Diagnosis and Management of Bacterial Pneumonia in Adult Horses

Harold C. McKenzie III, DVM, MS, Diplomate ACVIM

Author's address: Marion duPont Scott Equine Medical Center, VA/MD Regional College of Veterinary Medicine, Virginia Polytechnic and State University, 17690 Old Waterford Road, Leesburg, VA 20176; e-mail: hmckenzi@vt.edu.

1. Introduction

Lower respiratory infections in adult horses often have an initial viral component because the effects of lower respiratory viral infections on local clearance and immune function may predispose to secondary bacterial involvement. Bacterial lower respiratory infections have greater clinical impact than viral infections because of the substantial risk of complications ranging from focal abscessation to pleuropneumonia. The development of complicated pneumonia cannot always be prevented, but, once present, requires early and aggressive intervention to achieve acceptable outcomes. Bacterial pneumonia can present substantial therapeutic challenges to the clinician that requires careful consideration of both patient factors and pharmacologic principles when formulating one's therapeutic plan.

2. Development of Disease

The respiratory tract is the largest mucosal surface in the body, with an enormous surface area constantly exposed to the external environment. The respiratory mucosa is exposed to large amounts of potentially infectious material because each breath carries thousands of microscopic particles and microorganisms into the respiratory tract. There are numerous mechanisms that function to minimize and mitigate this exposure, thereby preventing disease. The normal defense mechanisms consist of the barrier represented by the filtration provided by the upper respiratory tract, the physical barrier represented by the epithelial lining fluid and the respiratory mucosa, and the innate and specific immune responses that eliminate or inactivate infectious organisms that reach the lower respiratory tract. The development of infectious lower respiratory tract infections requires that these respiratory tract defenses be overcome, and this may occur as a result of impairment of the defenses or by overwhelming exposure.

Viral respiratory infections can impair mucociliary clearance and suppress local immunity within the lower respiratory tract, thereby creating an environment favoring the development of secondary infections.[1] Transport represents a well-described risk factor for lower respiratory infections, due to the combined effects of prolonged periods of head elevation, which physically impairs lower respiratory clearance, with the immunosuppressive effects of physiologic stress.[2] Management situations that result in the intermingling of large numbers of horses increase the risk of exposure to potential pathogens and induce stress that impairs pulmonary immunity. Individuals undergoing anesthesia are at risk of lower respiratory infections due to

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the temporary loss of the filtering function of the upper respiratory tract and the immunosuppressive effects of general anesthesia.[3] Horses with dysphagia are also susceptible to lower respiratory tract infections caused by aspiration of foreign material and large numbers of bacteria.

Inhaled or aspirated bacteria from the upper respiratory tract are the primary causes of bacterial pneumonias in adult horses, unlike the situation in neonates, in which bacterial pneumonias are often of hematogenous origin. These infections develop initially on the surface of the respiratory mucosa but often progress to involve the pulmonary parenchyma. Pulmonary abscessation can develop in situations in which physical and immunologic clearance of the infectious organisms is incapable of completely resolving the infection. Pleuropneumonia develops when inflammation-associated injury to the lung tissue secondary to bacterial bronchopneumonia breaks down the lung parenchyma and visceral pleura, allowing the infectious organisms access to the pleural space. When infection extends into this space, it is difficult to resolve because it is difficult for the immune system to mount an effective immunologic response at this site, and the accumulation of inflammatory cells and serous fluid within the pleural space provides an expanding reservoir for infectious organisms.

3. Diagnostic Evaluation

The clinical signs of pneumonia may include fever, cough, nasal discharge, tachypnea, dyspnea, depression, anorexia, and pain on palpation of the thoracic wall (pleurodynia). The physical examination is key in determining the extent and severity of lower respiratory tract involvement, and this should include a rebreathing examination in most cases. The rebreathing test will greatly enhance the clinician's ability to detect lower respiratory inflammation on auscultation. This test should be avoided in patients that are exhibiting severely increased respiratory effort at rest. The presence of a cough on rebreathing is indicative of large airway inflammation/irritability. Abnormal breath sounds indicate the presence of lower respiratory inflammation, with wheezes occurring as the result of small airway narrowing and crackles being secondary to the presence of fluid material in the small airways. The presence of very loud airway sounds or the absence of airway sounds may indicate the presence of consolidated lung tissue or pleural effusion. The percussion test should not be overlooked as a simple tool that can facilitate the identification of consolidated lung and/or pleural effusion. Reluctance to move or the presence of pleural pain on palpation and/or percussion may indicate the presence of pleural inflammation.

Clinical pathology is important in evaluating the animal with lower respiratory tract disease, with leukocytosis, neutrophilia, left shift, and hyperfibrinogenemia often accompanying the progression of lower respiratory bacterial infections. Arterial blood gas analysis may reveal hypoxia and hypercapnea in patients with diffuse lower respiratory inflammation. Imaging studies may aid in the staging and localization of lower respiratory infections, with ultrasonography being particularly useful in assessing the superficial pulmonary tissues and the pleural cavity. This can be performed in the field, and even a linear reproductive probe can provide useful images when oriented lengthwise within the rib spaces. Thoracic radiographs are more challenging to obtain and are often not available in the field setting but provide a more global assessment of pulmonary inflammation, allowing for evaluation of the lung tissue below the pleural surface. The sensitivity and specificity of radiographs can be low at times, however. Radiography is most useful in the detection of pathology deep within the lung and can be critically important in the diagnosis of conditions such as pulmonary abscessation, neoplasia, and equine multinodular pulmonary fibrosis.

Though not usually required in the initial evaluation of patients with lower respiratory disease, airway cytology is critical in the assessment of severe or persistent lower respiratory infections. Airway cytology provides a clearer indication of the character of pulmonary inflammation, especially regarding the predominant type of inflammatory cells and the presence and type of bacteria, and is strongly indicated in patients that have undergone an unsuccessful course of antimicrobial therapy or those presenting with evidence of severe lower respiratory infection. Tracheal aspirates are easily obtained in a sterile manner by either the percutaneous approach or the endoscopic approach, using a guarded endoscopic aspiration catheter, allowing for culture of the sample. Bronchoalveolar lavage is less commonly used for the assessment of lower respiratory infections because of the potential for contamination occurring when the sampling device is advanced through the upper respiratory tract that renders culture results suspect. Despite this limitation, the use of bronchoalveolar lavage can provide an important indication of small airway inflammation and involvement, and the presence of suspected focal pulmonary involvement is an indication for bronchoscopy and directed bronchial lavage.[4]

Thoracocentesis is indicated in cases in which there is documented evidence of pleural fluid accumulation. This procedure can have both diagnostic and therapeutic applications because it yields a sterile sample for cytology and culture but also allows for the removal of fluid from the pleural cavity. Draining of pleural effusion can be beneficial in decreasing the degree of pulmonary dysfunction, increasing patient comfort, and removing large amounts of inflammatory debris and large numbers of bacterial organisms. Sterile lavage of the pleural cavity through an indwelling thoracic drain can help to remove additional inflammatory debris, and antimicrobials can be added to the lavage fluid to achieve high local concentrations in the pleural cavity.

Repeated airway cytology can also be useful in documenting the status of lower respiratory inflammation but should not be required in most cases showing clinical resolution. Changes in clinical status often represent important indicators in the progression of lower respiratory infections, however, and these include persistence and/or worsening of fever, changes in the character of coughing, and signs of systemic inflammation. Such changes in clinical status represent an indication for thorough reassessment of the patient, potentially to include physical examination, clinicopathologic evaluation, imaging studies, and collection of respiratory secretions for cytological assessment and culture.

4. Therapy

Rest represents a critical component of the therapeutic plan for any lower respiratory infection, regardless of etiology, because the resolution of infection may take 1 to 2 weeks or more, and the resolution of inflammation and healing of the respiratory epithelium may require an additional 2 to 4 weeks. Exercise before full resolution can expose the lower respiratory tract to cold, dry air and high-flow volumes, potentially resulting in further respiratory epithelial injury and a resurgence of lower respiratory inflammation.[5] This inflammation could create an environment conducive to the recurrence of infection or the development of secondary infection. Simple management tools may be of benefit as well, and these would include feeding a diet that minimizes the volume of inhaled antigenic material, such as a chopped forage or pelleted feed, as well as feeding from the floor level to encourage drainage of secretions from within the trachea. Bedding the stall in a low-dust material such as wood shavings, cardboard, or newspaper will decrease the volume of environmentally inspirable particles, potentially decreasing the antigenic load on the lower respiratory tract.[6]

The treatment of bacterial lower respiratory infections obviously depends on antimicrobial therapy, but delivery of antimicrobials to the site of infection can be challenging because of the barrier by the respiratory epithelium.[7] The presence of infection and/or inflammation can enhance the ability of antimicrobials to cross the epithelium, but this effect may lessen as the inflammation resolves, impairing antimicrobial delivery at the stage of final bacterial eradication. Therefore, the choice of antimicrobial is dictated not only by a presumptive or established sensitivity pattern but also by an understanding of the drug's intrapulmonary pharmacokinetics.[8] Penicillins, cephalosporins, and aminoglycosides[9] penetrate only poorly into bronchial lining fluid, whereas macrolides[10] and fluoroquinolones[11] can accumulate in the bronchial lining fluid and airway macrophages to concentrations greater than the peak serum concentration. Other classes of antimicrobials, specifically the tetracyclines and potentiated sulfas, are expected to penetrate fairly well into respiratory secretions but only to levels less than observed in the systemic circulation.[12] Because anaerobic involvement is likely in cases of pleuropneumonia, the treatment regimen should include agents that will address this type of bacteria. Metronidazole is effective and well tolerated and represents the gold standard for therapy of anaerobic infections.

Alternate routes of administration may be utilized to achieve high concentrations of antimicrobials within the bronchial lumen, including intrabronchial and aerosol delivery.[4,13] Concentration-dependent antimicrobials are preferred for intrapulmonary administration, with aminoglycosides being most commonly used in the horse.[13,14] Time-dependent antimicrobials such as the cephalosporins may be used by the intrapulmonary route but probably will require more frequent dosing, with ceftiofur typically being administered at 12-hour intervals.[14]

Once an appropriate antimicrobial regimen has been selected, care should be taken to ensure that the duration of therapy is adequate to ensure eradication of the infectious organisms within the lung, which may take as long as 7 to 14 days for uncomplicated pneumonias but can require weeks to months in cases of pleuropneumonia. Repeated airway cytology may be useful in monitoring the response to antimicrobial therapy because the determination of resolution can be challenging, based on clinical grounds alone.

Ancillary therapies such as bronchodilators and anti-inflammatories are not indicated in all cases of lower respiratory infection and may be counterproductive by masking the clinical signs of lower respiratory involvement and encouraging owners or trainers to exercise these horses before healing is complete. Horses exhibiting severe dyspnea or airway hyperreactivity may benefit from bronchodilatory therapy, however, because this may aid in minimizing the severity of ventilation/perfusion mismatching as well as lessening the airway response to irritation. The beta-2 agonists (albuterol, clenbuterol) are frequently used because they are readily administered and have additional benefits, including enhancement of mucociliary clearance. The author prefers the aerosol route to the systemic route to achieve an immediate effect and to avoid systemic toxicity. The beta-2 agonists should not be administered continuously for more than 3 to 4 weeks regardless of route because of the downregulation of the beta-2 receptors on the airway smooth muscle cells, which results in a loss of responsiveness to these drugs. Anticholinergics, such as ipratropium bromide, are very useful and can be used alone or in combination with a beta-2 agonist. Ipratropium bromide can only be administered as an aerosol, most commonly using a metered-dose inhaler. The aerosol route minimizes the risk of ileus associated with other anticholinergics and provides very effective bronchodilation for up to 8 hours. Combination therapy with a be-

ta-2 agonist provides for a rapid but short-term effect (1.5 hours) from the beta-2 followed by a longer-term effect from the anticholinergic (2 to 8 hours).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used in the treatment of bacterial lower respiratory infections, primarily to aid in suppressing fever and to decrease patient discomfort. There is some evidence from other species that NSAIDs not only control fever but also improve the clinical signs associated with lower respiratory infections and modulate the inflammatory response, both within the lower respiratory tract and systemically.[15,16] Flunixin meglumine is the NSAID most commonly used by the author in adult horses and appears to be effective while also exhibiting reasonable safety. Firocoxib is a promising new drug that appears to be clinically effective as an analgesic, but less is known about the anti-inflammatory capability of this drug when treating bacterial infections. Regardless of the drug used, care should be taken to discontinue NSAID therapy as soon as it is no longer clearly indicated because of the risk of renal and gastrointestinal toxicity. Care should be taken when monitoring the response to treatment in patients on NSAID therapy because the suppression of fever by NSAIDs may be interpreted as a positive response to antimicrobial therapy. For this reason, it is recommended to monitor the patient's rectal temperature immediately before administration of the next dose of NSAID because one may be able to appreciate an upward trend in the temperature at this time that would otherwise be missed.

Immunomodulatory therapy may be of some benefit in shortening the time to recovery, and, although well-controlled studies are lacking, these compounds are used in many settings. Examples would include *Propionibacterium acnes* preparations[a], mycobacterial cell wall extracts[b], *Parapoxvirus ovis* preparations[c], and products with undefined bacterial components (BI-KB®, Bacterial Immunomodulator–Killed Bacteria).

5. Prevention

Management is critical in reducing the incidence of viral respiratory infections, specifically Equine Influenza virus and Equine Herpes viruses 1 and 4 to decrease the risk of secondary bacterial infections. Quarantine of new arrivals on the farm for a minimum of 2 weeks decreases the likelihood of exposure for the resident horses on the farm and is critical in situations with frequent travel and high turnover. Vaccination, though not consistently effective in preventing disease, may be helpful in enhancing the individual's immunity to these viruses and lessening the severity of clinical disease and may aid in slowing the spread of disease throughout the farm population after exposure. High stocking densities should be avoided because these promote the spread of infectious respiratory diseases. Transport should include periods of rest at intervals of every 6 to 8 hours, during which time horses are allowed to lower their heads to eat and drink. There may be some benefit to the use of immunomodulators before transport to enhance lower respiratory immunity during this period of stress. Horses with suspected viral respiratory disease should be closely monitored for changes in their condition, such as persistence of fever beyond the first 2 to 3 days or a change in the character of the cough to moist and productive, because these changes may signal the onset of secondary bacterial infection.

References and Footnotes

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[a]Eqstim®, Neogen Corporation, 944 Nandino Blvd., Lexington, KY 40511-1205.
[b]Equimune IV®, Bioniche Animal Health Inc., 1551 Jennings Mille Rd., Bogart, GA 30622.
[c]Zylexis®, Pfizer Animal Health, Exton, PA 19341.