Update on Noninfectious Inflammatory Diseases of the Lower Airway

Melissa R. Mazan, DVM

KEYWORDS

• Inflammatory airway disease • Recurrent airway obstruction • Bronchodilator
• Environmental remediation • Airway inflammation • Corticosteroid • Lung function

KEY POINTS

- Inflammatory airway disease and recurrent airway obstruction are 2 nonseptic diseases with a shared cause of exposure to particulate matter and are likely 2 ends of a spectrum of disease.
- Diagnosis and differentiation of the 2 conditions can be made based on clinical signs, lung function testing, and cytologic analysis of bronchoalveolar fluid.
- Treatment consists of environmental modification and pharmacologic treatment, with each equally important.
- Corticosteroids, either systemic or inhaled, along with environmental remediation, are the cornerstone of successful treatment with bronchodilators indicated for short-term, rescue therapy.

Both inflammatory airway disease (IAD) and recurrent airway obstruction (RAO, better known as heaves) are inflammatory but *not* septic diseases of the equine respiratory system. The causes of both IAD and RAO share similarities, both being diseases of domestication and exposure to particulate matter, whereas it is at present unclear if it is the pathogenesis itself or the severity of pathogenesis that differs. The distinction between the 2 diseases becomes more apparent when history, clinical signs, and response to treatment are considered. Although they are considered separate diseases, there are recent data[1] to support the idea offered by Viel[2] decades ago that a spectrum of disease exists, with low-grade IAD on one end and RAO on the other end. This review begins with a discussion of what is known about the cause and pathogenesis of IAD and RAO and then considers the clinical signs; diagnostic approach, including sampling of respiratory fluids, lung function testing, and imaging; and concludes with a discussion of treatment options, including environmental modifications and pharmacologic treatments.

Disclosures: None.
Large Animal Department of Clinical Sciences, Cummings School of Veterinary Medicine at Tufts University, 200 Westborough Road, North Grafton, MA 01536, USA
E-mail address: Melissa.mazan@tufts.edu

Vet Clin Equine 31 (2015) 159–185
http://dx.doi.org/10.1016/j.cveq.2014.11.008 **vetequine.theclinics.com**
0749-0739/15/$ – see front matter

CAUSE OF INFLAMMATORY AIRWAY DISEASE

The exact cause of IAD is as yet unknown. It is probable that there is no one cause of this pervasive disease; rather, many different causes likely contribute to the constellation of signs that is recognized as IAD. The most commonly invoked contributors remain high levels of particulates in the environment, viral disease, air pollution, genetic predisposition, and bacterial infection. Although IAD is often referred to as allergic airway disease, this entity, defined as an immunoglobulin E (IgE)–mediated airway inflammatory condition, has not been shown to exist in horses.[3] This finding does not, however, imply that the immune system is uninvolved in the cause and pathogenesis of IAD.

Environment has long been associated with airway inflammation in horses. More than a decade ago, Sweeney and colleagues[4] noted that racehorses with clinical signs of IAD lived in poorly ventilated stables and speculated that organic dusts and molds were to blame. There is more than just an association of environment with airway inflammation: previously unaffected horses were shown in multiple studies to develop bronchoalveolar lavage (BAL) neutrophilia when introduced to a stable environment.[5] There is a plethora of substances found in bedding and feed that may be responsible for this response. The 2 components of the barn environment that have been best studied are particulate matter and endotoxin. The role of ammonia in inducing airway inflammation is being increasingly scrutinized as well. Airborne particulate matter in the stable environment is largely organic, including plant debris, mold spores primarily from hay, β-glucans, live and dead microbes, proteases, and animal dander to name a few. Inorganic particulates are of less importance, but still contribute, with silicates from dusty arenas or oil fly ash from diesel machinery being used inside large barns.[6]

It has long been recognized that the stable environment frequently presents an unacceptably high level of airborne particulates. Even the best of hay contains mold spores, such as *Aspergillosus fumigatus*, *Faenia rectivirgula*, and *Thermoactinomyces vulgaris*.[7] The role these molds play in disease cause is more clearly understood in RAO (see later discussion), but there is increasing evidence that exposure to hay and its accompanying organic particulates is important in the cause of IAD as well. When unaffected horses are exposed to endotoxin, they develop airway neutrophilia,[8] and the unsurprising finding that endotoxin concentrations are higher in stables than at pasture[9] goes far in explaining hay-eating as a risk factor for increased tracheal mucus in pleasure horses.[10] Not only is stabling a risk factor, but the horse's position in the stable may also affect development of IAD: being in a stall near high levels of activity, such as near the trainer's office, near entrances to the stable, or where fans are being used to improve ventilation are all risk factors.[5] Recent studies have found that levels of particulates and endotoxin at the horse's immediate breathing zone can be significantly and importantly greater than in the surrounding barn environs, and that the worst offender in increasing exposure to airborne particulates is the hay net.[11]

Previous exposure to respiratory viral disease is often invoked, especially by trainers, as a predisposing factor in the development of IAD. Recent infection with a respiratory virus is the most common trigger for exacerbation of the similar disease, asthma, in humans, so it is logical to make the connection to IAD. There are no clear data to support this idea, but indirect evidence is building. Recently, a large study looking for evidence of herpesvirus in horses with a clinical diagnosis of IAD or poor performance, but specifically excluding horses with signs of acute infectious disease, found that the affected group was more likely to have a positive tracheal wash (polymerase chain reaction [PCR]) for herpesvirus, with EHV-2 being most prevalent.[12] Long-lasting airway neutrophilia (21 days) was seen with experimental induction of EHV-2, but clinical signs concordant with IAD were not seen.[13] A recent study in the