

# Recurrent Airway Obstruction (Heaves)\*

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**H**eaves is the layman's term for allergen-induced airway obstruction in mature horses. Alternative terms for the condition include *recurrent airway obstruction*, *chronic obstructive pulmonary disease* (COPD), *emphysema*, and *broken wind*. *Recurrent airway obstruction* and *heaves* are the preferred terms; the terms *emphysema* and *COPD* have fallen out of favor because the pathogenesis of heaves differs from that of these human conditions. The pathophysiology of heaves is small airway inflammation and bronchoconstriction in response to allergen exposure. The most common environmental factor to precipitate an episode of airway obstruction in heaves-affected horses is organic dust from moldy hay and straw. A similar syndrome, termed *summer pasture-associated obstructive pulmonary disease* (SPAOPD), occurs in pastured horses in the southeastern United States and may be triggered by mold spores on grass.

Horses with classic heaves present with flared nostrils, tachypnea, wheezing, and a heave line. The typical respiratory pattern is characterized by a prolonged, labored expiratory phase and a short inspiratory phase. Intrapleural pressures are positive during expiration, contributing to the collapse of inflamed/constricted small airways and

preventing expulsion of air from the lower respiratory tract. The abdominal muscles are recruited to assist with expiration, and hypertrophy of the external abdominal oblique muscles produces the classic heave line. Wheezes are generated by air-flow through narrowed airways and are most pronounced during expiration. Crackles are often present and are associated with excessive mucus production. Just as in humans with asthma, there is a broad spectrum of sensitivity to antigens and severity of clinical signs. Mild to moderately affected horses may present with minimal clinical signs at rest, but coughing and exercise intolerance are noted during performance.

## DIAGNOSTIC CRITERIA

### Historical Information

**Breed and Gender Predispositions:** None.

**Age Predisposition:** Average age of onset is 9 years.

**Genetic Predisposition:** The incidence of heaves in horses with two affected parents is approximately 40%; in those with healthy parents, it is approximately 10%. A candidate gene (interleukin-4, receptor  $\alpha$ ) with potential locus heterogeneity for heaves has been identified, which may allow breeding decisions in the future.<sup>1</sup>

### Other Predispositions/Considerations:

- The prevalence of heaves is unknown (range 12% to 80%) and is likely to vary geographically.

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<sup>a</sup>Dr. Rush discloses that she has received an honorarium from Fort Dodge Animal Health within the past 3 years.

- Clinical signs may wax and wane with changes in weather and housing.

**Owner Observations:** The most common presenting complaints include cough, exercise intolerance, and respiratory distress.

## Physical Examination

### Findings

Affected horses are usually alert and afebrile. Signs include:

- Respiratory difficulty (pronounced double effort of expiration).
- Flared nostrils.
- Heave line (from hypertrophy of abdominal muscles).
- Wheezing (most prominent during expiration).
- Coughing, especially during exercise or eating.

### Laboratory Findings

- Complete blood count (CBC) and serum chemistry analysis results are usually unremarkable in horses with heaves. Horses with secondary bacterial infection have a moderate elevation in white blood cell count and serum fibrinogen concentration.
- Bronchoalveolar lavage (see box on page 200 and Figure 1) should be performed in horses with mild to moderate disease (exercise intolerance) to confirm the presence of lower airway inflammation. Heaves-affected horses demonstrate neutrophilic inflammation (20% to 90% neutrophils). Curschmann's spirals may be observed on cytologic evaluation and represent inspissated mucus/cellular casts from obstructed small airways. Bronchoalveolar lavage may be helpful

### Bronchoalveolar Lavage

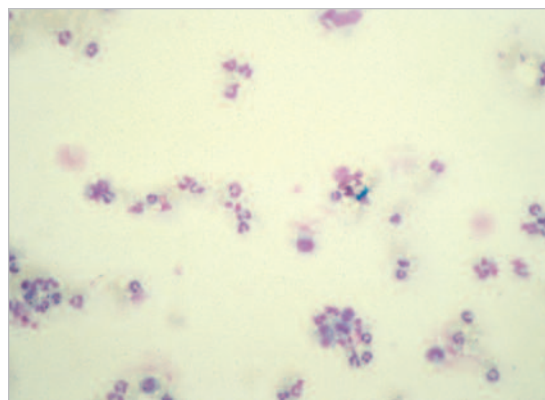
- Bronchoalveolar lavage is performed using a 300-cm, 10-mm diameter bronchoalveolar lavage catheter with an inflatable cuff (Bivona Inc., Gary, IN).
- Horses are sedated with IV xylazine hydrochloride (0.4 mg/kg) and restrained with a nose twitch.
- The catheter is passed through the nasal passage into the lower airways and advanced until it is wedged in a fourth- to fifth-generation airway.
- Sterile, isotonic fluid (300 mL) is infused by hand and recovered via immediate manual aspiration.
- Differential cell counts should be determined using slides prepared by cytocentrifugation and Wright's-Giemsa stain.
- Cytologic characteristics of bronchoalveolar lavage fluid from a normal horse include the following:
  - Macrophages and lymphocytes constitute 60% to 70% and 30% to 40% of the total cell count, respectively.
  - Neutrophils constitute <5% of the total cell count.
  - Mast cells, eosinophils, and epithelial cells may occasionally be present.

in differentiating low-grade heaves from lungworm infestation or eosinophilic pneumonitis.

- Bronchoalveolar lavage should be avoided in horses with respiratory distress.
- During a period of clinical exacerbation, arterial blood gas analysis reveals:
  - Hypoxemia (50 to 80 mm Hg; normal: 95 to 100 mm Hg).
  - Normocapnia (normal: 40 mm Hg).

### Other Significant Diagnostic Findings

- **Thoracic radiography** reveals peribronchial infiltration and overexpanded pulmonary fields (flattening of the diaphragm). Thoracic radiographs are of little benefit in confirming the diagnosis of heaves but may be helpful in eliminating diagnostic differentials such as interstitial pneumonia, pulmonary fibrosis, or bacterial pneumonia.
- **Transtracheal wash** provides little assistance in differentiating heaves from infectious respiratory disease. Both conditions have neutrophilic inflammation, and bacterial culture of tracheal aspirates from heaves-affected horses often recovers opportunistic pathogens, including *Streptococcus zooepidemicus* and *Actinobacillus* spp.



**Figure 1. Bronchoalveolar lavage from a horse with recurrent airway disease.** (Neutrophil count: >70% [normal: <5%]; Wright's-Giemsa stain; original magnification  $\times 20$ ).

- **Forced oscillatory mechanics and bronchoprovocation challenge** may be used at referral centers to detect hyperreactive airways in performance horses with exercise intolerance due to small airway inflammation. In this system, pulmonary function (forced oscillatory mechanics) is determined after aerosolization of incremental doses of histamine. In horses with airway hyperreactivity, lower doses of aerosolized histamine induce more rapid deterioration in pulmonary function compared with the response of normal horses.
- Horses rarely (2%) develop a patent infection; however, larvae may be identified using Baermann sedimentation of feces or cytologic evaluation of bronchoalveolar lavage fluid.
- Eosinophilic pulmonary inflammation may be identified via bronchoalveolar lavage; peripheral eosinophilia may be observed on CBC.

#### Bacterial Pneumonia

- Clinical signs include fever, depression, and anorexia.

### Summary of Diagnostic Criteria

- In most horses, diagnosis is based on history, physical examination, and unremarkable serum chemistry analysis and hematology findings.
- Horses that fail to respond after 14 days of treatment should be reevaluated. Thoracic radiographs should be obtained to determine if pulmonary fibrosis or interstitial infiltration is present.
- Bronchoalveolar lavage should be performed in horses that appear normal at rest but demonstrate poor performance and cough during exercise. Neutrophilic inflammation (>20% of total cell count) confirms the presence of lower airway inflammation.

### Differential Diagnosis

#### Interstitial Pneumonia

- *Restrictive* pulmonary disease that produces *inspiratory* difficulty.
- Thoracic radiographic examination reveals marked interstitial pattern with discrete or diffuse nodular infiltration.

#### Lungworm (*Dictyocaulus arnfieldi*) Infestation

- History includes exposure to donkeys.

**Table 1. Aerosolized Bronchodilators**

Drug	Dosage	Notes
<b>Short Acting (rescue therapy)</b>		
Albuterol	360–900 µg q4–6h for 14 d	Powerful, rapid onset (5 min); duration of action: 1 h
Fenoterol	1,000–1,500 µg q4–6h for 14 d	—
<b>Long Acting</b>		
Ipratropium	180 µg q4–6h for 14 d	Onset of action: approximately 30 min; duration of action: 4–6 h

- CBC reveals leukocytosis with mature neutrophilia and increased serum fibrinogen concentration.
- The typical obstructive breathing pattern is less likely to occur with bacterial pneumonia.

### Inflammatory Airway Disease (IAD)

- Characterized by poor performance and mucus in the lower respiratory tract.
- Bronchoalveolar lavage should be performed in horses with IAD to determine the type of airway inflammation. Cytologic evaluation will dictate the therapeutic plan.
- Horses with IAD may have mast cell (2% to 5% of the total cell count), eosinophilic (10% to 40% of the total cell count), or neutrophilic (10% to 15% of the total cell count) inflammation.
- Horses with neutrophilic IAD may be difficult to distinguish from horses with low-grade heaves.
- In general, horses with IAD are a younger population than horses with heaves, and the condition is transient rather than recurrent.

## TREATMENT RECOMMENDATIONS

The single most important treatment is environmental management to reduce allergen exposure. Medication will alleviate clinical signs of disease, but respiratory disease will return after medication is discontinued if the horse remains in the allergen-challenged environment. The most common offending agent is organic dust from moldy hay and straw. Hay does not have to appear overtly moldy to precipitate an episode in a sensitive horse. If possible, horses should be maintained at pasture with fresh grass as the source of roughage. Round bale hay is particularly allergenic and a common reason for treatment failure in horses on pasture. Horses that must be kept in a stall should be maintained in a con-

trolled environment and fed soaked hay, hay cubes, or a pelleted diet.

In the southeastern US Gulf Coast states, the offending allergens may be molds present on pasture grasses from July through September (summer pasture-associated obstructive pulmonary disease [SPAOPD]). Horses that develop signs of airway obstruction on pasture in this part of the country should be managed in a controlled stall environment and offered soaked hay, hay cubes, or a pelleted diet. Some horses with SPAOPD are also sensitive to the molds present in hay and straw.

The key to remission of clinical signs in horses suffering from recurrent airway obstruction is reduced inflammation. Pulmonary inflammation is the underlying pathophysiology of bronchoconstriction, and excessive mucus production contributes to obstructed airflow. Drug therapy should consist of an **antiinflammatory agent** and a **bronchodilator**. It is inappropriate to chronically administer bronchodilators as solo therapy; bronchodilators do not address the underlying inflammatory process and do not provide prolonged relief from airway obstruction, and some drugs have adverse effects.

### Treatment of Respiratory Distress

#### Corticosteroid Therapy

Systemic corticosteroids (dexamethasone) and aerosolized corticosteroids (beclomethasone dipropionate and fluticasone) have proven beneficial in the treatment of recurrent airway obstruction based on pulmonary function testing and bronchoalveolar fluid analysis results and improved airway hyperresponsiveness. Systemic corticosteroids are considered more effective for severe cases of respiratory distress because pulmonary distribution of aerosolized medication is poor in horses with severe airway obstruction. Aerosolized corticosteroids are effective in horses with mild to moderate air-

way obstruction because they deliver the drug directly to the respiratory tract. Aerosolized corticosteroids have become an integral part of therapy in humans with asthma. Humans treated with aerosolized corticosteroids do not develop the systemic side effects associated with adrenosuppression. However, the sensitivity of horses to aerosolized corticosteroids is evidenced by adrenosuppression.

- Dexamethasone—0.05 to 0.1 mg/kg IV q24h until the horse is breathing more comfortably (2 to 3 days), followed by administration every other day for 14 days. Dexamethasone administration has been shown to improve pulmonary function within hours and reduce pulmonary inflammation within 3 to 7 days.
- Aerosolized beclomethasone dipropionate—1,500 to 3,500 µg given twice daily when using the aerosol delivery device AeroMask Equine System. Beclomethasone therapy has been shown to reduce pulmonary inflammation and improve pulmonary function as well as produce clinical improvement within 24 hours after initiation of treatment.
- Aerosolized fluticasone propionate—2,000 µg given twice daily. Fluticasone therapy has resulted in reduced pulmonary neutrophilia, improved pulmonary function, and reduced airway hyperresponsiveness with possibly fewer systemic side effects.

### **Aerosolized Bronchodilator Therapy (Table 1)**

Bronchoconstriction plays an important role in the pathophysiology of recurrent airway obstruction in horses. The relief of smooth muscle contraction through bronchodilator therapy improves clinical signs. Combined short-acting (rescue therapy) and long-acting aerosolized bronchodilators should be used to treat horses with severe airway

obstruction. Anticholinergic agents and  $\beta_2$ -adrenergic agonists are considered to be the most reliable bronchodilators.

- Albuterol sulfate is the most commonly used short-acting  $\beta_2$ -adrenergic agonist. The beneficial effects of albuterol may last for up to 1 hour. In cases of severe airway obstruction, albuterol may be administered every 15 minutes for up to 2 hours.
- Ipratropium bromide is an antimuscarinic bronchodilating agent that improves pulmonary function by 50% within 60 minutes, with beneficial effects lasting 4 to 6 hours.



**Table 2. Treatment of Horses with Mild to Moderate Disease**

Drug	Dosage	Notes
<b>Inhalation Therapy</b>		
<b>Corticosteroids</b>		
Beclomethasone	1,500–3,500 µg bid for 14 d	
Fluticasone	2 mg bid for 14 d	
<b>Bronchodilators<sup>a</sup></b>		
Ipratropium	180 µg q4–6h for 14 d	Onset of action: approximately 30 min; duration of action: 4–6 h
Salmeterol	210 µg bid for 14 d	Onset of action: approximately 30 min; duration of action: approximately 8 h
<b>Systemic Therapy</b>		
<b>Corticosteroids</b>		
Prednisolone	1–2 mg/kg PO sid for 7 d, followed by 1 mg/kg PO every other day for 7 d	
Dexamethasone	0.05–0.1 mg/kg IV sid; 0.165 mg/kg PO q24h for 7 d <sup>b</sup>	
<b>Bronchodilator</b>		
Clenbuterol	0.8–1.6 µg/kg PO bid for 14 d	

<sup>a</sup>Long-acting bronchodilators should be administered twice daily and 30 min before exercise in horses with mild to moderate airway obstruction.

<sup>b</sup>Deluca L, Erb HN, Young JC, et al. The effect of adding oral dexamethasone to feed alterations on the airway cell inflammatory gene expression in stabled horses affected with recurrent airway obstruction. *J Vet Intern Med* 2008;22(2):427–435.

- Recommended dosages for other aerosolized drugs in Table 1 are based on administration with the AeroMask Equine System.

### Treatment of Horses with Mild to Moderate Disease (Table 2)

Horses with mild to moderate disease can be treated with inhalation therapy or systemic drugs. Aerosolized drugs reduce the total therapeutic dose and allow direct delivery of the drug to the lower respiratory tract but are generally more expensive.

#### Aerosol Delivery Devices

- **The AeroMask Equine System** (Trudell Medical, Ontario, Canada) is a versatile delivery system because it can be used for administration of aerosolized drugs via metered dose inhalers (MDIs) and nebulization solution. The mask must fit snugly around the muzzle to ensure adequate negative inspiratory pressure to

facilitate drug delivery and may cause distress in horses with respiratory difficulty.

- **The Equine Haler** (Equine Healthcare APS, Hillerød, Denmark) is a spacer device that fits over the entire left nostril of the horse and is designed for administration of an aerosolized drug using any human MDI. Unlike the AeroMask, the Equine Haler can accommodate any size horse without difficulty in creating an airtight seal over the muzzle. Pulmonary drug delivery can be poor if the administrator does not align the MDI with the spacer and the spacer apparatus with the nasal passages.

#### Patient Monitoring

Horses should be breathing more comfortably within 2 to 5 days of initiation of treatment and environmental change.

- **Failure to respond within 7 days:** Drug therapy and management changes should be reevaluated.

- **Failure to respond within 14 days:** Diagnosis should be reevaluated.

### Farm Management

Horses with heaves should be maintained on pasture with grass as their primary source of roughage. Round bale hay should be removed from the pasture. Although horses with heaves are not allergic to “dust,” their airways are hyperreactive to nonspecific stimuli, and they should not be pastured near a dry, dusty road or paddock. Horses maintained in a stall (SPAOPD or heaves) should not be housed in a building with an indoor arena, and hay should not be stored overhead. Straw bedding should be avoided. If hay is fed, it should be soaked with water and fed from the ground.

### Milestones/Recovery Time Frames

- There is no cure for heaves.
- The primary goal of therapy is to prevent episodes of airway obstruction by avoiding allergen exposure.
- Moderate to severely affected horses will have two to three episodes of airway obstruction per year that require medical therapy, despite efforts to control environmental allergens.

### Treatment Contraindications

- NSAIDs are ineffective to reduce pulmonary inflammation in horses with recurrent airway obstruction.
- Antihistamines have demonstrated minimal to no efficacy for horses with classic heaves.

## PROGNOSIS

### Favorable Criteria

- Rapid response to treatment (<48 hours).

### Unfavorable Criteria

- Failure to respond to therapy within 14 days.
- Relapse of clinical signs after discontinuation of medication despite environmental management.

## REFERENCE

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## RECOMMENDED READING

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