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PART II

Disorders of Specific Body Systems

CHAPTER 7

DISORDERS OF THE RESPIRATORY SYSTEM

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Disorders of the respiratory system are second in importance only to those of the musculoskeletal system in limiting the athletic performance of the horse. Owners sustain major economic losses when respiratory diseases interrupt the training programs of horses or when horses must be retired because of lung damage sustained from respiratory disease. Thus early detection and treatment of respiratory problems is essential for the rapid return of athleticism to performance animals.

Diagnostic Approach to Respiratory Disorders

HISTORY

The clinician should direct questions to the person most familiar with the performance and medical history of the horse. Accurately defining the problem, devoid of subjective impressions, can be the most difficult part of taking the history.

Age and Breed

The age and breed of the animal exhibiting respiratory-related signs may provide clues as to the problem. Congenital defects (nasal septal deviations, choanal atresia, subepiglottic cysts, and hypoplastic lungs) are typically evident at birth, whereas other conditions, such as chronic bacterial pneumonia *(Rhodococcus equi),* may not be evident until the foal is older (1 to 3 months of age). Viral and bacterial upper respiratory tract infections tend to occur in the weanling and yearling, whereas conditions such as inflammatory airway disease, pleuropneumonia, or exercise-induced epistaxis are found more commonly in performance horses 2 years or older. In contrast, recurrent airway disease (heaves) or neoplasia of the respiratory tract are diagnosed primarily in the middle-aged or older horse.

Considering the breed of the horse is also important in investigating respiratory disorders. For example, one should evaluate Arabian foals with chronic infections for combined immunodeficiency syndrome, a heritable condition in which cell-mediated and humoral limbs of the immune system are deficient. In addition, solitary defects in the humoral immune system also predispose horses to develop chronic respiratory and enteric infections. Selective immunoglobulin M (IgM) deficiency tends to occur more frequently in Arabians and Quarter Horses, whereas agammaglobulinemia has been documented in Thoroughbreds and Standardbreds.[1,2]

Environment

One should ascertain the environment to which the horse was or presently is exposed. For example, is the horse stabled at a racetrack where population turnover is high and the potential for viral respiratory outbreaks is increased, or is the horse a sole inhabitant of a small pasture, seldom exposed to other horses? Does the farm have a history of endemic infections, as often occur with *Streptococcus equi* outbreaks? Has the horse been exposed to pastures grazed by donkeys? This, along with information regarding the diet (hay, pelleted rations, or pasture), the nature of the bedding materials (straw, peat, or shavings), and the amount of time the horse is stabled are important considerations in establishing the risk factors for some respiratory disorders such as recurrent airway obstruction or lungworm infections. One also should obtain the deworming and vaccination schedules. Young horses are at risk for developing verminous pneumonia resulting from *Parascaris equorum* migration. Nematode eggs can survive for prolonged periods on a pasture. Thus establishing whether the foal was exposed to pastures grazed by yearlings or 2-year-olds may help in establishing the diagnosis and treating the problems. If the horse is a performance animal and is at an increased risk for developing upper respiratory tract infections, one should determine how frequently equine influenza and equine herpesvirus type 1 (EHV1) and type 4 (EHV4) vaccinations are administered.

Prior Medical Problems

Has the horse had a previous history of illness or trauma that might be related to the present complaint? Viral respiratory conditions often precede the development of bacterial pneumonia. Sequelae to *S. equi* infections include internal abscessation, guttural pouch empyema, retropharyngeal abscesses, and purpura hemorrhagica, which ultimately may affect the respiratory and cardiovascular systems. Trauma may be implicated in the development of diaphragmatic herniae, pneumothorax, or tracheal injury and subsequent stricture formation.

Present Medical Problem

The clinician should direct questions to define the exact problem, establishing the chronicity of the disorder and the rapidity of its development. Is the problem insidious in onset or an acute disorder of less than 2 weeks' duration? Is the onset associated with a stressful event such as racing or a prolonged van ride? Does the farm have new arrivals that have not been quarantined? One should also determine the effect of the respiratory complaint on the expected athletic performance: Are clinical signs evident during eupneic (resting) breathing or only noticeable during the hyperpnea of exercise? Has the horse received any medication and did the clinical condition improve? Amelioration of signs during therapy suggests that the previous treatment protocols were not of sufficient duration or that an underlying immunodeficiency exists.

PHYSICAL EXAMINATION

Before examining the horse, simply stepping back and evaluating the demeanor and mental status (alert or depressed), posture, and manner of movement of the horse is helpful. Has the horse adopted a particular stance (extended head and neck), or is it reluctant to move because of pain (pleurodynia)? Are changes in the pattern of breathing from the normal eupneic state obvious (Box 7-1)? Is the breathing pattern rapid and shallow? Does nostril flaring accompany a pronounced expiratory effort? The normal respiratory rate of the adult horse varies from 8 to 15 breaths per minute, with a slightly noticeable abdominal component during expiration (an active process in the horse).

Abnormalities of the respiratory system are evident also by the production of unusual sounds associated with respiration; the presence of a cough; a nasal or ocular discharge; lymphadenopathy; epistaxis; facial, pharyngeal, or cervical swellings; and cyanotic mucous membranes. Ataxia or reluctance to move, the presence of ventral thoracic or limb edema, foul odors associated with breathing, and a history of weight loss may occur with respiratory disorders.

BOX 7-1

BREATHING PATTERNS

Eupnea The normal quiet and seemingly effortless breathing pattern adopted by the healthy horse at rest. Inspiration and expiration in the horse are active processes.

Tachypnea A breathing pattern characterized by rapid frequency and shallow depth or small tidal volume.

Hyperpnea A breathing pattern characterized by an increase in the depth and rate of breathing, as might be found during exercise.

Apnea A period of time in which no discernible respiratory effort is made and air flow has ceased. Apnea may accompany sleep-related disorders or excessive ventilation (hypocapnia-induced apnea).

Hypoventilation A pattern of breathing that alters gas exchange sufficiently to cause hypercapnia or elevations of arterial carbon dioxide tension.

Hyperventilation A pattern of breathing that increases alveolar ventilation and results in arterial hypocapnia.

Dyspnea A breathing pattern that appears to reflect difficulty in breathing. The animal appears to be distressed, and increased work of breathing is obvious.

The clinician should assess the airflow from both nostrils to rule out potential obstructions or masses within the nasal cavity. One can detect atheromata, which may restrict airflow during exercise, by palpating the false nostrils. Any peculiar breath odors are detectable at this time. Percussion of the frontal and maxillary sinuses, performed by gently tapping over the sinuses while one holds the mouth of the horse slightly open, may reveal a dullness because of accumulations of fluid or inflammatory products, but the absence of a percussable change does not rule out a sinus disorder. One also should determine evidence of swelling in the submandibular space (lymphadenopathy) or in the pharyngeal (guttural pouch or retropharyngeal disorders) and cervical areas (accessory lungs[3]). Palpation of the larynx and trachea is routine and should not elicit coughing episodes in the normal horse. One also can detect evidence of muscle atrophy or prior surgeries (laryngoplasty, laryngotomy, myotomy) during the physical examination of the upper respiratory tract. One should check for patency of the jugular veins (thrombophlebitis and secondary pulmonary abscessation) or for evidence of perivascular injections that may contribute to upper respiratory tract obstructions by involving the recurrent laryngeal nerve or vagosympathetic trunks.

The clinician then should conduct a complete physical examination, paying attention to all organ systems (and not simply focusing on the respiratory system). In respiratory emergencies, one conducts an abbreviated initial examination and directs efforts at patient stabilization until that time when a more thorough physical examination can be conducted.

Auscultation of the Lung Fields

The clinician should examine the horse during eupneic and hyperpneic (by use of a rebreathing bag) breathing patterns. Normal *breath sounds* are those produced by turbulent air movement through the tracheobronchial tree and vary in intensity and quality depending on the portion of the lung field auscultated. The *vesicular sounds,* over the middle and diaphragmatic lung lobes, are the quietest sounds; the *bronchial sounds,* over the trachea and the base of the lung, are the loudest.[4-6] In the normal horse one can hear breath sounds more easily on the right side than on the left. Considerable variation exists between normal patients in the intensity of the breath sounds. For example, vesicular sounds are often barely audible during eupneic (normal) breathing in the obese patient and are perceived as soft rustling sounds. However, one may hear breath sounds easily in the thin or young animal because of less attenuation of lung sounds by the chest wall. The intensity of breath sounds also increases with increased airflow. Thus breath sounds are accentuated in febrile or excited animals or in animals hyperpneic from a variety of causes (exercise, hypoxia, pain). However, auscultatory findings do not always correlate well with the degree of alveolar ventilation.[5] For example, in horses with lung consolidation the transmission of breath sounds from adjacent areas gives the false impression that that region is well ventilated. Breath sounds also may become more difficult to hear in cases of (1) alveolar overinflation in which the aerated tissue of the lung is a poor conduction medium of sound or (2) pneumothorax and pleural effusions in which the sound is reflected at the pleural surface (acoustic impedance).[5]

Adventitious lung sounds are abnormal sounds superimposed on the normal breath sounds and have been described as crackles or wheezes. Crackles are short, explosive, discontinuous sounds that have been likened to the sound of salt thrown in a hot frying pan or the sound of cellophane being crumpled. They are usually of low intensity and are audible during the inspiratory phase of respiration. Their production has been attributed to the sudden equalization of pressure in two compartments after airways have reopened. Crackles are audible in cases of interstitial pneumonia and pulmonary edema (restrictive pulmonary diseases) and in cases of bronchopneumonia or airway diseases (obstructive disorders). Breathing 100% oxygen also may produce crackles because the nitrogen stent maintaining alveolar distention is eliminated.[7] Crackles are also audible in cases of subcutaneous emphysema. Wheezes are musical sounds thought to arise from the vibration of airway walls or tissue masses in close contact with the airway walls and may be audible during inspiration or expiration. Wheezes may be monophonic or polyphonic, the latter indicative of multiple sites of airway obstruction. Pleuritic friction rubs have been described as sandpaper-like sounds generated by the movement of the visceral and parietal pleurae across each other. One may detect them (infrequently) in the early stages of "dry" pleuritis, before the effusive stage.

Percussion of the Thorax

One percusses by methodically tapping the intercostal spaces of the thorax using a plexor and pleximeter (foals) or a large spoon and neurologic hammer (adults) and evaluating the nature of the sound produced. Aerated tissues produce a resonant sound, whereas fluid-filled structures (bowel, heart, lung abscesses, consolidated lung) produce a dull sound. One should identify the transitional site where sound quality changes during percussion by using a piece of tape. One then compares the limits of the percussed field with those of the normal horse. The cranial limit is the shoulder musculature, the dorsal limit is the back musculature, and the caudoventral limits are the seventeenth intercostal space at the level of the tuber coxae, the sixteenth intercostal space at the level of the tuber ischii, the thirteenth intercostal space at the midthorax, the eleventh intercostal space at the level of

the scapulohumeral articulation, and the sixth intercostal space at the olecranon.[8] Thoracic percussion should not be painful: resentment by the horse may indicate pleuritis or rib fractures. A ventral dullness suggests pleural effusion, pleural thickening, lung consolidation, or pericardial effusion. Occasionally, caudal borders may be expanded, suggesting alveolar overinflation, which may accompany recurrent airway disease.

Endoscopy

Fiberoptic endoscopy provides an invaluable method for assessing the equine respiratory tract. Endoscopy is helpful in establishing (1) the origin of respiratory noises that accompany laryngeal hemiplegia, dorsal displacement of the soft palate, epiglottic entrapment, rostral displacement of the palatopharyngeal arches, arytenoid chondritis, tracheal collapse or stenosis, and pharyngeal narrowing; (2) the existence of congenital defects such as subepiglottic cysts, cleft palate, or choanal atresia; (3) the source of exudate or hemorrhage occurring with guttural pouch mycosis or empyema, ethmoidal hematoma, pulmonary epistaxis, retropharyngeal abscessation, and chronic pulmonary disease; and (4) in extracting foreign bodies from the tracheobronchial tree. Videoendoscopic examination of the upper respiratory tract during maximal treadmill exercise (12 to 14 m/sec) is a routine diagnostic modality at many referral centers, allowing visualization of dynamic collapse of the upper airway structures during exercise in certain pathologic conditions. Accumulations of mucopurulent exudate within the pharynx or the trachea following exercise are compatible with a diagnosis of inflammatory airway disease. Endoscopy is a potential means of obtaining tracheobronchial aspirates (guarded swabs or catheters).[9] A number of different fiberoptic endoscope models are available but an 11-mm (outer diameter) endoscope usually is used in adult horses, and a smaller, 7.8-mm (outer diameter) pediatric scope is recommended for foals.

Sinuscopy

Sinuscopy, direct examination of the interior of the paranasal sinuses using an endoscope or an arthroscope that is introduced through a small trephine opening, is useful for diagnosing or treating sinus disease.[10,11] In selected cases, sinuscopy may be a diagnostic or therapeutic alternative to flap sinusotomy. One can access the caudal maxillary sinus at a point 2 cm rostral to the midpoint of a perpendicular line drawn from the medial canthus of the eye to the facial crest. One can access the rostral maxillary sinus 2 cm caudal to the midpoint of a line drawn from the rostral end of the facial crest to the infraorbital foramen. The frontoconchal sinus is accessible through a portal placed 40% of the distance of a perpendicular line drawn from 0.5 cm caudal to the medial canthus from the midline. The frontoconchal site affords excellent visualization of the frontoconchal sinus and, via the large frontomaxillary opening, the caudal maxillary sinus. Following sedation of the horse and surgical preparation and local anesthesia of the selected site, the clinician makes a small skin incision and opens the bone with either a ¼-inch Steinman pin (for a 4-mm diameter arthroscope) or a 10-mm trephine (for a 9-mm endoscope). The endoscope provides better illumination and a greater field of view. In addition to direct examination of the sinus interior for diagnosis (Figure 7-1), sinuscopy allows the examiner to biopsy tissues under direct visualization and to apply therapeutic procedures such as formalin injection of mass lesions (Figure 7-2), cyst removal, and removal of sequestered bone fragments. Following examination, the clinician may close the portal with cutaneous sutures or leave it open for therapeutic lavage.

Computed Tomography

Interpretation of conventional radiographs of the equine head is notoriously difficult because of the complex anatomy and the spectrum of radiographic densities: air, soft tissue, bone, and tooth. Thus radiographs and clinical examination may not define accurately the location and extent of lesions in the head region.[12] Computed

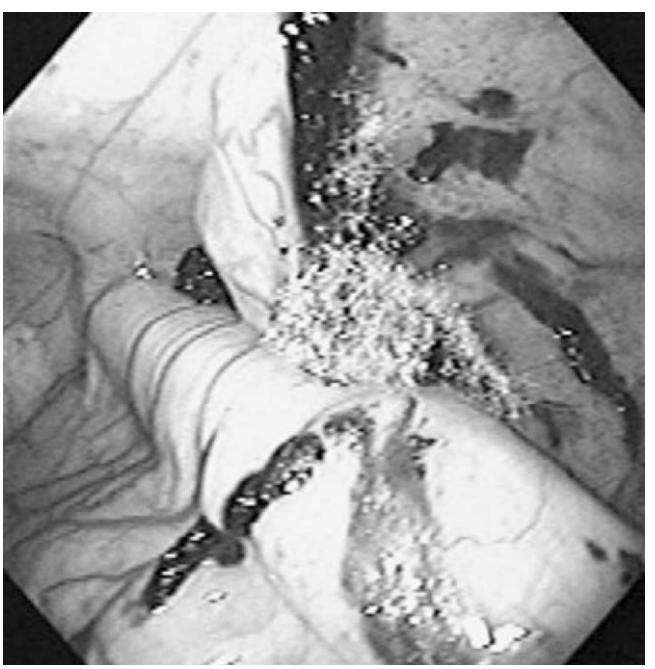


Figure 7-1 Sinuscopic view of the caudal maxillary sinus in 16-year-old Thoroughbred gelding with a history of epistaxis. A large fungal colony is on the infraorbital canal, and several small blood clots are visible.

(Courtesy R.P. Hackett, Ithaca, New York, 2001.)

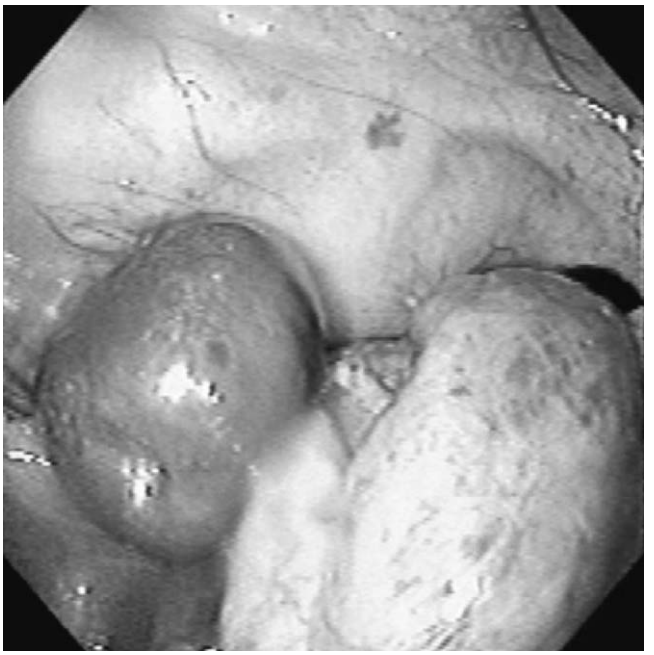


Figure 7-2 Sinuscopic view of small ethmoidal hematoma in 12-year-old Thoroughbred gelding. This lesion was injected with formalin transendoscopically.

(Courtesy R.P. Hackett, Ithaca, New York, 2001.)

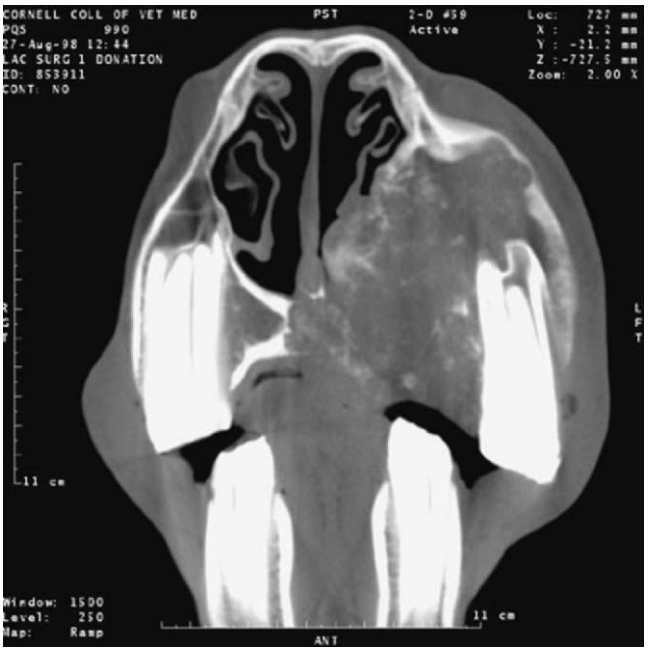


Figure 7-3 Cross-sectional image of an amelioblastoma involving the upper left premolars of a 4-year-old Warmblood gelding. A large soft issue mass is encroaching on the nasal passages, and significant osseous destruction of the hard palate, ventral concha, and premaxilla is visible.

(Courtesy R.P. Hackett, Ithaca, New York, 2001.)

tomography uses a rotating, highly columnated x-ray beam to generate digital cross-sectional images.[13,14] These cross-sectional images afford a much better evaluation of normal and pathologic anatomy than can be achieved through conventional radiographs (Figure 7-3). Additionally, the digital format enables three-dimensional reconstruction of structures and manipulation of images to optimize interpretation (Figure 7-4). Constraints for this technique are its expense, limited availability, and the need for general anesthesia of the horse.

Computed tomography has proved particularly useful for examining the anatomically complicated structures such as the nasal turbinates, paranasal sinuses, teeth, nasopharynx, and guttural pouches and for evaluating areas obscured by overlap of adjacent structures on conventional radiographs (Figure 7-5). Improved evaluation of these structures has enhanced considerably the diagnosis, the selection of surgical approaches, and the ability to render an appropriate prognosis.

Computed tomography has been of limited usefulness in evaluating the lower respiratory tract structures in adult horses because of the size constraints of the gantry. However, computed tomography is an excellent diagnostic modality for detecting and defining the extent of pulmonary or mediastinal masses in the thorax of foals, ponies, and miniature horses.[15]

Sampling of Respiratory Tract Secretions

Centesis of the Paranasal Sinuses The clinician can perform centesis of the paranasal sinuses when radiographic or computed tomographic examination reveals fluid lines or soft tissue densities in the sinuses. One performs the technique aseptically using local anesthesia on the sedated horse, using a Steinmann pin for the initial puncture of the sinus. One enters the rostral maxillary sinus at a site 2.5 cm dorsal to the facial crest and 2.5 cm caudal to the infraorbital foramen. One enters the caudal maxillary sinus (which communicates with the frontal sinus) at a site 2.5 cm dorsal to the facial crest and 2.5 cm rostral to the medial canthus. The clinician should submit aspirates for cytologic examination and bacterial culture.

Guttural Pouch Catheterization and Culture of the Exudate One performs guttural pouch catheterization in cases of empyema, chondroids, or distention of the pouches. With the horse sedated, the clinician passes a fiberoptic endoscope into the guttural pouch using the biopsy instrument or a Chambers catheter as a guide for the endoscope. One obtains a sample of the exudate with a triple-guarded catheter or protected swab. A technique for obtaining percutaneous aspirates of the guttural pouches recently has been described, but the authors prefer to use endoscopic visualization for sample collection.[16] Cytologic examination of guttural pouch aspirates from

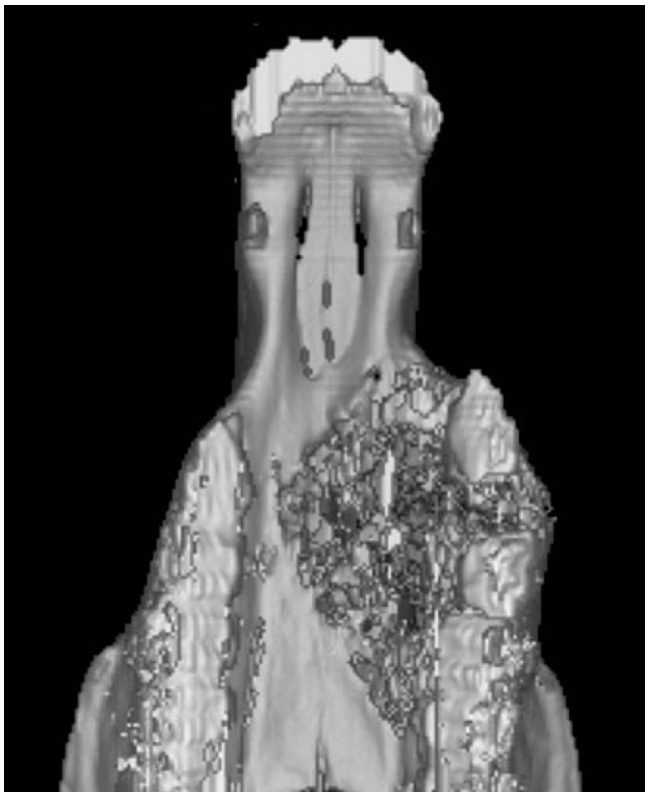


Figure 7-4 Three-dimensional reconstruction of the premaxilla in Figure 7-3. The extent of osseous destruction of the hard palate can be delineated clearly, as can separation of the second and third premolars.

(Courtesy R.P. Hackett, Ithaca, New York, 2001.)

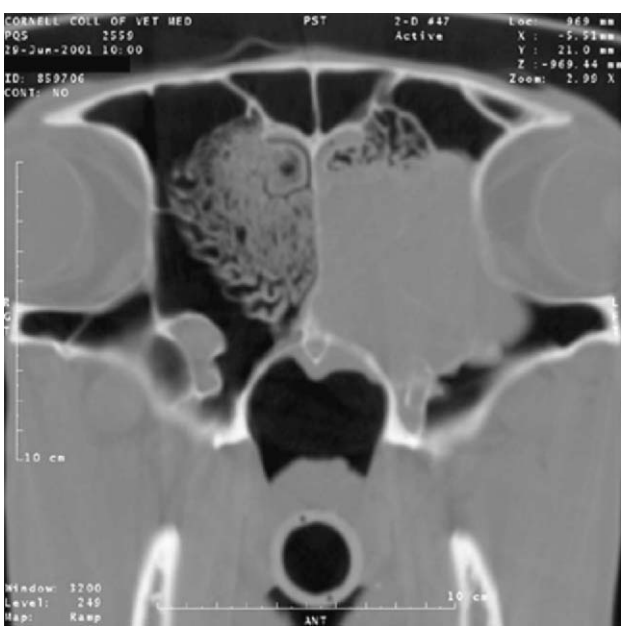


Figure 7-5 Cross-sectional image of an adenocarcinoma affecting the ethmoid turbinate in a 23-year-old hinny.

(Courtesy R.P. Hackett, Ithaca, New York, 2001.)

normal horses demonstrates the presence of mucus; a predominance of ciliated columnar epithelial cells; neutrophils; and a few (<1%) macrophages, lymphocytes, and eosinophils. Aspirates are not normally sterile: common bacterial isolates include α-hemolytic *Streptococcus, Staphylococcus,* and *Moraxella* species.[17] *Streptococcus equi* is not a normal inhabitant of the guttural pouch.

In horses suspected of having guttural pouch epistaxis, one should exercise caution regarding catheterization or endoscopic examination of the pouch. The procedure may dislodge a blood clot and cause fatal hemorrhage.

Sampling of Tracheobronchial Secretions Several techniques have been advocated for obtaining tracheobronchial samples. The site of the collection sample (tracheal versus bronchoalveolar) depends on the nature of the respiratory disorder. The appropriateness of using tracheal samples to evaluate chronic inflammatory disorders has been challenged, because little correlation exists between tracheal and bronchoalveolar lavage cytologic findings or between tracheal and pulmonary histopathologic findings.[18,19] In contrast, a good correlation exists between bronchoalveolar lavage cytologic findings and pulmonary histopathologic findings.[20] Bronchoalveolar lavage is indicated in the investigation of chronic *inflammatory* diseases but may be performed with collection of transtracheal aspirates if one cannot dismiss an infectious process. Table 7-1 shows representative cytologic findings from bronchoalveolar lavage studies of normal horses. Sedation of horses before bronchoalveolar lavage is recommended. Using a fiberoptic endoscope (permitting direct visualization of the lung segment to be lavaged) or using a thick-walled flexible tube with a cuffed end (which is passed blindly into the distal airways), the clinician instills 100 to 500 ml of physiologic saline solution within the pulmonary segment. One can retrieve 50% to 75% of the fluid and examine it cytologically. Before lavage, one may instill 20 to 40 ml of 2% lidocaine to desensitize the airways.

In the absence of a suitable method for collecting bronchoalveolar lavage fluid aseptically, tracheobronchial aspirates remain the method of choice for investigation of *infectious* lower respiratory tract disorders. Collection of culture samples by fiberoptic endoscopy simplifies the procedure and eliminates some of the complications formerly associated with the transtracheal technique, such as cellulitis and pneumomediastinum. Guarded tracheal swabs[21] and the telescoping plugged catheter of Darien[9] are convenient techniques for obtaining representative samples. However, oropharyngeal contamination still may occur when one obtains tracheobronchial aspirates endoscopically using telescoping plugged catheters.[22,23] The authors prefer to obtain tracheobronchial aspirates percutaneously.

Characterization of the normal bacterial isolates from tracheobronchial aspirates in healthy horses has been well

TABLE 7-1

Differential Counts in Bronchoalveolar Lavage Fluid*

NEUTROPHILS	MACROPHAGES	LYMPHOCYTES	EOSINOPHILS	MAST CELLS	EPITHELIAL	REFERENCE
8.9 ± 1.2	45.0 ± 2.8	43.0 ± 2.7	<1.0	1.2 ± 0.3	3.5 ± 0.7	18
5.0 ± 4.0	72 ± 10	18 ± 3.0	2.0 ± 4.0	1.0 ± 1.4	—	20
6.2 ± 5.0	70.3 ± 15.2	7.6 ± 3.9	1.0 ± 1.4	0.6 ± 1.4	14.3 ± 13.4	516
6.2 ± 2.4	48.5 ± 2.5	35.3 ± 2.5	2.5 ± 0.9	5.2 ± 0.8	2.3 ± 1.4	517

*Percent of total white blood cell count plus-or-minus standard error or standard deviation.

documented. When examining a horse with suspected respiratory disease, one must evaluate culture results in light of the cytologic findings and clinical examination. The tracheobronchial aspirates of approximately 8% of normal horses (pastured or stabled) were found to be culture-positive for *Klebsiella,* β-hemolytic streptococci, *Pasteurella* species, and *Pseudomonas aeruginosa*. For a microorganism to be implicated in a lower airway disorder, one would expect (1) to obtain a moderate to heavy growth of the organism on culture ($\geq 1 \times 10^3$ colony-forming units); (2) to identify organisms within phagocytic cells; and (3) to have evidence of degenerative neutrophils. In contrast, anaerobes, which are a normal component of the oropharyngeal flora, normally are not isolated from aspirates of healthy horses, emphasizing their importance in diseased processes when recovered from respiratory cases. Based on their studies, Sweeney, Beech, and Roby[24] also have described a group of transient bacterial flora of questionable pathogenicity such as *Enterobacter, Bacillus, Acinetobacter,* α-hemolytic streptococci (except for *Streptococcus pneumoniae* type 3), and *Staphylococcus epidermidis,* which may be isolated from tracheobronchial aspirates. In contrast, *S. pneumoniae* now is recognized as a pathogen of the respiratory tract in horses.[25-27] Fungal hyphae may be found free or engulfed within mononuclear cells in normal horses.

RADIOGRAPHY

Radiographs may be helpful (1) in detecting soft tissue masses (abscesses, granulomata, neoplasms, hematomas, polyps) or fluid accumulations within the paranasal sinuses, the nasal cavity proper, the guttural pouches, and the retropharyngeal areas; and (2) in evaluating orofacial deformations or fractures following trauma. Radiography also allows assessment of the anatomic dimensions of the pharyngeal and laryngeal structures (thickened soft palate, hypoplastic epiglottis, hyoid bone fractures). When one suspects nasal or sinus disorders, one should take lateral, dorsoventral, and oblique views. The clinician usually can achieve proper restraint of the horse for positioning of the cassette with xylazine, detomidine, or butorphanol sedation. In the horse that one can anesthetize safely, one may obtain a more thorough definition of the extent of nasal and upper respiratory tract diseases using computed tomography scans (see the previous discussion).

Radiographic evaluation of the equine thorax remains preferable to ultrasonography for detecting diffuse parenchymal diseases such as interstitial pneumonia, pulmonary edema, and chronic airway disorders or for detecting mediastinal or deep parenchymal abscesses.[28] Imaging the thorax of the standing horse requires three to four overlapping lateral radiographs. However, compared with human or small animal medicine, in which correlations between the pulmonary disorders and the radiographic findings are well-established, the radiographic changes in equine respiratory disorders tend to be rather nonspecific. In addition, many pulmonary diseases such as inflammatory airway disease, exercise-induced pulmonary hemorrhage, lungworm infections, and recurrent airway obstruction may be associated with normal radiographs.[29]

Four types of radiographic patterns have been described: an alveolar (airspace), an interstitial, a bronchial, and a vascular pattern. In the alveolar pattern, opaque areas coalesce and completely obliterate the vessels and bronchi. Air bronchograms may be notable. This pattern occurs with pulmonary edema, hemorrhage, lung consolidation, or neoplastic infiltration. Interstitial patterns are found most commonly and are associated with a variety of conditions. This pattern causes a blurring of the edges of the pulmonary vessels, a diffuse increase in lung opacity, and variable reticular, linear, or nodular opacities.[29,30] A reticular pattern occurs with viral, bacterial, or parasitic pneumonia; pulmonary edema; interstitial pneumonia; and pulmonary fibrosis. An irregular linear pattern occurs with resolving bronchopneumonia, and a nodular pattern occurs with abscesses, granulomata, or neoplasms. Bronchial patterns alone are not found commonly but usually occur in association with interstitial patterns. Paired linear opacities or numerous small circular opacities represent thickening of the large- and medium-sized airways or of the septa around the lobules. This pattern occurs in cases of equine bronchitis and bronchiolitis. Variations in the size, shape, and number of the

pulmonary vessels cause a vascular pattern and may be visible in horses following exercise or in horses with left-to-right cardiac shunts.

Extraparenchymal disorders that are evident radiographically include the presence of free pleural fluid or of free gas (pneumothorax) represented by the separation of the right or left or both caudal lung lobes from the dorsal and dorsolateral body wall by a free-air density.

ULTRASONOGRAPHY

Thoracic ultrasonography is useful for diagnostic, therapeutic, and prognostic evaluation of peripheral parenchymal lung or pleural disorders. Unlike thoracic radiography, which requires technology limited to specialty practices or veterinary medical teaching hospitals, ultrasonography is a method readily available to the practicing veterinarian. Ultrasonography is considered to be superior to thoracic radiography for detecting pleural effusion, pulmonary consolidation, pulmonary or mediastinal abscesses, tumors, or granulomata[28] and should be performed when clinical examination or thoracic percussion reveals pain and areas of dullness within the thorax.

Normal lung tissue reflects the ultrasound beam, producing an echogenic pulmonary periphery (thin white line) and reverberation artifacts or concentric equidistant echoes. Normal pleural fluid appears as an anechoic (black) area separating the parietal pleura from the lung tissue, and one commonly detects a small amount of pleural fluid in the ventral thorax of racehorses.[31] In respiratory disorders, one may detect accentuated amounts of anechoic or hypoechoic (gray) pleural fluid. The clinician can determine the character of the pleural fluid, the presence of fibrin or gas, the degree of loculation, and the existence of pleural adhesions during the examination. Pulmonary abscesses appear in ultrasonography as encapsulated cavitated areas filled with fluid or echogenic (white) material, whereas areas of pulmonary consolidation appear as dense patterns of homogeneous internal echoes with a gray tone.[32] Depending on the degree of consolidation, one may visualize bronchial and vascular structures more easily on the sonogram, as well as mediastinal masses. Detection of caudal mediastinal masses improves when pleural effusion is concurrent, because the aerated caudal lungs impair examination. One may visualize masses located in the cranial mediastinum at the third right intercostal space in the absence of pleural effusions.

Diagnostically, certain limitations are inherent in ultrasonography. One may not detect a deep parenchymal lesion if the overlying aerated lung reflects the ultrasound beam. In addition, cases of pneumothorax may be difficult to identify because the free air in the dorsal thorax and the aerated ventral lung appear similar with ultrasound.[28] One also may use ultrasonography prognostically. The detection of free gas echoes (associated with anaerobic bacterial infections or bronchopleural fistulae), extensive fibrinous tags, or areas of loculations within the pleural fluid are associated with a poorer prognosis requiring a more extensive therapeutic regimen.[33]

THORACOCENTESIS

Sampling of the pleural fluid by means of thoracocentesis is beneficial for diagnostic, prognostic, and therapeutic purposes. Abnormal pleural fluid accompanies numerous respiratory disorders, including pulmonary abscessation (pleuropneumonia), chronic pneumonia, systemic mycoses, neoplasia, pulmonary granulomata, and equine infectious anemia. One may perform the technique easily at the sixth or seventh intercostal space approximately 10 cm dorsal to the olecranon by aseptically inserting a teat cannula through an anesthetized site in the intercostal space, just cranial to the border of the rib. To reduce the amount of air aspirated into the pleural cavity, one attaches a three-way stopcock to the cannula. The clinician should take samples from both sides of the thorax and submit the aspirate for cytologic and microbiologic examination. One may obtain up to 100 ml of pleural fluid, although smaller amounts (10 to 30 ml) are more routine.[34] Normal pleural aspirates contain less than 10,000 nucleated cells per μl (60% of which are neutrophils) and less than 2.5 g/dl of protein. Samples should be cultured aerobically and anaerobically. Fluid with a putrid odor is associated with anaerobic bacteria and carries a less favorable prognosis for the horse.[35]

NUCLEAR MEDICINE IMAGING

Scintigraphy, or nuclear medicine imaging, is a specialized technique available at some university and practice facilities. Using γ-emitting radioisotopes such as krypton-81m or technetium-99m, the clinician can assess pulmonary ventilation and perfusion in the horse.[36,37] The horse, breathing through a closed circuit, inhales aerosolized technetium particles generated by a nebulizer. Aerosolized particles are of sufficiently small diameter to be deposited in the alveoli and small airways. Thus their distribution mirrors ventilation. A gamma camera records the sites of deposition within the lung fields. For the perfusion scan, one injects technetium-labeled macroaggregated albumin intravenously. The large protein particles lodge in the blood capillaries of the lung, enabling imaging of the pulmonary perfusion by the gamma camera. Hence lung scintigraphy permits evaluation of the ratio of regional ventilation to perfusion ($\dot{V}/\dot{Q}$) not possible by radiography or ultrasonography. Scintigraphic images may provide additional insights into the diagnosis and pathogenesis of such disorders as chronic obstructive pulmonary disease or exercise-induced pulmonary hemorrhage (EIPH) or in the evaluation of the

horse with poor performance.[38,39] For example, horses with EIPH appears to have a perfusion deficit in the caudodorsal lung lobe that results in a high V/Q area.[38] Horses with chronic obstructive pulmonary disease may produce several patterns, including V/Q deficits in the costophrenic angle (caudoventral diaphragmatic margin), ventilation deficits in the middorsal lung area, or patterns similar to those seen in EIPH.[40] In addition to assessment of pulmonary ventilation and perfusion, scintigraphy can show tracheal mucus transport after intratracheal injection of technetium. One performs the technique by timing the movement of the radioactive bolus over a given tracheal distance.[41,42] Normal values for the unsedated horse range from 16.6 to 20.7 mm/min. Further studies are needed to examine alterations in tracheal mucus transport during disease. For further information, the reader is referred to additional reviews.[40]

PULMONARY FUNCTION TESTING

Measurements of lung volumes, pleural (esophageal) pressure changes, and airflow, coupled with nitrogen washout studies and arterial blood gas determinations, have been used to assess horses with pulmonary disease. Pulmonary function testing requires that the horse wear a breathing apparatus to which an airflow meter has been attached. Pleural pressure changes occurring during each breath are estimated by catheters placed in the midesophagus, exteriorized through the nares, and attached to pressure transducers. By integrating airflow relative to time, one obtains the inspiratory and expiratory volumes. Additional parameters obtained from measurements of airflow include inspiratory and expiratory times, breathing frequency, and peak airflows. In general, the simple measurement of tidal volume, breathing frequency, or minute volume (the product of tidal volume and breathing frequency) provides limited information regarding the functionality of the lung, because these values tend to be maintained near normal limits until the respiratory disease is advanced.[43]

Measures of lung distensibility (dynamic compliance) and airway obstruction (pulmonary resistance) provide more meaningful information regarding pulmonary health. One measures dynamic compliance (C_{dyn}) by dividing the tidal volume by the change in pleural pressure occurring between the start and end of inhalation. One measures pulmonary resistance by several different techniques, depending on whether one measures the resistance at peak airflow or at specific ventilatory volumes (e.g., 50% tidal volume), and calculates it by dividing airflow by the change in pleural (esophageal) pressure. Alterations in these two values can provide information on the nature of the lung disorder. For example, in obstructive disorders of the tracheobronchial tree, dynamic compliance decreases and pulmonary resistance increases. A decrease in dynamic compliance in the absence of a change in pulmonary resistance suggests that the lung parenchyma has been stiffened by alveolar disease or by obstruction of the peripheral bronchioles. (One may recall that peripheral bronchioles, because of their immense cross-sectional area, contribute little to the resistance of breathing until the disorder is well advanced.) Conversely, an increase in pulmonary resistance in the absence of a change in dynamic compliance suggests that the obstruction exists in the upper airway, trachea, or bronchus.[44]

Currently, measures of airway hyperreactivity in horses are becoming more routine at referral centers.[45-47] In this technique, one determines the dosage of a nebulized bronchoconstrictor agent, such as histamine or methacholine, that causes a 35% increase in baseline respiratory resistance or a 35% decrease in baseline lung compliance. As might be predicted, the dosage to achieve this in a horse with inflammatory airway disease or recurrent airway disease is much smaller than that needed to achieve a similar effect in a healthy horse. Measurement of airway hyperreactivity requires that the horse be sedated and outfitted with an airtight breathing mask. Laboratory assistants should wear protective masks to prevent inhalation of the bronchoconstrictor agent.

Pulmonary function testing of *exercising* horses and its use in assessing the poor performer is a new diagnostic approach offered at select referral centers. With the availability of high-speed treadmills and the ability to measure airflow during exercise,[48] analysis of tidal volume, breathing frequency, dynamic compliance, lung resistance, end-expiratory lung volume, and flow-volume and pressure-volume loops may provide additional insights into the cause of the poor performance, the recognition of expiratory flow limitation, and the documentation of EIPH on respiratory mechanics.

LUNG BIOPSY

A histopathologic diagnosis may prove useful in the therapeutic management of certain lung disorders. Percutaneous lung biopsy has been used to investigate disorders (1) characterized radiographically by a pulmonary miliary pattern and (2) disorders for which radiographic or ultrasonographic results are compatible with pulmonary neoplasia or granuloma.[49] Raphel and Gunson originally described the methodology and application of this technique in equine medicine.[50] The clinician inserts the biopsy instrument aseptically through the seventh or eighth intercostal space, approximately 8 cm above a horizontal line through the scapulohumeral articulation. The technique is not recommended in patients that are tachypneic, are in respiratory distress, exhibit uncontrollable coughing, or have bleeding disorders. The technique is not indicated in cases of pulmonary abscessation, pleuropneumonia, or pneumonia.[49]

The most common complications observed with lung biopsy are epistaxis, pulmonary hemorrhage, tachypnea, and respiratory distress. Hemothorax also may develop following lung biopsy.[51]

Disorders of the Upper Respiratory Tract

One may encounter a variety of disorders of the upper respiratory tract in horses. Presenting complaints for upper airway disorders may include dyspnea (especially inspiratory), nasal discharge, dysphagia, lymphadenopathy, swelling or pain in the throatlatch region, or decreased exercise tolerance. Endoscopic or radiographic examination of the head and upper airway facilitate a diagnosis of most such disorders.

SINUS DISORDERS

Sinusitis

Anatomic Considerations Six pairs of sinuses communicate with the nasal cavity in the horse: the dorsal, middle, and ventral conchal and the maxillary, frontal, and sphenopalatine.[52] The conchal sinuses, extensions of the turbinates, communicate with the frontal (dorsal conchal) or maxillary sinuses (middle and ventral conchal). However, most clinically important conditions involve the maxillary and frontal sinuses. The sinuses are lined by a respiratory epithelium—pseudostratified ciliated columnar—interspersed with goblet cells and underlying serous glands.[53]

The maxillary sinus is divided into a rostral and caudal compartment by a bony oblique septum. In most horses the division is complete so that no communication exists between the two compartments. Each compartment communicates with the middle nasal meatus by the nasomaxillary opening, a narrow slit that is occluded easily during inflammation of the mucosa. This process leads to retention of exudate within the sinuses. In horses less than 5 years of age, the last three cheek teeth—the first, second, and third molars—occupy most of the maxillary sinus. As the horse ages and the residual root decreases, the sinus cavity enlarges. The larger frontal sinus communicates with the caudal compartment of the maxillary sinus via the frontomaxillary opening, thus establishing a natural drainage route of the frontal sinus with the nasal cavity.[54]

Causes Primary sinusitis or empyema reflects accumulation of exudate within the sinus cavities and is a sequela of viral or bacterial upper respiratory tract infections. Streptococcal (and rarely staphylococcal) organisms are the usual bacterial isolates. Secondary sinusitis (empyema) of the maxillary sinus usually is associated with dental disorders such as fractured teeth, patent infundibula, and alveolar periostitis. The first molar is the most commonly involved tooth. However, secondary sinusitis may follow traumatic head injuries or the development of congenital paranasal cysts. The latter usually are found in the maxillary sinus but also have been identified in the frontal sinus.[55,56] Neoplasms associated with secondary sinusitis include squamous cell carcinoma (most common), osteogenic sarcoma, lymphosarcoma, myxoma, osteoma, sarcoids, neurofibroma, and mast cell tumor.[57,58] Although rare, fungal granulomata induced by *Cryptococcus neoformans* and *Coccidioides immitis* may cause secondary sinusitis.[59,60] Progressive hematomas also may occur in the maxillary sinus.[57]

Clinical Signs Clinical signs depend on the inciting agent, its location, and the chronicity of the disorder. A unilateral nasal discharge suggests unilateral sinus involvement; a bilateral nasal exudate suggests that the right and left sinuses are involved. Sinusitis following dental disease or invasive neoplastic masses is characterized by a purulent foul-smelling and persistent nasal discharge, whereas a serosanguineous exudate is more typical of sinus cysts, slowly growing neoplasms, and certain stages of mycotic granulomata and hematomas. Inflammatory reactions of the skin, subcutaneous tissues, teeth, and bones may produce facial asymmetry. When sinus inflammation extends into the periorbital region, exophthalmos may ensue. Other clinical signs associated with sinusitis include breathing difficulties, epistaxis, epiphora, headshaking, weight loss, and neurologic signs if the sinusitis extends through the cribriform plate and causes meningoencephalitis.

Diagnosis Diagnosis is based on the history of the disorder, the age of the animal, and the nature of the clinical signs. Percussion of the sinuses may reveal dullness. Endoscopic examination helps to eliminate other potential sources of nasal discharge and demonstrates the presence of an exudate from the nasomaxillary opening, visualized from the middle meatus just proximal to the ethmoids. This visualization confirms that the exudate originates from the sinus compartment. One may further define the sinus disorder by sinuscopy or computed tomography scan. The clinician always should conduct a thorough oral examination of the upper dental arcade even if it requires short-acting anesthesia. The presence of fractured or displaced teeth, receding gum lines, exudate around a specific tooth, or patent infundibula suggests that dental disease is the cause of the disorder. Lateral and dorsoventral radiographs are helpful in diagnosing sinusitis and may demonstrate single or multiple horizontal fluid-air interfaces, abnormalities of the teeth, lysis of alveolar bone, or a combination of these (Figures 7-6 and 7-7). Nuclear scintigraphy may indicate increased uptake of radioisotope around an infected tooth root.[61] Neoplastic lesions may be visible radiographically as loculated or diffuse soft tissue densities. Culture and cytologic examination of the sinus fluid or biopsy of the tissue mass is

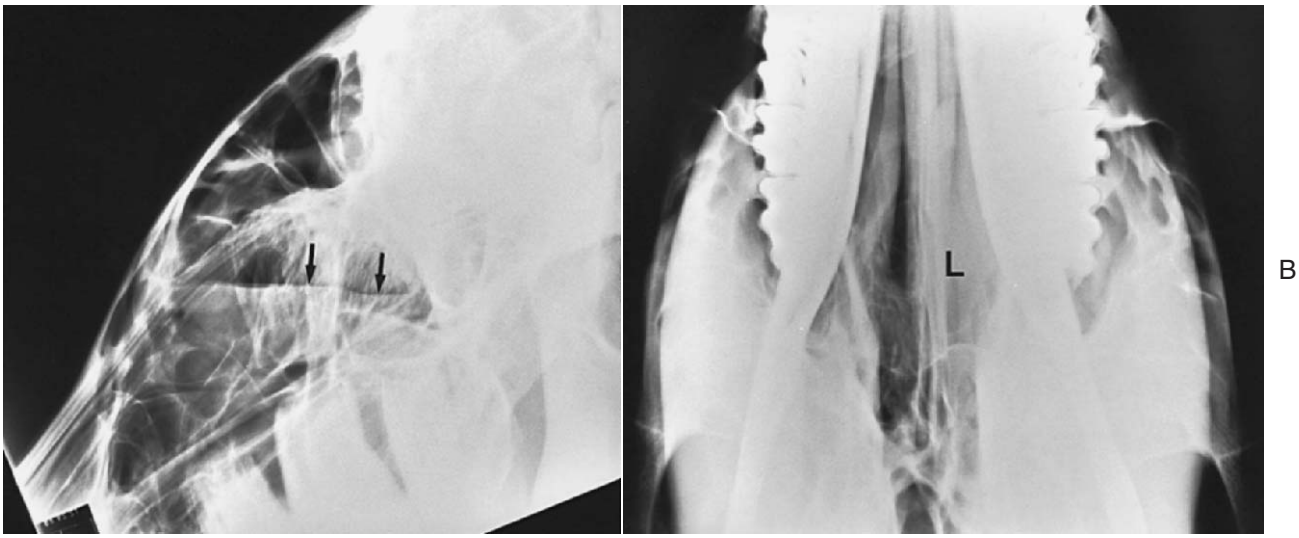


Figure 7-6 Five-year-old Thoroughbred with 7-month history of left-sided nasal discharge. **A,** Air-fluid interface *(arrows)* in the caudal maxillary sinus on the lateral radiograph resulting from dental disease and consistent with maxillary sinusitis. **B,** Increased soft tissue opacity in the left *(L)* maxillary sinus on the dorsoventral radiograph is notable.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

helpful in the diagnosis, although differentiating between a neoplastic or dysplastic process or inflammatory reaction may be difficult. Tumors may vary in consistency but usually have gelatinous areas mixed with combinations of cysts and solid tissue (fibrous tissue).[62]

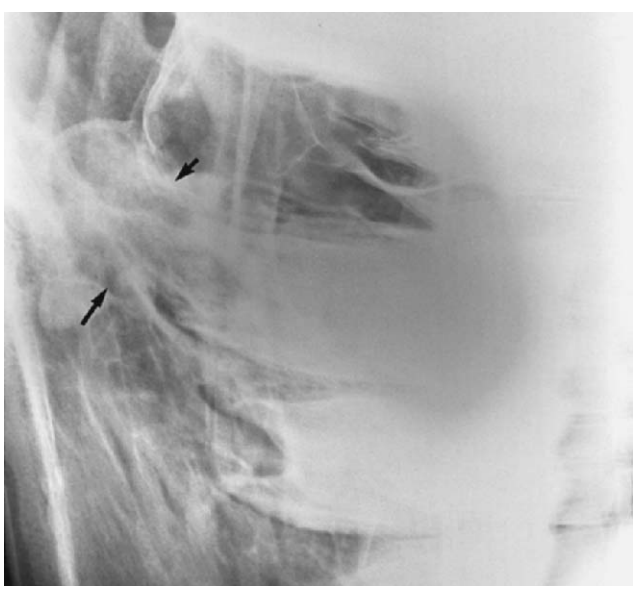


Figure 7-7 Lateral oblique radiograph of midmaxillary cheek teeth. The fourth cheek tooth had been removed previously. Sclerotic bony reaction *(arrows)* surrounds the root of the third cheek tooth.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

Treatment Treatment requires surgical removal of the affected teeth or tumorous or granulomatous tissue and establishment of adequate drainage. Extensive flushing of the sinuses has been recommended until the trephine sites have healed. Surgical removal of paranasal cysts has been associated with a favorable prognosis,[56] whereas fungal granulomata and neoplasms have a poor prognosis. With neoplastic lesions, surgical resection or ablation apparently achieves a low rate of success because of extensive infiltration of the neoplasm or recurrence of the tumor.[58,62]

Ethmoid Hematomas

Definition Ethmoid hematomas are encapsulated, expansive angiomatous masses that appear to develop from the mucosal lining of the ethmoid conchae but also may originate from the walls of the maxillary and frontal sinus. The inciting factor in their development is not known. Some have speculated that ethmoid hematomas develop following chronic infection, repeated episodes of hemorrhage, or congenital or neoplastic conditions.[63] They appear bilaterally in 50% of the cases and are more prevalent in older horses.[64]

Clinical Signs Clinical signs include intermittent unilateral discharge consisting of frank blood or serous or mucopurulent exudates. Stertorous breathing because of obstruction of nasal air flow also may occur.[63] Clinical signs also may include facial swelling, exophthalmos, malodorous breath, headshaking, and coughing.[59]

Diagnosis Diagnosis is based on the clinical signs, endoscopic examination, radiographic evaluation, and in some cases computed tomography scan. Confirmation of a diagnosis is by histopathologic study of the removed tissue. Endoscopy (see Figure 7-2) reveals a yellow, yellow-green, yellow-gray, red to red-purple smooth glistening mass originating from the ethmoid region.[63] One also may note petechial hemorrhages or surface erosions. The mass may protrude beyond the nasal septum (and in those cases may cause a bilateral nasal discharge). Radiographs reveal a space-occupying soft tissue density with smooth margins. Single or multilobular rounded opacities may be visible radiographically in the ventral aspect of the caudal maxillary sinus superimposed on the ethmoid turbinates. The ethmoid hematoma in some cases may extend dorsally into the frontal sinus (Figure 7-8).

Treatment Treatment options include surgical resection, cryosurgery, laser ablation, and formalin injection. Surgical removal is associated with extensive hemorrhage, and surgery may require blood transfusions. A preoperative crossmatch is warranted, and the horse may require a postoperative tracheotomy if one uses extensive packing of the nasal cavity to effect hemostasis. Antimicrobials and antiinflammatory agents are indicated. Following surgical removal, approximately 20% to 50% of the hematomas recur.[63,64] Postoperative complications may include facial wound dehiscence, suture periostitis, facial bone sequestration, persistent nasal discharges, fungal sinus plaque formation, and encephalitis.[65]

Transendoscopic injection of lesions with formalin is an alternative to surgical resection, particularly for smaller lesions. Most cases require multiple injections.[66] Severe complications also may ensue if the cribriform plate is fenestrated, allowing communication of the ethmoidal hematoma with the cranial vault.[67]

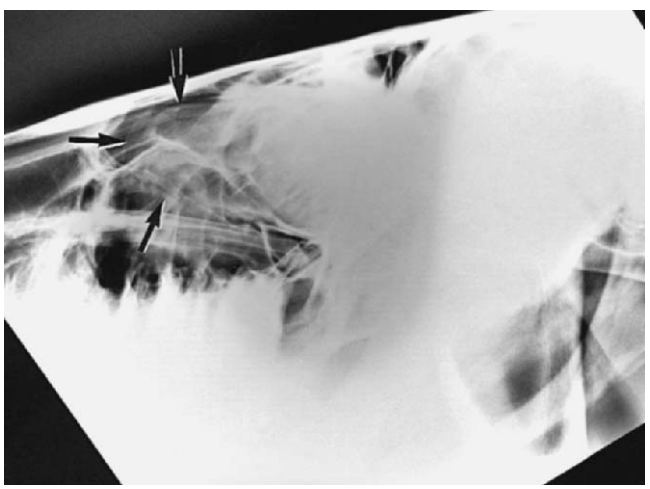


Figure 7-8 Ethmoidal hematoma. Focal increased soft issue opacity *(arrows)* adjacent to the ethmoids is notable.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

GUTTURAL POUCH DISORDERS

Anatomic Considerations

The guttural pouches are caudoventral diverticula of the auditory tubes the functions of which remain undefined, although some investigators have suggested that the pouches play a role in cooling the arterial supply to the brain.[68] Each pouch has a capacity of 300 ml and is divided into a medial and lateral compartment by the invagination of the stylohyoid bone. The mucosal lining of each pouch is secretory, being covered by ciliated pseudostratified epithelium with goblet cells and glands.[69] The mucosal lining is generally thinner than that found in the nasopharynx and also contains small aggregates of subepithelial lymphocytic tissue.[53]

Disorders of the guttural pouches often induce dysfunctions of the surrounding neural structures—cranial nerves VII, IX, X, XI, and XII and the sympathetic trunk, or cause erosion of the vascular structures—the internal carotid, the external carotid, and the maxillary arteries.

Tympany

Definition Tympany is a nonpainful distention of the guttural pouch by air that may produce an external swelling in the parotid region. Congenital tympany occurs in young foals (predominantly fillies), and acquired tympany usually affects older horses.[70]

Pathogenesis The cause of congenital guttural pouch tympany is unknown. An abnormal mucosal flap at the pharyngeal orifice has been proposed to function as a unidirectional valve, trapping air or fluid within the pouch. Tympany is more likely a functional defect rather than an anatomic defect because no abnormality is visible endoscopically or during surgical exploration. Acquired tympany typically is associated with upper respiratory infection and is thought to be caused by swelling of tissues around the pharyngeal orifice, causing a one-way valve effect. This problem is transient, and rarely does pouch distention become severe.

Clinical Signs Clinical signs depend on the degree of pouch distention and hence the degree of compression of the nasopharynx. If distention is significant, the foal may exhibit stertorous breathing, respiratory distress, dysphagia, nasal discharge, or evidence of pneumonia caused by aspiration. Regurgitation of milk from the nostrils also may be evident.[71] Endoscopic examination may reveal significant compression of the nasopharyngeal area because of distention of the pouches.

Diagnosis Confirmation of diagnosis is by the presence of tympanitic swelling in the Viborg's pouch area. Radiographs reveal a large, air-filled guttural pouch with or without fluid accumulation (Figure 7-9). The distinction

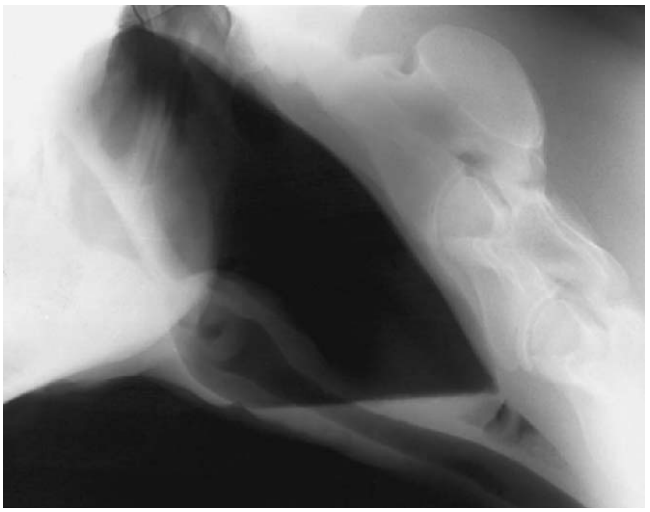


Figure 7-9 Guttural pouch tympany. Lateral radiograph of 5-month-old Arabian colt demonstrating a greatly distended gas-filled pouch.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

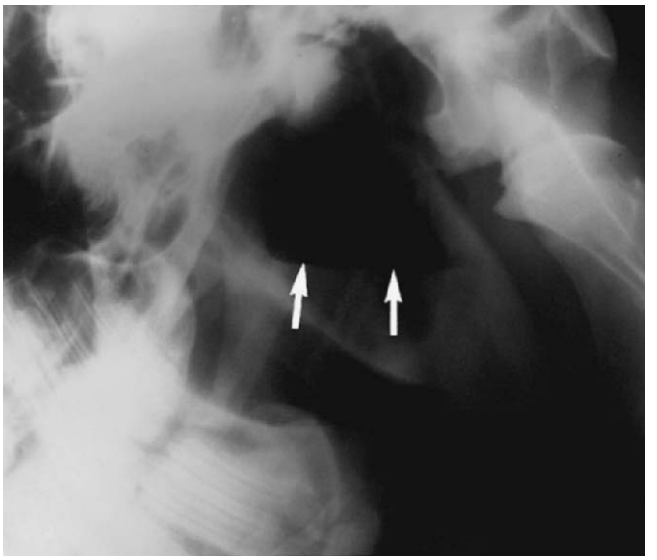


Figure 7-10 Guttural pouch empyema. Lateral radiograph shows a fluid line *(arrows)* or air-fluid interface within the guttural pouch.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

as to whether the problem is unilateral or bilateral can be difficult. Catheterization of one guttural pouch should correct the problem if a unilateral tympany exists. Dorsoventral radiographic views may help in diagnosing bilateral involvement.

Treatment Guttural pouch tympany requires surgical correction. For unilateral tympany, one performs fenestration of the median septum separating the two guttural pouches by conventional surgery or transendoscopic laser surgery. Bilateral involvement may necessitate resection of the excessive plica salpingopharyngeal flap.[72] Because many cultures of the pouches yield β-hemolytic streptococci and the potential for the development of aspiration pneumonia exists, administration of antimicrobials is justified.[70] The prognosis for uncomplicated cases of guttural pouch tympany is favorable.

Empyema

Definition *Empyema* is an accumulation of exudate within the guttural pouches and is usually a sequela of upper respiratory tract infections (*Streptococcal* spp.). In a recent survey, *Streptococcus equi* was isolated from 32% of the cases evaluated for empyema.[73] Empyema may also result from the rupture of abscessed retropharyngeal lymph nodes into the pouches[71] or may accompany cases of guttural pouch tympany. The condition may be unilateral or bilateral.

Clinical Signs Clinical signs include a white nonodorous nasal discharge (unilateral or bilateral), lymphadenopathy, painful distention in the parotid region, stertorous breathing, dysphagia, and occasionally epistaxis.[71] Inspissation of the material may occur with chronic infections, forming masses called chondroids.

Diagnosis Confirmation of diagnosis is by radiographic examination or endoscopy. Radiographs demonstrate a fluid line or an opacity in the pouch (Figure 7-10). Inspissated material also may be evident radiographically (Figure 7-11). Endoscopic examination may reveal a

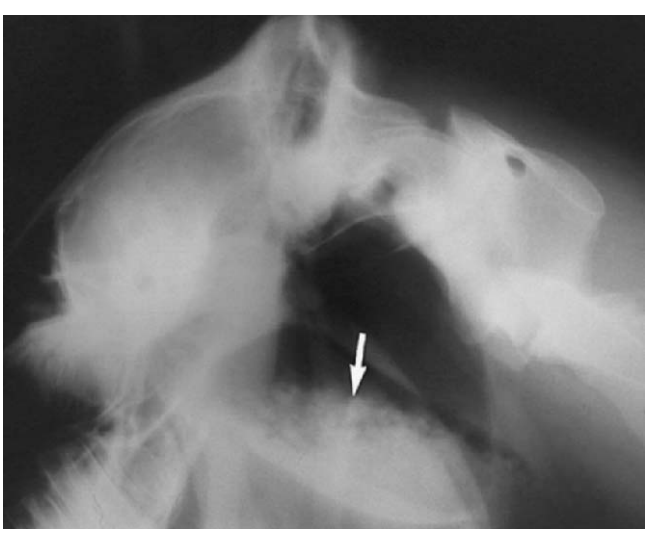


Figure 7-11 Guttural pouch chondroids. Lateral radiograph demonstrates irregular soft tissue opacities in the ventral guttural pouch outlined by gas *(arrow)*.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

purulent material at the pharyngeal orifice of the auditory tubes and within the medial or lateral compartments of the guttural pouches. Small pebblelike structures, chondroids, also may be visible endoscopically. Distortion of the pharynx may occur if distention is significant.

Treatment Because *S. equi* may be involved, the clinician should isolate affected horses and take precautions to avoid spread of the bacteria (see the following discussion). Treatment may entail medical and surgical modalities. Aggressive lavage of the guttural pouch with saline solutions and the administration of systemic antimicrobials is a first step in therapeutic management.[73] One may attempt removal of chondoids with an endoscopic snare, avoiding the complications or risk of surgery and minimizing the cost of treatment.[74] Surgery may be necessary if medical therapy is unsuccessful.[71]

Mycosis

Definition Guttural pouch mycosis is characterized by development of fungal plaques on the mucosal walls of the guttural pouches. The plaques usually are found at two sites, with the majority of them located on the roof of the medial compartment and less frequently on the lateral wall of the lateral compartment of the pouch. The plaques are associated closely with the underlying vascular structures, the internal and external carotid arteries, or the external maxillary artery.[75]

Pathogenesis The events leading to the formation of fungal plaques are not known. Some workers have suggested that aneurysmal dilations of the vasculature, visualized radiographically,[76] provide a suitable environment for fungal organisms to proliferate. Fungal colonization leads to erosion of the underlying mucosa and vascular structures or inflammatory injury to the adjacent nerves.

Clinical Signs Clinical signs depend on the integrity of the neural and vascular structures surrounding the guttural pouch. Horses may exhibit episodes of spontaneous epistaxis, dysphagia, nasal catarrh, laryngeal hemiplegia, Horner's syndrome, abnormal head extension, swelling in the parotid region, facial paralysis, mycotic encephalitis, and atlantooccipital joint infections.[77] The stress of being handled may precipitate fatal epistaxis in the horse.

Although guttural pouch mycosis is uncommon in the young horse, it has been reported in foals less than 6 months of age.[78,79]

Diagnosis Confirmation of diagnosis is by endoscopic observation of a fungal plaque in the guttural pouch. Shortly after an acute bout of epistaxis, endoscopic examination can confirm that blood is exiting the pouch, but attempts to visualize the interior of the pouch may be unsuccessful if blood obscures the visual field of the endoscope. Some risk exists of dislodging a blood clot if one performs endoscopic examination of the pouch.[75] Endoscopic confirmation of secondary neuropathies such as pharyngeal paralysis or laryngeal hemiplegia supports the diagnosis of guttural pouch mycoses.

Radiographs of the guttural pouch may show evidence of fluid accumulation or osteolytic changes in the stylohyoid bone or may suggest mycotic plaque formation. Angiographic demonstration of aneurysms of the internal or external carotid artery supports the diagnosis and may aid in surgical planning.

Treatment Treatment depends on surgical occlusion of the affected vessels. Several different techniques have been advocated.[75,80-83] Current therapies of choice use an intravascular balloon or coil to allow obliteration of arterial flow proximal and distal to the fungal lesion. Complications, including ischemic optic neuropathy and those associated with aberrant vasculature, have been reported.[84,85] Lane[75] has recommended that surgical treatment be combined with topical therapy (natamycin irrigation of the guttural pouch) and supportive care. Horses that have dysphagia may need enteral support via nasogastric intubation or esophagostomy. Medical treatment alone, with topical or parenteral antimycotic drugs, is not efficacious in eliminating the mycotic plaques.

PHARYNGEAL AND LARYNGEAL DISORDERS

Lymphoid Hyperplasia

Definition Acute inflammation of the lymphoid (and surrounding) tissues in the pharynx is termed *pharyngitis.* The condition occurs with equine influenza, EHV1, EHV2, and EHV4 and with *Streptococcus equi* infections. Acute pharyngitis also may develop with prolonged nasogastric intubation. Chronic inflammation of the pharynx, also termed *pharyngeal lymphoid hyperplasia, lymphoid follicular hyperplasia,* and *pharyngeal folliculitis,* is a condition frequently observed in weanlings to performance horses 2 to 3 years of age.[86]

Causes The cause of chronic pharyngitis is not known but probably is multifactorial. Many horses have a history of upper respiratory tract infections, causing some clinicians to speculate that lymphoid hyperplasia is a sequela of chronic antigenic stimulation. The condition has been reproduced experimentally with inoculation of EHV1 and EHV2.[87,88] The severity of the pharyngeal lymphoid hyperplasia does not correlate with EHV1 titers or with the isolation of EHV2.[89]

Streptococcus zooepidemicus, Bordetella bronchiseptica, and *Moraxella* species have been isolated from nasopharyngeal swabs of horses with lymphoid hyperplasia, but their role in the development of the lymphoid hyperplasia is also unknown. In one study the pharyngeal flora was similar in normal control horses and in those exhibiting grade I lymphoid hyperplasia. As the severity of the pharyngitis increased, the number of bacterial organisms that were isolated (colony-forming units per gram of swab material) also increased.[90]

BOX 7-2

GRADING SCHEME FOR LYMPHOID HYPERPLASIA

From Raker CW: The nasopharynx. In Mansmann RA, McAllister ES, editors: *Equine medicine and surgery,* Santa Barbara, Calif, 1982, Veterinary Publications.

The contribution of husbandry factors to the development or maintenance of lymphoid hyperplasia also has been examined. Young horses that are stabled indoors have a more severe pharyngitis than when kept outdoors with access to a three-sided shelter.[91]

Epidemiology An inverse relationship appears to exist between the age of the horse and the prevalence of pharyngeal lymphoid hyperplasia. Approximately 60% to 90% of 2-year-olds exhibit a grade II or more (Box 7-2). Between 35% and 65% of 3- and 4-year-olds and 10% to 20% of 5-year-olds still show grade II or greater lymphoid hyperplasia. With aging, lymphoid follicles regress and tend to disappear.

Clinical Signs Some horses may show a nasal discharge and mild submandibular lymphadenopathy. Manipulation of the larynx may induce a cough. Unless severe, lymphoid hyperplasia has not been associated with poor performance or alterations in arterial blood gases.[92]

Diagnosis Endoscopically, one observes raised hyperemic and edematous follicles distributed throughout the nasopharyngeal walls. Some follicles may have an ulcerated edge to them; others may appear thickened and fibrotic. Raker[93] proposed a gradation scheme based on the severity of the nodule formation, as outlined in Box 7-2. Histopathologic examination reveals lymphocytic proliferation and necrosis, the degree of which does not correlate with endoscopic findings.

Treatment In the absence of a clear understanding of the pathogenesis of this disorder, the most appropriate therapy has not been determined. One treatment that has been tried is nebulization (30 min/day) using an anti-inflammatory solution (350 ml nitrofurazone, 125 ml dimethyl sulfoxide, and 500 mg prednisolone acetate). Stabling changes to reduce dust and mold exposure may be helpful.

Dorsal Displacement of the Soft Palate

Definition During respiration, the caudal free border of the soft palate normally occupies a position ventral to the epiglottis. This position reverses abruptly during swallowing as the palate moves dorsally and the epiglottis covers the adducted arytenoid cartilages and vocal folds. These motor activities ensure that food or saliva is directed dorsally into the esophagus and not into the trachea.[94] The positioning of the palate is complex, controlled in part by the palatine, the tensor, and the levator muscles, which are innervated by the trigeminal, vagus, and glossopharyngeal nerves, respectively. Intermittent or persistent malpositioning of the soft palate dorsal to the epiglottis is termed *dorsal displacement of the soft palate* (DDSP).[95]

Causes On occasion, persistent displacement is evident endoscopically at rest. This finding may be associated with pharyngeal paralysis of numerous causes, but in the absence of signs of dysphagia, the condition often is caused by mechanical or inflammatory mechanisms that obliterate the subepiglottic space (subepiglottic cyst, epiglottitis, epiglottic entrapment, subepiglottic fibrosis, etc.). In most cases of DDSP, palate position is normal on resting and displacement occurs only during strenuous exercise. The cause of displacement in such cases is unclear. Formerly suggested mechanisms including excessively negative intrapharyngeal pressures,[96] excessive poll flexion,[97] epiglottic shortening,[98] and caudal retraction of the larynx by the sternothyrohyoideus[94] now appear largely unfounded. Recent studies have focused on palatal innervation and on factors controlling the relative positions of the larynx and hyoid apparatus as potential causes of palate displacement. Bilateral blockade of the pharyngeal branch of the vagus nerve with local anesthetic has been shown to cause DDSP, implicating a dysfunction of the palate musculature or its innervation as the cause.[99] Furthermore, the observation that some horses with displacement have lymphadenopathy of retropharyngeal nodes that lie in close proximity to the pharyngeal nerves supports the hypothesis that a neuropathy is contributory.[100] Other investigators have evaluated the effects of altering the relationships between the larynx and hyoid apparatus through denervation or transection of various muscles inserting on those structures. Selective transection of the thyrohyoideus muscle causes intermittent

dorsal displacement of the palate in some horses, leading to speculation that neuromuscular disorders of this muscle may predispose to displacement.[101] Recent observations that DDSP and nasopharyngeal collapse were observed in horses following desensitization of the laryngeal mucosa with local anesthetic suggests that receptors within the laryngeal mucosa may be important in maintaining upper airway patency in exercising horses.[102]

Pathogenesis Along with dorsal displacement of the soft palate is a reduction in the cross-sectional area of the nasopharynx. This increases the resistance to airflow and may occlude the passageway completely, temporarily inducing asphyxia (choking down). The displacement creates a stertorous noise most obvious during expiration as the soft tissues vibrate. Because of the obstruction, airflow may be diverted through the mouth during expiration. A study of 10 horses exercising on a high-speed treadmill found that the time of displacement relative to exercise intensity varied, occurring in two horses at peak speed, in two horses before obtaining peak speed, and in six horses as they started to slow down during the exercise protocol.[96] The time of displacement relative to the breathing-swallowing cycle also varied, with displacement occurring during inspiration in three horses, during expiration in three horses, and being associated with a swallow in four horses.[96]

Clinical Signs The cardinal signs of DDSP are respiratory noise and decreased exercise tolerance. Signs are often dramatic, leading to the descriptor "choking down." Affected horses typically make an inspiratory and expiratory noise, but the latter is much more prominent. The noise often is described as snoring, rattling, or gurgling. Occasionally, a horse may show an expiratory noise at rest or while eating. Clinical signs are ordinarily apparent only during strenuous exercise. In racehorses, a history of acute onset of noise and respiratory embarrassment is frequent. Normal respiratory function returns immediately when the horse swallows.

Diagnosis Given the intermittent nature of the displacement, diagnosis is often difficult to confirm. Definitive diagnosis is by observation of displacement during endoscopic examination while the horse is exercising rigorously on a high-speed treadmill. With displacement the caudal border of the palate moves dorsal to the epiglottis, obscuring its shape. The caudal free border of the palate is evident, as is dorsal billowing of the palate on expiration. Before the actual displacement, a lowering of the pharyngeal roof, an elevation of the rostral portion of the soft palate, and a caudal retraction of the larynx are apparent.

In the absence of treadmill access, diagnosis is based subjectively on typical historical findings and resting endoscopic examination. An important note is that most horses examined at rest have no evidence of DDSP. This examination primarily enables the clinician to rule out other causes of upper respiratory obstruction. In some horses, endoscopic findings such as ready displacement by nasal occlusion, ulceration of the free border of the soft palate, or epiglottic hypoplasia or deformity may support a diagnosis of DDSP. Normal horses often exhibit palate displacement during resting endoscopy, especially if sedated, excessively restrained, or subjected to tracheoscopy.

Radiographs of the larynx may demonstrate a hypoplastic epiglottis, that is, one less than 7 cm in length. The clinician should perform a thorough examination of the lower respiratory tract (e.g., auscultation and endoscopy) on these horses to rule out concomitant pulmonary disease.

Treatment Treatment varies and includes medical and surgical approaches. Medical therapy includes tying the tongue, use of a cavesson or figure-eight noseband to keep the mouth closed and treatment of concurrent upper respiratory disorders. One uses the tongue tie in an attempt to prevent caudal retraction of the larynx and subsequent displacement of the soft palate. Keeping the mouth closed is thought to protect the laryngopalatal seal. A short course of nebulization therapy using a solution of 350 ml of liquid nitrofurazone (Furacin), 125 ml of dimethyl sulfoxide, and 500 mg of prednisolone acetate (30 min/day for 7 to 10 days) may be helpful in horses with guttural pouch or pharyngeal inflammation.

The variety of surgical options for treating DDSP reflects the limited understanding of the cause of this disease. Described surgical treatments include resection of the caudal margin of the soft palate (staphylectomy) to increase the size of the ostium intrapharyngeum,[95] partial sternothyrohyoideus myectomy to prevent caudal retraction of the larynx, and epiglottic augmentation by injection of Teflon into the epiglottal submucosa.[103] The current procedure of choice in North America is a combination of conservative staphylectomy and resection of the musculotendinous junction of sternothyroideus muscle, the Llewellyn procedure.[104] Dorsal displacement of the soft palate is a difficult condition to treat: the success rate for the myectomy and staphylectomy approaches 50% to 60%.[105]

Rostral Displacement of the Palatopharyngeal Arch

Definition In the horse the soft palate terminates caudally by the confluence of the caudal pillars to form the palatopharyngeal arch that covers the esophageal orifice.[95] In rostral displacement of the palatopharyngeal arch, this fold of tissue appears to be displaced forward, overlying the apices of the arytenoid cartilages. Cook[106] first described the condition in 1974; others have diagnosed the condition since that time.

Causes The displacement of the palatopharyngeal arch is associated with malformation of the thyroid cartilage and the cricopharyngeal and cricothyroid muscles. Goulden, Anderson, Davies, et al.[107] have speculated that the anomaly results from developmental defects of the fourth branchial arch, which normally forms the thyroid cartilage.

Pathogenesis Cartilaginous and muscular defects have been found in this condition. A deformation of the thyroid cartilage, a lack of the cricothyroid articulation, and often an absence or agenesis of the cricothyroid and cricopharyngeal muscles occur.[107,108] Abnormal pharyngeal configurations prevent normal deglutition, predisposing horses to develop aspiration pneumonia.

Clinical Signs The condition may be present from birth. In most cases, abnormal respiratory noise and poor athletic performance are the presenting complaints. In severe cases, horses may exhibit dysphagia, nasal discharge of food material, persistent coughing, and belching.[106,107]

Diagnosis The diagnosis is based on the clinical signs and history confirmed with endoscopic examination. The rostrally displaced palatopharyngeal arch obscures the normal view of the apices of the arytenoid cartilages. Postmortem examination or surgical exploration of the larynx confirms the presence of developmental defects.

Treatment Rostral displacement of the palatopharyngeal arch is an endoscopic sign representing a major deformation of the laryngeal structures. Resection of the arch by conventional surgery or laser surgery has not enabled successful athletic performance.[109] Severely affected horses are euthanized.

Epiglottic Entrapment

Definition The aryepiglottic fold is the mucous membrane that extends from the lateral aspect of the arytenoid cartilages to the ventrolateral aspect of the epiglottis, where it blends with the subepiglottic mucosa and the glossoepiglottic fold. In epiglottic entrapment, this membrane envelops a portion of or all of the epiglottis.[95,110]

Causes The cause of epiglottic entrapment is not understood completely. In most cases, the epiglottic cartilage and associated soft tissues appear normal. In occasional cases, congenital epiglottic hypoplasia or inflammation of the upper respiratory tract structures appears to contribute to entrapment.

Epidemiology Epiglottic entrapment occurs predominantly in Standardbred and Thoroughbred racehorses, with males and females equally affected.[111]

Pathogenesis Billowing of the entrapping membranes during respiration decreases the cross-sectional area of the pharynx and effectively obstructs the airflow, particularly during expiration.

Clinical Signs Most horses show exercise intolerance and respiratory stertor. Horses occasionally may cough during exercise or while eating. Because entrapment may be an intermittent finding, one should confirm the persistence of the entrapment during exercise by endoscopic examination during exercise or immediately following completion of exercise.

Diagnosis Diagnosis is based on endoscopic examination. The membrane obscures the normal serrated margin of the epiglottis and its dorsal vasculature. In contrast to dorsal displacement of the soft palate, one still can appreciate the shape of the epiglottis. Ulceration of the free margin of the fold and erosion of the entrapped epiglottis may be apparent.[95] Epiglottic length may be determined radiographically.[98] One also may visualize the entrapment on lateral radiographs (Figure 7-12).

Treatment Entrapment requires surgical correction. A number of different approaches have been advocated. One may accomplish resection or division of the tissue (1) under general anesthesia via pharyngotomy, laryngotomy, or by an oral approach; (2) transendoscopically, using a contact Nd:YAG laser; or (3) transnasally, using a hooked bistoury.[111,112] Augmentation of the hypoplastic epiglottis by Teflon submucosal injections has been advocated to increase the bulk of the epiglottis and thus offset some of the structural defects that may predispose to entrapment.[103] One performs this procedure through a ventral laryngotomy.

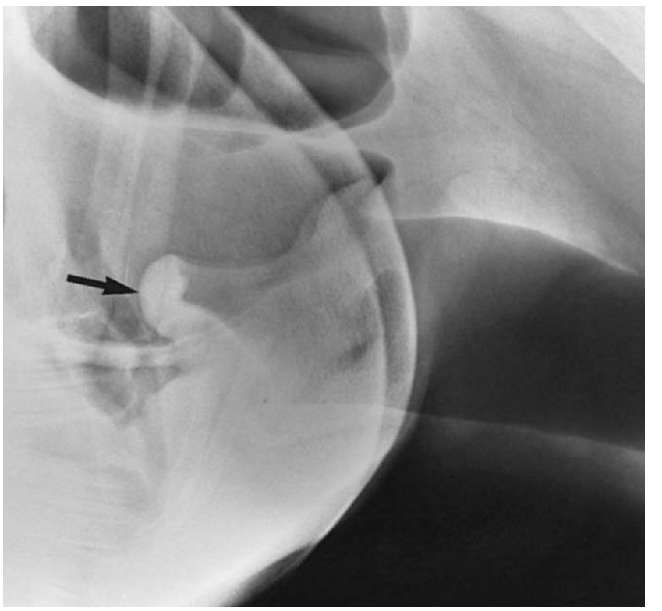


Figure 7-12 Seven-year-old male Standardbred with an entrapped epiglottis. Lateral radiograph of the larynx demonstrates a rounded distal end to the epiglottis *(arrow)*. The epiglottis also appears shortened.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

Epiglottitis

Definition Epiglottis is an acute inflammatory disorder affecting the epiglottis.

Causes The cause of epiglottitis is unknown. Racehorses in active training are affected most commonly. Suggested causes include respiratory tract infection, allergens, palate displacement, epiglottic entrapment, inhaled foreign material, poor quality hay, and the stress of race training.[113]

Clinical Signs Primary clinical signs include exercise intolerance, respiratory noise, and coughing. Dysphagia and respiratory distress are less common signs.

Diagnosis Diagnosis is by endoscopic examination. Signs include epiglottic thickening and ulceration, edema and discoloration of the epiglottic mucosa and aryepiglottic folds, and dorsal elevation of the epiglottic axis. Ulceration may expose the cartilage at the tip of the epiglottis or may be evident as granulation tissue on the underside of the epiglottis. Dorsal displacement of the soft palate is a frequent accompanying finding and may obscure visualization of the epiglottis. In such cases, lateral pharyngeal radiographic or transoral endoscopic evaluation of the epiglottis is of diagnostic value. Epiglottitis frequently is misdiagnosed as epiglottic entrapment on endoscopy.

Treatment Treatment is conservative, consisting of stall rest, systemic antiinflammatory drugs, and topical treatment with antiinflammatory drugs and antibiotics. Most horses respond satisfactorily to treatment, but some occasionally require surgical resection of fibrotic or abscessed subepiglottic tissues. Long-term complications include epiglottic deformity, intermittent or persistent palate displacement, and epiglottic entrapment.

Pharyngeal Cysts

Definition Pharyngeal cysts are fluid-filled structures that have been found in the subepiglottic tissues, in the dorsal nasopharynx, and within the soft palate.[114,115] Depending on their location, the cysts may represent embryonic remnants of the thyroglossal and craniopharyngeal ducts. The cysts usually are considered congenital. Acquired cysts are associated with secretory cells and may occur following obstruction or inflammation of the mucous glands.[95,115] Pseudostratified cuboidal or columnar epithelium or squamous epithelium usually line the cysts, which often contain thick, yellow mucus.

Clinical Signs A foal affected with a large pharyngeal cyst may exhibit signs of respiratory obstruction or dysphagia in the immediate postnatal period. Cough, nasal discharge, nasal milk reflux, and signs of pneumonia may be evidence of accompanying aspiration pneumonia. More typically, the affected horse is asymptomatic until rigorous training begins and signs of abnormal respiratory noise and exercise intolerance become evident. Horses may cough occasionally as well. Dorsal displacement of the soft palate may coexist.

Diagnosis Confirmation of diagnosis is by visualization of smooth-walled structures 1 to 5 cm in diameter. Subepiglottic cysts may distort the appearance of the epiglottis, causing it to assume a more upright position in the pharynx. Endoscopic differentiation between subepiglottic and soft palatal cysts may be difficult. Lateral radiographs of the pharynx and larynx or transoral endoscopic examination of the epiglottis may be useful in distinguishing cysts from conformational defects of the epiglottis.

Treatment Treatment is surgical resection of the cyst via a ventral midline laryngotomy. Some cysts may be accessible via Nd:YAG laser techniques, eliminating the need for general anesthesia. Broad-spectrum antimicrobials are indicated because of the potential for development of aspiration pneumonia, and the clinician should initiate therapy immediately. A course of 7 to 10 days may be indicated postoperatively, depending on the involvement of the lower respiratory tract structures.

Arytenoid Chondritis

Definition *Arytenoid chondritis* is an abnormal enlargement of the arytenoid cartilages associated with chronic inflammation.[116]

Epidemiology The condition is primarily a disease of horses performing at high speeds. Although the racing Thoroughbred or Standardbred primarily is affected, the condition has been described in other breeds.[117]

Pathogenesis The cause of arytenoid chondritis is unknown, but trauma, inflammation, and infection have been cited as potential causes. In most cases the onset of clinical signs is insidious and progressive, but occasionally, arytenoid chondritis may follow an acute episode of laryngeal infection. Histopathologic findings in this condition are consistent with a chronic recurrent inflammatory process. Involved cartilage is greatly thickened and laminated with fibrous connective tissue. Intralumenal granulomata and sinus tracts are observable in some cases. Airway obstruction is caused by physical enlargement of the affected arytenoid cartilage and axial movement of the cartilage as it enlarges. The condition is typically unilateral, though often secondary contact damage ("kissing lesion") occurs to the contralateral cartilage. In most cases the condition is progressive and debilitating, and thus the clinician should give a guarded to poor prognosis.[115]

Clinical Signs Clinical signs include exercise intolerance and inspiratory stridor during exercise. In some horses one easily can elicit a cough with tracheal compression. Palpation of the larynx suggests that the cartilages are less resilient than normal.[118] In severe cases of chondritis, dyspnea at rest may be evident.

Diagnosis Diagnosis is based on endoscopic examination. Mildly affected horses retain arytenoid mobility yet have

ulcerations of the body of the affected cartilage or granulomata that project into the laryngeal lumen. In more advanced cases, the affected arytenoid cartilage is immobile and deviated axially. Such cases may mimic laryngeal hemiplegia, but most have additional findings of ulceration, granuloma, deformity of the corniculate process, or a kissing lesion on the contralateral cartilage.[117] Other abnormalities, such as aryepiglottic entrapment or dorsal displacement of the soft palate, may be evident. Radiographs may reveal excessive mineralization of laryngeal cartilages.

Treatment Treatment includes medical and surgical approaches. Rest, nonsteroidal antiinflammatory therapy, antimicrobials, and throat sprays or nebulization may be helpful in some cases.[117] In horses that retain arytenoid mobility yet have an intralumenal granuloma, transendoscopic laser debulking is indicated. More advanced cases require surgical resection of the affected cartilage. Several techniques have been advocated. Arytenoidectomy involves removal of the corniculate and arytenoid cartilages, including the muscular process. Partial arytenoidectomy (with ventriculectomy and cordectomy) involves resection of the laryngeal saccule, vocal fold, and arytenoid cartilage, excluding the muscular process and the rostral strip of the corniculate.[119] Subtotal arytenoidectomy involves removal of the arytenoid cartilage except for the muscular process.[120,121]

Laryngeal Hemiplegia

Definition *Laryngeal hemiplegia* is a failure of abduction of a structurally normal arytenoid cartilage because of decreased or absent motor activity in the cricoarytenoideus dorsalis muscle, the primary arytenoid cartilage abductor. The fundamental defect is neuropathy of recurrent laryngeal nerve that innervates all of the intrinsic muscles of the larynx with the exception of the cricothyroideus. Paralysis of the cricoarytenoideus dorsalis prevents phasic abduction of the arytenoid cartilages during inspiration or maintained abduction of the cartilages during exercise. Denervation of the arytenoideus transversus, cricoarytenoideus lateralis, ventricularis, and vocalis also prevents adduction of the arytenoids and slackening of the vocal folds.[94]

Causes In the majority of cases no cause for the laryngeal paralysis is found; thus it has been termed *idiopathic laryngeal hemiplegia* (ILH). Most of the clinically detectable cases of ILH involve the left recurrent laryngeal nerve. ILH is a manifestation of a generalized distal axonopathy affecting all long nerves in large-statured horses. The left recurrent laryngeal nerve is the longest nerve in the horse and typically the only one in which axonopathy leads to a clinically evident deficit. Other theories advanced to explain the recurrent laryngeal neuropathy include (1) mechanical compression or stretch of the left recurrent laryngeal nerve as it courses over the aortic arch, (2) bacterial- or viral-induced neuropathies, and (3) vitamin deficiencies.[122] In occasional cases, laryngeal hemiplegia has been known to occur following perivascular or perineural injections, organophosphate intoxication,[123,124] lead poisoning, plant poisoning, guttural pouch mycosis, neoplasia, traumatic accidents to the neck, and paralaryngeal abscessation.[123,125]

Epidemiology ILH generally is considered to be a disorder of larger-breed horses and rarely is reported in Arabians and ponies. Clinical signs usually occur after 3 years of age at a time when work begins. However, left laryngeal asymmetry has been observed endoscopically in foals.[125] Males are reported to be affected more commonly than females, although the physical size difference may be an important consideration in this regard because ILH occurs more frequently in larger horses (>160 cm in height) with long necks and narrow chests.[122] ILH has been reported more frequently in certain family lines of horses, thus causing some to propose it to be a heritable disorder.[126,127] However, the exact mode of transmission remains uncertain.

Pathogenesis In ILH, distal degeneration of the nerve fibers in the left recurrent laryngeal nerve and subsequent atrophy of the intrinsic laryngeal musculature occur.[128,129] Similar, although less severe changes also occur in the right recurrent laryngeal nerve of hemiplegic horses. Mild involvement of other peripheral long nerve fibers—for example, of the distal hindlimb—also occurs. The finding of bilateral recurrent neuropathy, along with changes in other peripheral nerves, is inconsistent with the hypothesis that neuropathy is a sequela of compression or stretching of the nerve as it courses along the aortic arch. The findings, however, are not inconsistent with the development of a distal axonopathy following an energy-dependent disorder, an antioxidant disorder, or a filamentous neuropathy.[130]

Pathophysiology Inadequate abduction of the arytenoids provides an inspiratory resistance to air flow. In experimentally induced hemiplegia, a significant increase in inspiratory or expiratory resistance at rest is not evident. However, during moderate exercise intensities, a significant increase in inspiratory resistance and a subsequent inspiratory airflow limitation develops.[131] The effect of this limitation on gas exchange has been evaluated. During eupneic breathing, no detectable alterations in gas exchange occur. However, during exercise, the physiologic hypercapnia and hypoxemia normally found worsens.[132,133] The ensuing hypoxemia may contribute to the exercise intolerance. The inspiratory resistance increases the work of breathing and *may* predispose to the development of respiratory muscle fatigue.

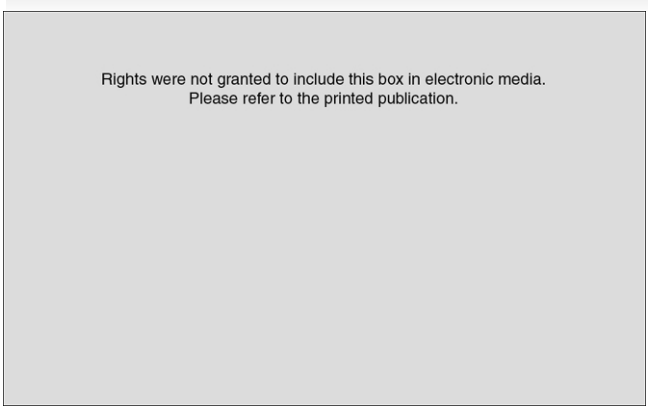
Clinical Signs Most horses with unilateral laryngeal hemiplegia have a history of exercise intolerance and the production of an inspiratory noise described as a whistle

or a roar. In contrast, horses with bilateral laryngeal paralysis may show respiratory distress and require emergency tracheostomies. In cases of bilateral paralysis secondary to toxins (e.g., organophosphate overdose), clinical signs may not be apparent for several weeks following the toxic insult.[134]

Diagnosis Physical examination and palpation of the larynx may reveal atrophy of the cricoarytenoideus dorsalis muscle. The slap test has been used to evaluate the adductor function of the intrinsic laryngeal muscles. In normal horses, when one slaps the saddle area of the horse, contralateral arytenoid cartilage adduction occurs. This adduction is detectable endoscopically or by palpation of the larynx during the procedure. The reflex is absent in horses with idiopathic recurrent laryngeal neuropathy.[135] However, the demonstration of a normal laryngeal reflex when the horse is at rest does not indicate that the horse is completely free of laryngeal hemiplegia.[126] Ultimately, the clinician usually makes the diagnosis by an endoscopic examination wherein one observes asymmetric positioning or range of motion of the arytenoid cartilages and relaxation of the vocal folds on the affected side. Box 7-3 provides a proposed grading scheme and may aid in the decision for surgical intervention. For example, horses with grade IV can be expected to benefit from surgery, whereas horses with grades I and II usually are not compromised during exercise and thus are not good surgical candidates. Horses with grade III are considered suspect, some of these horses demonstrating dynamic collapse of the airway and thus requiring surgical intervention. Ideally, one should perform endoscopic examination of the horse during treadmill exercise to ascertain the importance of slight asymmetry at rest in the production of exercise intolerance. A recent study documented progression of laryngeal hemiplegia, as judged by clinical signs and endoscopic examination, in 15% of horses.[136] The mean age of onset of progression was 7 years.

BOX 7-3

GRADING SCHEME FOR LARYNGEAL ANATOMY



From Ducharme NG, Hackett RP: The value of surgical treatment of laryngeal hemiplegia in horses, *Compend Cont Educ Pract Vet* 13:472, 1991.

Treatment Surgical correction of the airflow obstruction is necessary. Laryngoplasty, a prosthesis that maintains the affected arytenoid in abduction, is implemented most commonly. Complications associated with the surgery include failure to maintain abduction of the arytenoid cartilage, dysphagia leading to coughing while eating or rarely aspiration pneumonia, chronic infection of the prosthesis leading to a suture sinus, ossification of cartilage, esophageal obstruction, intralaryngeal granulomatous polyps, right-sided laryngospasm during exercise, laryngeal edema, and chondritis.[137] Ventriculectomy, surgical ablation of the lateral ventricles in an effort to induce adhesions between the vocal cords and laryngeal walls, also has been performed, singly or with the laryngoplasty. Prosthetic laryngoplasty prevents the increase in inspiratory resistance and flow limitation during moderate exercise.[132] However, ventriculectomy alone fails to alleviate the increased inspiratory impedance during exercise.[133] Surgical procedures that attempt to restore innervation to the cricoartyenoideus dorsalis muscle minimize the risk of serious postoperative complications. Described techniques include transplantation of a nerve-muscle pedicle into the cricoartenoidus dorsalis muscle, implantation of the cut end of the second cervical nerve into the left cricoarytenoideus muscle and anastomosis of the first cervical nerve to the abductor branch of the left recurrent laryngeal nerve.[137-139] A modest improvement was notable in the experimental models but a report of nerve-muscle pedicle graft in racehorses revealed results comparable to those of prosthetic laryngoplasty.[140] Reinnervation of the cricoarytenoideus muscle following nerve-muscle pedicle grafting takes 6 to 12 months depending on the amount of muscle atrophy and thus is used primarily in young, unraced horses or in horses in which a rapid return to athletic performance is not necessary.

In horses with bilateral laryngeal paralysis, tracheostomy may be required until resolution or lessening of paralysis occurs. Affected horses should not be stressed or subjected to undue movements. The clinician should institute broad-spectrum antimicrobial and antiinflammatory therapy.

Streptococcus equi Infections (Strangles)

Causes *Streptococcus equi* subspecies *equi*, a gram-positive β-hemolytic bacterium of the Lancefield Group C, is the causative agent of strangles, a highly contagious disease

of equidae. The disease was recognized in the thirteenth century and occurs worldwide.[141] Recent multilocus enzyme electrophoresis studies have confirmed a close genetic relationship of *S. equi equi* and *S. zooepidemicus,* indicating that the former is a clone derived from the more genetically diverse *S. zooepidemicus.*[142] This finding has led to the recommendation that *S. equi equi* be reclassified as a biovar of *S. zooepidemicus.*[143] Although isolates of these two organisms show greater than 92% DNA homology, immunity is species specific: immunization with *S. zooepidimicus* does not protect against challenge by *S. equi equi*.

S. equi equi (hereafter referred to as *S. equi*) is not a normal inhabitant of the equine upper respiratory tract and does not require prior viral infections for successful colonization and infection.[144] Based on morphologic features of the bacterial colony, three strains of the organism occur that differ in virulence. The typical and highly virulent encapsulated *S. equi* strains produce golden, honey-colored mucoid colonies on blood agar. Atypical *S. equi* colonies exhibit a matte appearance within 24 hours of incubation. Nonencapsulated colonies are glossy, dry, and small.[145] Differences in the hyaluronic acid content of the capsule are responsible for the morphologically distinctive features of *S. equi* colonies.

Laboratory diagnosis of Lancefield group C streptococci *(S. equi, S. zooepidemicus, S. equisimilis)* traditionally is based on fermentation patterns of lactose, sorbitol, and trehalose. Typical *S. equi* isolates fail to ferment any of these sugars, whereas atypical *S. equi* isolates may ferment lactose or trehalose but not sorbitol.[146] In some laboratories, polymerase chain reaction (PCR) assays aid in confirming *S. equi* isolates.[147]

Epidemiology The infection occurs primarily in horses 1 to 5 years old but is not restricted to this age group. Foals up to 3 months of age born from immune mares are known to be resistant to the development of strangles.[148] In susceptible equine populations, morbidity is nearly 100%, whereas mortality is low (up to 10%) if appropriate therapy is instituted.[149] Once having been infected, approximately 75% of the horses are immune to the organism for 4 years.[150] In another study, 83% of young horses affected with clinical strangles as foals were resistant to co-mingling exposure 6 months later.[151] Immunity is not lifelong: epidemiologic studies report attack rates in horses greater than 3 years of age of 18%, 29%, and 35%.[149,152,153]

The organism is transmitted (1) via direct contact with nasal secretions or lymph node discharges from infected horses or (2) via exposure to fomites such as contaminated equipment, pails, halters, leads, brushes, clothing, horse vans, or stalls. Recent additions to a stable are most often the cause of a strangles outbreak because a recovering horse may shed the organism for several weeks. In closed herds, epidemics have been attributed to exposure of horses to asymptomatic chronic carriers of the organism. Such horses harbor the organism in the guttural pouches for as long as 39 months in the absence of clinical signs. Other sites of long-term carriage of the organism include the paranasal sinuses.[154]

The organism also can survive for long periods in the environment depending on the temperature and the substrate. Jorm[155] found that *S. equi* survived for 63 days on wood at temperatures of 2° C and for 48 days on glass or wood at temperatures of 20° C. A 1:200 dilution of phenol and disinfectants such as povidone-iodine, chlorhexidine, and glutaraldehyde kill the organism within 90 minutes.

Although the organism traditionally is thought to infect only equidae, a fatal pneumonia attributed to *S. equi* infection in a dromedary camel was reported recently.[156] In the literature on human beings, descriptions of two cases of *S. equi* bacteremia exist, but infections in human beings are considered rare.[157]

Pathogenesis After infective droplets are inhaled or ingested, the organism adheres to the epithelial cells of the buccal and nasal mucosa of the horse. Within hours of adhesion, the organism has translocated below the mucosa and gained access to the local lymphatics and lymph nodes where replication occurs extracellulary.[141] Spread of the organism to sites other than the upper respiratory tract lymphoid tissue may occur by hematogenous or lymphatic pathways.

At least three virulence factors of *S. equi* contribute to its pathogenicity and include the hyaluronic acid capsule, the M-like protein, and a leukocidal toxin.[158] The hyaluronic acid capsule possesses a strongly negative charge and apparently repels phagocytic cells. Nonencapsulated strains of *S. equi* are able to colonize the surface of the upper respiratory tract and stimulate production of serum antibody but are unable to induce detectable pathologic changes in the retropharyngeal and submandibular lymph nodes.[159] The second virulence factor, the M-like protein (SeM), is a 58-kd cell wall antigen. This protein functions by limiting deposition of complement components (C3b) on the bacterial surface and preventing activation of the alternative complement pathway. SeM also binds fibrinogen and impairs neutrophil killing of the organism.[142] The M-like antigen also appears to be important for adherence of the organism to the oropharyngeal epithelium. Another recently identified M-like protein, SzPSe, exhibits antigenic cross reactivity with the M-like proteins of *S. zooepidemicus.* Its contribution to the virulence of *S. equi* is currently unknown.[142]

Additional factors that may contribute to the pathogenicity of *S. equi* include extracellular proteins that are mitogenic for peripheral blood mononuclear cells.[160] These mitogenic factors have been hypothesized to induce

release of interleukin-1 (IL-1) and tumor necrosis factor α from antigen-presenting cells (macrophages, monocytes) and to contribute to the development of fever, malaise, neutrophilia, and hyperfibrinogenemia.[160]

Clinical Signs The incubation period ranges from 2 to 6 days. In typical cases, horses are febrile, exhibit malaise, and develop a serous nasal discharge that becomes mucopurulent. Submandibular and retropharyngeal lymph nodes are initially firm but become fluctuant before rupturing 7 to 10 days after the onset of signs. Lymphadenopathy may be asymmetrical and may become so severe that dysphagia and respiratory distress ensue. Swelling of the throat-latch area or of Viborg's triangle may be apparent. The affected horse may stand with its neck stretched out and be reluctant to swallow. A soft moist cough may be heard. The average course of the syndrome is 23 days.[144]

In atypical *S. equi* infections, a mild inflammation of the upper respiratory tract occurs and is characterized by a slight nasal discharge, cough, and fever. Abscessation of the lymph nodes occurs only in a small number of the cases.[145,146,161]

Clinical Pathology A marked neutrophilic leukocytosis, hyperfibrinogenemia, and an anemia of chronic infection are found in typical strangles cases.

Diagnosis Diagnosis usually is based on clinical signs and the isolation (culture) or detection (PCR) of *S. equi* from a lymph node, a nasopharyngeal swab, or lavage fluid from the guttural pouches. Blood cultures may become positive for *S. equi* on days 6 to 12 following infection.[162]

Identification of chronic asymptomatic carriers can be difficult. In one recent study, endoscopic abnormalities in the guttural pouches were evident in most asymptomatic carriers.[163] However, the absence of visible pathologic signs in one asymptomatic carrier emphasizes the need to obtain samples for microbiologic studies. When PCR and culture results from asymptomatic carriers were compared, many more samples were found to be positive using PCR than with culture alone.[164]

Treatment Treatment is a function of the stage of the disease. Sweeney, Benson, Whitlock, et al.[165] suggested a treatment protocol that is outlined next. Penicillin is the drug of choice, although *S. equi* is sensitive to oxytetracycline and the potentiated sulfonamides.[141,154]

The treatment plan is as follows:

1. For horses exposed to the organism, penicillin therapy is indicated to prevent seeding of the pharyngeal lymph nodes. Antimicrobial therapy should continue for as long as the horse remains exposed to the organism. Once the therapy stops, a risk exists that the horse may develop strangles.
2. For horses exhibiting signs of infection in the absence of lymph node abscessation, penicillin G therapy can arrest the progression of the disease. One should isolate the horses during their treatment protocol.
3. For horses exhibiting evidence of lymph node abscessation, administration of penicillin slows the progression of lymph node abscessation and generally is contraindicated. Hot-packing the area(s) promotes abscess formation. Once achieved, the clinician should lance the abscess and flush it with a 2% tamed iodine solution. One should treat horses in isolation.
4. For horses that are systemically ill or that develop complications such as dysphagia and respiratory distress require supportive care in addition to high levels of intravenous penicillin. This therapy may entail intravenous fluid therapy, a tracheostomy, nonsteroidal antiinflammatory drugs, and feeding via the nasogastric tube.

Sequelae Complications most frequently result from metastasis of the organism to other organ systems with the formation of purulent foci.[165] These complications include the following:

1. Internal abscessation of the mesentery or of parenchymatous organs. The causes of internal abscessation are not known, although inadequate antimicrobial therapy during respiratory catarrh and lymphoid abscessation may be contributory.[166] The horse may have a history of intermittent colic, periodic pyrexia, anorexia, depression, and weight loss. The clinician should direct diagnostic techniques, including rectal palpation, thoracic radiography, thoracocentesis, abdominocentesis, ultrasonography, computed tomography, and nuclear scintigraphy,[167] at determining the location of the abscess. Cases of internal abscessation can be difficult to differentiate from neoplastic causes of weight loss and colic because both processes may induce similar abnormalities in the peritoneal fluid (leukocytosis and hyperproteinemia). Differentiation between the two processes may not be possible unless exfoliated neoplastic cells are identified.[168] Hematologic and serum biochemical abnormalities in cases of internal abscessation include (1) a neutrophilic and monocytic leukocytosis, (2) hyperfibrinogenemia, (3) hyperglobulinemia and hypoalbuminemia, and (4) hypocalcemia.[166,168] However, these changes are not unique to abscesses and may not be found in horses with intraabdominal neoplasms.[168] Thus the diagnosis of internal abscessation represents a medical challenge. Once one confirms the diagnosis, long-term penicillin therapy is indicated and may be required for several months. Clinical signs, rectal palpation, repeated abdominocentesis, and multiple complete blood counts (CBCs) are useful to monitor the progress of therapy.
2. Purpura hemorrhagica. This aseptic vasculitis occurs following reexposure to *S. equi* by natural infection or following vaccination. In horses with purpura hemorrhagica, IgA titers to the SeM and to nonspecific proteins in the *S. equi* culture supernatant (SC-P)

are significantly greater than those titers found in horses with uncomplicated strangles.[169] Furthermore, the isolation of immune complexes consisting of IgA and M-like proteins in the sera of horses with purpura hemorrhagica has led to the suggestion that this isotype is involved in the development of purpura.[169,170] The immunologic basis for the increase in serum IgA levels is not known: possible explanations include uncontrolled expansion of B cell populations that produce IgA against antigens of *S. equi* or failure of IgA removal mechanisms because of hepatic dysfunction. In the horse, purpura hemorrhagica has been likened to Henoch-Schönlein purpura, an immune complex–mediated disease of human beings.[170]

The clinical signs of purpura vary and range from a mild transient reaction to a severe and fatal form. Horses with purpura develop pitting edema of the limbs, head, and trunk and petechiation and ecchymoses of the mucous membranes. Horses also may have colic following edema and hemorrhage of the bowel. The vasculitis may cause skin sloughing and infarcts of skeletal muscle. Death may ensue as a result of pneumonia, cardiac arrhythmias, renal failure, or gastrointestinal disorders.

Confirmation of diagnosis is by skin biopsy characterized as a leukocytoclastic vasculitis, isolation of the organism, or demonstration of elevated IgA titers to *S. equi*. Treatment entails administration of intravenous penicillin (20,000 IU/kg 4 times daily), dexamethasone (0.1 mg/kg intravenously or intramuscularly), intravenous fluids, and antiinflammatory drugs. Clinical recovery occurs as the source of the antigen is removed and as the immune response is suppressed. Coincidental with recovery is the production of IgG to *S. equi* antigens.[169]

3. Guttural pouch empyema and chondroid formation (see the previous discussion).
4. Septicemia and the development of infectious arthritis, pneumonia, and encephalitis. These conditions warrant a poor prognosis.[171]
5. Retropharyngeal abscessation. Upper respiratory tract obstruction may cause the horse to develop respiratory distress and dysphagia. Endoscopy of the nasopharynx demonstrates collapse of the nasopharynx, deviation of the larynx, or drainage of purulent material into the nasopharynx when external pressure is applied to the parotid region.[172] Radiographs demonstrate a soft tissue density in the retropharyngeal area, thickening of the roof of the pharynx, reduction in the diameter of the pharyngeal airway, and distortion or compression of the guttural pouches, pharynx, and trachea.[173] The retropharyngeal abscess may rupture into the pharynx and cause a secondary pneumonia or may rupture dorsally into the guttural pouches.[165,172,173]
6. Laryngeal hemiplegia. The condition occurs when abscessed lymph nodes encroach on the recurrent laryngeal nerve.[174]
7. Tracheal compression following abscessation of the cranial mediastinal lymph nodes. Tracheal compression has been reported. The horse may show respiratory distress or exhibit stertorous breathing. Laryngeal hemiplegia may be an additional complication if the abscess compressing the trachea involves the recurrent laryngeal nerves.[174]
8. Endocarditis or myocarditis following abscess formation.
9. Agalactia in periparturient mares.
10. Suppurative necrotic bronchopneumonia, which may result in death.
11. Abscess formation in the central nervous system.[175]
12. Myopathies. Two types of muscle disorders associated with *S. equi* infection have been described recently. One fatal form is characterized by a vasculitis and infarction of skeletal muscle and pulmonary and gastrointestinal tissues. Horses typically have signs of colic and usually are euthanized because of unrelenting pain. Postmortem examination reveals muscle infarctions that are compatible with purpura hemorrhagica. The second type of muscle disorder affects Quarter Horses that have malaise, significant muscle atrophy, and chronic active rhabdomyolysis. Immunocytochemical stains of fast-twitch fibers are positive for equine IgG. Horses responded to treatment with penicillin and dexamethasone with the muscle mass normalizing within 2 months.[176]

The clinician should follow these control measures to reduce transmission of *S. equi* during an outbreak[177]:

1. Prevent spread of infection to horses on other premises and to new arrivals immediately by stopping all movement of horses on and off the premises.
2. Identify symptomatic and asymptomatic carriers by sampling nasopharygneal or guttural pouch regions at weekly intervals and testing for *S. equi* by culture and PCR.
3. Isolate infectious horses from those screened negative for *S. equi*. Cordon off the isolation area and have infectious horses looked after by a dedicated staff wearing protective clothing and footgear. Disinfect stalls, aisles, and equipment.
4. Once clinical signs have disappeared, perform at least three consecutive swabs or lavages for *S. equi* culture, coupled with endoscopic examination of the guttural pouches to confirm that horses are noninfectious.

Prevention Vaccines currently available include Strepguard with Havlogen (*S. equi* extract); Strepvax II (aluminum hydroxide adjuvanted *S. equi* extract), and Pinnacle I.N. (an attenuated live culture of *S. equi*). None of the vaccines guarantees prevention of strangles

in vaccinated horses. Parenteral (killed) vaccines induce strong serum bactericidal activity, but these antibodies are not necessarily protective because mucosal immunity plays a significant role in the resistance to infection.[178] In contrast, mucosal immunization induces a combination of systemic and local responses associated with the production of a greater variety of immunoglobulin isotypes and specificities that closely mimic those induced by natural disease. Although intranasal vaccines are expected to produce fewer adverse reactions than parenteral vaccines, lethargy, inappetence, fever, lymphadenopathy, lymph node abscessation, purpura hemorrhagica, and intramuscular abscesses have occurred after vaccination. One should not administer intranasal vaccines concurrently with other parenteral injections because of the risk of abscess formation at the site of the intramuscular injection. One should wash one's hands thoroughly following vaccination. Vaccination of infected horses during an outbreak on a farm may be associated with the development of purpura hemorrhagica. Because of the lack of scientific studies, whether the clinician should implement vaccination in the face of an outbreak is uncertain. During vaccination, effective immune response takes 7 to 10 days to develop.

VIRAL INFECTIONS

Viruses of known pathogenicity to the horse that produce or are associated with respiratory tract disease include equine influenza virus, EHV1, EHV2, EHV4, equine arteritis virus (EAV), and equine rhinovirus A and B.

Equine Influenza

Causes The influenza viruses are enveloped myxoviruses containing single-stranded RNA. Based on the internal nucleoproteins and matrix antigens, influenza viruses have been classified as three types: A, B, and C. Types B and C infect only human beings, but type A infects many different species, including human beings, horses, swine, and avian species.[178] Natural cross-species infections have occurred between human beings and swine, and experimental infection of human beings with equine influenza virus (subtype 2) is possible, although natural infections do not occur.[179] Type A is classified further into subtypes based on the surface antigens, the hemagglutinin (H) and neuraminidase (N). Two subtypes are recognized as infectious for the horse: subtypes H7N7 and H3N8. Subtype H7N7 was first isolated in Prague in 1956 and has been called equine-1 influenza (A/equine/Prague/56). Subtype 1 is thought to have disappeared from horses worldwide because an isolate has not been confirmed since 1980. Subtype H3N8 was first isolated in Miami in 1963 (prototype) and was designated as equine-2 influenza (A/equine/Miami/63). Several variants of subtype 2 (antigenic drift) have been identified and include A/equine/Fontainebleau/79, A/equine/Kentucky/81, A/equine/Saskatoon/90, and A/equine/Newmarket 2(N2/93).[178,180,181] Compared with the human influenza virus, the equine influenza virus is stable antigenically, not experiencing major antigenic shifts. This stability has been postulated to result from the shorter life span of horses relative to human beings and the lower mutation pressure placed on the equine influenza viruses because of low specific antibody titers.[179]

Epidemiology Influenza most commonly affects 2- and 3-year-old horses and may be the most common cause of respiratory illness in racehorses, with some tracks experiencing influenza outbreaks 2 to 3 times within a racing season.[180-182] This phenomenon may reflect poor ventilation systems (closed shedrows), lack of adequate immunization protocols, and rapid transmission of the virus from exercise ponies to racehorses.[180] The reservoir of equine influenza virus between epizootics remains unknown. Some speculate that the virus is maintained in the horse population itself and that asymptomatic carriers shed virus when stressed. Alternatively, the virus may be harbored in other species such as birds, which are asymptomatic but shed the virus in their feces.[179]

Pathogenesis The incubation period is 1 to 3 days, with the virus infecting the upper respiratory tract and the lungs to a lesser extent. Healthy respiratory tract epithelium is ciliated and contains mucus that forms a protective layer over the cell surface. The mucus normally acts as a mechanical barrier between air and tissue and contains antibody and protein substances that deter the attachment of viral particles to the epithelium.[183] Neuraminidase activity of the viral particles alters the efficiency of the mucociliary apparatus, allowing the virions to attach via hemagglutinin antigens to sugar groups (sialic acid) on the surface of the epithelial cells. The epithelial cell internalizes the bound virus and surrounds it with an endosome. However, in the mildly acidic conditions of the mature endosome, the hemagglutinin antigen protein becomes activated and promotes fusion of the viral and cellular membranes, leading to release of the nucleocapsid into the cytoplasm.[184] Cell necrosis and desquamation follow viral replication within the respiratory tract epithelium. Exposure of irritant receptors causes hypersecretion of submucosal serous glands and further damage to the mucociliary apparatus. Inflammation leads to massive lymphocyte infiltration and edema. Recovery of the normal epithelial architecture can require more than 6 weeks.[185] Humoral and cellular immunity are important in providing protection against viral disease: IgA blocks viral penetration but is not bactericidal; certain IgG isotypes, IgGa and IgGb, opsonize the virus particles and enhance phagocytosis.[186]

Clinical Signs Signs of influenza appear 3 to 5 days following exposure to the virus. Horses exhibit a sudden

onset of fever (103° to 105° F), which may be biphasic; a serous nasal discharge; anorexia; depression; and a dry, deep cough. Some horses exhibit myalgia, myositis, and limb edema and are thus reluctant to move.[179] A mild form of azoturia (myoglobinuria) occurs in some cases. One may find submandibular lymphadenopathy, as well as endoscopic evidence of pharyngitis and tracheitis. A mild bronchitis with minimal changes in lung sounds may occur. From experimental studies, inoculation with A/equine-1 produces a milder (subclinical) syndrome unless the animal is stressed before infection, whereas A/equine-2 usually generates the typical clinical signs. The course of the infection usually lasts 2 to 10 days in uncomplicated cases. Exercise exacerbates the clinical signs.[187] Secondary bacterial infections may occur, and donkeys and mules appear to have greater susceptibility to secondary infections than horses.[188] Horses remain infectious for 3 to 6 days after the last signs of illness.

In young foals, influenza is severe, producing signs of viral pneumonia, which may lead to death within 48 hours.

Clinical Pathology Horses initially may exhibit a lymphopenia followed by a monocytosis.

Diagnosis The clinician may diagnosis equine influenza by two methods:

1. Detection of virus. Based on studies of influenza outbreaks, viral culture and isolation alone from nasopharyngeal swabs appears to be the least sensitive method for diagnosing influenza,[180] probably because the chances of viral isolation are greater when samples are collected within the first 24 hours.[182] However, a stallside assay (Directigen Flu-A test, Becton Dickinson, Franklin Lakes, New Jersey), allows rapid detection of influenza antigen and an immediate diagnosis.[185] Detection of viral particles in materials obtained from nasopharyngeal swabs via PCR permits diagnosis of influenza infections within 48 hours of sample submission.
2. Serologic testing. Several diagnostic methods for detecting influenza virus antibodies in the horse are available and include complement fixation, hemagglutination inhibition, single radial hemolysis, viral neutralization, and enzyme immunoassay.[189] Acute and convalescent serum samples are needed to establish a definitive diagnosis, and although viral neutralizing antibodies may be detectable within a week of infection, the horse may take up to 28 days to exhibit a rise in hemagglutination titers.[179] Serologic testing has been considered to be a sensitive method for diagnosing influenza outbreaks, although in one epidemic, approximately 24% of horses with clinical signs of influenza failed to seroconvert.[180]

Treatment Treatment is primarily symptomatic, ensuring that the horse continues to maintain adequate hydration and is not subjected to undue stresses. Nonsteroidal antiinflammatory drugs may be indicated to reduce the fever, eliminate the myalgia, and improve the appetite. The risk is that the owner will return the horse to strenuous exercise before the horse has rested a sufficient time. Horses that suffer severe infections may be unfit for competition for 50 to 100 days after infection. During the infection, frequent examinations of the respiratory tract are indicated to detect the development of secondary complications such as pneumonia, pleuropneumonia, and myocarditis.

Prevention Regular vaccination significantly reduces the population at risk. In fact, the suggestion has been made that at least 70% of the equine population (horses, ponies, donkeys) should be vaccinated to prevent epidemics of influenza.[190] Killed and modified live vaccines are commercially available. The inactivated vaccines contain both subtypes of influenza virus and some of their strain variants (e.g., A/equine-2/KY 81). Equine subtypes 1 and 2 do not immunologically cross-react: exposure to one subtype does not protect against exposure to the other. The modified live vaccine (Flu Avert, Heska, Fort Collins, Colorado) contains only A2 strains and is administered intranasally.

In one study the use of a killed vaccine reduced neither the rate of respiratory tract disease nor the severity of clinical scores compared with nonvaccinates.[191] This vaccine failure may be a function of the number of boosters horses received before infection and of the strain of A2 contained within the vaccine.

Little data is currently available concerning the performance of the modified live vaccine during influenza outbreaks. From experimental trials, the vaccine appears to have phenotypic stability, is efficacious against heterologous virus challenge, and can be administered safely to strenuously exercised horses.[192,193] The modified live vaccine is not recommended for pregnant mares.

Vaccination of young athletic horses is recommended more frequently (at 4- to 6-month intervals) than for horses that have received regular boosters for years. Vaccinating foals before 6 months of age may be ineffective in inducing an antibody response to influenza (killed vaccine) because of interference by maternally derived antibodies.[194,195] Some undesirable side effects of vaccination occur, including fever, depression, pain, swelling at the vaccine site, and muscular stiffness, but these usually resolve within 1 or 2 days.[182] Administering two intranasal vaccines simultaneously is not recommended.

Sequelae Secondary bacterial pneumonia and pleuropneumonia are potential complications that may follow viral respiratory diseases in horses that have not been rested adequately before being returned to training or that have undergone other potentially stressful events such as long trailer rides. Myocarditis, pericarditis, and cardiac

arrhythmias are other possible sequelae to influenza infections.

Equine Herpesvirus Types 1 and 4

Causes Currently, five equine herpesviruses are recognized as causing disease in horses. Three are classified as α-herpesviruses (EHV1, EHV3, and EHV4), and two are grouped with the γ-herpesviruses (EHV2 and EHV5). EHV4, formerly called EHV1 subtype 2, serologically cross-reacts with EHV1 but is genetically distinct from that virus.[196] EHV1 and EHV4 share many common clinical features. EHV1, in addition to causing respiratory disease, also causes abortions, myeloencephalitis, and neonatal deaths. EHV4 is associated predominantly with respiratory disease in young horses but *sporadically* causes abortion, neonatal deaths, and neurologic disease.[197-200]

Epidemiology EHV1 and EHV4 may persist within a herd because of recrudescence of latent infections during periods of stress or immunosuppression. Dexamethasone or cyclophosphamide administration is a reliable reactivation stimulus for viral shedding in experimental studies.[201] For some years the site of viral persistent was unknown. However, in a study of 40 abattoir horses, EHV1 and EHV4 were detectable by PCR methods in the bronchial lymph nodes of 88% of the horses examined. Of the trigeminal ganglia examined in nine of the horses, one was found to contain only EHV1, four had detectable EHV4 in the ganglia, and three had evidence of EHV1 and EHV4.[202] EHV2 also was isolated from all of the horses examined, leading some researchers to speculate that EHV2 activates the promoter gene of EHV1.[203] In addition to the clinical trials, experimental studies of EHV1 and EHV4 also have provided data supporting the fact that lymphoid and neural tissues are sites of viral latency.[201,203]

Realizing that virus can establish latency, one easily can understand why respiratory infections by EHV1 or EHV4 can develop in foals, weanings, and yearlings in closed herds. Immunity to EHV1 or EHV4 is short-lived (3 to 5 months) so that most horses are reinfected during their breeding or racing careers. Reexposure usually results in mild or inapparent infections, except in the case of broodmares in which reinfection may lead to abortion in the last trimester. Immunity following abortion is generally of longer duration, and in the field, repeat abortions rarely occur in the same mares. No clear relationship exists between gestational age or the level of virus-neutralizing antibody and the incidence of virus-induced abortion.[204] Perinatal disease characterized by weakness and respiratory distress is usually evident within 18 to 24 hours of birth, with foals dying within 24 to 72 hours.[205]

Pathogenesis Infection occurs via inhalation of the virus or contact with infected tissues. The virus is delicate and does not survive in the environment; thus close contact appears to be important for transmission.[205] Kydd, Smith, Hannant, et al.[206] have suggested that EHV1 enters the upper respiratory tract and, in the absence of mucosal antibody, immediately infects the epithelium lining of the nasopharynx and tonsils. Subsequent events depend on whether EHV1 becomes a productive or limited infection. Productive infection results in the intercellular spread of EHV1 through susceptible cells (including leukocytes) in the stroma until the vascular or lymphatic endothelium becomes infected. Thereafter infection spreads via leukocyte adhesion to infected endothelium, leading to the development of cell-associated viremia. As a result of viremia and of inhalation of viral particles, the virus disseminates to the lower respiratory tract. In a limited infection, infected cells are phagocytized and viral antigens are processed and presented to lymphocytes in mucosal lymphoid nodules or lymph nodes. The studies of Burrell[89] and Sutton, Viel, Carman, et al.[207] have demonstrated lower respiratory tract involvement in which hyperemia and mucous accumulations develop 2 to 12 weeks after the initial infection. EHV1 also has a tropism for lymphocytes and is reported to cause immunosuppression.

The pathogenesis of EHV4 has not been investigated completely and may be similar to that of EHV1.

Clinical Signs Clinical signs of rhinopneumonitis appear 1 to 3 days following infection and are indistinguishable from influenza. Horses are febrile and exhibit a cough and a serous nasal discharge, which may become mucopurulent with secondary bacterial infections. Horses develop rhinitis, pharyngitis, and tracheitis detectable endoscopically. A severe disseminated EHV1 infection that caused fever, depression, respiratory distress, and eventual death has been described in yearlings and 2-year-old horses.[208,209]

Clinical Pathology An epidemiologic survey by Mason, Watkins, McNie, et al.[210] during an outbreak of EHV1 infection on a racetrack in Hong Kong documents a monocytosis in infected horses (>500 cells/μl) during the first 5 days of clinically apparent infections. In experimental infections of EHV1, a decrease in neutrophils and monocytes occurs on day 3 after infection, but the absolute values of both cell types remain within normal limits.[207]

Diagnosis One may attempt viral isolation from citrated blood samples. Virus has been recovered from mononuclear cells for up to 2 weeks after infection or from nasopharyngeal swabs. PCR on clinical materials is rapid and enables distinction between EHV1 and EHV4.[211] Serologic diagnosis is made by demonstrating a fourfold increase in titers. Virus neutralization, immunoassay, complement fixation, and a radial immunodiffusion enzyme assay can detect antibodies against EHV1.[212] Postmortem examination of foals who died from EHV1 or EHV4 infection revealed interstitial pneumonia, pleural and

peritoneal effusions, hypoplasia of the thymus and spleen, focal necrosis of the liver, and viral inclusion bodies within the hepatic parenchyma. Similar pathologic findings are observed in aborted fetuses.

Treatment Treatment is supportive, minimizing stresses and ensuring adequate rest. Limited trials using antiviral drugs experimentally or clinically have been described. Acyclovir, is an acyclic nucleoside analog that inhibits viral DNA polymerases. Acyclovir is activated by virus-induced thymidine kinase before being converted to acyclovir triphosphate by cellular kinases. During outbreaks of EHV1 involving neurologic disease or neonatal deaths, acyclovir has been administered at doses ranging from 8 to 16 mg/kg orally 3 times daily to 20 mg/kg orally 3 times daily.[213,214] The efficacy of acyclovir in treating respiratory disease has not been demonstrated. One potential drawback of acyclovir use is the development of viral resistance in strains lacking thymidine kinase. Another antiviral drug, (s)-1-[(3-hydroxy-2-phosphonyl methoxy)-propyl]cytosine, or HPMPC, has been shown to be efficacious when given before EHV1 challenge in naïve foals but has not been used clinically in North America.[215]

Because evidence of immunosuppression during herpetic infections exists, the clinician should give horses broad-spectrum antimicrobials for 7 to 10 days and order rest for 4 to 6 weeks before the horse commences light exercise.

Prevention Currently available vaccines are produced from EHV1 and EHV4, and although the vaccine does not prevent infection, it reduces the severity of clinical signs.

Equine Herpesvirus 2

EHV2 is a slowly replicating virus, often referred to as equine cytomegalovirus. Opinions as to the role of EHV2 in producing equine respiratory diseases have been equivocal because the virus can be recovered from various sites from ill and apparently healthy horses.[87,216] Foals that are infected experimentally with EHV2 develop pharyngitis and lymphoid hyperplasia, thus implicating this as a causative agent of chronic lymphoid hyperplasia in young horses.[87] The virus also has been isolated from young horses in race training with pharyngeal lymphoid hyperplasia.[89] EHV2 has been isolated from 2- to 3-month-old foals during outbreaks of pneumonia in Hungary, Japan, Australia, New Zealand, and in the United States.[216-220] In some of these outbreaks, EHV2 was the sole infectious agent isolated from the respiratory tract, whereas in other outbreaks, bacterial agents—*Streptococcus zooepidemicus* and *Rhodococcus equi*—complicated the pneumonitis.[219] This has led some to speculate that if the foals are stressed or infected with a large dose of virus during a period in which maternal antibodies are waning, then the virus may invade the cells of the immune system and cause further immunosuppression. Blakeslee, Olsen, McAllister, et al.[87] reported a dose-related immunosuppression following in vitro infection of lymphocytes with EHV2, and this effect has been documented in vivo using a rabbit model.

EHV2 also has been isolated from ocular, nasal, and tracheobronchial swabs of horses with keratoconjunctivitis, implicating it in the production of this clinical sydrome.[221]

The suggestion has been made that most foals are exposed to EHV2 at 2 to 3 months of age and shed the virus for 2 to 6 months until a humoral antibody response develops and eventually is associated with low viral recovery.[216] Nearly 100% of older horses are seropositive for EHV2.[222]

After natural exposure, EHV2 is recoverable from nasal and nasopharyngeal swabs, from the kidney, bone marrow, spleen, mammary gland, salivary gland, vagina, tracheal mucus, neural tissue, and from the cornea and conjunctiva.[222,223] Leukocytes and lymph nodes draining the respiratory tract are major reservoirs of EHV2 DNA.[222]

Diagnosis of EHV2 depends on isolation of the virus, serologic evidence of an active viral infection, and the presence of clinical signs. Treatment is symptomatic. Efficacy of antiviral agents has not been examined in EHV2 infections.

Equine Viral Arteritis

Causes Equine arteritis virus, an enveloped single-stranded RNA virus, is a member of the order Nidovirales and family Arteriviridae. EAV is genetically similar to coronaviruses (also a member of Arteriviridae) but has a dissimilar viral structure and complement-fixing antigen.[224] Only one strain has been identified, the Bucyrus strain, but isolates vary in virulence.[225]

Epidemiology Before the 1984 epizootic of equine viral arteritis (EVA) in Kentucky, little attention was paid to this virus.[226] Most infections were assumed to be transmitted by inhalation until the important role of venereal transmission was demonstrated in those outbreaks. The virus is maintained in the equine population by long-term and short-term carriers in stallions. The duration of the carrier status ranges from several weeks to years. Testosterone is essential for maintenance of persistence. Long-term infections do not occur in colts exposed to the virus before the onset of peripubertal development or in mares.[226-228] During the carrier state, the virus is present solely in the reproductive tract, principally in the ampulla of the vas deferens. Primary exposure to the virus is presumed to be via the venereal route. Susceptible mares bred to carrier stallions almost always become infected with EAV. Viral shedding into the respiratory tract allows secondary horizontal transmission of the virus to occur.

A significant difference in seropositivity to EAV exists among the horse breeds. Approximately 84% of

Standardbreds and 93% of Austrian Warmblood stallions have circulating antibodies to EAV, whereas less than 5% of Thoroughbred and less than 1% of Quarter Horses are seropositive.[229]

Pathogenesis Following intranasal challenge (aerosolization), the virus invades the respiratory tract epithelium and the alveolar macrophages. By 72 hours after infection, replicating virus are detectable in the bronchopulmonary lymph nodes, endothelium, and circulating macrophages. Dissemination of the virus by hematogenous routes allows infection of mesenteric lymph nodes; spleen; liver; kidneys; nasopharyngeal, pleural, and peritoneal fluid; and urine.[226] By 6 to 8 days after infection, the virus has localized within the endothelium and medial myocytes of blood vessels, where it causes a necrotizing arteritis, a panvasculitis.[224] The vascular lesion may be caused by a direct cytopathic effect of the virus on the endothelium and medial myocytes or from the effects of anoxia or thrombosis induced by cell damage.

With venereal transmission (by natural cover or by artificial insemination), the virus can be isolated from swabs of the rectal and vaginal mucosa during the febrile periods.

Clinical Signs Clinical signs vary, ranging from severe disease to subclinical infections. The variation may be a function of host factors, such as age and immune status, and virus factors, including the virulence, the amount of infective virus, and the route of infection.[230] The incubation period ranges from 3 to 14 days (6 to 8 days if transmitted venereally). In the acute disease, horses are febrile (105° F) for 1 to 5 days, anorectic, and depressed and may cough. Other clinical signs include a serous nasal discharge, congestion of the nasal mucosa, intermandibular lymphadenopathy, conjunctivitis, lacrimation, and less frequently, corneal opacification. Edema of the sheath, scrotum, ventral midline, limbs, and eyelids occurs because of vasculitis. Other signs may include respiratory distress, stiffness, soreness, diarrhea, icterus, skin rash on the neck, and papular eruptions on the inside of the upper lip. Most adult horses recover uneventfully.

Abortions occur from the tenth to the thirty-fourth day following exposure (during the third to tenth months of gestation), but the mechanism is not known. Abortion can occur with or without preceding clinical evidence of infection.[231] EVA has not been associated with teratologic abnormalities in fetuses or foals.

Neonates may die suddenly or develop severe respiratory distress followed by death.[226,232]

Clinical Pathology Infection causes leukopenia, lymphopenia, and thrombocytopenia.

Diagnosis EVA is a reportable disease. Although virus may persist in the buffy coat for up to 36 days after infection, viral isolation can be difficult.[230] The clinician should submit citrated blood samples and should attempt isolation of virions from nasopharyngeal and conjunctival swabs, vaginal swabs, and semen from an infected stallion.[233] PCR enhances viral detection and specificity. One also should attempt serologic diagnosis. Virus neutralization, complement fixation, immunodiffusion, and immunofluorescence are techniques used to demonstrate changes in antibody titers. A fourfold or greater rise in titer or a change in status from seronegative to seropositive may indicate a recent infection. Postmortem examinations of aborted fetuses do not show signs of arteritis as seen in adults. Fetuses do have evidence of edema, excessive pleural fluid, and petechiation on the mucosal surfaces of the respiratory and gastrointestinal tracts, but focal necrosis of the liver or intranuclear inclusions are not features of the disease.[225]

Treatment Treatment is primarily symptomatic, keeping the horse hydrated and providing analgesics (nonsteroidal antiinflammatory drugs) as needed. Fever in stallions can lead to sperm damage and temporary infertility, so one should administer nonsteroidal antiinflammatory drugs. The clinician should isolate horses for 3 to 4 weeks to minimize the chances of transmission.

Prevention Vaccination of seronegative stallions with a commercially available modified live vaccine is credited with preventing the establishment of carrier states in the stallion or with further increases in the carrier state during the 1984 epizootic in Kentucky. Stallions were bred only to mares that were vaccinated or seropositive from previous natural exposure to EVA. Following vaccination, clinical immunity was found to develop rapidly and to last for 1 to 3 years.[226] Primary vaccination does not prevent reinfection and limited shedding of virus. Clinicians should vaccinate mares 3 to 4 weeks before breeding to an EAV carrier stallion and should isolate such mares for another 3 weeks after being bred to a carrier stallion for the first time.[231] Vaccination is not recommended for pregnant mares or in foals less than 6 weeks of age. Passively derived antibodies to EAV decrease to undetectable amounts by 8 months postpartum for foals born to seropositive mares. Vaccination should be effective at this time if necessary.[234]

Equine Rhinoviruses

Among those viruses that formerly were called equine rhinoviruses—classified as members of the family Picornaviridae and genus *Rhinovirus*—two serotypes were identified. Serotype 1 recently has been renamed equine rhinitis A virus (ERAV) and has been reclassified as a member of the genus *Aphthovirus*. The reclassification is based on (1) homology of the nucleotide sequence of the ERAV genome with that of foot-and-mouth disease virus, (2) the physicochemical properties of ERAV, and (3) the production of viremia and persistent shedding following ERAV infection.[235] Serotype 2 has been renamed

equine rhinitis B virus (ERBV) and has been reclassified as the sole member of the genus *Erbovirus*. A third serotype designated P313/75 also has been identified and currently is assigned to the family Picornaviridae. However, based on sequence similarity and serologic data, investigators have proposed that P313/75 be classified as a distinct serotype of *Erbovirus* and tentatively have named it ERBV2.[236]

Infection of horses with ERAV causes acute fever, nasal discharge, coughing, anorexia, pharyngitis, laryngitis, and submandibular lymphadenitis.[237,238] Infection produces moderate increases in the neutrophil-to-lymphocyte ratios (from 50:49 in healthy horses to 57:43 in infected horses) and in plasma fibrinogen.[238] The importance of ERAV as a cause of respiratory disease has not been recognized previously because clinical signs may be mild and because viral isolation is difficult.[239] The incubation period is 3 to 8 days, with shedding of viral particles from pharyngeal secretions, urine, and feces a feature of the infection. Young horses are infected more commonly and in one study, 73% of 2-year olds showed serologic evidence of ERAV infection.[238]

Equine rhinovirus A has a broad host range that includes rabbits, guinea pigs, monkeys, and human beings. Experimental and epidemiologic evidence of ERAV infection of human beings exists. High antibody titers were found in the sera of 3 of 12 stable workers, whereas no ERAV antibody was found in the sera of 159 non–stable workers.[240] One can attempt diagnosis of ERAV infection by serologic testing (fourfold changes between acute and convalescent titers) or PCR identification of the virus in nasopharyngeal swabs.[239]

Equine rhinovirus B is also an equine respiratory tract pathogen. In a survey of horses with acute respiratory disease, researchers isolated ERBV from 30% of the horses sampled. Of the 28 horses from which the virus was recovered, a serologic diagnosis was made in only 6 horses. Researchers attributed the low diagnosis rate to the difficulty of initially collecting samples during the acute phase: antibody levels rise rapidly from day 6 after infection to peak between days 14 and 18.[241] Thus in contrast to ERAV, viral isolation may be the more successful diagnostic method.

The clinical significance of ERBV2 (P313/75) is unknown. ERBV2 was isolated from a horse with a history of 6 days of intermittent fever that began 4 days after an umbilical hernia operation and castration.[242] The clinical importance requires further investigation.

No vaccine is currently available for ERAV or ERBV.

Tracheal Disorders

Definition Inflammations, obstructions, compressions, lacerations, and containment of foreign bodies are the predominant disorders of the trachea in the horse.[243-246] Tracheitis often accompanies viral upper respiratory tract diseases (see previous discussion) and manifests as areas of hyperemia and epithelial desquamation. Lacerations usually result from trauma, whereas compressions may result from extraluminal masses such as streptococcal abscesses or neoplasms such as lymphosarcomata or lipomata. Intraluminal obstructions may follow fibrotic stricture formation following trauma, tracheostomy, or pressure necrosis from inflated cuffs of endotracheal tubes or may be caused by granulomatous reactions within the trachea.[243] Foreign bodies, such as twigs, probably are inhaled during deglutition. Tracheal collapse may represent a congenital defect in miniature horses and ponies.[247,248]

Clinical Signs Clinical signs vary and range from stertorous breathing and dyspnea to chronic and persistent coughing and bilateral nasal discharge with a foul odor. Mild manipulation of the trachea also may induce paroxysmal bouts of coughing.

Diagnosis The diagnosis is made on physical examination or endoscopic evaluation of the trachea. A history of a tracheal surgery or traumatic episode should alert the diagnostician to the possibility of an intraluminal obstruction or stricture. The clinician may visualize foreign bodies on examination but may need radiographs to delineate the extent of their involvement. One also should perform radiographic examination of the thorax to determine if a concomitant pneumonia, pneumomediastinum, or pneumothorax exists.

Treatment One directs treatment at the primary cause. One does not treat primary inflammations following viral infections unless a persistent fever and a secondary bacterial tracheitis and pneumonia develop. The clinician may extract foreign bodies but may require tracheotomy to retrieve them if the endoscope is not long enough. In the adult horse a 2-m endoscope is necessary to reach the level of the carina located at the fifth to sixth intercostal space. Extraluminal masses require careful drainage or excision, with the potential for spread of infection into the mediastinum. The clinician should isolate horses with *Streptococcus equi* infections from other equids. Rupture of the trachea may require temporary tracheotomy distal to the rupture to ensure patency of airflow. A 2-week course of broad-spectrum antimicrobial therapy may be indicated, especially if the mucociliary clearance mechanism is compromised. Complications such as subcutaneous emphysema, cellulitis, and pneumomediastinum usually resolve over 2 weeks. Horses with tracheal defects have a poor to guarded prognosis for return to athletic potential.

The Normal Lung

ANATOMY

The lungs of the horse differ from those of other domestic species in that they lack deep interlobar fissures and

distinct lung lobes. Superficially, however, the left lung consists of a cranial and caudal lobe, whereas the right lung contains a cranial, an intermediate, and a caudal lobe.[249] The intrathoracic trachea bifurcates into the right and left main stem bronchi at the level of the fifth or sixth intercostal space and enters the hilum of each lung. At its division from the trachea, the right bronchus assumes a straighter, more horizontal position relative to the left bronchus, a configuration that may predispose the horse to develop right-sided pulmonary disorders. Each bronchus divides into lobar, segmental, and subsegmental bronchi with the eventual formation of bronchioles. In the distal part of the bronchial tree the terminal bronchioles lead into poorly developed respiratory bronchioles or open directly into alveolar ducts.[249,250] The tracheobronchial lining consists of tall columnar, pseudostratified epithelium interspersed with serous and goblet cells. The goblet cells and the underlying submucosal mucous glands function to produce mucus consisting of an outer gel and an inner sol layer.[251] Mucus serves to prevent epithelial dehydration, contains protective factors that guard against infectious agents, and is an integral part of the mucociliary apparatus. The rapid beating of the cilia moves mucus and any particulate matter to the pharynx to be swallowed. Approximately 90% of material deposited on the mucinous layer is cleared within 1 hour.

Ciliated cells decrease in frequency with successive divisions of the airways so that at the level of the bronchioles the epithelium is composed predominantly of low ciliated and taller nonciliated Clara cells.[252] Glands are also absent at this level. The bronchiolar epithelium becomes contiguous with that of the alveoli, which are characterized by two distinct cell types. Type I pneumocytes cover most of the alveolar surface with thin cytoplasmic extensions 0.2 to 0.5 μm thick.[251] Type II cells are cuboidal and contain the characteristic lamellar cytoplasmic inclusions thought to constitute surfactant components. Type II cells also are considered to be stem cells, replacing the type I cells when damaged.

Lymphocytes are scattered throughout the pulmonary epithelium, are associated with the bronchioles and bronchi, and occur in discrete nodules or patches.[253] These cells, along with alveolar macrophages, provide an integral component of the pulmonary immune surveillance system. Macrophages are derived from blood monocytes via the interstitium and are cleared continuously from the alveoli. They are the predominant cell type recovered from the bronchoalveolar lavage in normal horses (see Table 7-1). Pulmonary interstitial macrophages are able rapidly to ingest particles introduced within the pulmonary circulation.[254] The ability of these macrophages to localize antigenic particles within the pulmonary vasculature may predispose the equine lung to development of acute pulmonary inflammation (e.g., during endotoxemia).

Additional cells within the lung parenchyma include the subepithelial and free mast cell. These cells bear IgE on their cell surface and release biogenic amines in response to specific antigen stimulation. They appear to be important in the pathogenesis of several equine pulmonary disorders, including anaphlaxis and lungworm infections.

Tracheobronchial secretions consist of substances secreted from mucous and serous glands, as well as serum transudates. The principal component of the secretions is water, with approximately equal amounts of protein, carbohydrate, lipid, and inorganic material. Contained within the protein fraction of the tracheobronchial secretions are albumin, IgA, IgG (the predominant immunoglobulin in the lower lung), lysozyme, lactoferrin, haptoglobulin, transferrin, and complement components.[251]

VASCULAR SUPPLY

The lung has two sources of blood flow. The major source of blood is the pulmonary circulation, a low-pressure, low-resistance system that serves primarily to deliver blood to the alveoli for participation in gas exchange but also provides nutrients to the alveolar constituents. The distribution of the pulmonary arterial flow to the various lung regions depends largely on mechanical forces: gravity and pulmonary arterial, pulmonary venous, and alveolar pressures.[255] In the standing horse, a vertical perfusion gradient of the lung has been demonstrated,[256] the most dorsal part of the equine lung being less well perfused than the ventral dependent regions. The distribution of pulmonary blood flow also is influenced by vasoactive compounds such as catecholamines, histamine, and eicosanoids and by changes in alveolar oxygen and carbon dioxide. Alterations in pulmonary vascular resistance may help to match ventilation with perfusion and optimize gas exchange.

The bronchial circulation, the second source of blood flow to the lungs, provides nutrient support to the lymphatics and vascular and airway components. Bronchial circulation provides arterial blood to the pleural surface and anastomotic connections with the alveolar capillary bed derived from the pulmonary circulation.[250] The magnitude of the anastomotic flow depends on the relative pressure in the bronchial and pulmonary microvasculature and on the alveolar pressure. Thus in the dorsal part of the lung, where pulmonary arterial flow is poor, blood flow from the bronchial circulation may be favored.[257] The degree of anastomotic bronchial blood flow through the alveolar capillaries also increases with systemic arterial hypoxemia and alveolar hypoxia.[255] The bronchial circulation undergoes hypertrophy (angiogenesis) in response to inflammatory pulmonary diseases such as chronic bronchitis, bronchiolitis, and bronchiectasis.

INNERVATION

The autonomic nervous system supplies innervation to the pulmonary structures. This nervous system influences (1) airway smooth muscle tone, (2) secretion of mucus from the submucosal glands, (3) transport of fluid across airway epithelium, (4) permeability and blood flow in the bronchial circulation, and (5) release of mediators from mast cells and other inflammatory cells.[258] In the horse the autonomic nervous system can be classified functionally into three categories: (1) parasympathetic, (2) sympathetic, and (3) nonadrenergic noncholinergic (NANC) pathways.[259] The vagus nerve is an integral component of the parasympathetic and NANC systems. The vagus nerve not only contains the efferent fibers of these pathways, which help to alter airway resistance, lung volume, and compliance, but also contains the afferent fibers the central input of which regulates the pattern of breathing. Stimulation of the parasympathetic fibers within the vagus nerve (i.e., the efferent limb) releases acetylcholine from the postganglionic fibers and combines with the muscarinic receptors of the airway smooth muscle to cause bronchoconstriction. Yet because atropinization (antagonism of muscarinic receptors) does not normally change airway resistance, the parasympathetic system appears to exert little influence on resting airway tone in the *healthy* horse.[260] However, vagal efferents are important in reflex bronchoconstriction during pulmonary disease.

As described previously, the vagus nerve also contains afferent nerve fibers that transmit information detected by three types of pulmonary mechanoreceptors: (1) the slowly adapting receptors, (2) the rapidly adapting receptors, and (3) the nonmyelinated C fibers. The receptors relay information to the central respiratory neurons located within the ventral medulla and pons. Changes in breathing depth and frequency occur in response to mechanical deformations or chemical stimulation of these receptors. Thus these receptors mediate the tachypneic breathing pattern that occurs in response to inhalation of irritant substances. Stimulation of these receptors also influences airway smooth muscle tone,[261] inducing reflex bronchoconstriction in response to inhaled irritants.

In the lung, α- and β-adrenergic receptors mediate sympathomimetic effects. Postsynaptic fibers course from the sympathetic ganglion to airway smooth muscle where released norepinephrine interacts with α- and β-receptors. Postganglionic sympathetic fibers also innervate parasympathetic ganglia. The released norepinephrine inhibits cholinergic neurotransmission.[259] However, numerous β_2-adrenergic receptors are distributed throughout the pulmonary parenchyma that lack innervation by the sympathetic fibers. Circulating catecholamines are probably important in activating these receptors and in causing subsequent bronchodilation. It is of interest that β_2-adrenergic stimulation does not alter airway diameter in the healthy horse[262] but does increase airway caliber in horses with recurrent airway disease. β-agonists also promote ion transport and water secretion across human airway epithelium (in vitro) and may cause similar effects in vivo in the horse. This effect would benefit mucociliary clearance by increasing the sol component of the mucus. In addition, β-agonists stimulate surfactant secretion by type II pneumocytes, inhibit antigen-induced mast cell degranulation, and modulate cholinergic neural transmission.[258] Such effects remain to be demonstrated in the horse, however.

α-Adrenergic receptors also exist in the equine lung, but their stimulation induces bronchoconstriction only in heavy and not in normal ponies.[263] This finding suggests that, in health, these receptors are probably unimportant in the regulation of bronchomotor tone.

An additional autonomic pathway, the NANC inhibitory system, also has been demonstrated in the equine lung, and its fibers course within the vagus nerve.[259] Although the mediators involved in neural transmission have not been identified definitively, some speculate that vasoactive intestinal peptide or peptide histidine isoleucine or both may be the neurotransmitters.[264] Stimulation of this pathway causes a 50% reduction in smooth muscle tone and thus exerts a vasodilating effect.[265] Interestingly, horses with recurrent airway disease appear to lack NANC innervation in the bronchioles, and this dysfunction may contribute to the airway hyperactivity observed.[259]

LYMPH DRAINAGE

Lymph drainage from the lung is accomplished by (1) the deep lymphatics, which begin at the level of the alveolar ducts and run with the conducting airway and arteries toward the hilar lymph nodes, and (2) the superficial lymphatics, which drain the visceral pleura through a plexus converging on the hilum.[251]

PULMONARY PHYSIOLOGY

The major function of the lung is gas exchange: diffusion of oxygen and elimination of carbon dioxide. During eupnea, an adult horse breathes at a frequency of about 12 breaths per minute and a tidal volume near 6.5 L. This represents a total minute ventilation of 77 L/min, or more than 100,000 L/day. During this same period, the resting horse consumes approximately 2.1 L/min of oxygen (3000 L/day) and produces approximately 1.7 L/min of carbon dioxide (2400 L/day).[266] Thus the lung provides an important means by which normal arterial oxygen and carbon dioxide tensions and arterial pH are maintained. In the absence of lung disease, pulmonary arterial oxygenation (Pa_{O_2}) depends on the inspired fraction of oxygen (normally 0.21) and the

effective level of alveolar ventilation. This is approximated by a version of the alveolar gas equation:

$$PA_{O_2} = PI_{O_2} (PA_{CO_2})/R$$

where PA_{O_2} is the alveolar oxygen tension, PI_{O_2} is the inspired oxygen tension, PA_{CO_2} is the alveolar carbon dioxide tension, and R is the respiratory exchange quotient (the ratio of CO_2 production to O_2 consumption). Because an admixture of venous blood with the pulmonary arterial circulation occurs, alveolar oxygen tension exceeds arterial oxygen tension by approximately 10 mm Hg.

In the absence of alterations in inspired oxygen tensions, arterial hypoxemia (Pa_{O_2} <85 mm Hg) may result from basically four processes, including (1) hypoventilation, (2) diffusion impairment, (3) V/Q ($\dot{V}/\dot{Q}$) inequality, and (4) shunts.[267]

Alveolar and thus arterial CO_2 levels depend on the rate of CO_2 elimination relative to its production, given by the following equation:

$$PA_{CO_2} \approx \dot{V}CO_2/\dot{V}A$$

where $\dot{V}CO_2$ is the rate of CO_2 production and $\dot{V}A$ is alveolar ventilation. *Hypoventilation* is defined as inadequate CO_2 elimination relative to production, resulting in an elevated Pa_{CO_2} (hypercapnia, hypercarbia). Hypoventilation can result from a variety of abnormalities. A convenient diagnostic approach follows the control of breathing from (1) the respiratory center in the medulla, (2) the efferent nerves (phrenic), (3) the bellows (diaphragm and chest wall muscles), (4) the pleural space, and (5) the airways. Some situations in which hypoventilation may develop include (1) drug administration (barbiturates, diazepam, xylazine); (2) diseases of the brainstem following infection (encephalitis), trauma, hemorrhage, or neoplasia; (3) diseases of the respiratory muscles, including botulism, trauma, or fatigue; (4) pleuritis and space-occupying lesions; and (5) choke and upper airway obstruction.

In patients suffering from hypoventilation, arterial oxygenation improves with oxygen administration (by increasing PI_{O_2}), but the most efficacious mode of correcting the hypercapnia and consequent hypoxemia is by mechanical ventilation. Diffusion impairment occurs when time is inadequate for equilibration of alveolar oxygen tensions with pulmonary capillary oxygen tensions. Under normal resting conditions, equilibration of oxygen tensions occurs within 0.25 second, approximately one third of the contact time of the blood in the pulmonary circulation.[267] Some evidence suggests that in the exercising horse, the arterial hypoxemia that normally develops at high exercise intensities in part is caused by the decrease in time available for oxygen diffusion.[268,269] During rest, diffusion impairment is unlikely to occur. Arterial hypoxemia caused by diffusion impairment can be corrected by administration of supplemental oxygen.

$\dot{V}/\dot{Q}$ inequalities are the primary cause of arterial hypoxemia and occur when alveolar ventilation and pulmonary blood flow are mismatched despite the existence of several reflexes that normally tend to prevent this problem. For example, a fall in the $\dot{V}/\dot{Q}$ ratio causes alveolar hypoxia, which induces pulmonary vasoconstriction and decreases perfusion to that lung region. (But this reflex also increases pulmonary vascular resistance and thus the work of the right side of the heart.) A second reflex is hypocapnic bronchoconstriction. When the $\dot{V}/\dot{Q}$ ratio increases, regional ventilation of those lung units is reduced by smooth muscle constriction. $\dot{V}/\dot{Q}$ inequalities interfere with O_2 and CO_2 transfer so that hypoxemia and hypercapnia may ensue. Usually the consequent hypercapnia increases chemoreceptor drive and thus increases alveolar ventilation, which restores normocapnia. However, because of the shape of the oxyhemoglobin dissociation curve, the increase in oxygen tension in the normal alveoli caused by the hyperventilation does not increase the oxygen content of the blood coming significantly from these units. Several factors can exacerbate the hypoxemia of $\dot{V}/\dot{Q}$ inequalities, including hypoventilation (sedation) and decrements in cardiac output (mechanical ventilation with positive end-expiratory pressure). $\dot{V}/\dot{Q}$ inequalities respond to oxygen therapy, although this may lead to increases in arterial carbon dioxide tension by (1) a reduction of the chemoreceptor (hypoxic) drive, (2) an increase in $\dot{V}/\dot{Q}$ inequalities, and (3) a shift in the carboxyhemoglobin dissociation curve to the right, decreasing its affinity for carbon dioxide.[270] Mechanical ventilation may be indicated in severe $\dot{V}/\dot{Q}$ inequalities if hypercapnia is progressive.

Passage of blood through abnormal cardiovascular communications (atrial septal defects, ventricular septal defects, patent ductus arteriosus) or through pulmonary capillaries within the walls of atelectatic or fluid-filled alveoli causes shunts and consequent hypoxemia. Such defects may be considered as one extreme of $\dot{V}/\dot{Q}$ inequality ($\dot{V}/\dot{Q} = 0$) and are resistant to correction by oxygen therapy.[270] In shunts caused by pulmonary disease, mechanical ventilation and positive end-expiratory pressure increase end-expiratory lung volume and thus the alveolar surface area available for gas exchange. The incremental increase in end-expiratory lung volume also may help to redistribute the excessive extravascular lung water from the alveoli to the interstitium.

METABOLIC FUNCTIONS

The entire cardiac output passes through the pulmonary circulation, thus providing an ideal means by which

hormones and drugs may be metabolized to inactive compounds. Indeed, relative to the hepatic blood flow (approximately 25% of the cardiac output), the contribution of the lungs to the total body clearance of drugs or xenobiotics may be significant. The lung contains hydrolytic enzymes that cleave peptides such as bradykinin and angiotensin I, thus serving to inactivate (bradykinin) or to bioactivate (angiotensin) compounds. The enzymatic activity responsible is concentrated within the caveolae of the pulmonary capillary endothelium or in pouchings in the plasma membranes of these cells.[271] Other pulmonary enzymes exist that are capable of cleaving phosphate groups from nucleotides (adenosine triphosphate, adenosine diphosphate, and adenosine monophosphate), of oxidizing steroid hormones (testosterone), of inactivating prostaglandins E and F, and of metabolizing biogenic amines such as 5-hydroxytryptamine, norepinephrine, and tyramine.[255,271,272]

DEFENSE AGAINST INFECTION

The sterile environment of the lung results from several mechanisms, including the mucociliary apparatus, which clears particulate debris from the lung at a rate of approximately 17 mm/min,[273] and vagally mediated reflexes, which serve to initiate coughing and concomitant bronchoconstriction. However, the predominant line of defense against noxious agents and bacteria is the alveolar macrophages of the distal airways and alveoli. Recent investigations have shown depression in alveolar macrophage function following exercise or long van rides.[274,275] Viral infections also depress macrophage function. Helping to maintain immunosurveillance and the sterile pulmonary environment are polymorphonuclear cells that respond to chemotactic stimuli and lymphocytes.

Disorders of the Lower Respiratory Tract

Disorders of the lower respiratory tract are common in horses of all ages. Presenting complaints vary with these disorders and may include exercise intolerance, cough, nasal discharge, fever, dyspnea, increased respiratory rate or effort, or generalized depression and inappetance. Careful clinical examination including auscultation while rebreathing often confirms the anatomic site of the problem. Ancillary diagnostic testing such as bronchoalveolar lavage, transtracheal wash, thoracic ultrasound, or thoracic radiography often are indicated to confirm a suspected diagnosis.

BACTERIAL PNEUMONIA

Causes

Normally the lungs contain only small numbers of bacteria (colony-forming units) that are considered to be transient contaminants in the process of being removed by clearance mechanisms.[276] When pulmonary defense mechanisms are overwhelmed, aspirated bacteria from the oropharynx may proliferate and cause pneumonia. The most common gram-positive bacteria involved are *Streptococcus zooepidemicus* (β-hemolytic), *Staphylococcus aureus,* and *Streptococcus pneumoniae* (α-hemolytic). The most frequent gram-negative isolates are *Pasteurella* and *Actinobacillus* spp., *Escherichia coli, Klebsiella pneumoniae,* and *Bordetella bronchiseptica*.[26,27,277-280] *Pseudomonas* is rarely a cause of equine pneumonia, and its isolation from tracheobronchial aspirates suggests environmental contamination of equipment (endoscope). *Nocardia* organisms also have been isolated from horses with pulmonary infections, but these are rare and appear to require significant derangements of the defense mechanisms.[281] The anaerobic bacteria most commonly isolated are *Bacteroides fragilis, Peptostreptococcus anaerobius,* and *Fusobacterium* spp. Polymicrobic infections are not uncommon in cases of equine pneumonia and may represent a synergy between aerobic/facultatively anaerobic and anaerobic bacteria. Mechanisms of synergy may involve protection from phagocytosis and intracellular killing, production of essential growth factors, and lowering of local oxygen concentrations.[278]

Pathogenesis

Bacterial pneumonia develops following viral infections, athletic events (races), trailor rides, and general anesthesia and also occurs in horses that are overcrowded, maintained on poor nutrition, or are exposed to inclement weather. Laryngeal and pharyngeal dysfunction also may predipose the horse to develop pneumonia by aspiration of oropharyngeal bacteria. Such predisposition occurs in horses (1) with primary neuropathies of the ninth and tenth cranial nerves (equine protozoal myeloencephalitis, botulism, *Streptococcus equi* infections, guttural pouch mycoses), (2) with primary myopathies of the pharyngeal, laryngeal, or esophageal musculature (vitamin E and selenium deficiency, megaesophagus), (3) following laryngeal surgery, or (4) with esophageal obstructions.

The pathogenic mechanisms described subsequently apply to the development of lung abscesses and pleuropneumonia.

Viral-induced modifications of respiratory tract defenses include (1) enhanced susceptibility to bacterial attachment and colonization following damage to the epithelial cells, (2) diminished mucociliary clearance and physical translocation of bacterial particles deposited on the bronchial ciliated epithelium, and (3) decreased surfactant levels and collapse of the airways because of viral destruction of alveolar type II cells.[282] The ensuing anaerobic environment predisposes to macrophage dysfunction. In addition, the alveolar exudate that

accompanies viral pneumonitis may provide a nutrient medium for multiplication of aspirated bacteria.

Exercise, with aspiration of track debris and oropharyngeal secretions and with the development of exercise-induced pulmonary hemorrhage has been suggested as creating an ideal environment for bacterial growth and pneumonia.[283] An exercise-associated increase in bacterial contaminants of the lower respiratory tract has been demonstrated experimentally. Strenuously exercised horses exhibit a ten- and a 100-fold increase, respectively, in the number of aerobic and anaerobic bacteria isolated from transtracheal aspirates relative to preexercise samples.[284] The bacterial contamination, along with exercise-associated increases in bronchoalveolar cortisol concentrations, decreased pulmonary alveolar macrophage viability, and impaired phagocytic function, enable bacteria to proliferate and cause pneumonia.[274,275,283,285,286]

Transportation remains one of the most common causes of pneumonia and pleuropneumonia in the horse because physically restraining the head of the horse and preventing postural drainage enhances bacterial colonization of the lower respiratory tract.[283,287] Inflammation and increased numbers of bacteria are found in the transtracheal aspirates of horses within 6 to 12 hours of confinement with the head elevated.[288] Another hypothesis is that dehydration, associated with reduced fluid consumption before or during transportation, reduces mucociliary clearance and contributes to bacterial proliferation. Neither the prophylactic administration of antibiotics nor the intermittent release from the confined head posture reliably reduces tracheal bacterial numbers or prevents the accumulation of purulent tracheobronchial secretions in horses confined with their heads elevated.[288,289]

Horses undergoing general anesthesia may develop pneumonia when endotracheal intubation introduces oropharyngeal contaminants to the lower respiratory tract. Anesthesia may compromise mucociliary clearance, and compression atelectasis and vascular congestion may cause regional ischemia and necrosis of lung regions, providing local conditions suitable for bacterial multiplication.[283]

Clinical Signs

In early cases, clinical signs may not be obvious, being limited to a gurgling sound of exudates in the trachea, fever, or depression. As the pneumonia progresses, horses may exhibit intermittent fever, tachypnea or respiratory distress, nasal discharge, coughing, inappetence, exercise intolerance, and weight loss. Nasal discharge is usually mucopurulent but may be hemorrhagic in some cases.[278] Auscultation of the thorax reveals increased harsh breath sounds dorsally, crackles, and wheezes and dullness of respiratory sounds ventrally. Manipulation of the trachea or larynx may induce a cough. Halitosis and a foul-smelling nasal discharge suggest an anaerobic infection. Submandibular lymphadenopathy may be apparent in aspiration pneumonia associated with strangles or with viral infections.

Diagnosis

Clinical signs and history aid in diagnosis. Clinical pathologic data supportive of a bacterial pneumonia include a leukocytosis and an absolute neutrophilia, with or without a left shift. Neutropenia also may be evident if gram-negative organisms are involved. A hyperfibrinogenemia (>500 mg/dl), hyperglobulinemia, hypoalbuminemia, and anemia of chronic inflammation are compatible with the diagnosis of chronic bacterial pneumonia. Endoscopic evaluation of the upper respiratory tract may demonstrate a defect in the laryngeal pharyngeal function if this is the inciting cause. One may observe a mucopurulent exudate with or without traces of blood by endoscopy in the lower respiratory tract. Thoracic radiographs demonstrate a radiopacity in the anteroventral thorax and a loss of clarity in the lung fields caudal to the heart. Air bronchograms occasionally are found in the adult horse with bacterial pneumonia (Figure 7-13). Ultrasound may demonstrate consolidation of ventral lung lobes and extension of the pneumonia to the pleural surfaces. Tracheobronchial aspirates yield degenerative neutrophils, damaged epithelial cells, and microorganisms. The presence of squamous epithelial cells supports a diagnosis of

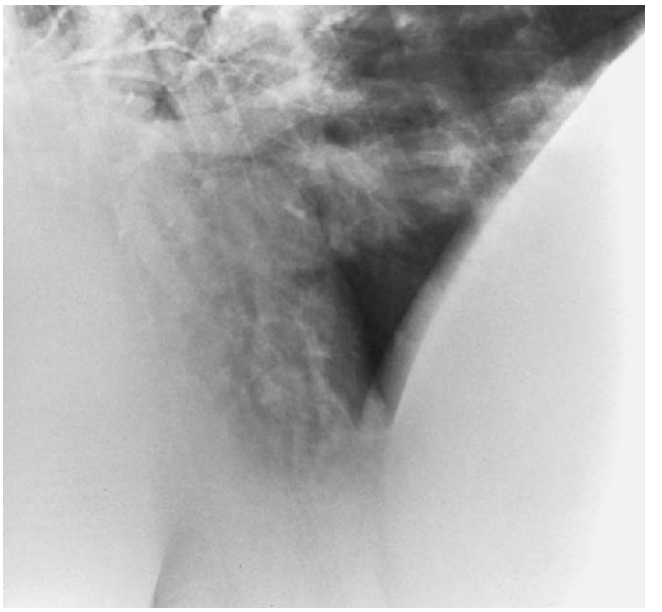


Figure 7-13 Two-year-old Thoroughbred with pneumonia. A patchy area of pulmonary consolidation is notable in the ventral dependent portion of the lung silhouetting the heart and diaphragm.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

aspiration pneumonia, provided that the tracheal catheter was not misplaced in the pharynx during sampling. The clinician should perform aerobic and anaerobic cultures on the tracheal aspirates.

Treatment

The clinician should direct treatment at the causative organism, but in the absence of culture sensitivity results, one should administer broad-spectrum antimicrobials. Appropriate therapy might include intravenous aqueous sodium or potassium penicillin and an aminoglycoside or third-generation cephalosporin (Table 7-2). The aminoglycosides are efficacious against most gram-negative aerobes, but lack efficacy against anaerobes. However, metronidazole is effective against most anaerobes, including the penicillin-resistant *Bacteroides fragilis* and routinely is included in the treatment protocol. Depending on the culture sensitivity results, one also may administer potentiated sulfonamides. The clinician should use aminoglycosides judiciously in animals that have renal compromise or are dehydrated. (See the section on treatment for parapneumonic effusions.)

With gram-negative infections and the potential for endotoxemia, small doses of flunixin meglumine (0.25 mg/kg 3 times daily) may be given to inhibit arachidonic acid metabolism. Other treatment modalities that have been advocated include nebulization of mucolytics, the use of bronchodilators and expectorants, and prophylactic measures against laminitis. The goal of supportive care should be to minimize stress and ensure adequate ventilation and hydration. Ideally, horses should be bedded on paper or on other materials free of dusts or molds and should be fed forages of excellent quality. One should also direct attention to correcting the primary cause of the pneumonia. Depending on the chronicity of the pneumonia, one should note clinical improvement in 48 to 72 hours. The prognosis can be excellent if the pneumonia is treated aggressively, but the clinician should forewarn the owner of potential complications (see the following discussion). The clinician should administer treatment for 2 to 6 weeks depending on the extent of the pneumonia and the underlying inciting cause. (See the section on treatment for parapneumonic effusions.)

Preventive measures that help deter the development of pneumonia include (1) adequate immunization protocols with vaccination against equine influenza virus, EHV1, and EHV2, every 4 to 6 months (in the performance horse); (2) the minimization of stresses such as long van rides in which the head is restrained constantly; and (3) the use of management or husbandry methods that minimize dust or noxious gas accumulations within the stall, prevent exposure to inclement weather, and provide adequate nutrition for the horse.

TABLE 7-2

Antimicrobials Commonly Used to Treat Respiratory Conditions

ANTIMICROBIAL	DOSAGE*
Amikacin	16-18 mg/kg, IV, s.i.d.
Ampicillin sodium	11-22 mg/kg, IV or IM, t.i.d. or q.i.d.
Ceftiofur	2.2 mg/kg, IV or IM, b.i.d.
Chloramphenicol	50 mg/kg, PO, q.i.d.
Enrofloxacin	7.5 mg/kg, PO or IV, s.i.d.
Gentamicin	6.6 mg/kg, IV or IM, s.i.d.
Metronidazole	15-25 mg/kg, PO, t.i.d. or q.i.d.
Oxytetracycline	5.0 mg/kg, IV, b.i.d.
Potassium Penicillin G	22,000 IU/kg, IV, q.i.d.
Procaine Penicillin G	22,000 IU/kg, IM, b.i.d.
Rifampin	5-10 mg/kg, PO, b.i.d.
Sodium Penicillin G	22,000 IU/kg, IV, q.i.d.
Trimethoprim-sulfonamide	15-20 mg/kg, PO or IV, b.i.d.

**b.i.d.,* Twice daily; *IM,* intramuscularly; *IV,* intravenously; *PO,* orally; *q.i.d.,* 4 times daily; *s.i.d.,* once daily; *t.i.d.,* 3 times daily.

LUNG ABSCESSES

Causes

In foals less than 6 months of age, *Rhodococcus equi* and *Streptococcus zooepidemicus* are the most common bacterial isolates recovered.[290] In adult horses, *Streptococcus* and *Actinobacillus* species are the most gram-positive and gram-negative organisms implicated in the development of pulmonary abscesses.[290-292] This discussion predominantly addresses lung abscesses in the adult horse.

Pathophysiology

Lung abscesses may develop as a consequence of inhaling bacterial organisms resident to the oropharynx or contaminating the environment *(Rhodococcus equi)*. The abscess may develop as a consequence of a focal pneumonia or may be a component of pleuropneumonia complex. Racehorses may be at an increased risk for developing lung abscesses when bacteria proliferate in the blood in the airways and alveoli following episodes of EIPH. The regional location of lung abscesses in these cases supports this hypothesis.[292]

Clinical Signs

Clinical signs may vary, but most horses have periods of pyrexia, inappetance, lethargy, mild tachycardia, and respiratory-related signs ranging from tachypnea to distress.[291,292] Other signs that may be evident include cough, purulent nasal discharge, thoracic pain, epistaxis, and halitosis.

Diagnosis

The adult horse may have a history of transport, strenuous exercise, surgery, prior pneumonia, or administration of

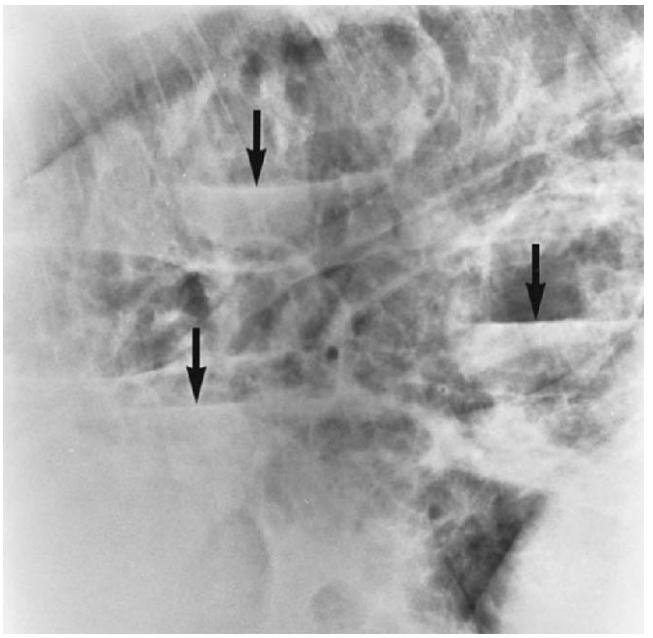


Figure 7-14 Nine-year-old saddle horse. Multiple cavitating pulmonary abscesses are present within the lungs. Arrows indicate air-fluid interfaces within the abscesses.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

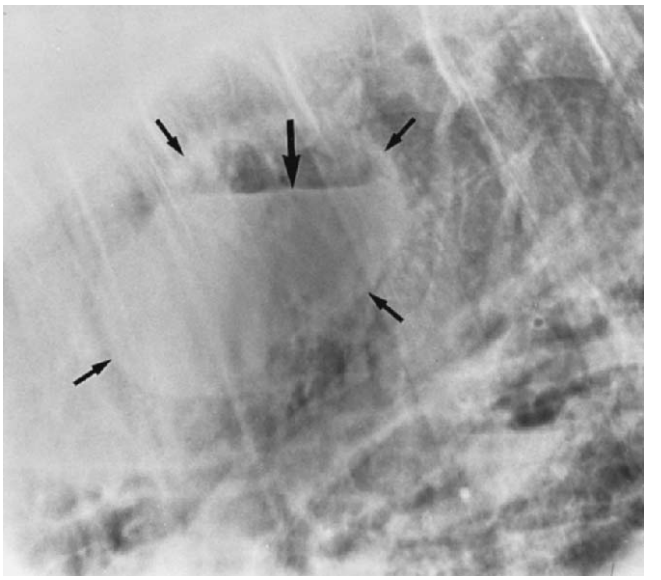


Figure 7-15 A large air-capped pulmonary abscess. Small arrows indicate an abscess; large arrow indicates the air-fluid interface.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

medications. In most cases, evidence of an infection is found on the CBC and serum chemistry panel: a mature neutrophila, hyperfibrinogenemia, hyperglobulinemia, and anemia. Radiography and ultrasound are useful imaging modalities, and one may use them concurrently to detect lung abscesses (Figures 7-14 and 7-15). Pulmonary abscesses appear on ultrasonography as encapsulated cavitated areas filled with fluid or echogenic (white) material. Cardiac structures or air-filled lung may overlie an abscess, obscuring its detection. In one study, two thirds of the abscesses were located in the caudodorsal lung field, whereas the remaining abscesses were located in the caudoventral region.[292]

Transtracheal aspirates or percutaneous aspirates of lung abscesses adhered to the body wall may help the clinician decide the choice of antimicrobials. One should culture isolates under aerobic and anaerobic conditions.

Treatment

Long-term antimicrobial therapy (8 to 10 weeks) along with prolonged periods of rest (5 to 6 months) before resuming strenuous exercise is recommended. (See the section on treatment for parapneumonic effusions for specific antimicrobial recommendations.) In human beings receiving antimicrobial treatment for pulmonary absceses, an 80% reduction in the size of abscess cavities less than 3 cm in diameter usually occurs within 1 month of appropriate therapy.[293] Furthermore, 70% of cavitary lesions in human cases of lung abscessation resolve completely by 3 months.[294] For lung abscesses unresponsive to therapy, the clinician should consider drainage via a thoracotomy or thoracoscopy.[295]

Prognosis for resumption of athleticism is good if treatment is initiated early. In one study, 23 of 25 Standardbreds and 13 of 20 Thoroughbreds raced after the diagnosis and treatment of a lung abscess with no significant effect on race performance.[292]

PARAPNEUMONIC EFFUSIONS AND SEPTIC PLEURITIS

Causes

Between two thirds and three quarters of cases of septic pleuritis arise as an extension of pneumonia or pulmonary abscessation.[296-298] Septic pleuritis also may occur in cases of thoracic trauma, esophageal rupture, or penetration of the esophagus or stomach by a foreign body.[283,299-301] The aerobic or facultatively anaerobic organisms most often isolated from horses with pleuropneumonia are bacterial species that normally reside in the oropharyngeal cavities: *Streptococcus* spp., *Pasteurella* and *Actinobacillus* spp., *Escherichia coli*, and *Enterobacter* spp. Anaerobic organisms frequently isolated include *Bacteroides* spp., *Peptostreptococcus* spp., *Fusobacterium* spp., and *Clostridium* spp.[301-303]

Epidemiology

Risk factors for the development of pleuropneumonia are the same as those associated with pneumonia (see the previous discussion) and include long-distance transport,

strenuous exercise, viral respiratory tract disease, surgery, dysphagia, general anesthesia, and systemic illness (enteritis). These conditions may enhance aspiration of oropharyngeal organisms or may impair clearance of such organisms.[283,297,304]

Pathogenesis

The causative factors of equine pleuropneumonia are those that suppress the pulmonary defense mechanisms and allow bacterial contamination of the lower respiratory tract to progress to pneumonia or abscess formation. The subsequent extension of the infectious process into the pleural space causes pleuritis. The distribution of the pulmonary lesions—cranioventral with the right cranial and middle lung lobes more severely afflicted—is consistent with inhalation or aspiration of bacteria rather than infection from a hematogenous spread. Fluid accumulates within the pleural cavity as the parenchymal inflammation increases the permeability of the capillaries in the overlying visceral pleura, causing an outpouring of protein and cells. Bacteria also may invade the pleural fluid.

Clinical Signs

Depending on the chronicity of the disease, the clinical signs may vary and may be confused with signs of colic or rhabdomyolysis. In the acute stages, horses are febrile and lethargic, have a slight nasal discharge, and exhibit a guarded cough, shallow breathing pattern, and painful, stilted gait.[303] The right hemithorax is affected more often than the left, presumably because of the more direct route of the right main stem bronchus.[283] Thoracic auscultation may be abnormal as evidenced by pleural friction rubs and ventral dullness. In severe acute cases the horse may exhibit nostril flaring; tachycardia; jugular pulsations; toxic mucous membranes; a guarded soft, moist cough; and a serosanguinous fetid nasal discharge. In chronic cases of pleuropneumonia (duration greater than 2 weeks), horses may have bouts of intermittent fever and exhibit weight loss and substernal and limb edema.

Diagnosis

Diagnosis is based on historical information, clinical examination, imaging results, and microbiologic and cytologic analysis of tracheal and pleural fluid aspirates.

On auscultation of the thorax, one may hear vesicular sounds only dorsally, with an absence of lung sounds ventrally. One may hear bronchial or tracheal sounds if lung consolidation exists. Cardiac sounds radiate over a wider area of the lung field than normal, a finding distinct from clinical cases of pericarditis. On percussion of the chest, the clinician may elicit a painful response (pleurodynia) and detect an area of dullness or decreased resonance ventrally.

Laboratory assessment may demonstrate normal or toxemic leukogram and chemistry findings in the acute cases, whereas in chronic cases, one may find anemia, neutrophilia, hyperfibrinogenemia, and hyperproteinemia.

Ultrasound is the diagnostic technique of choice in cases of pleuropneumonia or pleural effusion. Using a 3.5- to 5-MHz transducer (sector scanner or linear probe), one can detect free or loculated fluid, pleural thickening, pulmonary and mediastinal abscesses, pulmonary consolidation, inundation of airways with fluid, fibrinous adhesions, and concurrent pericarditis. Pleural fluid may displace the lungs axially and dorsally. The fluid may appear anechoic or hypoechoic depending on the relative cellularity.[303] Free gas echoes within the pleural fluid may reflect (1) the presence of anaerobic organisms,[33] (2) the presence of air introduced during a thoracocentesis, or (3) the presence of air introduced by a bronchopleural fistula.

Ultrasonography enables accurate placement of the catheter during thoracocentesis and ensures productive yields during placement of a chest drain (Figures 7-16 to 7-18). Ultrasound examination fails to demonstrate deep parenchymal lesions if the overlying lung is normally aerated.

Thoracic radiography also remains a useful technique for evaluating horses with pleuropneumonia, permitting detection of a pneumothorax or an abscess located deep in aerated lung tissue. Pneumothorax may develop following transtracheal aspiration, thoracocentesis, thoracic drainage, or pleuroscopy. Pneumothorax also may develop as a sequela to gas-producing organisms in the pleural cavity or to air leaks from bronchopleural fistulae.[283]

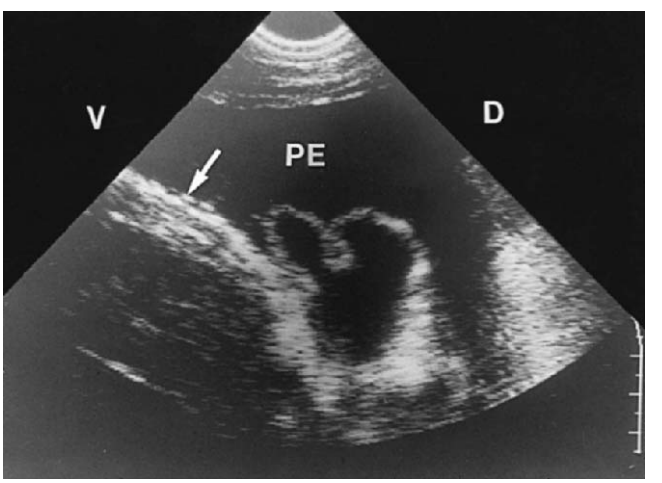


Figure 7-16 Ultrasound of pleural effusion. Anechoic *(black)* area represents pleural effusion *(PE)*. The echogenic *(white)* tortuous fibrin strand is attached to the parietal pleura of the diaphragm. *V,* Ventral; *D,* dorsal; *arrow,* diaphragm.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

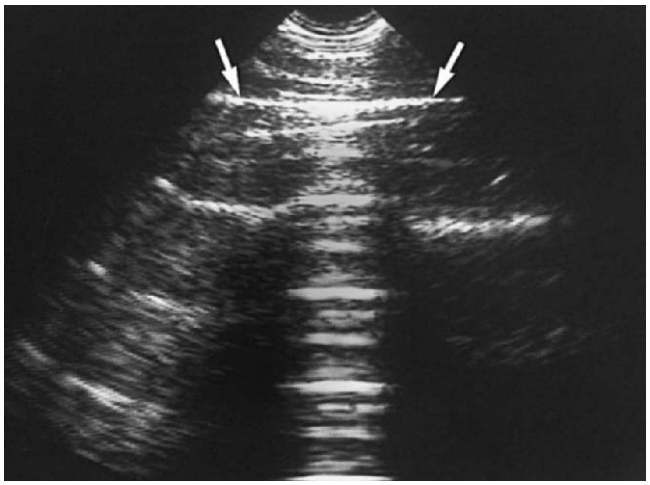


Figure 7-17 Normal thoracic ultrasound demonstrates a highly echogenic interface *(arrows)* between the chest wall and normal lung. A reverberation artifact is notable deep to the chest wall–lung interface.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

Although radiographs may detect pulmonary abscesses, they may fail to detect lesions obscured by the cardiac silhouette.

Thoracocentesis of both sides of the chest is indicated if one notes fluid bilaterally. Not only is thoracocentesis diagnostic and prognostic, it may be a therapeutic life-saving procedure in horses with severe respiratory distress.[305] In healthy horses the fenestrated caudal mediastinium allows communication of the fluid between the two sides of the chest. In horses with pleuropneumonia, fibrin may close mediastinal fenestrations, allowing for differences to develop in the pleural fluid of the two hemithoraces. The clinician should submit fluid for cytologic examination and for aerobic and anaerobic culture. Pleural fluid in healthy horses contains fewer than 10,000 cells per µl, approximately 60% of which are neutrophils, and has a total protein of less than 2.5 g/dl. In cases of pleuropneumonia, pleural fluid white blood cell counts and protein are elevated and glucose levels may be low (<40 mg/dl). The fluid may have a foul odor if anaerobes are contributing to the infection, but the absence of an odor should not preclude the possibility of an anaerobic component.

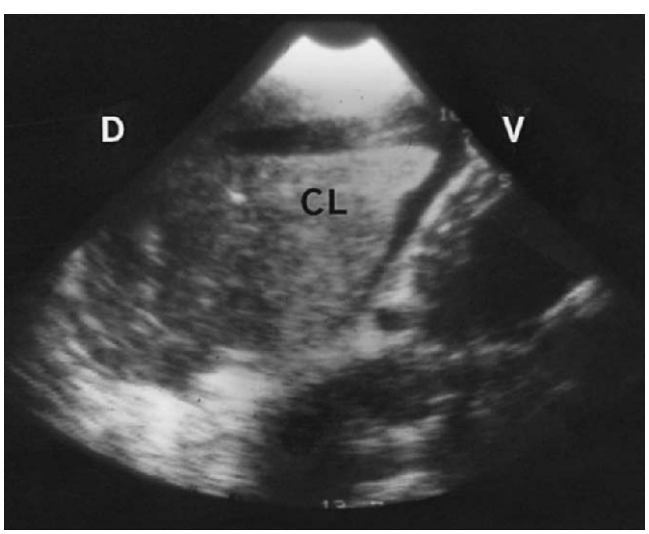


Figure 7-18 Ultrasound of ventrally consolidated lung *(CL)* surrounded by a small amount of pleural effusion. *V,* Ventral; *D,* dorsal.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

The clinician always should obtain a tracheobronchial aspirate to recover the inciting bacterial agents and to examine tracheobronchial secretions cytologically (Gram stain, cell types). One should submit aspirates for aerobic and anaerobic culture and a Gram staining to provide guidance on antimicrobial selection. During the course of the disease, one may obtain multiple tracheobronchial aspirates to identify new or resistant bacterial organisms.

One can use thoracoscopy, performed in standing sedated horses or in horses under general anesthesia, in acute and chronic cases of pleuropneumonia (1) for guided placement of drains into abscesses and loculated pleural effusions; (2) for assessment of the extend and progression of pleural disease; and (3) for the evaluation of therapeutic responses and the efficacy of pleural lavage/drainage.[306]

Treatment

Treatment aims at (1) removing excessive pleural fluid; (2) administering systemic antimicrobials to inhibit bacterial growth; (3) providing antiinflammatory and analgesic drugs that deter the development of secondary complications; and (4) providing supportive care.

Under ultrasound guidance, one can remove pleural fluid aseptically through the seventh or eighth intercostal spaces at a locale dorsal to the costochondral junction using a 24-32 French chest tube. One may remove as much as 30 to 50 L. If blood discoloration of the pleural fluid is caused by the underlying disease, the fluid remains blood-tinged throughout the drainage.[305]

The clinician should place indwelling chest tubes (1) if large volumes of foul-smelling fluid with microorganisms are obtained; (2) if the pleural fluid has a pH less than 7.2 or a glucose concentration less than 40 mg/dl; or (3) if the horse responds poorly to intermittent drainage.[298-305] One should avoid the rapid removal of large volumes of fluid from the chest to guard against the development of hypovolemia. To the end of the indwelling chest tube one should attach a Heimlich valve or a nonlubricated condom with its tip snipped off. Complications of chest tube placement include pneumothorax; lung laceration; hemothorax; cardiac arrhythmias; bowel, liver or heart puncture; and localized swelling.[305]

Appropriate antimicrobial therapy is based on the results of the culture and sensitivity. Pending microbiologic test results, one should administer broad-spectrum intravenous antibiotics in most cases of pleuropneumonia because the infections are polymicrobic. Penicillin is one of the drugs of choice, for it is efficacious against *Streptococcus* spp., *Staphylococcus* spp., and many anaerobes. Metronidazole is added routinely to the penicillin to broaden bactericidal activity against anaerobes, especially *Bacteroides fragilis.* Aminoglycosides lack efficacy against anaerobic bacteria and have poor penetration into respiratory tract secretions but still are administered with penicillin. Third-generation cephalosporins such as ceftiofur sodium, with activity against gram-negative aerobes and facultative anaerobes, showed excellent efficacy in the treatment of spontaneous clinical and posttransport pneumonia associated with *Streptococcus zooepidemicus, Actinobacillus* spp., and *Pasteurella* spp.[307]

Depending on the clinical response of the horse, 10 to 14 days after the onset of initial therapy, the clinician usually replaces parenteral antimicrobials with oral antibiotics. Chloramphenicol, a bacteriostatic drug, has excellent broad-spectrum activity against gram-negative, gram-positive, and anaerobic bacteria and can be given orally. (One must use caution when handling the drug.) Enrofloxacin, a fluoroquinolone, has excellent antibacterial action against aerobic gram-negative bacteria, many gram-positive bacteria, and mycoplasma bacteria but has limited activity against *Streptococcus* spp. and anaerobes.[308] Concentrations of the enrofloxacin in lung tissue are similar to those in serum.[309] Erythromycin and rifampin attain good concentrations in the lung and pleural fluid and within phagocytic cells, but rifampin is expensive and erythromycin may induce a fatal colitis, precluding their use in adult horses.[310]

Antimicrobial therapy should continue for 2 to 4 months until the horse is gaining weight, hematologic and serum chemistry values have normalized, and no evidence of respiratory tract disease exists. One should implement limited exercise (hand walking) and avoidance of stress. One should reevaluate refractory cases using the techniques of ultrasonography, thoracocentesis, or transtracheal aspiration to determine if drug resistance has developed, if additional pathogens are involved, or if untoward sequelae have occurred (see the following discussion).

In refractory cases, drainage of pulmonary or mediastinal abscesses or mechanical debridement of fibrinous material (decortication) may become necessary. One should consider initially attempting drainage using a large-bore chest tube (24F) directed through the chest wall and then the capsular wall of the abscess followed by suction of the abscess contents. Lavage of the contents of the abscess may improve removal of the purulent material. One should take care to prevent spillage of the contents into the pleural cavity. For removal of fibrinopurulent material or necrotic lung segments, a standing thoracotomy may provide necessary access.[311] After removing accessible exudates and fibrin manually, one lavages the chest cavity with a warm 1% Betadine solution, packs it with a large lap sponge, and covers it with a self-adhering dressing and pad. One must lavage the pleural cavity daily. Fistulae formation is a common sequela in these clinical cases, but this does not preclude horses from returning to racing or breeding careers.

Nonsteroidal antiinflammatory drugs (flunixin meglumin, 0.25 to 0.50 mg/kg intravenously 2 to 3 times daily) provide analgesia, increase appetite, increase the comfort of the horse, and decrease the inflammatory response.

Many horses with pleuropneumonia benefit from the administration of intravenous fluids for the first 48 to 72 hours, until the horse is comfortable enough to resume drinking and the danger of endotoxemia has lessened. Nasal insufflation of oxygen (10 to 15 L/min) may be indicated if the horse is hypoxemic or in respiratory distress. One may achieve bronchodilation using inhaled or nebulized albuterol (600 to 720 μg 3 to 4 times daily). Because gram-negative organisms are often involved in pleuropneumonia cases, one should implement prophylactic measures against laminitis.

Prognosis

A favorable response most often relates to early identification and aggressive treatment of pleuropneumonia. Survival rates[297,312] of horses treated for acute pleuropneumonia range from 49% to 98%. Prognosis deteriorates with increased duration of illness because of involvement of anaerobic bacteria and the development of complicating factors such as pleural adhesions, pulmonary necrosis, cranial mediastinal abscesses, bronchopleural fistulae, constrictive pericarditis, and laminitis.[312,384] In a recent study, 61% of Thoroughbreds treated for pleuropneumonia raced after recovery, with 56% winning at least one race.[313]

Complications

Long-term medical treatment of pleuropneumonia may induce complications such as venous phlebitis or thrombosis (from intravenous catheter placement), cellulitis or pneumothorax following thoracocentesis, diarrhea resulting from antimicrobial and antiinflammatory therapy or endotoxemia, and laminitis. With minor changes in the therapeutic approaches, many of these complications resolve and do not impede the eventual return to health of the horse. The more complicated sequelae of infectious pleuropneumonia have been described in detail by Byars, Dainis, Seltzer, et al.[314] and Byars and

Becht.[315] In a survey of 153 horses brought to their veterinary hospital over a 4-year period with pleuropneumonia, they detailed the development of cranial thoracic masses (7.2%), bronchopleural fistulae (6.5%), pericarditis (2.6%), and laminitis (1.3%).

One should suspect cranial thoracic masses when horses exhibit tachycardia, jugular distention, forelimb extension (pointing), and caudal displacement of the heart. One can confirm the presence of empyema, loculations, or encapsulated abscesses cranial to the heart by ultrasonography. In most cases, medical therapy is effective at reducing the abscess, and thus one should elect this conservative approach initially. Additional therapeutic modalities include the administration of a diuretic (furosemide) and a chronotropic agent (digitalis) to improve cardiac performance. However, refractory cases may require ultrasound-guided drainage of the abscess performed under short-term anesthesia (xylazine-ketamine combination).

Bronchopleural fistulae develop when necrotic pulmonary tissue sloughs, providing a direct communication of the airways with the pleural cavity. One confirms diagnosis by visualization of the airways following pleuroscopy or by the intratracheal appearance of contrast media injected into the pleural cavity. Bronchopleural fistulae may close eventually as the pulmonary tissue adheres to the chest wall or as the airways close. Thoracoscopic-guided closure of the bronchopleural fistualae may be necessary in long-standing cases.

PLEURAL EFFUSION

Causes

Accumulation of fluid within the pleural space most often results from imbalances in Starling's law of fluid fluxes. As described previously, pleural effusions in the horse most commonly occur with bacterial pneumonia or lung abscesses.[316] (See the section on treatment for parapneumonic effusions.) Pleural effusions also may accompany a number of thoracic neoplasms such as fibrosarcoma, gastric squamous cell carcinoma, hepatoblastoma, hemangiosarcoma, melanoma, mesothelioma, and metastatic mammary or ovarian adenocarcinoma but most commonly are associated with lymphoma.[317-326] Pleural effusion also develops in a number of other conditions, including thoracic trauma; pericarditis; peritonitis; viral, mycoplasmal, and fungal infections; congestive heart failure; liver disease; diaphragmatic herniation; hypoproteinemia; equine infectious anemia; pulmonary granulomata; and damage of the thoracic duct.[298,327-329]

Pathogenesis

Pleural fluid is really the interstitial fluid of the parietal pleura. A pressure gradient driving its formation exists because the parietal pleura is supplied by the systemic circulation and because the pressure of the pleural space is more negative than that of the subpleural interstitium.[330] Pleural liquid and protein exit the pleural space via the parietal pleural stomata. Fluid production in the pleural space increases if any of the following occur: (1) an elevation of the hydrostatic pressure gradient (congestive heart failure, portal hypertension); (2) a decrease in the colloid osmotic pressures (hypoproteinemia); (3) an increased permeability of the capillary vessels (infection, malignancy, inflammation); or (4) a decreased removal of fluid because of impaired lymphatic drainage (neoplasia) or a decrease in the pleural space (atelectasis).[331] Excessive amounts of peritoneal fluid may accumulate in the pleural cavity as the fluid moves through diaphragmatic defects or through diaphragmatic lymphatics.[330]

Diagnosis

A physical and rectal examination, CBC and chemistry panel, cardiac evaluation, thoracic and abdominal ultrasound, and abdominal centesis may be helpful in determining the cause of the pleural effusion. When one suspects infectious agents, one should perform a transtracheal aspirate. One also should obtain a Coggins test and titers against *Coccidioides immitis, Cryptococcus neoformans,* and *Mycoplasma felis,* depending on the nature of the effusion and the geographic location of the affected horse.

Cytologic and microbiologic evaluation of the pleural fluid may help to identify neoplastic cells or fungal elements. Transudates, fluid with a total protein less than 2.5 g/dl, and few cells usually are associated with congestive heart failure, liver fibrosis, hypoalbuminemia, or early neoplastic processes. Modified transudates have low nucleated cell counts (<10,000 cells/μl) and moderate to high protein levels (>2.5 g/dl) and can be found in many disorders including neoplasia. Exudates have nucleated cell counts exceeding 10,000 cells/μl and total protein levels greater than 3.0 g/dl and are found in infections and intraabdominal diseases.[316] One can distinguish septic effusions from nonseptic effusions by biochemical analysis of pleural fluid aspirates. For example, fluid that has a pH less than 7.2, a glucose concentration less 40 mg/dl, and a lactate dehydrogenase concentration greater than 1000 IU/L has been suggested to indicate septic effusions. Chylous effusions (which are milky white to pale pink) have triglyceride concentrations exceeding that of simultaneously measured serum.[316]

Treatment

Treatment aims at the primary cause, but neoplastic conditions and pleural effusions associated with an end-stage organ failure carry a poor prognosis. Therapeutic thoracocentesis is indicated in malignant effusions when horses are experiencing breathing difficulties. Chest tube drainage and chemical pleurodesis or thoracoscopy with

talc poudrage may be one treatment option. The clinician should consider these procedures if (1) significant improvement in the status of the horse occurs with pleural fluid evacuation and (2) reexpansion of the lung is achieved once fluid is removed. Adapting protocols from human medicine[332] (as successful management of malignant effusions in equine medicine has not been described) requires that the horse first be sedated. Then one administers a sclerosing agent in 100 to 500 ml of sterile solution through a chest tube. One clamps the tube for 1 hour before reconnecting it to continuous suction. One sclerosing agent that has been used is doxycyline (500 mg in 50 to 100 ml saline for human beings).

Poudrage is the most widely used method of instilling talc into the pleural space and usually is performed under thoracosopic guidance. Before spraying the talc over the visceral pleura, one should remove all pleural fluid: complete collapse aids in distributing the talc. In human medicine, one usually instills 5 g (8 to 12 ml) evenly over the pleural surface, places a chest tube, and applies progressive suction until the amount of fluid aspirated per day is less than 100 ml.[332]

FUNGAL PNEUMONIA

Causes

Primary fungal pathogens causing respiratory tract disease in the horse include *Blastomyces dermatitidis, Coccidioides immitis, Cryptococcus neoformans,* and *Histoplasma capsulatum.*

B. dermatitidis is a thermally dimorphic fungus: it exists as a mold at room temperature and as a budding, round yeastlike cell when cultured at 37° C or when replicating in the host. As a soil saprophyte, *B. dermatitidis* can be found near decomposed vegetation or rotting wood.[333] Although respiratory tract disease caused by this organism is rare in the horse, inhalation of the spores may cause a pyogranulomatous pneumonia.[334]

Coccidioides immitis, a soil saprophyte, is also dimorphic, existing as a mold on most culture media and as a nonbudding spherical form in the host tissue. Fungal pneumonia and pleuritis result from inhalation of windborne arthrospores. Lymphohematogenous dissemination of the organisms may lead to the development of lesions in the bones, skin, and meninges.[335]

Cryptococcus neoformans is a yeastlike fungus that reproduces by budding, forming cells 4 to 7 μm in diameter. The organism has a predilection for the respiratory tract and for the central nervous system. The proposed route of infection is via inhalation with secondary hematogenous spread to the central nervous system. When *C. neoformans* replicates within the host or on culture media, the organism forms a large polysaccharide capsule that appears as a clear halo around the cell when organisms are stained with India ink.[336] The capsule is antiphagocytic and immunosuppressive: secretion of capsular antigens into the body fluids binds opsonizing antibody before it reaches the organism. Based on the capsular antigens, two varieties of *C. neoformans* exist: *C. neoformans* var. *neoformans* (serotypes A and D) and *C. neoformans* var. *gatti* (serotypes B and C).

Histoplasma capsulatum is a dimorphic fungus found in the soil and on decaying vegetation. Heavy concentrations of the organism accumulate in soils containing bat or bird feces. The organism is highly infectious as an airborne spore (microconidia) but is of low virulence when it converts to the yeast phase (2 to 4 μm) in the host.[336] Systemic histoplasmosis is uncommon in proportion to the equine population exposed: the horse seems particularly resistant to infection.[337] The propose route of infection is via inhalation or ingestion of the microconidia. Because the organism parasitizes mononuclear phagocytes and has an affinity for the reticuloendothelial system, it may disseminate to the liver, spleen, lymph nodes, and bone marrow.[338]

Opportunists such as *Aspergillus* spp. and *Pneumocystis carinii* cause fungal pneumonia in horses that are immunocompromised, that are neutropenic, or that have enteritis/colitis, bacterial pneumonia, or neoplasms.[339-345]

Aspergillus is a mold with septate hyphae 2 to 4 μm in diameter. The most prevalent pathogenic species is *A. fumigatus,* but *A. flavus, A. nidulans,* and *A. niger* also may cause disease.[346] These fungi are ubiquitous in the environment, growing on dead leaves, stored grain, compost piles, hay, and decaying vegetation.[336] Inhalation of *Aspergillus* spores is suspected to be common, but disease is rare unless the patient is immunocompromised. Infection is characterized by hyphal invasion of blood vessels, thrombosis, necrosis, and hemorrhagic infarction. Because *Aspergillus* occurs widely as an environmental contaminant, diagnosis may require repeated isolation or histologic demonstration.

Pneumocystis carinii formerly had been considered a protozoan organism because of its morphologic features and its susceptibility to antiprotozoal agents.[347] However, the genes encoding the small subunit ribosomal RNA (16s) and the large subunit of mitochondrial rRNA demonstrate similarities to the genes encoding for the rRNA of several different fungal species.[348] As a result, *P. carinii* recently has been reclassified as a fungus. Electron microscopy has revealed two parasite forms: trophozoite and cystic. The trophozoite is an ameboid form 2 to 5 μm in diameter with filopodia that attach to the surface of the type I epithelial cells. The trophozoite is visible with hematoxylin and eosin stains. The mature cyst is 4 to 6 μm in diameter and contains eight uninucleate intracytic bodies. The cyst stains with Gomori's methenamine silver stain and periodic acid–Schiff stain. In keeping with the new taxonomic classification, some

authors recommend replacing the terminology of the different parasite forms by the terms *yeast cell* (trophozoite), *sporangia* (cyst), and *spores* (intracystic bodies).[348]

The infective stage or source of *P. carinii* is unknown, although several studies have reported discovery of *P. carinii* DNA in water and air samples, suggesting that these are environmental reservoirs.[349] In rodent models, *P. carinii* can be transmitted from one animal to another via the airborne route. Researchers also believe that once the organism enters the lower respiratory tract of an immunocompetent host, it remains as a lung saprophyte only to be reactivated during periods of immunosuppression.[347]

Epidemiology

Fungal pneumonia in the horse as a primary entity is uncommon. Disease usually results when debilitating conditions that favor the penetration or growth of fungi exist. Contributory factors include (1) exposure to large numbers of mycotic organisms in the environment[350]; (2) the stabling of horses within a moist environment[351]; (3) the prolonged administration of antibiotics that upset the microfloral balance or interfere with vitamin synthesis; (4) the existence of an immunosuppressive state primarily (combined immunodeficiency disorder) or secondarily because of the administration of drugs, the development of an endocrinopathy, or neoplasia.[345,346]

For the pathogenic fungi, prevalence of the disease may be determined geographically. For example, *Blastomyces dermatitidis* is endemic to the Mississippi, Missouri, and Ohio River basins; the Canadian provinces of Quebec, Ontario, and Manitoba; the Great Lakes region; and the Eastern seaboard.[334] Although *Histoplasma capsulatum* is also endemic to the Mississippi, Ohio and St. Lawrence River valleys, it also is found in the southern United States.[338,352] *Coccidiodoes immitis* is endemic to the arid and semiarid regions of North America, including the states of California, Texas, Arizonia, New Mexico, Nevada, and Utah.[335,353] In contrast, *Cryptococcus neoformans* is widespread, being found in high concentrations in the soil and in avian manure *(C. neoformans* var. *neoformans)*. In Australia, an epizootiologic relationship of *C. neoformans* var. *gatti* exists with the eucalyptus tree *(Eucalyptus camaldulensis)*. Environmental dispersal of the fungus coincides with flowering of the eucalyptus tree in the spring, resulting in greater exposure and more cases of disease during that time.[354]

For the opportunistic fungus *Pneumocystis carinii,* human clinical infections develop only in immunodepressed subjects, those individuals with low $CD4^+$ counts, with certain viral infections (cytomegalovirus), or in weakened nutritional states.[347,348] To date, all reported cases of equine pneumocystosis have occurred in foals 1.5 to 4 months of age. Predisposing factors include the existence of a combined immunodeficiency disorder,[343] *Rhodococcus equi* or chronic bacterial pneumonia,[344,355] low $CD4^+$ counts,[356] and chronic debilitation or weight loss.[357,358] In two reports of equine pneumocystosis, predisposing factors could not be identified.[359,360] The occurrence of pneumocystosis in young foals may reflect an age-dependent maturation of the immune system. Cell-mediated immune responses (in vitro) of foals less than 2 months of age are reduced relative to those of adult horses, perhaps increasing the susceptibility of the foal to pneumocystosis.[361]

Clinical Signs

Horses with primary fungal pneumonia (blastomycosis, histoplasmosis, cryptococcosis, and coccidioidomycosis) may have a chronic cough, anorexia, weight loss, exercise intolerance, and nasal discharge.[362-364] Tachypnea or respiratory distress may or may not be a clinical feature of the fungal pneumonia. Pleural effusion is found more commonly with coccidioidomycosis but also has been reported in cases of cryptococcosis and blastomycosis.[334,335,364]

In addition to causing pneumonia, these fungal organisms may cause disease in other body systems. *Blastomyces dermatitidis* causes superficial abscesses around the anus, vulva, and udder.[365] In a review of 15 cases of equine coccidioidomycosis, 43% of the cases had hepatic lesions, 29% had bone or periosteal involvement, 22% had lesions in the peritoneum, and 64% had pulmonary parenchymal disorders.[335] Other reports describe *Coccidioides immitis* lesions in the mammary gland,[366] the placenta and fetus,[367,368] and the skin.[369] *Cryptococcus neoformans* has been reported to cause granulomata in the skin, nasal cavity, paranasal sinuses, orbits, intestines, bones, meninges, placenta, and fetus.[354,370-373] *Histoplasma capsulatum* has been associated with abortions, disseminated histoplasmosis of foals, and granulomatous colitis of adult horses.[337,352,374]

Horse developing pneumonia caused by opportunistic fungi (aspergillosis, pneumocystosis) may have evidence of a debilitating or immunosuppressive problem such as colitis, peritonitis, septicemia, endotoxemia, an endocrinopathy, or chronic bacterial pneumonia. Young horses (foals) may be at an increased risk for developing opportunistic infections.

In the majority of cases of pulmonary aspergillosis, pneumonia appears to be a sequelum to mycotic invasion of the intestinal tract, the integrity of which has been compromised by severe acute enterocolitis.[339,340,342,350] Such horses typically also have received broad-spectrum antimicrobials and nonsteroidal antiinflammatory drugs and are neutropenic—factors that may also predispose them to the development of systemic aspergillosis. Nevertheless, pulmonary aspergillosis also has been reported in horses with pleuropneumonia, myositis,

renal failure, pituitary adenoma, and myelomonocytic leukemia.[342,345,346]

Horses with pulmonary aspergillosis suddenly may become febrile and tachypneic and may exhibit adventitious lung or pleural sounds and have a nasal discharge. Other horses with pulmonary aspergillosis may show only mild respiratory signs or fail to demonstrate any abnormalities of the respiratory tract.[342,374,375]

Pneumocystosis is a rare clinical entity. In the majority of cases, foals have evidence of chronic respiratory disease that has progressed to respiratory distress. Weight loss, dehydration, and inappetence also may be evident.[344,356-358,360]

Diagnosis

Tracheobronchial aspirates may reveal degenerated neutrophils, yeast cells, and bacteria. In the case of aspergillosis, the diagnosis may be difficult because one may recover fungal elements from the tracheal washings of normal horses.[24] Definitive diagnosis may require repeated isolation of the *Aspergillus* organisms or histologic demonstration of hyphal elements in the pulmonary parenchyma. Transtracheal aspirates may be of limited usefulness in diagnosing pneumocystosis because the organism rarely is isolated by this method. For horses not in respiratory distress, isolation of the organism may be possible by bronchoalveolar lavage or endobronchial brushings.[344,356-358]

In horses with fungal pneumonia, radiographs may reveal circular masses with or without fluid lines and an accentuated interstitial pattern. Radiography or ultrasonography may detect pleural effusion.

Serologic detection of an antibody response to *Coccidioides immitis, Cryptococcus neoformans,* and *Histoplasma capsulatum* has been useful in diagnosing fungal pneumonia. In cryptococcosis, serologic detection of capsular antigens (serum latex agglutination test) also has proved effective in the diagnosis.[364,370] However, the histoplasmin skin test is of little diagnostic value: in one endemic area, 73% of horses had a postive skin test.[376]

Serologic diagnosis of pulmonary aspergillosis can be difficult because titers are detectable in healthy and diseased horses.[342] Nevertheless, Moore, Reed, Kowalski, et al.[377] reported the existence of two precipitin bands against *Aspergillus* antigens in a horse confirmed to have an *Aspergillus* mediastinal granuloma. Precipitin bands were not evident in the eight control horses sampled. Recently, Guillot, Sarfati, DeBarros, et al.[378] reported the usefulness of an immunoblot analysis for the diagnosis of aspergillosis, detecting reactivity to low-molecular-mass antigens (22 to 26 kd) in the sera of diseased horses that was not evident in clinically healthy horses. The investigators suggested that these antigens were released during mycelial growth in the tissues, a phase that would not develop in clinically healthy horses. However, until this experimental assay is commercially available, one should use serologic diagnosis cautiously in suspected cases of pulmonary aspergillosis. One may confirm the diagnosis with lung biopsy and by the presence of other systemic alterations.

The clinician should investigate cases of immunosuppression by quantitation of immunoglobulin levels, by performing mitogen stimulation tests, by quantitation of $CD4^+$ and $CD8^+$ cells and by ruling out endocrinopathies and neoplasia.

Treatment

Treatment against the primary fungal pathogens requires long-term administration (10 to 12 weeks) of antifungal drugs and correction of the inciting cause of the fungal pneumonia. Two basic classes of antifungal drugs are used commonly in equine medicine. The polyene antibiotics—amphotericin B, nystatin, and natamycin—combine with ergosterol in the cytoplasmic membrane of the fungi to increase cell permeability. The second class of drugs, the azoles—miconazole, ketoconazole, itraconazole, and fluconazole—inhibit synthesis of ergosterol and cause an accumulation of aberrant sterols in the membrane. This inhibition affects nutrient utilization and causes leaky cell membranes.[336] Because fungal pneumonia is uncommon, the efficacy of various protocols has not been assessed rigorously. Selection of the antifungal drug to use also should depend on sensitivity patterns of the fungal isolates.

Amphotericin B has been used successfully to treat histoplasmosis[338] and pulmonary aspergillosis.[378] The recommended dose is 0.1 to 0.5 mg/kg administered in a 5% dextrose solution intravenously over 30 minutes, 3 times per week. The possible side effects include anorexia, anemia, arrhythmias, hepatic and renal disyfunction, and hypersensitivity reactions.[372] Neither amphotericin B nor ketaconazole were found to be curative in a series of cases of coccidioidomycosis,[335] although long-term administration of itraconazole (2.6 mg/kg orally twice daily) was eventually effective in treating coccidioidomycosis vertebral osteomyelitis in a foal.[353]

Pneumocystis carinii infections require treatment with antiprotozoal drugs: Ewing, Cowell, Tyler, et al.[358] reported success using trimethoprim sulfamethoxazole (25 mg/kg orally twice daily) in combination with procaine penicillin G in foals with pneumocystosis. Furthermore, Flaminio, Ruch, Cox, et al.[356] supplemented trimethoprim sulfamethoxazole (30 mg/kg orally twice daily) with interferon-α (100 U orally once daily) and *Propionibacterium acnes* (EqStim) in an effort to increase $CD4^+$ and $CD8^+$ counts in a foal with pneumocystosis. The pneumonia eventually resolved and lymphocyte counts returned to normal.

MYCOPLASMAL PNEUMONIA

One can isolate several species of mycoplasma from the upper and lower respiratory tracts of healthy horses and from the nasal cavities of healthy foals soon after birth.[379] *Mycoplasma felis* has been isolated from clinical and experimental cases of parapneumonic effusions[327,380,381] and foal pneumonia.[382] *M. felis* and *M. equirhinis* have been isolated, along with bacterial organisms, from the tracheobronchial aspirates of young athletic horses with inflammatory airway disease.[383] Furthermore, a recent Canadian survey documented serologic evidence of *M. felis* or *M. equirhinis* infection in 9% and 10%, respectively, of horses showing clinical signs of acute respiratory disease.[241] The pathogenesis of the inflammatory or infectious airway disease generally is believed to involve adherence of the organism to ciliated epithelium, causing loss of the cilia and subsequent death of the cell. This belief is supported by the finding of degenerative epithelial cells in the tracheobronchial aspirates of horses with mycoplasma infections.[383] Diagnosis of mycoplasmosis depends on isolation of the organism from tracheobronchial aspirates or from pleural fluid and on demonstration of seroconversion. The clinician should initiate treatment with broad-spectrum antibacterials (oxytetracycline) until antimicrobial sensitivity reports are available.

ACUTE RESPIRATORY DISTRESS SYNDROME

Causes

Acute respiratory distress syndrome (ARDS) is a syndrome of lung injury characterized by alveolar damage, high permeability pulmonary edema, and respiratory failure. Primary lung injury may result from aspiration (near drowning), improper administration of medications via nasogastric tubes, inhalation of smoke or noxious gases, oxygen toxicity, or pulmonary infection by viral, bacterial, mycoplasmal, or fungal agents. Secondary lung injury may be a sequelum of anaphylaxis, gram-negative sepsis/endotoxemia, trauma and embolism, and hypertransfusion.[384-389] In human medicine, strict criteria have been established to define ARDS: impaired oxygenation (ratio of Pao_2/Fio_2 <200), detection of bilateral pulmonary infiltrates in chest radiographs, and a pulmonary artery wedge pressure less than 18 mm Hg or no clinical evidence of elevated left atrial pressures.[390,391] Similar criteria have not been established in equine medicine.

Pathogenesis

Based on the human literature, the thought is that although many different insults (causing capillary permeability) may lead to ARDS, a common final pathway ultimately results in alveolar damage. This pathway may include complement and leukocyte activation with release of oxygen free radicals and inflammatory mediators (IL-1, tumor necrosis factor) and secondary destruction of surfactant.[392] The net result is a deterioration of gas exchange and pulmonary mechanics. Whether horses that survive are more predisposed to the development of interstitial lung disease is uncertain (see the following discussion).

Clinical Signs

Horses are tachypneic or in respiratory distress or both. A red-tinged or yellow frothy material, indicative of pulmonary edema, may be evident at the nares. Fever may be a component of the syndrome depending on the primary cause. In cases of smoke inhalation, clinical signs may not become evident for several days following exposure to noxious gases.

Diagnosis

Diagnosis depends on the physical findings and history. One may detect crackles on auscultation and may auscultate fluid within the trachea. Endoscopic examination (if performed without stressing the horse) may reveal the extent of airway edema, inflammation, mucosal necrosis or sloughing, and the presence of soot (smoke inhalation). Radiographs reveal an interstitial pattern, although an alveolar pattern caused by ventral consolidation of the lung fields may follow aspiration pneumonia. Arterial blood gases reveal hypoxemia and hypocapnia, although with carbon monoxide poisoning, oxygen tensions may be normal. In such cases, carboxyhemoglobin concentrations (measured at human hospitals) exceed 10%, indicating carbon monoxide toxicity.[389]

Treatment

The clinician should direct treatment at the primary cause with the understanding that prognosis is guarded. Lipoid pneumonia resulting from aspiration of mineral oil is fatal.[385] Cases of near drowning and smoke inhalation have been treated successfully with return to athletic function in some cases.[386,387,393]

One should administer intravenous fluid cautiously. Plasma may be needed if hypoproteinemia develops. Furosemide (1 mg/kg intravenously) helps to mobilize lung extravascular water and repetitive dosing at 2- to 4-hour intervals may be required. (One should monitor electrolytes.) Humidified intranasal oxygen (10 to 15 L/min) or mechanical ventilation through a tracheotomy may be necessary. Although technically difficult to perform, adult horses in respiratory failure have been ventilated mechanically.[394] The clinician may perform tracheal suction to remove cell debris and other materials through the endoscope or through a tracheotomy. Surfactant, although expensive, may improve oxygenation and pulmonary mechanics when administered by intratracheal instillation. One may use bronchodilators

to treat bronchospasm. (See the section on recurrent airway obstruction for dosages.) Nonsteroidal antiinflammatory drugs and corticosteroids also are indicated for treating severe permeability edema. One should administer broad-spectrum antimicrobials, including metronidazole, in many of these cases but especially those involving aspiration pneumonia, bacterial and viral pneumonia, and smoke or noxious gas inhalation lung injury.

RECURRENT AIRWAY OBSTRUCTION (HEAVES)

Definition

Recurrent airway obstruction is a naturally occurring respiratory disease characterized by periods of reversible airway obstruction caused by neutrophil accumulation, mucus production, and bronchospasm. The condition has been termed *chronic obstructive pulmonary disease, chronic pulmonary disease, chronic airway reactivity, hyperactive airway disease, broken wind,* and *hay sickness.* The consensus at the International Workshop of Equine Chronic Airway Disease was that the term *chronic obstructive pulmonary disease* not be used to describe this condition in horses, because the pathophysiologic and morphologic aspects of the equine disease are different from human chronic obstructive pulmonary disease.[395]

Pulmonary function testing demonstrates a decrease in lung compliance, an increase in lung resistance, an increase in the work of breathing, and the development of arterial hypoxemia, usually in the absence of hypercapnia.[396,397] During airway obstruction, affected horses are hyperresponsive to nonspecific stimuli such as histamine, methacholine, and water.[398]

Epidemiology

The condition occurs worldwide, but the highest prevalence in the United States is in northeastern and midwestern horses that are fed hay and stabled. A similar condition, found in horses in the southeastern United States maintained on pasture is termed *summer pasture associated obstructive disease.* These horses improve when stabled.[399] Recurrent airway obstruction effects middle-aged or older horses, the median age of which is 12 years.[400] No breed predilection occurs, but a familial tendency has been found: a horse born to a dam and sire with heaves is at an increased risk for developing heaves.[401]

Causes

Much debate still occurs concerning the cause of heaves. Many consider heaves to be a hypersensitivity reaction to organic dusts or molds commonly found in poorly cured hay or straw. Dust in horse stables contains well more than 50 species of molds, large numbers of forage mites, endotoxins, and inorganic components—a variable mixture of agents any one of which might induce pulmonary inflammation in a susceptible horse. The two most frequently implicated molds are *Aspergillus fumigatus* (fungus) and *Micropolyspora faeni* (a thermophilic actinomycete).[402]

Pathogenesis

The condition is characterized by periods of reversible small airway obstruction caused by smooth muscle contraction and accumulations of mucus and neutrophils. One hypothesis is that inhalation of the organic molds, dusts, and endotoxin induces an immune response, the nature of which is controversial. A T helper cell type 2 response (TH2), involving IgE-mediated degranulation of mast cells, has been proposed as the inciting cause because of the findings of (1) increased anti–*Micropolyspora faeni* and anti–*Aspergillus fumigatus* IgA and IgE concentrations in the bronchoalveolar lavage (BAL) fluid of asymptomatic and symptomatic heaves-affected horses,[403] (2) increased histamine levels in the BAL fluid of heaves-affected horses 5 hours after natural challenge,[404] (3) increased serum IgE levels against recombinant *Aspergillus* antigens in heaves-affected horses,[405] and (4) increased numbers of BAL cells that are positive for IL-4 and IL-5 messenger RNA in heaves-affected horses.[406]

A T helper cell type 1 immune reaction with secondary neutrophil influx and release of cytokines also has been implicated in the pathogenesis of heaves because (1) correlation of antigen-specific IgE levels with expression of disease is not absolute,[405,407] (2) pulmonary eosinophilia, as occurs in the TH2 disorder of human asthma, is not a feature of heaves,[408] (3) increases in BAL fluid allergen-specific IgGa and IgGb noted by Halliwell, McGorum, Irving, et al. are more compatible with a TH1 rather than with a TH2 response,[403] and (4) quantitative PCR analysis of BAL lymphocytes demonstrates an increase in TH1 (interferon-γ) but not TH2 (IL-4, IL-5) associated cytokines.[409,410]

In horses with heaves, IL-8 concentrations in the bronchoalveolar fluid are increased relative to levels found in healthy horses.[410,411] This cytokine may be derived from macrophages, neutrophils, or airway epithelial cells and is one of the primary chemoattractants for neutrophil migration into the airways. Interestingly, in murine models of obstructive airway disease, airway epithelial cell production of IL-8 is upregulated by interferon-γ and IL-17.[412] Because the mRNA levels of IL-17, a T cell–derived cytokine, also increased in airway lymphocytes isolated from heaves-affected horses (Ainsworth, unpublished data), a link between the airway TH1 responses and epithelial-derived chemokines may exist.

Neutrophil- and macrophage-derived products such as reactive oxygen species and proteases also may contribute

to the inflammatory process of heaves. Art, Kirschvink, Smith, et al.[413] suggested that an oxidative stress caused by the release of reactive oxygen species from granulocytes and macrophages develops in the airways of heaves-affected horses. Their conclusion is based on the finding that oxidized glutathione levels and glutathione redox ratios (the ratios of oxidized glutathione to total glutathione levels) are elevated in the pulmonary epithelial lining fluid of heaves-affected horses relative to controls. They further suggested that the oxidant stress does not incite but rather exacerbates the existing inflammation. Interestingly, oxidative stress[414] has been found to activate NFκB, a transcription factor that regulates the expression of many proinflammatory cytokines and adhesion molecules including tumor necrosis factor α, IL-1β, IL-8, and intercellular adhesion molecule 1.[415] Recently, Bureau, Bonizzi, Kirschvink, et al.[416] demonstrated that levels of NFκB in the bronchial brushing cells of heaves-affected horses were increased many times, the magnitude of which correlated with the severity of the clinical disease. Furthermore, the airway epithelial cell expression of intercellular adhesion molecule 1, a protein required for migration of neutrophils from the pulmonary vasculature into the lung parenchyma, paralleled the expression of NFκB, suggesting that this protein, along with IL-8, enhances the airway neutrophilia.

Proteases released from neutrophils (and macrophages) in the airways of heaves-affected horses may contribute further to inflammatory cell influx and possible tissue damage. Researchers have found that the tracheal epithelial lining fluid of horses with heaves has increased concentrations of matrix metalloproteinases that exhibit collagenolytic, gelatinolytic, and elastinolytic activities.[417-419] The importance of these proteases, as well as other inflammatory mediators and arachidonic acid metabolites, to the initiation and development of bronchospasm, mucus secretion, and neutrophil influx needs to be determined.

Clinical Signs

Horses with heaves have a chronic spontaneous cough, a mucopurulent nasal discharge, an accentuated expiratory effort, and adventitious lung sounds. Hypertrophy of the external oblique and rectus abdominis muscles caused by continued recruitment is evident (heave line). The respiratory rate may be normal or increased (tachypnea). Exercise intolerance, weight loss, and cachexia also may be evident in severe cases. Horses are usually afebrile.

Diagnosis

Diagnosis is based on the clinical signs and history of a seasonal disorder associated with husbandry alterations such as being fed hay, stabled, transported in a trailer, or maintained in a dusty lot. Auscultation may reveal inspiratory or expiratory wheezes, crackles, or tracheal rattles. Percussion may be normal or an expanded lung field may be detectable.

Endoscopic examination reveals excessive mucopurulent exudate within the trachea. A bronchoalveolar lavage supports a *nonseptic* inflammatory reaction with increases in mucus and the percentage of intact neutrophils. Albumin and immunoglobulin levels within the bronchoalveolar lavage may not increase.[420] Gram-positive organisms may be retrieved by tracheobronchial aspirates if a concurrent septic inflammation exists. Pollen, fungal hyphae, and Curschmann's spirals (inspissated mucus plugs) also may be visible.

Thoracic radiography may demonstrate an increase in the interstitial and bronchial pattern throughout the lung fields. However, these changes may be difficult to interpret relative to the normal aging changes that occur. One also may detect exudate within the trachea by thoracic radiography (Figure 7-19).

Some have advocated intradermal skin testing for diagnosing heaves and for detecting sensitizing allergens. Its usefulness is questionable. Theoretically, heaves-affected horses should react if sensitized to a given allergen, but (1) clinically normal horses have positive skin test reactions to the allergens and (2) heaves-affected horses lack positive reactions. Thus intradermal skin testing is not indicated for diagnosing heaves.[421-423] Furthermore, a poor correlation exists between skin test results and serum allergen testing, leading some clinicians to conclude that these assays should not be used as screening tests for allergen hypersensitivities in the horse.[423]

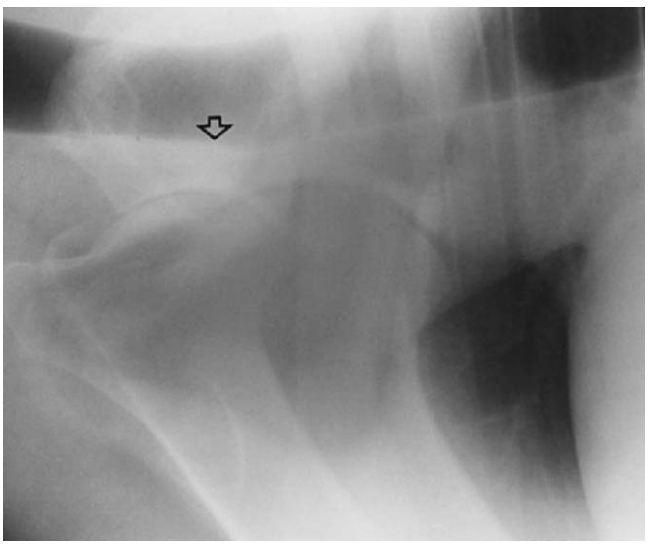


Figure 7-19 Tracheal fluid or exudates *(arrow)* is visible ventrally in the trachea at the level of the thoracic inlet.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

A CBC and serum chemistry panel is of limited usefulness in diagnosing heaves because no abnormalities are detectable in the leukogram or in serum biochemistries.[400]

Pathologic Signs

Postmortem examination reveals a diffuse bronchiolitis with goblet cell metaplasia, airway smooth muscle hypertrophy, excess mucus, and inflammatory cells in the small airways. Eosinophilic infiltration around the bronchioles is a variable finding, present in approximately one third of the horses. Varying degrees of alveolar overinflation and atelectases also are found, as well as evidence of fibrosis of the alveolar septa.[424] The larger airways—the bronchi and trachea—also may show variable changes, including epithelial hyperplasia with loss of ciliated cells, goblet cell hyperplasia, and inflammatory cell infiltration.[425]

Treatment

Elimination of the source of the mold or dust is the most beneficial step in the treatment regimen but also the most difficult management change to implement.[400] Horses should be fed a pelleted alfalfa or a complete pelleted feed with the transition from a hay diet to one of a complete pelleted feed made gradually over 7 to 10 days. Unless pasture exacerbates the condition, the owner should keep horses outside, blanket them in the winter, and allow access to a three-walled shelter affording protection from the wind and rain. If the horse is stabled, the stall bedding should be shredded paper, shavings, peat moss, or clay to eliminate dusts and molds. The surrounding stalls should be bedded similarly. Although such stabling changes improve lung function somewhat, airway hyperreactivity still remains.[426,427]

Medical management also has been indicated in clinical cases because stabling alone takes several weeks to quiet the pulmonary inflammation. Corticosteroids are efficacious in reducing the inflammatory reaction in the lungs, whereas nonsteroidal antiinflammatory drugs provide no benefit. The clinician initially may give prednisolone (not prednisone) at 2.2 mg/kg orally once daily in the morning for 7 to 10 days, 1.1 mg/kg once daily for 7 to 10 days, 0.50 mg/kg once daily for 7 to 10 days, and 0.50 mg/lb every other day for 7 to 10 days. Alternatively, one may give a course of dexamethasone parenterally. For the 500 kg horse, the course is 40 mg intramuscularly once daily every other day for three treatments, followed by 35 mg intramuscularly once daily every other day for three treatments, 30 mg intramuscularly once daily every other day for three treatments, etc., until the horse is weaned off of the dexamethasone. Corticosteroid use may be contraindicated in horses predisposed to laminitis or exhibiting endocrinopathies.

Inhaled steroids have been used to treat the pulmonary inflammation of heaves but may not provide a therapeutic benefit for 24 to 72 hours. Thus for horses in respiratory distress, inhaled steroids should not be the main route of glucocorticoid administration. Metered dose inhalers attached to a spacer on the Aeromask (Trudell Medical, London, Ontario, Canada) administer the drug when the horse initiates inspiration. Frequent administration of steroids to effect improvement in lung function may make this medical treatment less desirable. Some suggested corticosteroid dosages (using the Aeromask) are beclomethasone (3750 μg twice daily) or fluticasone (2 μg twice daily).

Bronchodilators also are recommended for treating recurrent airway obstruction. Three types of compounds are used to relax airway smooth muscle: the β-adrenergics, the methylxanthines, and the anticholinergics. The β_2-adrenergic compounds include clenbuterol, albuterol, salmeterol, and fenoterol. Experimental investigations with clenbuterol suggest that when given at a dose of 0.8 μg/kg once daily by mouth, the drug may be efficacious in alleviating some of the signs of heaves. In addition to a direct smooth muscle effect, clenbuterol also may stabilize mast cells, increase mucociliary clearance, and improve airway secretions.[428] Albuterol is absorbed poorly from the gastrointestinal tract, so inhalation is the recommended method of administration. Some suggested dosages of β_2-agonists that can be administered by metered dose inhalers through the Aeromask are these: albuterol, 720 μg 3 to 4 times daily; fenoterol, 1 to 2 μg 3 to 4 times daily; and salmeterol, 210 μg once or twice daily. Administration of the β_2-agonist before corticosteroid dosing enhances the deposition of the latter in the smaller airways.[429] Long-term use of β_2-agonists has been associated with a downregulation of the β-receptors in human beings, but whether this occurs in horses is unknown.

The methylxanthines include aminophylline (theophylline), which dilates smooth muscle by increasing cyclic adenosine monophosphate levels intracellularly. Cyclic adenosine monophosphate also inhibits degranulation of mast cells and subsequent mediator release. One may give aminophylline at 4 to 6 mg/kg orally 3 times daily. However, in a recent study, aminophylline 18 mg/kg intravenously provided clinical improvement in only 50% of the cases.[430]

The third class of compounds used to effect smooth muscle dilation includes the anticholinergics, of which atropine and glycopyrrolate are representatives. Atropine provides clinical improvement when administered intravenously at 0.02 mg/kg, but the duration of effect is short-lived (2 hours) and atropine may be associated with the development of ileus, abdominal pain, tachycardia, mydriasis, and thickening of airway secretions.[430] Atropine

generally is used for emergency relief of airway obstruction. Glycopyrrolate has been reported to be efficacious at a dose of 0.007 mg/kg, but it also may cause colic. One also can administer ipratropium bromide by inhalation at a dose of 180 to 360 mg 3 times daily with a low risk of inducing systemic side effects.[395]

Disodium cromoglycate is considered efficacious by some, acting to stabilize mast cell degranulation and inhibit the vagal efferent component of histamine response. A suggested dose from the study of McPherson and Thomson[402] was 80 mg once daily for 4 days by nebulization. Mucolytics (acetylcysteine, dembrexine) and mucokinetics (iodides, bromhexine) may provide some relief.[431] Antimicrobials are indicated if microorganisms are isolated on the tracheobronchial aspirate.

Prevention

Once the clinician has diagnosed the condition, the horse always will be susceptible to recurrences of the disease. Husbandry changes should be implemented to decrease environmental dust and organic mold exposure. During periods of hot, humid, or dusty conditions, prophylactic administration of a steroid and bronchodilator via the metered dose inhaler may be indicated. Routine immunizations against the viral respiratory pathogens and good management practices are logical suggestions.

INFLAMMATORY AIRWAY DISEASE

Definition

Inflammatory airway disease (IAD) is characterized by the presence of excessive amounts of mucoid or mucopurulent exudate in the nasopharynx, trachea, and bronchial bifurcation. The condition is encountered predominantly in the young performance horse.[47,89] Auscultatable pulmonary abnormalities rarely are identified. Some horses with IAD may exhibit a cough and reduced athletic performance. The relationship between IAD in young horses and recurrent airway obstruction in mature horses is unknown: currently, the former condition is believed not necessarily to progress to the latter.[395]

Epidemiology

Depending on the study, a prevalence of 20% to 65% among racehorses in training has been noted.[89,432] The variation in prevalence may reflect the method of diagnosis: the amount of tracheal exudates detected endoscopically increases as a function of exercise intensity.[89] Thus one may miss the diagnosis of IAD if one performs endoscopic examination in the resting horse.[433]

Causes

The definitive cause of the lower airway inflammation is currently unknown and has been hypothesized to reflect the response of the lung to the presence of (1) low-grade persistent bacterial or viral infections, (2) autologous blood from exercise-induced pulmonary hemorrhage, and (3) inhaled dusts, molds, particulate matter or environmental pollutants such as H_2S, NH_3, ozone, SO_2, NO_2 and CO.

Studies in the United Kingdom and Australia suggest that bacterial agents are involved in the pathogenesis of IAD.[89,434-436] Using an inflammatory score based on the amount of mucus, total nucleated cell count, and neutrophil percentages in endoscopically obtained tracheobronchial aspirates, investigators found that as the inflammatory score increased, the percentage of positive bacterial cultures also increased.[437] The most commonly isolated organisms were *Streptococcus zooepidemicus, Streptococcus pneumoniae, Actinobacillus equuli,* and *Pasteurella* spp. Mycoplasma spp. also were isolated from some horses with IAD.[383] That the prevalence of IAD decreased with increasing age of the horse was attributed to the development of an effective immune response. In studies in the United Kingdom and in Australia (where equine influenza is not endemic), no association between the onset of IAD and seroconversion to EHV1, ERV1, ERV2, or equine influenza existed,[434,436,438] suggesting that IAD is not associated with a viral infection.

A viral cause has been proposed for IAD based on the cytologic improvements in BAL fluid constituents in horses treated with oral interferon-α. In their study of 32 Standardbred horses with a history of poor performance referable to the respiratory tract, Moore, Krakowka, Robertson, et al.[439,440] and Moore, Krakowka, McVey, et al.[441] found that relative to control horses, the BAL fluid total nucleated cell count and the percentages of BAL fluid neutrophils, lymphocytes, and monocytes increased significantly in horses with IAD. They considered the lymphocytosis and monocytosis to be consistent with a low-grade viral infection. A 5-day course of oral interferon-α (50 U per day) lowered total nucleated cell counts and converted the cell distribution to a noninflammatory profile for at least 15 days. The investigators did not describe whether the amelioration of pulmonary inflammation was associated with an improvement in athletic performance. They also did not evaluate horses endoscopically beyond 2 weeks to determine if cessation of interferon-α therapy was associated with a return of IAD.

Autologous blood, derived from pulmonary capillaries that rupture during intense exercise, also has been suggested to cause of IAD. In an experimental study, Tyler, Pascoe, Aguilera-Tejero, et al. found that instillation of blood caused a neutrophilic pulmonary inflammatory reaction in the lungs, leading them to conclude that pulmonary hemorrhage may contribute to IAD.[442]

Evidence that inhaled environmental allergens from hay or straw contribute to IAD is supported by the observations that episodes of IAD are shorter in horses bedded on shredded paper[434] and that stabling is associated with an increase in the proportion of BAL fluid neutrophils and a decrease in the percentage of lymphocytes.[91]

Hare and Viel[443] also have suggested that a type I (IgE-mediated) hypersensitivity reaction to inhaled environment allergens could be the cause of IAD. They studied young Standardbred racehorses with a history of poor performance and found evidence of peripheral blood and BAL fluid eosinophilia (12% eosinophils). Normally the percentage of eosinophils in BAL fluid is less than 2%. Because they found no evidence of pulmonary or intestinal parasitism in this group of affected horses, the investigators attributed the eosinophilic IAD to an allergic reaction.

Environmental pollutants also have been suggested as a cause of IAD. This hypothesis arises from the observation that many racetracks and training facilities are located in metropolitan areas that have significant accumulations of smog. No data exist verifying this as a cause of IAD.

Clinical Signs

Inflammatory airway disease is frequently subclinical but in some cases may be associated with poor athletic performance or a cough. With the exception of the cases described in England, pyrexia is generally not a feature of the disorder. Horses also may have evidence of EIPH.

Diagnosis

Definitive diagnosis requires endoscopic examination of the respiratory tract with the finding of exudate in the nasopharynx and in the trachea. One also may see lymphoid hyperplasia depending on the age of the horse. Other causes of poor performance—musculoskeletal and cardiovascular—must be ruled out to attribute reduced athleticism to IAD. This may require that the horse perform a standardized treadmill exercise test, enabling assessment of the upper respiratory tract (videoendoscopy), the cardiovascular system (electrocardiogram), and the musculoskeletal system (lameness exam, creatine kinase and aspartate transaminase measurement). One also should obtain a CBC and chemistry panel. With the exception of cases of IAD associated with pulmonary eosinophilia, CBC and chemistry profiles are usually within normal limits.

Further diagnostic evaluation of the respiratory system in horses with IAD should include a culture of a tracheobronchial aspirate to rule out a low-grade bacterial infection and a bronchoalveolar lavage to determine whether the cytologic profile is most representative of a bacterial, viral, or allergic cause.

Although instillation of autologous blood does decrease dynamic compliance and increase respiratory resistance[444] in the majority of investigations of IAD, pulmonary function tests have been unremarkable.[47,443] Measures of airway hyperreactivity, performed by determining dose-dependent alterations in respiratory tract resistance or dynamic lung compliance following nebulizing of methacholine or histamine, have demonstrated that some horses with IAD have hyperresponsive airways.[47,443,445]

Treatment

Because the cause of IAP remains uncertain, most treatment recommendations aim at environmental alterations to decrease exposure to dust, molds, and allergens. Horses should have pasture turnout whenever possible. Horses with bacterial infections should receive a 7- to 10-day course of an antibiotic, the selection of which is based on culture and sensitivity results from the tracheobronchial aspirate. Horses with pulmonary lymphocytosis and monocytosis may benefit from a 5-day course of orally administered interferon-α (50 U once daily). One also should implement efforts to decrease the severity or frequency of EIPH by having horses train and race with furosemide. In the absence of an infectious cause, horses also may benefit from a course of corticosteroids: prednisolone at 1 mg/lb orally once daily for 7 to 10 days, followed by 0.5 mg/lb orally once daily for 7 to 10 days, and then 0.5 mg/lb orally once every other day for 7 to 10 days.

LUNGWORMS

Causes

Lungworm infections in the equine species are caused by *Dictyocaulus arnfieldi*. Infections in the donkey and mule are asymptomatic but provide a source of viable eggs for clinically apparent infections in the horse and pony.

Epidemiology

Lungworm infections have been diagnosed by recovery of larvae in live animals by bronchoscopic examination[446] or at postmortem evaluation. Using this approach, the prevalence of lung worm infection is approximately 68% to 80% in donkeys, 29% in mules, and 2% to 11% in horses.[447,448]

Pathogenesis

Donkeys are asymptomatic reservoirs of the parasite, but instances of lungworm infections have occurred in horses in which no contact with donkeys could be established, suggesting horse-to-horse transmission may be possible.[448] Experimental studies provide evidence that under field conditions, *Pilobolus* fungi may facilitate the spread of lungworm infections in a manner similar to that which

occurs in cattle lungworm infections.[449] The infective larvae ascend the coprophilous fungus as it grows on the manure and invade the sporangia. When the sporangia rupture, the infective larvae disperse with the fungal spores. After the infective larvae (0.4 mm) are ingested, they migrate through the gut wall and are carried to the lungs via the lymphatics. In hosts in which infections are patent, the larvae mature to egg-laying adults in the peripheral bronchioles. The prepatent period is approximately 2 to 3 months. Eggs are transported out of the lungs by the mucociliary apparatus, swallowed, and excreted in the feces where they become infective by 4 days.[450] First-stage larvae have survived for at least 49 days but do not survive over the winter.[451] In horses and ponies, larval development in the lungs is arrested (fifth stage), but airway inflammation still occurs.

Clinical Signs

Horses exhibit chronic coughing and an increased expiratory effort. Auscultation reveals crackles and wheezes, especially over the dorsal and caudal parts of the lung fields.[452] Signs are often indistinguishable from those associated with heaves. Donkeys do not typically exhibit clinical signs of infection.

Diagnosis

Endoscopic examination may reveal a mild lymphoid follicular hyperplasia and copious amounts of exudate in the trachea and bronchioles. Tracheobronchial aspirates or bronchoalveolar lavage may contain a predominance of eosinophils. A peripheral eosinophilia is a variable finding in these horses. Definitive diagnosis is made by identification of *D. arnfieldi* larvae in the sediment of centrifuged mucus, although this may be difficult.[451] One should examine stained and unstained cytologic preparations. In donkeys and in horses with patent infections, bronchoscopic identification of the lungworm, 16 cm in length, confirms the diagnosis. The Baermann technique is useful for diagnosing lungworms when the infections are patent.

Diagnosis most often depends on the clinical signs, the history of exposure to donkeys, and the response to anthelmintic therapy.

Treatment

Ivermectin (200 μg/kg) is effective against *D. arnfieldi* in controlled studies and field evaluations and did not cause any detrimental side effects.[453] Moxidectin (0.4 mg/kg) was found to be 99.9% effective in treating lungworm infections in donkeys.[454]

Prevention

Horses should not be pastured with donkeys or mules unless they are confirmed to be free of lungworms.

EXERCISE-INDUCED PULMONARY HEMORRHAGE

Causes

Strenuous exercise is associated with exudation of red blood cells from the pulmonary vasculature into the alveoli and airways of the caudal dorsal lung segments.

Epidemiology

EIPH has been detected in most breeds of horses undergoing strenuous athletic events. The prevalence of EIPH is estimated to be between 44% and 75% in the Thoroughbred, 26% in the Standardbred, 62% in the racing Quarter Horse, 50% in racing Appaloosas, 68% in steeplechasers, 67% in timber racing horses, 40% in Three-Day Event horses, 10% in pony club event horses, and 11% in polo ponies.[455-459] Indeed, EIPH probably occurs in any breed of horse that is exercised strenuously. The prevalence of EIPH increases with the age of the horse. No clear correlation exists between EIPH and the location of stables, the condition of the track, or the track type.[460] No geographic variation exists in the prevalence of EIPH.

Pathogenesis

The mechanisms responsible for the development of EIPH are not known completely, although potential causes include (1) ventilation inhomogeneities caused by small airway disease, (2) mechanical constraints of abdominal viscera placed on the dorsocaudal lung field, and (3) stress failure of the pulmonary capillaries.

Robinson and Derksen[461] proposed that poor collateral ventilation in the horse coupled with small airway disease (and thus altered time constants for alveolar filling) caused underventilation of certain lung units. Extreme fluctuations in the alveolar pressure of these underventilated regions during exercise produced parenchymal tearing or alveolar capillary rupture. Small airway disease (IAD) has been detected in a large percentage of horses with EIPH[462]; however, its absence in the lungs of young racehorses that still exhibit evidence of EIPH suggests that small airway disease, at least, is not an inciting cause of EIPH.[463] The role of small airway disease in propagating the cycle of EIPH cannot be dismissed.

Clarke[464] speculated that visceral constraint of the diaphragm caused greater mechanical forces or stresses to develop in the dorsal thorax. Thus in the caudodorsal lung, these mechanical forces would be borne over a narrow area, leading to parenchymal tearing or rupture of capillaries during inspiration. However, evidence of widespread hemorrhage in the dorsal portions of the lung suggests that the distribution of extremely negative intrapleural pressures is more complex and not simply restricted to the region in close proximity to the caudal dorsal lung. An alternative mechanical theory has proposed that forelimb locomotory impact forces are transmitted through the chest wall, setting up waves converging

caudodorsally in the lung parenchyma.[465] Experimental evidence supporting the mechanical theories is currently not available.

Pulmonary hypertension and secondary stress failure of the capillaries also has been suggested as the cause EIPH. Stress failure is thought to occur following development of high transmural pressures, the pressure difference between the pulmonary capillary bed and the adjacent alveoli. Pulmonary capillary pressures (which may exceed 70 mm Hg in strenuously exercised horses) disrupt capillary endothelial and alveolar epithelial tight junctions leading to hemorrhage within the interstitium and alveoli. The pulmonary hypertension is a consequence of the high cardiac output, the lack of sufficient pulmonary vascular vasodilation and the increased blood viscosity during exercise. Evidence supportive of the stress failure theory is provided by electronmicrographs prepared from lung segments taken from strenuously exercised horses. These demonstrate a breakdown of the endothelial and epithelial tight junctions and exudation of red blood cells into the alveoli.[466] Although some investigators have found no correlation between pulmonary capillary pressures in exercising horses and the development of EIPH ascertained endoscopically,[467] others have found a correlation between mean pulmonary artery pressures in exercising horses and the number of erythrocytes in postexercise bronchoalveolar lavage fluid samples.[468]

A combination of these three mechanisms likely may contribute to the development of EIPH.

Clinical Signs

Evidence of frank blood occurs in less than 10% of the horses with EIPH. The effect of EIPH on racing performance varies. A clear association between finishing position in a race and the prevalence of EIPH in Thoroughbreds or Standardbreds has not been demonstrated. Often horses continue to perform at levels judged to be adequate. In other cases, horses may slow or stop, and some may exhibit difficult or labored breathing, coughing, or excessive swallowing. The affect of EIPH on athletic performance may be better understood when methods to quantitate the extent of bleeding have been developed.

Diagnosis

Endoscopic examination of the upper respiratory tract and detection of frank blood within the trachea is the usual method of diagnosis. Optimal time for endoscopic examination is within 90 minutes of a race or workout. However, EIPH is not a consistent finding; it may not be apparent in a given horse examined on different occasions after the same level of exercise. Transtracheal aspirates or bronchoalveolar lavage reveals hemosiderophages, intact and degenerating neutrophils, some with intracellular bacteria, and erythrocytes. Radiographs may demonstrate increases in interstitial patterns, a radiopaque region in the caudal lung lobe (rare), and possible dorsal displacement of the major pulmonary vessels[469] (Figure 7-20).

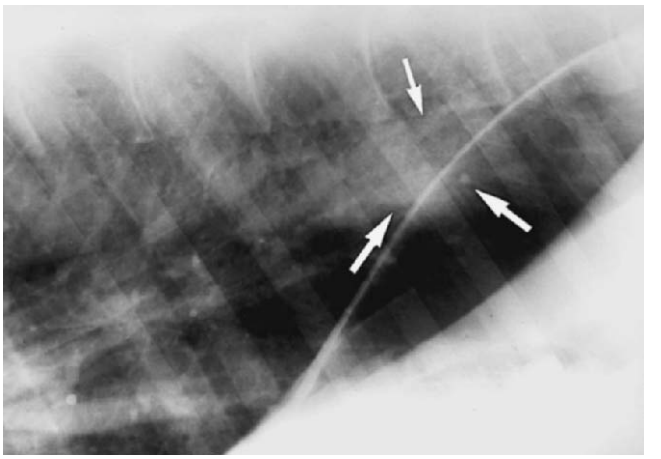


Figure 7-20 Focal area of increased interstitial pulmonary opacity *(arrows)* in the dorsal caudal lung field represents exercise-induced pulmonary hemorrhage.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

Treatment

Rest has been recommended, but pulmonary hemorrhage likely will recur once the horse resumes training. The finding of concomitant small airway disease (IAD) in some horses suggests that one should attempt to minimize environmental dusts and molds. Corticosteroids and bronchodilators, inhaled or administered parenterally, have not been shown to reduce EIPH but may lessen the severity of small airway disease. Cromoglycate, which is believed to stabilize mast cell membranes, has not been efficacious in the treatment of EIPH.[470]

Antimicrobials may be indicated in cases of severe hemorrhage because blood provides an excellent medium for bacterial growth to occur.

Drugs that reduce pulmonary capillary pressure have gained the most widespread use in the treatment and prevention of EIPH. Furosemide, 250 to 300 mg, is given 4 hours before a race or strenuous workout. Although furosemide admnistration has failed to prevent the development of EIPH in horses that were previously EIPH-negative,[471,472] some evidence indicates that it may reduce the severity of EIPH (red blood cell counts in bronchoalveolar lavage fluid). Nitric oxide, a potent vasodilator, also has been administered to horses in the form of nitroglycerin. However, nitric oxide reduces neither pulmonary artery pressures of strenuously exercising horses nor the severity of EIPH.[473,474]

Prevention

The efficacy of treatment regimens in the prevention of EIPH under race conditions has been difficult to determine even when speed handicapping methods are used. Variables such as the administration of drugs unknown to the investigators or the inability to diagnose or reproduce EIPH within a given horse on consecutive days makes interpretation of these studies difficult. And yet controlled studies conducted on a treadmill probably do not accurately simulate race conditions, so that one also may draw false conclusions.

INTERSTITIAL LUNG DISEASE

Definition

Although traditionally considered to be a chronic disorder, interstitial pneumonia encompasses acute and chronic inflammatory responses that predominantly involve the alveolar walls and interstitial tissues of the lung.[475] Interstitial lung disease includes a heterogeneous group of disorders characterized by damage to the alveolar walls and loss of functional alveolar capillary units. This is a morphologic characterization of a lung disease. These authors believe it possible that cases of ARDS may progress eventually to interstitial lung disease. However, longitudinal studies supporting this hypothesis have not been conducted.

Epidemiology

Buergelt[476] has suggested that two types of equine interstitial disorders exist: one occurring in foals 6 days to 6 months of age and one developing in adult horses greater than 2 year of age. This discussion focuses on interstitial lung disorders in the adult horse.

Causes

Most of the recognized spontaneously occurring interstitial lung disorders in animals have been attributed to toxic or infectious (viral or parasitic agents) agents or to allergens.[475] Toxic lung injury in the horse has been documented following consumption of Crofton weed, pyrrolizidine alkaloids, and *Perilla* ketones.[475-478] Interstitial pneumonia is a feature of viral infections (influenza, EHV1, EHV4, EVA), silicosis, and possibly oxygen therapy.[479,480] Other cases of interstitial pneumonia may not have a well-defined cause.[481-484]

Pathophysiology

An inciting agent initiates damage to pulmonary epithelial or endothelial cells, causing coagulative necrosis of the alveoli. Pulmonary congestion, interstitial edema, erythrocyte extravasation, and alveolar flooding characterize the acute (exudative) phase of the disease. Fibrin, protein-rich fluid, cellular debris, and inflammatory cells (neutrophils and macrophages) form hyaline membranes. During the acute phase (days 1 to 5), the horse may exhibit respiratory distress. The exudative phase is followed by a proliferative stage in which the type II pneumocytes, the pulmonary stem cells, replace damaged type I pneumocytes. Interlobar septa widen because of the proliferation of fibroblasts and inflammatory cell infiltration by neutrophils and macrophages.[475]

Clinical Signs

Clinical signs vary depending on the stage of the pneumonia and the causative agent. In the acute phase, horses may have respiratory distress: they are tachypneic, may be hypoxemic, and may or may not be febrile.[478,479] Horses also may have signs similar to those exhibited by heaves-affected horses with an increased respiratory rate and a significant expiratory effort, cough, and nasal discharge.[481-483] In chronic disorders, horses may exhibit exercise intolerance[482] or have a history of weight loss and anorexia. Interstitial lung disease also may be present in the absence of clinical signs.[482]

Diagnosis

The diagnosis is based on clinical signs, history, radiographic examination, isolation of a causative agent, and lung biopsy. Arterial hypoxemia may be evident on blood gas analysis. CBC and serum chemistry panels may be normal or may demonstrate leukocytosis and hyperfibrinogenemia.[485,486] Radiographs demonstrate (1) pulmonary infiltrates with discrete and diffuse nodules, suggesting neoplasia or mycotic pneumonia, or (2) an increase in the interstitial pattern of the lung (Figure 7-21). Serum titer levels may indicate a high titer

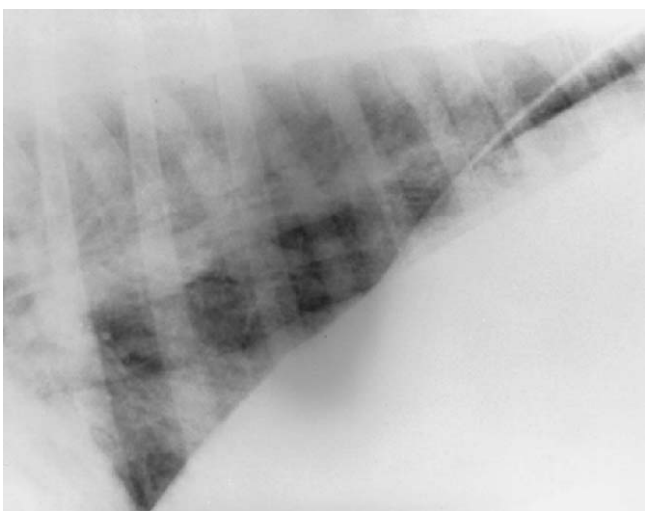


Figure 7-21 Overall increase in interstitial pulmonary opacity represents interstitial lung disease.

(Courtesy D.S. Biller, Manhatten, Kansas, 1991.)

to equine influenza virus.[479] Lung biopsy confirms the diagnosis of interstitial pneumonia. Silicosis, also a rare finding in the horse, is diagnosed by using x-ray diffraction techniques on lung tissue specimens.[480]

Pathologic Signs

The lung changes are a function of the stage and the causative agent. Postmortem examination may reveal diffuse pulmonary fibrosis and hypercellularity of alveolar septa and scarring of the interlobular septa and parts of the pleura. Severe chronic bronchitis and bronchiolitis also may be evident if concurrent airway disease exists, but this is typically not a feature of interstitial pneumonia.[482] Multifocal granulomata may be detectable.[480,483]

Treatment

The prognosis is poor for resolving the interstitial lung disorder. In one study of six adult horses presented to a veterinary clinic for chronic respiratory disease, one horse improved.[482] In another study, long-term glucocorticoid therapy improved the pulmonary disorder sufficiently to allow the horse to return to athletic performance.[485]

TUMORS OF THE RESPIRATORY SYSTEM

Causes

Based on postmortem surveys, the most frequently encountered equine tumors are sarcoids, squamous cell carcinomata, fibromata, melanomas, papillomata, fibrosarcomata, and lymphomata.[486-488] Neoplastic involvement of the pulmonary parenchyma or thoracic structures per se remains rare in horses, occurring at a prevalence rate of 0.15 to 0.62.[326,488]

Primary equine lung tumors include granular cell tumors (myoblastomata),[489-492] bronchial myxomata,[493] pulmonary carcinomata[486,494] pulmonary adenocarcinomata,[495,496] and pulmonary chondrosarcomata.[497,498] Primary thoracic tumors include pleural mesotheliomata,[432,499] thymomata,[326] and lymphomata.[326,500]

The incidence of primary lung tumors is much less than that of metastatic pulmonary tumors. The most common primary lung neoplasm is the granular cell tumor, with a prevalence rate of 0.15%. Most granular cell tumors involve the right lung, may be multiple or single masses, may be associated with airway obstruction, and are visible with endoscopic examination.[491,492] Based on immunohistochemical staining, granular cell tumors are thought to be composed primarily of myelinating Schwann cells with lesser numbers of scattered nonmyelinating Schwann cells.[501,502]

Metastatic lung tumors include adenocarcinoma (primary sites of origin are in the kidney, uterus, thyroid, ovary, and mammary gland),[323,324] hemangiosarcoma (primary sites of origin are in the skeletal musculature or are undetermined),[326,503-510] and lymphoma.[326,500]

Hemangiosarcoma remains a rare tumor, occurring in 2 in 1322 horses in a study by Sundbery, Burnstein, Page, et al.[487] and in 1 in 4739 cases in a survey reported by Hargis and McElwain.[506] Many of the reported cases of hemangiosarcoma involve horses less than 7 years of age.[503,507-510] Typically, horses exhibit pallor of the mucous membranes because of anemia, have evidence of pleural effusion (hemorrhagic fluid) or pulmonary hemorrhage,[508] and exhibit rapid clinical deterioration.

Although hemangiosarcoma may involve the thoracic cavity, the more common neoplasms include lymphoma and gastric squamous cell carcinoma.[326,511,512] Both tumors may be associated with the development of pleural effusion.

Clinical Signs

Horses with thoracic neoplasms may have a history of weight loss, inappetence, exercise intolerance, ventral edema, and intermittent fever. Depending on the tumor, physical examination may or may not reveal signs referable to the respiratory tract. In some cases, horses exhibited signs that were initially compatible with inflammatory airway disease, pleuropneumonia, and pulmonary epistaxis.[489,507,508] Hypertrophic pulmonary osteoarthropathy characterized by enlargement of the joints, bony swellings of the distal limbs, and generalized stiffness has been reported in cases of granular cell tumor.[513,514]

Diagnosis

Endoscopic examination may reveal the presence of masses occluding the bronchi, as in the case of primary granular cell tumors and bronchogenic carcinomata.[489,494] Pleuroscopy may reveal the extent of tumor involvement. Transtracheal aspirates, bronchoalveolar lavages, cytologic aspirates, histologic examination of biopsy specimens, and thoracocentesis may aid in the diagnosis. Radiographic or ultrasonographic evidence of multifocal interstitial densities (2 to 3 cm in diameter), tracheal elevation, or mediastinal densities also suggest neoplasms.

Treatment

The prognosis is poor for horses with neoplasms, and most patients are euthanized. In horses in which the tumor is localized and has a low metastatic potential, as exists with granular cell tumors, lung resection may be an option.[515] In cases with malignant effusion, the clinician may achieve temporary stabilization by thoracocentesis and possibly with pleurodesis (see the section on pleural effusion).

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