How to Diagnose Mild and Moderate Equine Asthma as a Cause of Poor Performance in Sport Horses

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1. Equine Asthma—Name Change
The chronic, non-infectious lower airway diseases of horses have been known under different names over the years and cause great confusion in both the equine veterinary scientific and lay communities. For these reasons, the medical term “equine asthma” is now being used to foster better communication between all stakeholders.\textsuperscript{1-3} Based on severity, the term “severe equine asthma” is now used to describe the condition previously known as heaves or recurrent airway obstruction (RAO; equine COPD, chronic bronchitis, equine emphysema, etc.), while “mild and moderate equine asthma” are used to describe what was known as “inflammatory airway disease (IAD).” “Moderate equine asthma” describes the condition of horses with clinical signs (e.g., cough) or clinical findings (abnormal lung sounds) of a lung disease but without the presence, or a history, of labored breathing at rest. The term “mild equine asthma” is used for horses presenting exercise intolerance and a lower airway inflammation or obstruction but without obvious clinical signs suggestive of lung diseases. Equine asthma may further be defined based on the triggering factors (barn/hay and pasture) and the inflammatory cells in bronchoalveolar fluid cytology (neutrophilic, mastocytic, eosinophilic, mixed granulocytic, and pangranulocytic). Other phenotypes (clinical findings) and endotypes (mechanistic pathways) are emerging in equine asthma and may eventually lead to personalized therapy.\textsuperscript{4}

2. Main Features
Inhalation of the offending antigens, especially those present in hay and bedding during stabling, causes inflammation and obstruction of the airways. This in turn is responsible for the development of the clinical signs observed in equine asthma, which include exercise intolerance and, for the more severe syndrome, cough, increased respiratory rate, and labored breathing at rest. While the severity of the clinical signs may progress in genetically susceptible horses, the condition may be transient or intermittent in some horses or even persist without further progression in mild and moderate equine asthma. The time between exposure and the development of clinical signs is variable, as is the severity of airway hyperreactivity and inflammation. While strong epidemiological studies are lacking, it has been proposed that up to 75-80\% of horses will develop milder forms of equine asthma in their lifetime.\textsuperscript{3} Recent findings suggest that inflammation-induced airway structural changes (remodeling) may be responsible for the progression of equine asthma in some horses.\textsuperscript{5}
3. How to Diagnose Moderate Equine Asthma

The diagnosis of moderate equine asthma is usually straightforward and is based on the presence of a chronic cough in an otherwise healthy horse. It is confirmed by demonstrating inflammation using bronchoalveolar lavage fluid (BALF) cytology. Exercise intolerance and tachypnea after exercise may also be present. Bloodwork, thoracic ultrasound, and radiographs are normal. Clinical signs include intermittent or frequent coughing episodes at rest, when eating, or during exercise. Physical examination may reveal a bilateral, intermittent, or persistent serous or seromucous nasal discharge. A tachypnea at rest, but without nasal flaring or increased abdominal excursions as in severe asthma, may be present. Thoracic auscultation may reveal localized or generalized crackles and wheezes when using a rebreathing bag. Physical examination is otherwise unremarkable. These findings indicate the presence of a lower airway condition and should raise suspicion for equine asthma. BALF cytology revealing increased percentages of neutrophils, mast cells, or eosinophils is confirmatory for the diagnosis of moderate equine asthma when combined with the presence of respiratory signs. In absence of BALF cytology, increased amount of tracheal mucus on endoscopy combined with a positive response to therapy is supportive of the diagnosis.

4. How to Diagnose Mild Equine Asthma

Mild equine asthma is a diagnostic challenge as decreased exercise tolerance or poor performance with a prolonged recovery period after exercise are the only presenting clinical signs in athletic horses. Because of the absence of clinical signs suggestive of a lung condition, it is a largely overlooked cause of exercise intolerance in high performance horses. The diagnosis is based on the presence of exercise intolerance and lower airway inflammation documented by an abnormal BALF cytology, combined with the exclusion of other common causes of exercise intolerance (upper airway obstruction, lameness, myopathy, cardiac pathology, arrhythmia, etc.). History, physical examination, and CBC and blood biochemistry are otherwise unremarkable. When present, crackles or wheezes on thoracic auscultation using a rebreathing bag or increased tracheal mucus on endoscopy will lead the clinician to investigate the lungs, but these findings are inconsistent. The response to therapy (decreased inhaled antigens and noxious gas, corticosteroids, bronchodilators) will often be required to confirm the diagnosis.

5. Diagnostic Aids for Equine Asthma

Bronchoalveolar Lavage Fluid Cytology

The different techniques used to collect BALF (type, volume, and temperature of the fluids, how it is infused and aspirated from the lower airways—syringe, pump, or tube of videoendoscopy—the method for the preparation—cytospins, sedimentation, smears—and staining of the cytopreparation, how the differential cell count is made, as well as the experience of the cytologist) may influence the BALF differential cell counts. For these reasons, there are no universal “normal values” for BALF cytology in horses. Of note, lower airway inflammation may have numerous causes and represents a normal response to inhalation of irritants, noxious gas, and various microbes. For these reasons, lower airway inflammation without the presence of abnormal clinical signs is not considered sufficient for a diagnosis of equine asthma. Nevertheless, the recent report that increased percentages of mast cells, and to a lesser extent, neutrophils, in BALF cytology of Thoroughbred racehorses was associated with decreased racing speed suggests that lower airway inflammation of any causes may lead to impaired performance. Inflammation documented from tracheal washes or aspirates is not considered appropriate for the diagnosis of equine asthma.

Tracheal Mucus on Endoscopy

The presence of tracheal mucus has been associated with decreased performance in sport horses. Excess tracheal mucus (score >1/5 for racehorses and >2/5 for sports/pleasure horses) is common in horses with mild and moderate asthma, but mucus accumulation may have many other causes. Therefore it has low sensitivity and specificity for diagnosis of severe equine asthma, but its presence is suggestive of the condition.

Airway Obstruction

The poor performance caused by equine asthma results from a decreased gas exchange in the alveoli due to airflow impairment. The asthma diagnosis would therefore be based ideally on the documentation of lower airway obstruction. Different methods have been developed to measure the airway function of horses. Bronchoprovocation with histamine or methacholine, lung mechanics detected using a rebreathing method, airflow measured after forced expiration, and PaO2 and decreased VO2 peak during exercise have been used for the diagnosis of mild and moderate equine asthma. However, their use is currently limited by the specialized equipment and expertise they require, lack or portability, or commercial availability.

Blood Biomarkers

Blood biomarkers may facilitate the diagnosis of equine asthma in clinical practice as there is evidence of systemic inflammation in affected horses. While more work is needed, the combination of acute phase proteins including serum amyloid A (SAA), haptoglobin, and C-reactive protein (CRP), with lung specific biomarkers such as surfactant protein (SP)-D and secretoglobin, appear promising. Of note, high concentrations of SAA and other acute phase proteins may be indicative of infection rather than equine asthma.
Performance Testing

Performance testing is increasingly available at referral centers or to individual practitioners and may help identify the cause of exercise intolerance. Diagnostics may include dynamic videoendoscopy with structured exercise testing and exercising heart rate, VO_{2} peak, ECG, arterial blood gases, and stress echocardiography.

Endobronchial Biopsies

The presence of a remodeling of the epithelium, the lamina propria, and the bronchial smooth muscle layer in the central and peripheral airways of horses with severe asthma is well documented. These structural changes correlate with decreased lung function in affected horses. Using endobronchial biopsies, which are easy to collect and are well tolerated by horses during bronchoscopy, it was recently observed that a remodeling of the airways is also present in the milder forms of asthma. Follow-up studies would be required to determine whether these tissue changes allow prognosticating on the outcome or are useful for the implementation of specific therapy (precision medicine).

6. Conclusion

Mild and moderate asthma are common and under-diagnosed causes of exercise intolerance in performance horses. The diagnosis is based on the presence of compatible clinical signs, lower airway inflammation documented by BALF cytology, and the exclusion of other causes of exercise intolerance. Response to therapy may be required to confirm the diagnosis.

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Declaration of Ethics

The Author has adhered to the Principles of Veterinary Medical Ethics of the AVMA.

Conflict of Interest

The Author has no conflicts of interest.

References