septicemia, such as occurs occasionally in human abusers of IV drugs.

High or repeated dosages of exogenous corticosteroids are to be condemned in dairy cattle and may represent the most dangerous drugs currently predisposing to fungal infections. There are few, if any, diseases in dairy cattle that require high doses of corticosteroids for effective therapy. Corticosteroid use as initial therapy for severe infectious/inflammatory diseases should not be repeated. The low dosages of corticosteroids (10–20 mg of dexamethasone) used by many veterinarians as daily treatment for ketosis generally are safe if limited to no more than 3 to 5 days but should not be used on several consecutive days in cattle with severe infections such as septic mastitis, septic metritis, pneumonia, or toxic rumenitis.



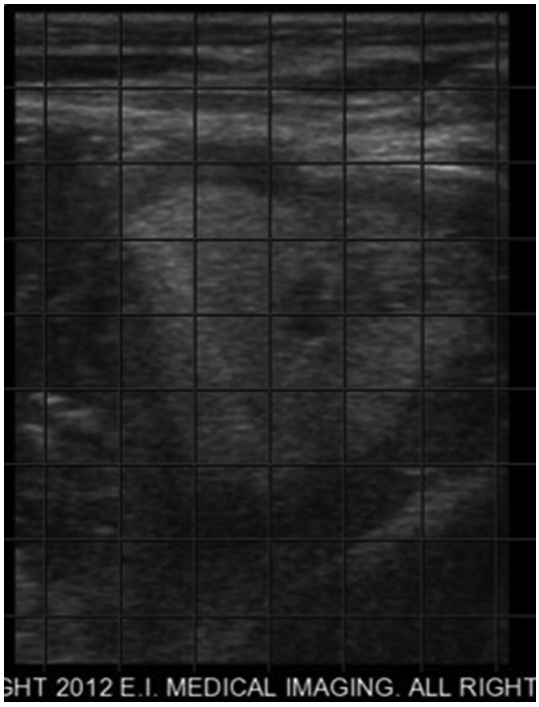
• **Fig. 4.89** Sonogram of caudal lung lobe abscess in 28-day-old Holstein bull calf. Note the mixed echogenicity to abscess content with some hyperechoic gas shadowing present within the luminal center of the lesion.

Space-Occupying Masses in the Thorax, Lung Parenchyma, or Lower Airway

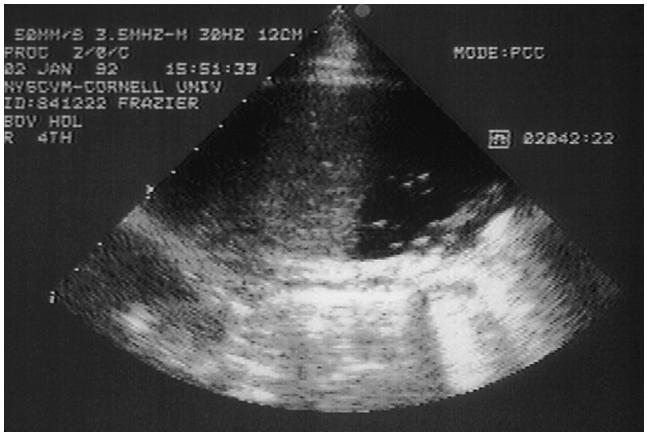
Etiology and Signs

Space-occupying thoracic masses involving the lung parenchyma, visceral or parietal pleura, mediastinum or other structures in the thorax cause subtle or marked progressive dyspnea and may cause signs similar to congestive heart failure. Other clinical signs vary with specific lesions; for example, fever that is only partially or transiently responsive to conventional antibiotic treatment might be present in cattle affected with thoracic abscesses or pleuritis, but fever may not be present at all in thoracic or mediastinal neoplasia.

Inflammatory lesions include thoracic abscesses (Figs. 4.89 and 4.90) and pleuritis (Fig. 4.91, see also Video Clip 4.10). Thoracic abscesses usually are unilateral and when substantial in size may result in detectable absence of lung sounds in the affected ventral hemithorax. Whereas ipsilateral heart sounds may be absent or muffled, contralateral heart sounds are louder than normal and accentuated by the displaced heart's proximity to the contralateral thoracic wall. When small in size, whether single or multiple, thoracic abscesses may be much harder to diagnose; auscultation may not reveal their presence and diagnostic imaging (radiography and ultrasonography) becomes the most helpful diagnostic tool. Fever that is only partially responsive to antibiotics, progressive dyspnea, venous distention and pulsation of the jugular and mammary veins, ventral edema, and a reluctance to move are other signs observed in cattle affected with thoracic abscesses. Etiology of thoracic abscesses sometimes is unknown, but penetration of the thorax by reticular foreign bodies and localized enlarging pulmonary abscesses from previous pneumonia have been confirmed at necropsy in several



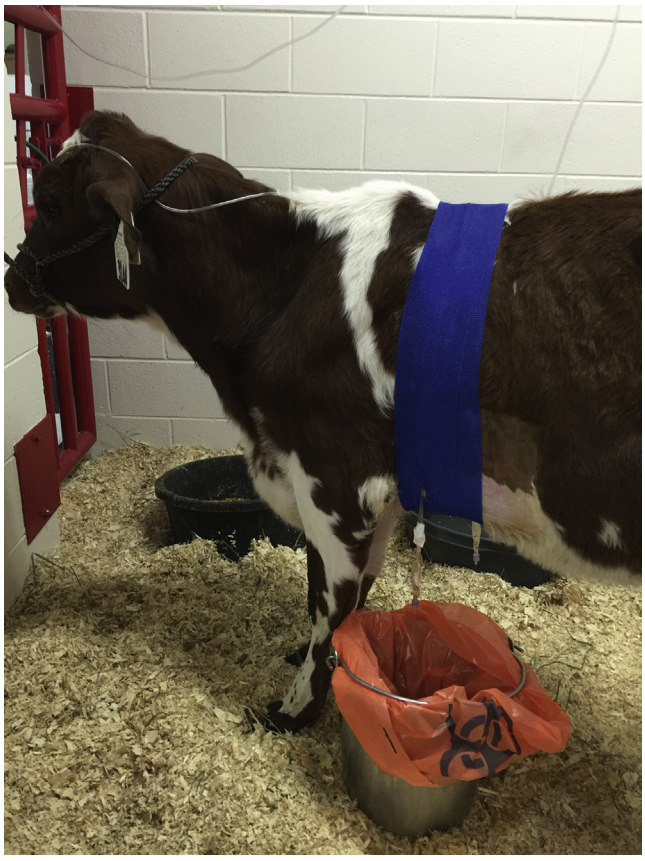
• **Fig. 4.90** Sonogram of the same caudal lung lobe abscess from the bull calf in Fig. 4.89 approximately 2 weeks later, showing more homogeneous appearance to abscess content, suggestive of inspissation.



• **Fig. 4.91** Sonogram of the thorax of a cow with septic pleuritis. The white echogenic spots in the black fluid suggest anaerobic infection and gas production.

fatal cases. Previous history of pneumonia or hardware disease may suggest the etiology in certain cases, but a specific etiology seldom is determined in surviving cattle. *T. pyogenes* is the organism isolated from most thoracic abscesses, either in isolation or in mixed infections involving gram-negative anaerobes such as *Fusobacterium* spp.

Pleuritis is rare in dairy cattle except when it accompanies severe consolidating bronchopneumonia of bacterial origin such as can occur with *Mannheimia haemolytica* pneumonia. As in other species, fever, progressive dyspnea, absence of lung sounds in the ventral thorax (unilateral or bilateral), and thoracic pain are typical. Although a fibrinous pleuritis with a low volume of free pleural fluid is more common in cattle,



• **Fig. 4.92** A 4-month-old Milking Shorthorn heifer with aseptic pleural fluid being drained from the left hemithorax. Fluid accumulation was associated with pulmonary hypertension and signs of congestive heart failure.

when large amounts of pleural fluid are present, venous distention and apparent pulsations may be present in the jugular and mammary veins. Rare cases of pleuritis resulting from rupture of a parenchymal pulmonary abscess into the pleural space, penetrating thoracic wounds or foreign bodies associated with traumatic reticuloperitonitis, erosion of the diaphragm by an abscess associated with hardware or perforating abomasal ulcer, and rupture of the esophagus secondary to chronic choke or trauma also have been observed.

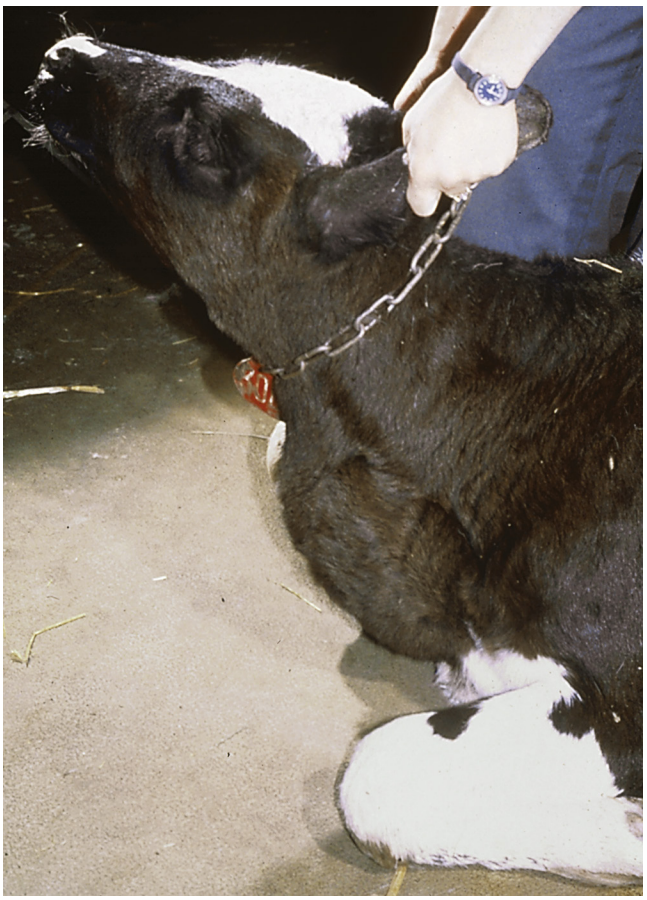
Pleural effusion may also occur with either nonseptic or septic pericarditis. We have had some patients with pericarditis and pleuritis in whom the cause could not be determined. In one cow with fibrinous pericarditis and pleuritis of mixed cytology on centesis (neutrophils, lymphocytes, plasma cells), a complete cure was achieved after pericardial injection of corticosteroids and systemic antibiotics. Although severe pleural effusion is not common in cattle with right heart failure, we have seen it in a few cases (Fig. 4.92). Pleural effusion of a mild to moderate volume does seem to be quite common in association with idiopathic hemorrhagic pericardial effusion, most likely caused by the cardiac tamponade that accompanies the sometimes massive volume of pericardial fluid. When pleural fluid accompanies pericardial effusion, cytologic evaluation of the two different cavity fluids is not always the same, emphasizing the relevance of pericardiocentesis in the evaluation of primary pericardial disease.

• **Fig. 4.93** A mature Holstein cow with a thoracic seroma or transudate secondary to traumatic injury at the costochondral region of the left thorax. A total of 40 L of transudative fluid had just been removed from the left hemithorax via thoracocentesis. The cow made a complete recovery.

Seromas and hematomas may develop after trauma to the thoracic wall. These masses occasionally extend into the thorax itself. In rare instances, apparent rupture or leakage of the seroma through the parietal pleura occurs. These seromas and hematomas may be associated with rib fractures or traumatic injuries at the costochondral junctions (Fig. 4.93). Dystocia can be a cause of these in neonatal calves. Signs may include progressive dyspnea, increased respiratory rate, venous distention and pulsation, normal temperature, absence of lung sounds ventrally in the affected hemithorax, absence or muffling of heart sounds in the affected hemithorax, and loud pounding heart sounds in the contralateral hemithorax caused by cardiac displacement.

Diaphragmatic hernias may cause dyspnea and absence of cardiopulmonary sounds in the affected thoracic area. Bloat is most commonly observed in cattle having diaphragmatic hernia because the reticulum is usually the herniated organ.

Neoplastic masses may occur in the pulmonary parenchyma, pleura, lymph nodes, or thymus. Cardiac neoplasms are discussed with other cardiac diseases in Chapter 3. Thymic lymphosarcoma may be the most obvious neoplasm within this group. Thymic lymphosarcoma is recognized in cattle between 4 and 24 months of age and causes progressive dyspnea, bloat, or both. It is a sporadic form of lymphosarcoma in cattle, meaning that it is not associated with bovine leukemia virus (BLV) infection. Swelling is often obvious in the distal ventral cervical area and extends through the thoracic inlet. Some thymic lymphosarcoma masses are soft, fluid-like swellings on palpation (Fig. 4.94), but others are firmer. Compression of the trachea, esophagus, and jugular veins results in dyspnea, interference with eructation, and jugular distention that varies with the size of the mass. Compression of the trachea, causing respiratory distress, may also occur in adult cattle with enzootic BLV–associated lymphosarcoma. Adult lymphosarcoma may be associated with tumor formation in the thorax as a result of lymph node, pleural, cardiac, and occasionally pulmonary



• **Fig. 4.94** Thymic lymphosarcoma in a 6-month-old calf presented because of worsening dyspnea and intermittent bloat.

involvement. Signs vary depending on the tumor numbers, size, and other organs affected. Occasionally, patients with lymphosarcoma have fever caused by tumor necrosis, and this may be a misleading sign because otherwise they should be afebrile. Severe pleural effusion with many neoplastic lymphocytes may occur. The pleural effusion caused by lymphosarcoma is often grossly discolored, having a bloody appearance. Thymomas are rare in cattle.

Primary pulmonary tumors of epithelial origin described as papillary adenomas have been observed in young cattle at slaughter. These were reported as benign, multicentric tumors because metastases were not observed. Signs were not reported because these were incidental findings during slaughter inspection. Several case reports have documented malignant neoplasms such as bronchiolar adenocarcinoma in older cows showing signs of progressive dyspnea. Dr. Rebhun documented one older cow and one bull with massive pulmonary adenocarcinomas that resulted in progressive dyspnea, weight loss, and reduced lung sounds. Mesotheliomas within the thorax originate from the pleura and tend to be multiple. They may enlarge collectively to create signs of progressive dyspnea, decreased lung sounds caused by massive pleural effusion, and weight loss, eventually leading to death. Of the small number of patients with mesothelioma that we have seen, they have all had dual body cavity effusions to some degree with both thoracic (pleural) and abdominal fluid accumulation.

Tuberculosis, although rare in dairy cattle because of regulatory control efforts, should be remembered as a potential cause of progressive dyspnea, coughing, weight loss, and signs of pneumonia. Enlarged thoracic lymph nodes associated with the infection may result in esophageal compression and bloat or obvious respiratory distress from tracheal compression. However, the condition is not commonly associated with significant pleural effusion.

Diagnosis

Diagnosis of space-occupying lesions in the thorax requires careful auscultation to detect differences in lung and heart sounds in each hemithorax. Abscesses, seromas, bronchial cysts, or masses occupying one hemithorax elevate the ipsilateral lung and push the heart toward the opposite hemithorax. Therefore in the affected hemithorax, lung sounds are absent ventrally, and heart sounds are muffled or absent. Auscultation of the opposite hemithorax reveals uniformly increased bronchovesicular sounds and a loud "pounding" heart beat caused by the proximity of the heart to the thoracic wall on this side. Thoracic percussion also may be helpful in detecting the area of involvement. Because cattle affected with these problems often have increased central venous pressure as a result of impaired venous return, they may be confused with heart failure patients. An incomplete physical examination may lead to an erroneous diagnosis such as endocarditis or pericarditis if the examiner only auscultates one hemithorax.

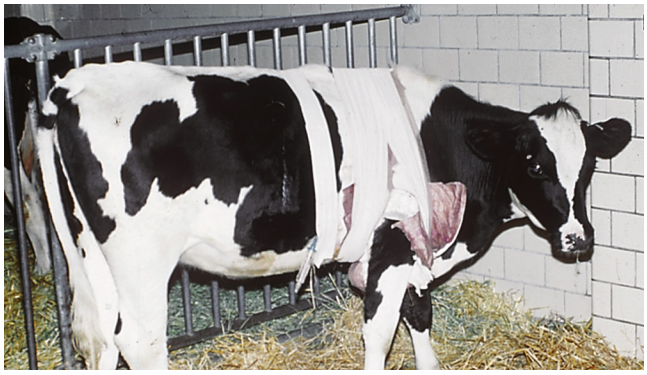
When an abnormality has been identified on physical examination, further diagnostics are indicated. Thoracic radiography and ultrasonography are appropriate if a complete diagnostic workup is to be performed. Blood work may be helpful in the case of thoracic abscesses in that the serum globulin level usually is elevated (≥5.0 g/dL), and neutrophilia may be present. Undoubtedly, ultrasonography has tremendous benefits diagnostically for the evaluation of pleural, cardiac, and mediastinal space-occupying lesions. Because of the extravagant fluid volumes that can be associated with neoplastic lesions in particular, it may be necessary to use low- to medium-frequency probes (2.5–5 MHz) that provide high-quality images at 20 to 25 cm depth to identify deeper space-occupying lesions. Drainage both facilitates cytologic diagnosis and permits better near-field visualization of any masses.

The most direct diagnostic aid remains thoracocentesis with a suitable needle. Although a 5.0-cm needle will enter the pleural space of cattle, it is seldom long enough to invade the capsule of an encapsulated abscess or seroma. Therefore an 8.75-cm, 18-gauge needle is preferred for initial thoracocentesis through the lower fifth or sixth ICS on the affected hemithorax. If fluid or pus is obtained, the material is submitted for cytology and culture. Biopsy of a mass lesion under ultrasound guidance may be indicated.

If thymic lymphosarcoma is suspected, aspirates for cytology or biopsies (True-Cut biopsy needle; Baxter Healthcare Corp., Valencia, CA) are indicated to allow definitive diagnosis. A hematoma of the ventral neck may appear clinically similar to thymic lymphosarcoma, but ultrasound examination and biopsy should allow differentiation of the two. As previously mentioned, some patients with thymic lymphosarcoma have a misleading fluctuant mass in the distal cervical region that appears fluid filled. Aspirate attempts yield no fluid, however, but biopsy will confirm the diagnosis. Biopsy of mediastinal masses that are confined to the thorax are challenging to perform safely, with the risk of iatrogenic cardiac, pulmonary, or great vessel injury being quite high. If accompanied by free pleural fluid, it is always prudent to obtain a sample of this first in hopes of identifying exfoliated neoplastic cells before rushing to a riskier biopsy procedure. Juvenile cattle affected with thymic lymphosarcoma usually are negative for BLV when tested by agar gel immunodiffusion (AGID), ELISA, or PCR.

Pleuritis or pleural effusion may be unilateral or bilateral. Careful auscultation and percussion should lead to suspicion of free pleural fluid because lung sounds usually are absent in the ventral aspect of the affected hemithorax. Dyspnea may be marked in cattle with large accumulations of pleural fluid. Pleural fluid does not displace the heart, as occurs in association with unilateral thoracic masses or abscesses. Therefore heart sounds are audible bilaterally and may appear to radiate caudodorsally by sound conduction through the pleural fluid. Pleural fluid must be differentiated from anterior ventral pulmonary consolidation. Whereas bronchial tones usually are heard in consolidated regions of lungs, absence of sounds is more typical of pleural fluid. Thoracocentesis is indicated to confirm pleural fluid accumulation; any sampled fluid should be analyzed using cytology and culture to differentiate infectious from neoplastic or other causes. Ultrasonography and thoracic radiography, if available, help in the management of a valuable cow affected with this problem. Ultrasonography is an extremely valuable tool for evaluating pleural disease in cattle. As more portable equipment becomes available, an ultrasound machine may be used with increasing frequency as part of the evaluation for sick cows. Ultrasonography can quickly determine whether the patient has pleural effusion, abscessation, consolidation, or pleural surface masses. It can also be used as an aid for collection of samples via needle or biopsy. If available, thoracic radiography is helpful to confirm or deny diaphragmatic hernia.

Thoracic tumors involving the lung parenchyma, pleura, or thoracic lymph nodes are difficult to diagnose unless thoracic radiographs and ultrasonography are available. Signs vary, and dyspnea and progressive weight loss occur despite symptomatic treatment. Thoracic lymphosarcoma may be suspected based on physical signs involving other sites or lymph nodes becoming obviously enlarged. A PCR test for BLV will be positive as will the AGID and ELISA tests in most cows with clinical lymphosarcoma. This does not confirm a diagnosis but does add to the index of suspicion if lymphosarcoma is suspected. Bloat and tracheal compression may occur if mediastinal masses or lymphadenopathy become severe. Thoracocentesis may offer the best means of diagnosis for unusual



• **Fig. 4.95** Yearling heifer with an encapsulated *Trueperella pyogenes* abscess in the right hemithorax. A chest trochar has been placed to facilitate drainage.

tumors such as adenocarcinomas because exfoliative cytology may help identify the tumor and allow proper prognosis. Thoracoscopy can be performed safely in cattle and allows direct observation of the mediastinal lymph nodes, thoracic portion of the esophagus, and dorsal branch of the vagus nerve, and it could aid in the identification and biopsy of intrathoracic masses.

Treatment

Therapy of unilateral thoracic abscesses and seromas involves drainage of the lesions through the thoracic wall. Because *T. pyogenes* is the usual causative organism of thoracic abscesses, a thick capsule often is present. After the location of the abscess is confirmed by thoracocentesis, a large-bore (20–28 Fr) chest trochar is placed into the abscess cavity (Fig. 4.95). The chest trochar is sutured in place, and the affected cow is started on penicillin (22,000 U/kg twice daily, SC or IM). When ultrasonography is available, it may be used to confirm pleural adhesions between parietal pleura and the abscess, allowing subsequent surgical thoracotomy coupled with rib resection to afford even more efficient drainage and exploration of the cause of the abscess. Complete drainage is the key to successful treatment. Lavage of saline or antibiotic and saline solutions through the indwelling trochar also has been used in some cases. Irritating solutions such as iodine products are contraindicated, however.

Cattle with seromas that are drained in this manner subsequently have a good prognosis. Abscesses require long-term antibiotic therapy and complete evacuation and drainage. Therefore, the affected cow must be of substantial value to justify the medical expenses and associated loss of milk sales for several weeks. Cattle affected with thoracic abscesses may lose significant body condition during early treatment, but absence of fever, decreased venous distention, increased appetite, weight gain, and a return to normal thoracic sounds on auscultation are all signs of improvement.

Treatment for pleuritis and pleural fluid requires drainage of the fluid and appropriate antibiotic therapy to control associated pneumonia. If pleural fluid is caused by effusion from neoplastic conditions, treatment is rarely indicated. Hardware perforations of the diaphragm may result in frank pleuritis associated with pleural fluid accumulation, thoracic abscessation, or diaphragmatic hernia. When *T. pyogenes* predominates, a thick-walled thoracic abscess develops, resulting in chronic illness. If a mixed infection develops and a fluid pleuritis that is not encapsulated results, the affected cow typically has an acute presentation with large amounts of septic fluid free in the pleural space.

Surprisingly few cattle with bacterial bronchopneumonia develop clinically significant pleural fluid accumulation. Nonetheless, pneumonia remains the most common cause of pleural fluid accumulation. The diagnosis of pleural fluid accumulation unilaterally or bilaterally in a cow affected with severe pneumonia dictates drainage of this fluid. Pleural effusion associated with bronchopneumonia will result in fever unresponsive to antibiotics and marked dyspnea. Drainage is provided by daily thoracocentesis or continuous drainage until negligible quantities of pleural fluid are obtained. Appropriate systemic antibiotics should be selected based on culture and susceptibility results and maintained for at least 1 week beyond the last thoracocentesis. Thoracotomy and drainage may be required in some cases, especially those associated with hardware and a foreign body residing within the abscess.

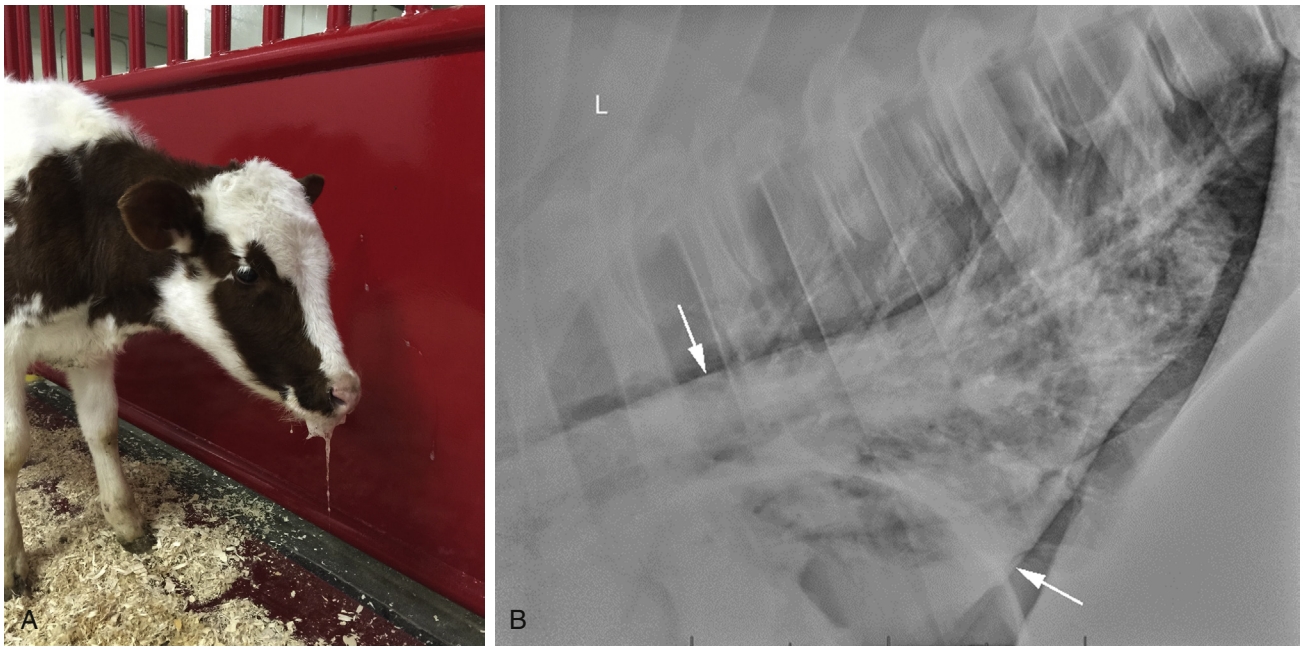
Pneumothorax

Etiology and Signs

Dyspnea accompanied by increased respiratory rate and effort coupled with absence of bronchovesicular sounds in the dorsal lung fields unilaterally or bilaterally characterizes pneumothorax or bullous pulmonary emphysema. Dyspnea may range from mild to severe. Some adult cattle appear very painful with pneumothorax. When severe dyspnea is present, open-mouth breathing and expiratory groan suggest a bilateral problem. Subcutaneous emphysema may be observed in some affected cattle.

Pneumoretroperitoneum may be appreciated on rectal exam in some cattle with pneumothorax or pneumomediastinum.

Auscultation of the affected hemithorax reveals increased bronchovesicular sounds in the ventral lung fields and absence of lung sounds dorsally. Body temperature is normal unless exertion, high environmental temperatures, or pulmonary inflammation associated with a primary infectious cause (e.g., BRSV) leads to pyrexia. Severe exertion during parturition, exertion during restraint for treatment or surgery, penetrating thoracic wounds, or pharyngeal or laryngeal injury causing a pneumomediastinum that ruptures into the chest may also cause pneumothorax (Fig. 4.96). Primary pulmonary pathology associated with chronic bronchopneumonia and emphysematous bullae formation is the most common cause of pneumothorax in adult dairy cattle in the northern United States. Fever may be present if primary pulmonary inflammation (BRSV, severe bacterial bronchopneumonia, acute bovine pulmonary emphysema [ABPE], among others) contributed to emphysema and resultant pneumothorax. BRSV is the



• **Fig. 4.96** **A,** A 6-month-old Milking Shorthorn with respiratory distress and severe aspiration pneumonia associated with pharyngeal trauma. **B,** Note pneumothorax with lung collapse and severe pneumonia on a thoracic radiograph. The collapsed lung is highlighted by *arrows*.

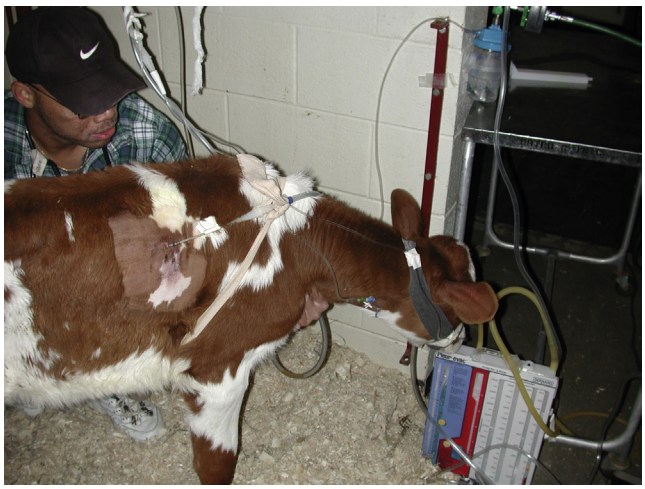
most common infectious agent associated with pneumothorax in cattle (see Fig. 4.60). In these inflammatory diseases, auscultation of the ventral lung fields helps to define etiology. Ultrasonography may be helpful in diagnosing the pneumothorax (there is no normal sliding of the dorsal air line) and determining the extent of more cranioventral lung pathology.

Diagnosis

Auscultation and percussion suggest the diagnosis. Pneumothorax must be differentiated from bullous emphysema and pulmonary edema because these two conditions should not be addressed therapeutically by chest drainage. Radiography or ultrasonography will confirm the diagnosis but may not be available. If history, auscultation, and percussion suggest a diagnosis of pneumothorax, thoracic puncture and vacuum evacuation of free air should be attempted through the dorsal 9th or 10th ICS. The presence of free air confirms the diagnosis, and airway sounds should return to the dorsal thorax after evacuation of the free air. Tracheal wash samples for cytology, culture, and BRSV diagnostics may be necessary to assess lower airway infection or inflammation. Care should be taken to avoid causing severe coughing while collecting samples as this could exacerbate the condition.

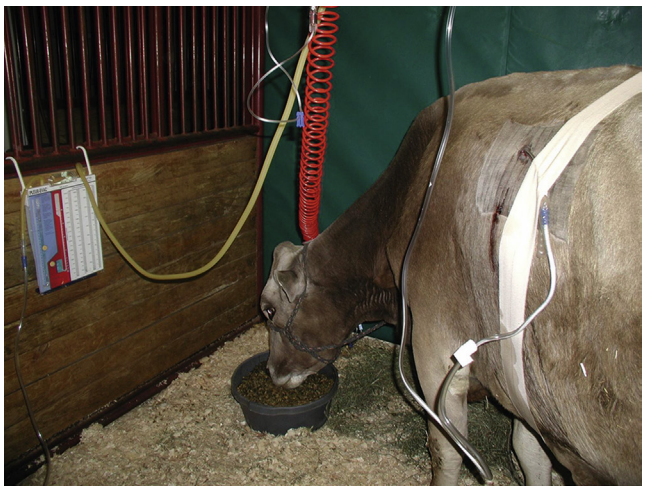
Treatment

Therapy requires evacuation of air from the affected hemithorax and treatment of any primary problem such as pneumonia, puncture wounds, and so forth. Cattle with pneumothorax resulting from chronic bacterial pneumonia have a guarded prognosis. Following evacuation, rapid improvement in the dyspnea should be anticipated when

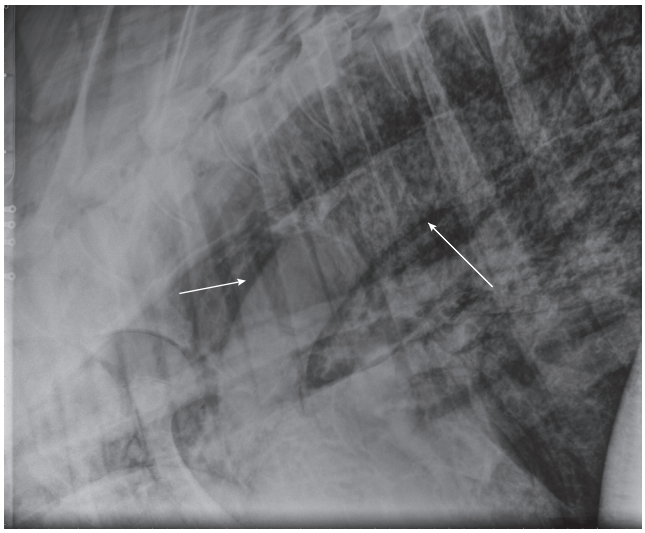


• **Fig. 4.97** A 5-week-old Holstein calf undergoing continuous flow evacuation of right-sided pneumothorax associated with acute bovine respiratory syncytial virus infection. The calf made a full recovery.

pneumothorax is the major problem. The clinician must remember that, except in exogenous puncture of the thorax or ruptured pneumomediastinum, pneumothorax originates from damaged pulmonary tissue that has "leaked" air. Simple evacuation of the free air in the thorax will improve the affected animal temporarily but does not guarantee the problem will not recur. Owners need to be instructed to watch the patient carefully for recurrence of dyspnea if the damaged lung continues to leak. Most cattle, however, respond to one or two evacuations of the thorax. A technique for continuous drainage has been described by Peek and coworkers in cattle that requires hospitalization and confinement (Figs. 4.97 and 4.98).



• **Fig. 4.98** A 4-year-old Brown Swiss cow being treated for pneumothorax associated with bullous emphysema and unilateral pneumothorax associated with chronic bronchopneumonia by continuous flow evacuation.



• **Fig. 4.99** "Double silhouetting" *(arrows)* of the aorta associated with pneumomediastinum in an adult cow with bovine respiratory syncytial virus infection and severe interstitial pneumonia.

Pneumomediastinum

Etiology and Signs

Pneumomediastinum most often accompanies severe pulmonary parenchymal diseases that result in emphysema and bullae formation. Subsequent leakage of air into the mediastinum occurs. Several of the causes of pneumothorax mentioned previously are also potential causes of pneumomediastinum. Pneumomediastinum is most common in postpartum cows. In some cases, there is old pulmonary pathology predisposing to the pneumomediastinum, but other cases may simply result from the exertion of calving. Signs may be mild or impossible to separate from those caused by the primary pulmonary pathology. Mild dyspnea, SC emphysema, and bilateral muffled heart sounds are present in most instances. The muffled heart sounds are the only consistent findings and are caused by air insulation of the cardiac sounds. The SC emphysema is mostly on the dorsum of the cow as the air migrates along the aorta and through the lumbar fascial planes. It can also be felt rectally along the aorta.

On rare occasions, respiratory distress may occur within a few minutes after a lidocaine epidural when air may have been heard entering the epidural space for a few seconds before the lidocaine injection. Affected cattle appear apprehensive and restless, have pronounced abdominal effort in breathing, and cough. Although anaphylaxis is often considered, there are no other signs of anaphylaxis, and the cattle slowly recover without treatment in 20 to 30 minutes. This is most likely a result of epidural air acutely entering the mediastinum, causing pneumomediastinum (see Video Clip 4.15).

Diagnosis

Subcutaneous emphysema in a postpartum cow is highly suggestive of pneumomediastinum. The presence of bilateral heart sound muffling requires differentiation of this condition from pericarditis. This differentiation is aided by obvious pulmonary pathology coupled with an absence of signs of heart failure in most cases. If physical examination findings cannot definitively differentiate these problems, ultrasonography and radiography are indicated. Pericardiocentesis is not indicated as an initial procedure because it may subject the patient to unnecessary risks. Thoracic radiographs demonstrate a very clear cardiac and aortic shadow because surrounding air highlights these tissues. "Double silhouetting" of the great vessels on chest radiographs is characteristic of pneumomediastinum (Fig. 4.99). On occasions this radiographic finding may even be incidental in a postpartum cow with no other signs of dyspnea.

Treatment

Specific treatment for pneumomediastinum is not required unless the cow has labored breathing and a probable pneumothorax. Therefore therapy should be directed against any primary pulmonary pathology in addition to oxygen, bronchodilator, and antitussive therapy.

Noninfectious Causes of Acute Respiratory Distress in Cattle

Acute respiratory distress in cattle may occur with a variety of noninfectious pathologic changes. Some causes have well-documented pathophysiology, but others are more poorly defined and controversial. Terminology varies tremendously among pathologists and clinicians, resulting in much confusion regarding these disorders. Most acute diseases discussed here require gross or microscopic pathology to enable positive diagnosis. The clinician cannot differentiate most of these diseases based on physical examination alone. Textbook

descriptions have confused the issue by using different synonyms and eponyms to characterize the problem.

Fortunately, as a collected group of respiratory problems, these diseases are uncommon and much less important than infectious causes of respiratory disease in dairy cattle. Therefore they will be described individually as best as possible in this section. Readers should realize that the nomenclature of these diseases has changed in the past and is likely to change in the future. Specific therapy is addressed when indicated. Respiratory distress may also be caused by methemoglobinemia (nitrate toxicity), cyanide toxicity (wilted wild cherry leaf ingestion), or acute and severe hemolytic anemia.

Acute Bovine Pulmonary Edema and Emphysema (Atypical Interstitial Pneumonia, Fog Fever, and Pneumotoxicosis)

Etiology and Signs

This acute disease of cattle classically develops within 2 weeks of the time cattle are moved to lush pasture. The exact composition of the pasture does not seem important because grasses, alfalfa, turnips, kale, and rape all have been incriminated. Consumption of *Perilla* (purple) mint *(Perilla frutescens)* or moldy sweet potatoes may cause identical syndromes. Although not as well documented, we have seen similar clinical and pathological outbreaks associated with grass silages and ryegrass pastures. Affected cattle develop acute, severe respiratory distress characterized by reluctance to move, open-mouth breathing, pulmonary edema, tachypnea, and hyperpnea. Temperatures are normal to only slightly elevated unless environmental temperatures are very high.

The etiopathogenesis of classic "fog fever" is well characterized. Rapid consumption of lush, postharvest pasture leads to ingestion of large amounts of L-tryptophan to which the rumen microbiota is not acclimated. Subsequent transformation of ingested L-tryptophan to indole acetic acid is followed by decarboxylation to 3-methylindole, which is the toxic metabolite of tryptophan. After absorption of 3-methylindole from the rumen into the systemic circulation the cytochrome P450 system metabolizes the chemical, producing pneumotoxicity in Clara cells and type 1 pneumocytes. Experimental studies have confirmed that 3-methylindole is the toxic metabolite of tryptophan involved in classic ABPE. Calves seldom are affected, but adult animals older than 2 years of age in good body condition appear most at risk.

The etiopathogeneses of AIP associated with *Perilla* mint and moldy sweet potato consumption are quite similar. *Perilla* mint is at its most toxic when the plant is flowering and in the seed-producing stage; cattle tend to only consume it when other more palatable pasture components are grazed out; subsequently, the condition is usually seen in the late summer on poor-quality pasture. The toxic principle is *Perilla* ketone rather than 3-methylindole. Cattle can develop identical signs when fed sweet potatoes blighted with the mold *Fusarium solani,* which produces the propneumotoxin 4-ipomeanol. Activation of 4-ipomeanol by pulmonary cytochrome P450 enzyme activity is thought to produce the toxic principle.

Fortunately, ABPE is rare in dairy cattle in the United States because pasture management is more stringent, and pasturing is practiced less commonly in confinement herds than in the beef industry. Dairy practitioners should be aware of ABPE but may never see a herd outbreak of the disease. We have on rare occasion diagnosed this or a similar disease in confined cattle fed silage where the pneumotoxicant was unknown.

Signs

Profound dyspnea, expiratory grunt, reluctance to move, auscultatable evidence of interstitial pneumonia (rhonchi and rales) in the ventral lung field, and quiet lungs dorsally secondary to emphysema and edema characterize the condition. Subcutaneous emphysema may be observed. The morbidity rate may approach 50%, and mortality rates range from 25% to 50%.

Diagnosis and Treatment

Diagnosis is by history, clinical signs, and pathologic study of the lungs from fatal cases. Treatment is seldom helpful, but a variety of drugs have been used in an effort to save badly affected animals. Simple movement or mild restraint may be fatal to these anoxic animals. Therefore treatment is controversial and empiric. Furosemide (0.5–1.0 mg/kg) may lessen pulmonary edema. Atropine (0.048 mg/kg or 1/30 grain/100 lb body weight twice daily), antihistamines, NSAIDs, vitamins A and E, and cortisone all have been used with varying anecdotal results. Animals that are rested, removed from the pasture, and not severely affected usually recover in 1 to 2 weeks. Some cattle may fall into the category of "chronic lungers," with chronic respiratory illness associated with proliferation of type 2 pneumocytes and pulmonary fibrosis.

Prevention

Prevention is the best treatment and may be accomplished by feeding susceptible cattle an ionophore such as monensin (200 mg/head/day) starting several days before they are introduced to lush pasture and for 7 to 10 days after being placed on that pasture. These drugs inhibit the metabolism of tryptophan to 3-methylindole.

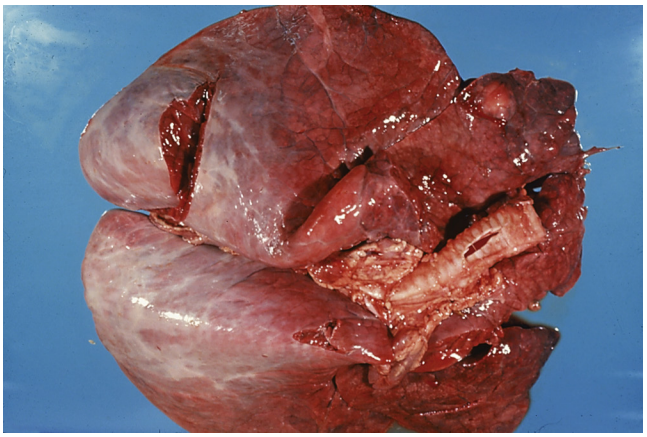
Proliferative Pneumonia

Etiology and Signs

Proliferative pneumonia is another cause of acute respiratory distress observed in dairy cattle. This condition occasionally has been observed to cause high morbidity within a herd but usually affects only one or a few cattle within a group. Acute onset of dyspnea characterized by hyperpnea, tachypnea, an occasional cough, open-mouth breathing, and pulmonary edema are observed (Fig. 4.100).

The term *proliferative pneumonia* derives from the characteristic gross pathology consisting of heavy, firm, wet lungs that are diffusely affected. Histologic study of these

• **Fig. 4.100** A Holstein cow with acute severe dyspnea and open-mouth breathing because of proliferative pneumonia.



• **Fig. 4.101** Necropsy specimen of the lungs from a calf with acute proliferative pneumonia superimposed on resolving cranioventral bronchopneumonia. (Courtesy of Dr. John M. King.)

lungs reveals obliteration of alveolar spaces by proliferating type 2 pneumocytes and interstitial edema. As such, there are some very comparable clinical and pathological features that are shared by both classic pneumotoxin-associated AIP and proliferative pneumonia. The principal difference is the grazing history in the former and the fact that the pneumotoxins described in the last section tend to affect larger groups of cattle rather than an individual animal or small group.

The gross pathology and histopathology are characteristic. Unfortunately, affected cattle show ante-mortem signs common to many other diseases also characterized by acute respiratory distress. Clinical signs include a low-grade fever (103.0° to 104.0°F [39.44° to 40.00°C]), which may range higher (105.0° to 106.0°F [40.56° to 41.11°C]) as a result of exertion and environmental factors. Auscultation of the lungs reveals diffuse reduction of airway sounds over the entire thorax. Proliferation of type 2 pneumocytes within the alveoli and interstitial edema contribute to the reduced lower airway sounds. Therefore, although the affected cow has severe lower airway dyspnea, the lungs are very quiet on auscultation.

Other diseases, such as ABPE, diffuse pulmonary edema, acute dyspnea associated with embolic showering from a CVCT, nitrogen dioxide inhalation, and other causes of acute respiratory distress, could lead to similar signs.

Not only is the disease difficult to diagnose accurately, but also the exact cause or causes remain unknown. Nitrogen gases have been incriminated, and the disease has similarities to silo filler's disease caused by nitrogen dioxide (NO_2). However, calves and adult cattle that develop proliferative pneumonia frequently have not been exposed to silo gas or other environmental nitrogen gases. Cytochrome P450 enzymatic activity within lung tissue has been demonstrated to be pivotal in the pathogenesis of interstitial pneumonia caused by 3-methylindole, 4-ipomeanol, and *Perilla* mint pneumotoxicosis. It is possible that activation of inhaled or absorbed propneumotoxins by a similar metabolic process plays a role in proliferative pneumonia. Alternatively, patients with proliferative pneumonia may be unfortunate enough to have a combined pneumotoxin and infectious insult. The question remains: Are all of these individual toxicities completely separate entities in cattle? It seems that the disease known as proliferative pneumonia may be a composite of these toxicities or may be caused by a yet-to-be-determined toxin common within the environment of dairy cattle.

Another form of pathologically confirmed proliferative pneumonia has been observed in dairy calves after previous infection with, and apparent recovery from, *Pasteurella* or *Mannheimia* pneumonia. The disease occurs in a single animal among a group of calves 2 to 4 weeks after apparent recovery from *Pasteurella* or *Mannheimia* pneumonia. This single animal develops an acute severe respiratory distress syndrome with tachypnea, hyperpnea, an elevated heart rate, open-mouth breathing, fever (103.0° to 106.0°F [39.44° to 41.11°C]), and pulmonary edema. An expiratory grunt may also be present. The animal is reluctant to move and may become cyanotic if stressed. The degree of respiratory effort makes it impossible to determine whether the pyrexia is caused by inflammation or exertion. The lungs are very quiet on auscultation and have reduced sounds throughout all fields. If the previous pneumonia resulted in consolidation of anterior ventral lung lobes, bronchial tones may be heard ventrally and reduced sounds elsewhere. Usually both lungs are involved, but occasionally one lung has much more serious lesions. Unless treated quickly and intensively, the calf dies within 24 hours. Gross necropsy reveals diffusely heavy, wet, firm lungs with evidence of resolved or resolving anterior ventral pneumonia (Fig. 4.101). Bacterial products resulting in a delayed hypersensitivity reaction are thought to be the cause of this problem. The 2- to 4-week interval between earlier signs of typical *Pasteurella* or *Mannheimia* pneumonia and subsequent acute proliferative pneumonia, as well as the pathologic lesions, differentiate this syndrome from the "relapse" respiratory distress sometimes observed in

BRSV infections. In addition, paired serum samples do not support BRSV as the cause.

Diagnosis and Treatment

Treatment of proliferative pneumonia is controversial because only lung biopsy or necropsy can definitively confirm the clinical entity at hand. Lung biopsy via a Tru-Cut biopsy needle is a useful diagnostic step to aid diagnosis and treatment in valuable animals. Thoracic radiographs, if available, will demonstrate a diffuse pulmonary edema and mixed alveolar–interstitial pattern. Treatment with atropine has reportedly been beneficial to affected herdmates when endemic proliferative pneumonia has been confirmed by necropsy study (see below). When proliferative pneumonia is confirmed or strongly suspected, the following therapy is suggested:

- Remove affected cattle from any source of toxic plants, nitrogen gases, or fumes; for example, if the only affected cows are confined near a silo chute or manure pit, move them. Affected cattle should be moved only when their ventilation and environment need to be improved. Otherwise, any movement constitutes a severe stress.
- Administer furosemide (0.5–1.0 mg/kg or 25 to 50 mg/100 lb body weight by injection once or twice daily) for the first 2 days of therapy if hydration status allows.
- Administer atropine (0.048 mg/kg or 1/30 grain [2.2 mg] per 100 lb body weight twice daily).
- Administer dexamethasone (10 to 20 mg once daily) for 3 days unless the affected cow is pregnant.
- Administer broad-spectrum antibiotics for 5 to 7 days to protect against secondary bacterial pneumonia.

Respiratory Distress in Newborn Calves

Etiology, Pathophysiology, and Signs

This is a relatively common occurrence and may result from aspiration of meconium, congenital heart disease, white muscle disease, fetal lung pathology, or more commonly from dysmaturity or immaturity of the lung with associated surfactant deficiency. It is especially common in premature, cloned, or in vitro fertilized calves (Fig. 4.102). Calves born in advance of 270 days' gestation are at risk, and the earlier the delivery, the higher the risk. It is true that some calves born as early as 6 weeks premature may have relatively normal pulmonary function, but this is unusual. Regardless of the causative factors, abnormal lung compliance present in these cases causes poor air exchange, hypoxia, pulmonary hypertension, and may eventually lead to right heart failure. Occasionally, rib fractures causing traumatic lung injury or hemothorax may also be a cause of respiratory distress in neonates. Because of protracted labor, these same newborn calves are also at great risk for hypoxemic injury to the central nervous system, GI tract, and other organs; rarely do they acquire or potentially absorb sufficient colostrum and consequently are at further and substantial risk for sepsis. Congenital heart defects may also cause respiratory distress in either newborn or slightly older calves.

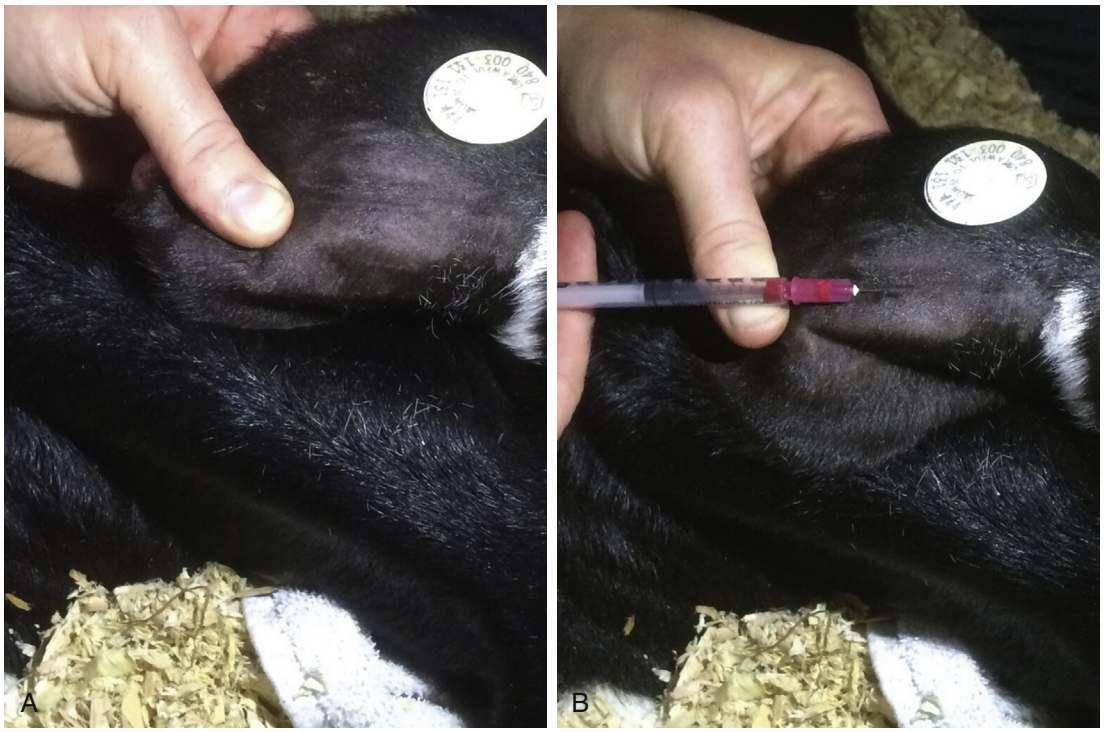
• **Fig. 4.102** A newborn cloned calf with hypoxemia being treated with intranasal oxygen.

Diagnosis

Calves should develop a fairly normal respiratory pattern within the first hour after delivery, whereas newborn calves with respiratory distress syndrome will have labored breathing that does not improve with time. There may be other signs of prematurity (e.g., small size, abnormally fine hair coat) in premature calves. Cloned calves may also have abnormally large umbilical vessels and other abnormalities including ascites. Lung sounds are diffusely harsh and generally do not have rales. The heart rate will be high, but loud murmurs are usually absent unless the respiratory distress is caused by a congenital heart defect. All newborn calves with respiratory distress should have their heart auscultated properly to rule out congenital heart defects. An arterial sample can be collected from the brachial or auricular arteries (Fig. 4.103) to confirm the severity of the hypoxemia. It should be noted that newborn healthy calves may have PaO_2 values of 55 to 60 mm Hg during the first 30 to 60 minutes of life. In many cases with respiratory distress, the PCO_2 will be elevated, and this can be confirmed by a venous sample (>45 mm Hg). If the CO_2 is elevated in a rapidly breathing calf, the PaO_2 will be extremely low. Pulse oximetry is useful in calves after the first hour of life to confirm the hypoxemia and for monitoring therapy. A chest radiograph will reveal diffuse underinflation of the lung and parenchymal collapse. Some premature calves will have moderate to severe respiratory acidosis, hypercapnia, and hypoxemia but because of inappropriate or underdeveloped central responses appear eupneic or only slightly tachypneic. Periodic assessment of preferably arterial blood gases, or at the very least venous blood pH and CO_2 tension, in the first day or two of life in premature calves is therefore recommended. Premature calves with respiratory difficulties can have a rapid downward spiral leading to hypoxic death.

Treatment

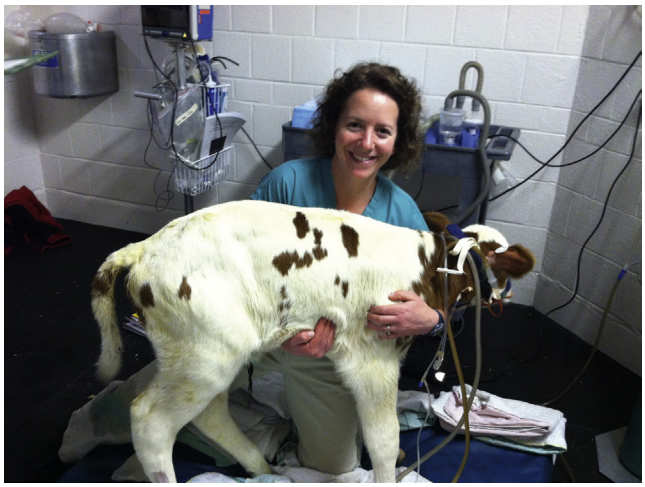
Treatment must be early and vigorous if there is hope for survival in neonatal calves with respiratory distress. Premature calves born by cesarean section and not taking a big



• **Fig. 4.103** Technique for arterial blood gas sampling from auricular artery. The artery is occluded distally along the dorsal edge of the ear to cause the artery to stand out (**A**), and then a heparinized tuberculin syringe with a 25-gauge needle is carefully introduced into the vessel (**B**) and gentle suction applied. (Courtesy of Dr. Chelsea Holschbach.)

breath immediately after delivery are at a high risk of having excessive fluid in the airways, and a loud fluid sound may be notable during labored breathing. Lifting those calves by the hind legs for 10 seconds, suctioning each nostril for 5 seconds, or irritating the nostril with a piece of straw may be helpful in removing excessive fluid from the airways. Prolonged suction or suspension by the hind legs should definitely be avoided because they would make the calf more hypoxic. Vitamin E and selenium should be given IM. Intranasal humidified oxygen must be administered at 5 to 8 L/min as soon as possible in an attempt to improve tissue oxygenation and decrease reflex pulmonary artery constriction (Fig. 4.104). If the calf is premature and the accompanying respiratory distress is severe, nasal cannulas in both nostrils and high-flow humidified oxygen may be needed. This is considered to have a number of physiological advantages compared with standard oxygen therapies, including reduced anatomical dead space, higher FiO_2, and positive end-expiratory pressure, which may keep the terminal airways and alveoli open, improving lung compliance. It is best to not let the calves lie in lateral recumbency as this has a negative effect on ventilation and oxygenation.

Newborn calves with respiratory distress are almost always given prophylactic antibiotics and a plasma transfusion if plasma immunoglobulin G is low. One dose of corticosteroid (10 mg of dexamethasone) is often given and empirically does seem to help, especially after meconium aspiration. Although it is proven that corticosteroids given to cattle in the last 2 weeks of gestation improve lung function at birth in cesarean section–delivered calves, there is limited proof that postnatally administered steroids will similarly accelerate lung maturation. It may be that



• **Fig. 4.104** A 2-day-old calf with respiratory distress caused by meconium aspiration. The calf is receiving intranasal oxygen through a small tube *(red)* sutured into one nostril. The calf also has an enteral feeding tube for feeding and intravenous fluid line for fluids and medication and a nebulizer in the background for nebulization of surfactant, corticosteroid, bronchodilator, and antibiotics. The calf made a complete recovery with the intensive care treatments.

• **Fig. 4.105** **A,** A newborn cloned calf with respiratory distress being ventilated with a mechanical ventilator. **B,** Mechanical ventilator settings for this calf. **C,** The calf was weaned off the ventilator 4 days later and is seen here still receiving intranasal oxygen. **D,** Same calf as in A and C ready for discharge.

postnatally administered steroids, if they help at all, inhibit oxidative lung damage in hypoxic calves. If surfactant is available, it should be given to the calf via intratracheal instillation or less commonly by direct tracheal injection, or it can be nebulized. Commercially prepared surfactant is preferred, but we have collected surfactant from healthy donor cows by BAL using 100 mL of sterile saline and then using the top (foamy) part of the collection for intratracheal administration or nebulization. The calf should be turned over in dorsal recumbency for 10 seconds immediately after surfactant is placed in the trachea to facilitate its distribution into all or most areas of the lungs. The surfactant seems to be more effective when given early in the disease process. If a response is noted it may need to be repeated several times as the life of the exogenous surfactant is short. We have also nebulized affected calves with acetylcysteine while they were being administered an aminophylline drip (5 mg/kg over 2 hours). The aminophylline not only serves as a bronchodilator but also has antiinflammatory properties and helps maintain diaphragm strength. In regions where beta agonist inhalation bronchodilator treatment is legal this might also improve both surfactant production and mucociliary clearance; however, the treatment is illegal in cattle in the United States.

Fluids (crystalloids and colloids such as plasma) may be given IV as a continuous drip if needed but the calf should not be overhydrated. The calf should be gradually warmed if it is hypothermic. We have also administered thyrotropin-releasing factor or thyroxine (2-5 μg/kg orally once daily) or both, in hopes of increasing surfactant production. Although thyroid hormones are known to be important in prenatal lung development, most studies have been unable to demonstrate a benefit of thyroxine treatment on lung maturation when administered after birth. If pulmonary gas exchange cannot be sufficiently improved with these methods and the owners request further treatment, the calf can be placed on a mechanical ventilator, but this is expensive (Fig. 4.105). It is sometimes more difficult to keep calves quiet on a ventilator compared with foals. Cloned calves with ascites and enlarged umbilical vessels have low survival rates even when placed on the ventilator. A short-term alternative to machine-driven mechanical ventilation is to continuously or intermittently use an Ambu bag to inflate the lung. Another alternative on

• **Fig. 4.106** A 2-day-old calf with pulmonary hypertension receiving oxygen and nitric oxide.

the farm is to use a commercially sold calf resuscitator/aspirator. Persistent pulmonary hypertension causes progression of right heart failure and sometimes reversion to fetal circulation patterns. The chronic hypoxia results in a mixed acidosis and often multiple organ failure. Nitric oxide (ratio of NO to oxygen, 1:9) can be administered through the oxygen line in hopes of decreasing the pulmonary hypertension (Fig. 4.106).

Prevention of Respiratory Failure in Calves Induced Prematurely

Occasionally, labor in a cow in late pregnancy will need to be induced, most often because of some medical disease of the dam. The likelihood of respiratory distress caused by premature delivery may be decreased by the administration of glucocorticoids and prostaglandin F2α to the dam. If the calf is at less than 260 days' gestation, this treatment might not improve lung function. If the premature delivery must occur before 260 days of gestation, then a 7-day induction protocol should be used if the dam can be kept humanely alive for that period. Induction begins with administration of 5 mg of dexamethasone intramuscularly every 12 hours for 4 days. On day 5, the dose of dexamethasone is doubled to 10 mg every 12 hours. In some cows, parturition occurs on day 6; in the remainder, 40 mg of dexamethasone and an abortigenic dose of prostaglandin F2α is given once on day 6. The cow must not be suffering during this time!

Other Less Common Causes of Respiratory Distress

Silo Filler's Disease (Nitrogen Dioxide Poisoning)

Etiology and Signs

Fumes of NO_2, a heavy yellow gas produced by anaerobic fermentation of fresh silage, may cause the same lower airway damage in exposed cattle as in humans. Because the gas is heavier than air, it lies on top of recently ensiled material, especially corn silage, and seeks out lower locations such as silo chutes. The major risk to farmers occurs when workers enter a silo chute or silo without first starting the blower in the silo loader to "wash out" NO_2. Cattle confined next to the silo chute are most at risk and may receive chronic low-exposure toxicity or severe acute toxicity. Gaseous NO_2 seeks water that then converts it to nitric acid, which is highly tissue damaging. In the respiratory tract, nitric acid causes acute chemical injury similar to anhydrous ammonia and subsequent obliterative bronchiolitis and interstitial fibrosis.

Affected cattle that have been chronically exposed to NO_2 have a chronic dry cough and increased respiratory rate greater than 40 breaths/min but few other symptoms. Cattle with severe acute exposure have a moist cough, more severe dyspnea (increased rate and effort), and pulmonary edema.

Diagnosis

Careful observation and history may be the key to diagnosis because the signs are nonspecific. Lung biopsy or necropsy is the only absolute means of diagnosis.

Treatment

Corticosteroids may be used judiciously in affected cattle. Cattle are very sensitive to dexamethasone, and 10 to 20 mg/day for a few days would be appropriate therapy. Risk of secondary infection and abortifacient properties of dexamethasone need to be considered. Atropine and furosemide may also be indicated at previously described doses.

Farmer's Lung: Hypersensitivity Pneumonitis (Extrinsic Allergic Alveolitis)

Etiology and Signs

Hypersensitivity pneumonitis may occur in cattle and result in respiratory distress or chronic respiratory disease. In humans, many specific inhalant antigens may cause similar symptoms, but frequently *Micropolyspora faeni* and related organisms are incriminated. Wet hay that ferments excessively remains the biggest cause of this condition in farmers and cattle. The resultant dusty, moldy hay releases tremendous numbers of spores when bales are opened into the faces of humans and animals. Large round bales also have been observed to cause the problem occasionally. A delayed hypersensitivity reaction is suspected.

Signs of acute experimental exposure include a sudden decrease in appetite and milk production, coughing, craniоventral pulmonary rales bilaterally, and transient fever. In natural cases, chronic cough without obvious illness remains the most common sign when this disease has been recognized in the northern United States. Usually more than 50% of the herd is affected, and herd production decreases 10% to 25% because affected cattle cough enough to interfere with normal consumption of feed. Auscultation of the lungs may reveal a few wheezes or may be normal. Signs lessen but do not stop entirely when animals are fed outdoors or go to pasture. Confinement and feeding the causative hay indoors accentuate the signs. Death is rare, but occasionally severe chronic cases have developed right heart failure. With the feeding of total mixed rations and the reduction in lifespan of dairy cattle in the United States, this disease has become less common. However, sporadic cases continue to be seen, not so much as a herd issue but as an individual, older multiparous cow problem on traditional stanchion and tie stall farms. We occasionally see a similar clinical syndrome in a hospitalized cow that is bedded heavily and has frequent bedding changes.

Diagnosis

The diagnosis can be aided by history, observation, lack of profound illness in affected cattle, and exclusion of other causes of lower airway disease. Tracheal wash samples suggest lymphocytic inflammation with macrophages, lymphocytes, and some plasma cells. The serum of affected cattle may be analyzed for precipitins to *M. faeni* and to other antigens known to be associated with the condition in humans. When results are positive, this is suggestive but not definitive evidence because many normal cattle have positive antibodies.

Lung biopsy also may be a very helpful diagnostic aid if the value of the affected cow precludes necropsy. Necropsy inspection of the affected lungs reveals gray spots indicative of lymphocyte accumulations around small airways in the interstitium. Histopathology shows infiltration of lymphocytes and plasma cells in the interalveolar septa. Provocative testing using the hay in question provides subjective, causative evidence. Lungworms definitely should be ruled out by Baermann's technique, tracheal wash cytology, and necropsy if necessary.

Treatment and Control

When a large percentage of the herd is affected, corticosteroids do not represent a wise treatment. Corticosteroids benefit acutely affected individual cattle or severe recurrent cases but should not be used on a wide scale. Changes in management constitute both treatment and prevention. Feeding hay outside may give some relief, especially if the bales are opened several minutes or more before the cows are allowed access to the hay. Wetting the hay may be helpful. If economics permit, getting rid of the hay is the best policy and may solve the problem. Farmers who consistently make poor-quality hay should be encouraged to consider haylage or at least include hay additives during harvesting that inhibit mold growth. Humans working with causative hay should consider the use of surgical masks or protective face masks to prevent symptoms of farmer's lung in themselves.

Bronchiolitis Obliterans

Etiology and Signs

This poorly described condition is observed occasionally in individual animals. A dry cough is the predominant sign in affected cattle, and Dr. Fox (personal communication to Dr. Rebhun) used to highlight the magnitude of the cough by quoting farmers who call only because a cow "coughs so hard she causes the milking machine to fall off." Auscultation of the lungs may reveal wheezes or abnormally quiet lung sounds. Although hyperpnea and tachypnea are present in addition to the dry cough, the affected cow does not otherwise appear ill.

The cause is unknown but probably involves chronic exposure to toxic gases, 3-methylindole, allergens, or other proposed causes of acute respiratory distress in cattle from which the individual has survived but with serious lung pathology. The chronic damage that ensues may result in bronchiolitis obliterans, a pathologic diagnosis.

Diagnosis

Lung biopsy or histopathology after necropsy is required for definitive diagnosis.

Treatment

Dexamethasone often gives some relief to affected animals when administered judiciously at 10 to 20 mg/day. Appropriate contraindications should be considered.

Fibrosing Alveolitis

Etiology and Signs

This is a chronic debilitating respiratory disease of mature cattle. Affected cattle do not act ill but have an obvious increased respiratory rate and effort, as well as obvious coughing. Moist or dry rales may be auscultated over the entire lung field. Morbidity is low, but subsequent mortality is high because the disease is chronic and progressive.

The cause is unknown and may simply be the result of chronic exposure to some of the pneumotoxic materials previously discussed in this section. Chronic exposure to 3-methylindole, NO_2 or other gases, antigens known to cause hypersensitivity pneumonia, survival from smoke inhalation, or unknown factors may result in diffuse fibrosis of the alveoli.

Diagnosis

Gross inspection of the lungs at necropsy reveals diffuse pale, heavy, firm lungs. The lobules are white and fleshy. Obliteration of alveolar air space by type 2 pneumocytes, macrophages, and other cells histopathologically explains the antemortem dyspnea. Lung biopsy is indicated if necropsy is not an option.

Treatment

No treatment is likely to be successful, but antiinflammatory drugs may be tried.

Anaphylaxis and Milk Allergy

Etiology and Signs

Respiratory distress often accompanies anaphylaxis induced by exogenous antigens such as vaccines, antibiotics, local anesthetics and feedstuffs, or endogenous antigens such as α-casein in milk.

In susceptible animals, signs usually develop within minutes after injection of biologics or antibiotics and consist of urticaria, edema of mucocutaneous junctions, and respiratory distress. Signs may be mild, with urticaria predominating, or severe, with collapse quickly following initial signs. Laryngeal edema may occur and be progressive over many hours. Certain biologics have been incriminated more than others in this regard. Antibiotic-induced anaphylaxis has been observed as a result of penicillin, tetracycline, sulfas, and other antibiotics. Penicillin may cause respiratory distress from a true anaphylaxis (usually hives accompany the respiratory distress) or as part of the procaine reaction. A procaine reaction causes hyperexcitement and snorting, but edema is not present because this is not an immunologic reaction. A procaine reaction is rare in cattle in comparison to horses and when it does occur is generally less severe than in horses. Biologics that cause an anaphylactic reaction in more than an occasional cow should be avoided unless suitable alternatives are not available. Many apparent anaphylactic crises may in fact be the result of endotoxins in certain biologics and cattle of certain genetic lines being more susceptible to such vaccine reactions.

Affected cattle appear apprehensive and restless, and their hair stands on end. The heart rate elevates, hives may develop, and frequent attempts to urinate and defecate may alternate with restless treading on the limbs. Dyspnea may be inapparent or obvious, with pulmonary edema, hyperpnea, and respiratory stertor. Cyanosis; cold, clammy skin; and hypotensive collapse ensue in severe cases.

Milk allergy occurs most commonly in Channel Island breeds but may occur in any breed. The onset of signs may follow drying a cow off or a reduction in milking frequency to "bag" a cow for a show. Any delay in the normal milking interval may trigger this reaction in cattle sensitized to their own α-casein. The signs may be mild or severe as previously described. Hives, edema of mucocutaneous junctions, and respiratory signs develop to varying degrees (also see Chapter 7).

A unique syndrome of collapse has been observed by many practitioners in cattle injected with concentrated vitamin E and selenium products. The reaction is observed within minutes of the IM injection, and collapse and dyspnea are the only signs. It is not known whether this represents true anaphylaxis, accidental intravascular administration (most likely), or specific toxicity. Most cases recover, but fatal outcomes may occur in 10% to 20% of the cases.

Diagnosis

History and physical signs suffice for diagnosis.

Treatment

Treatment is commensurate with the severity of disease and consists of drugs such as epinephrine, antihistamines, corticosteroids, and furosemide. Recommended dosages for adult cattle include:

- Epinephrine (1/1000 concentration), 2 to 10 mL IM or SC; 2 to 4 mL can be given IV in severe cases
- Tripelennamine HCl, 1 mg/kg IM or SC
- Furosemide, 0.5 to 1.0 mg/kg IM (if pulmonary edema is present)
- Dexamethasone, 20 to 40 mg IV or IM if the cow is not pregnant
- Flunixin meglumine, 1.1 mg/kg IV

For milk allergy, immediate milking out is indicated along with other symptomatic therapy (see earlier) if the cow shows a serious allergic reaction.

In most anaphylaxis cases, one treatment suffices, but in cattle with severe pulmonary edema or urticaria, several treatments at 8- to 12-hour intervals may be necessary for complete resolution.

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