Treatment and Management of Mild/Moderate and Severe Equine Asthma

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1. Introduction

Equine asthma is the most recent nomenclature to define a general disorder of noninfectious lung inflammation associated with respiratory clinical signs of variable severity. Equine asthma is a broad term that encompasses (1) mild/moderate equine asthma (previously known as inflammatory airway disease), (2) severe equine asthma (previously known as “heaves”/recurrent airway obstruction), and (3) summer pasture-associated recurrent airway obstruction (now also referred to as severe equine asthma). The updated equine asthma terminology has been adopted since the pathobiology of asthma found in horses shares similarities with human asthma.1–4 Specific information about the definitions and pathophysiology of equine asthma can be found in the in-depth manuscript from Dr. Couetil that is paired with the present manuscript. This manuscript will focus on the treatment and management of equine asthma. It is important to convey the message to horse owners that although equine asthma can be effectively managed, there is no cure for this disease. Effective management involves a combination of medical treatments and measures to control exposure to environmental organic particulates. Both must be implemented together to be successful over the mid- to long-term period.

2. Medical Treatment of Severe Equine Asthma

The literature disproportionately assesses the effects of medical treatments in horses with severe asthma as compared to mild/moderate asthma. This is likely because it is easier to objectively quantify responses to treatments in horses with severe versus mild/moderate equine asthma since the standard lung function techniques are not sensitive enough to document any of the small treatment responses in horses with mild/moderate asthma. However, since the roots of the pathophysiology are thought to be quite similar between the two types of asthma, practitioners commonly use a similar therapeutic approach for mild/moderate and severe asthma. Equine asthma involves a triad of lung inflammation, bronchoconstriction, and mucus production. Although each of these entities could be treated separately with specific medication for each of these processes, it has been shown consistently that controlling lung inflammation with corticosteroids will also positively impact the other two mechanisms.

Corticosteroids

There is an abundance of evidence supporting the use of corticosteroids in the treatment plan of equine asthma.5–15 It should be noted that an inhaled corticosteroid has been recently approved for commercialization to treat severe equine asthma, which will now have an impact on the treatment decisions made by practitioners.
Systemic Corticosteroids

Systemic Dexamethasone

Dexamethasone is the systemic corticosteroid of reference in equine asthma and has been used as a benchmark in many studies assessing the efficacy of therapies.5–12,16–25 It has been evaluated in equine asthma studies with oral, intramuscular, or intravenous administration. All the studies except for three,16,17,20 used horses with severe asthma. The most frequently measured outcomes were clinical signs, lung mechanics (lung resistance, elastance, and transpulmonary pressure), and bronchoalveolar lavage fluid (BALF) cytology. Systemic dexamethasone sodium phosphate is commonly used at a dose of 0.04 to 0.1 mg/kg IV once daily across studies, without side effects reported on the small number of horses studied.6–10,12,23 Authors have also reported the effects of dexamethasone sodium phosphate at a dose of 0.04 to 0.05 mg/kg IM once daily without reported local reactions using a product available in Canada and Europe.6,16,20 Systemic dexamethasone-21-isonicotinate has also been used at a dose of 0.04 mg/kg every 3 days in a study in the United States.26 Studies have assessed the efficacy of oral dexamethasone at doses between 0.05 and 0.16 mg/kg once daily.7,9,22

a) Lung function. Systemic dexamethasone positively influences the clinical signs and lung mechanics in horses with equine asthma in a way that is comparable to the responses obtained by turning horses outside on pasture in dust-free conditions. Systemic dexamethasone (IV and IM) has been shown to significantly improve the lung function of horses with severe equine asthma (9 horses enrolled in a crossover design) after only 3 days of treatment, even when the horses were kept indoors and without measures to decrease exposure to dust.12 One study reported that 7 horses with severe equine asthma kept in a dusty indoor environment but treated with oral dexamethasone (0.05 mg/kg) reached the same level of improvement in lung function as when they were put on pasture for a long period of time.9 This level of efficacy is not yet matched by any other corticosteroids tested in horses. The rapid and reliable efficacy of dexamethasone justifies its use in equine asthma; however, it comes at the price of potential side effects that can be life-threatening in some cases (e.g., severe laminitis). The side effects are thought to be mainly related to the effects of dexamethasone on the hypothalamic-pituitary-adrenal axis and adrenal suppression. Many studies using dexamethasone in severe equine asthma have reported a marked reversible decrease in blood cortisol, indicating a transient but strong adrenal suppression effect at the dosage used.6,7,10,11 Systemic dexamethasone has also been shown to induce a decrease in serum total proteins in horses, likely secondary to some subclinical gastrointestinal tract ulcerations.7 Dexamethasone therapy in horses also affects their glucose metabolism, which translates into an increased resting lactatemia.27 Systemic dexamethasone IV also affects the lung microbiota of horses with mild/moderate equine asthma, which show an increased abundance of Streptococcus sp. in their airways.28 The significance of this finding is still unknown, but it shows that the relationship between bacteria and the horse immune system in the lungs is affected by systemic corticosteroids therapy.

b) Bronchoalveolar cytology. Except for one study,12 there is an agreement in the literature that if horses with severe equine asthma are kept in a dusty environment, dexamethasone treatment will not decrease the percentage of neutrophils found in the BALF cytology.7–9,11 A similar trend was found in one study on mild/moderate asthma; however, a larger sample population would be required to statistically confirm this finding.25 As discussed in further detail in the environmental control section, airway accumulation of inflammatory cells will not persist when exposure to organic particulates is prevented. In comparison, there is some evidence that dexamethasone decreases the accumulation of mucus in the large airways of horses with severe asthma,6 even when they are kept in a dusty environment.29

c) Mucus. There is some evidence that dexamethasone decreases the accumulation of mucus in the large airways of horses with severe asthma,6 even when they are kept in a dusty environment.29

Oral Prednisolone

When prescribing oral corticosteroids in horses, oral prednisolone should always be chosen over oral prednisone since the latter has been shown to have a poor bioavailability and would be unlikely to have clinical efficacy in horses with asthma.26 Oral prednisolone (2 mg/kg) has been shown to have some efficacy at improving lung function of horses with severe asthma, even when kept indoors, but was not found to be as effective as oral dexamethasone (0.05 mg/kg).9 It seems that prednisolone therapy can only reach some clinical efficacy comparable to dexamethasone if it is combined with management measures to prevent exposure to aerosolized organic particulates.6

Isolupredone Acetate

Isolupredone acetate (0.03 mg/kg IM) has been commonly used in the past in large animal practice. This medication has been shown to quickly improve the lung function of horses with severe asthma and to have a lasting effect, on par with dexamethasone (0.04 mg/kg IV).10 Unfortunately, some significant hypokalemia was also noted in the treated horses, which has been associated with myopathies, recumbency, and death in cattle and humans.

Triamcinolone Acetonide

The long-acting triamcinolone acetonide was the first corticosteroid to be assessed in a controlled clinical trial in horses with severe asthma.13 It has been shown to improve the lung function of horses with...
severe asthma up to 4 weeks after systemic intramuscular administration of this medication at a dose of 40 mg. Interestingly, it has been recently shown that intra-articular injection (40 mg total) of triamcinolone acetonide also improved the lung function of horses with severe asthma for 3 weeks.30 Practitioners should discuss the potential side effects (particularly severe laminitis) with the owners and avoid repeating the treatment without a long washout period to decrease the likelihood of side effects.

Inhaled Corticosteroids
Because systemic corticosteroids are associated with hypothalamic-pituitary-adrenal suppression, inhaled corticosteroids present the advantage of having a local airway anti-inflammatory activity, while potentially decreasing the systemic absorption. In simple words, the goal of inhaled corticosteroids is basically “treat the lungs only, instead of treating the horse, including the lungs.” Furthermore, although little evidence is available, the withdrawal times are likely significantly less for inhaled than for systemic corticosteroids. However, inhaled therapy presents its own technical challenges, notably to achieve small enough particles to be respirable and reach a good lung distribution of the active product, while limiting ingestion (which could be associated with adrenal suppression). There are basically 3 ways currently used to deliver inhaled medication to the lower airway: mechanical nebulizers (e.g., vibration and jet), metered dose inhalers (MDIs), and a soft mist inhaler (SMI).31 All 3 techniques have been used in horses to deliver corticosteroids to the lower airways using various devices. The mechanical nebulizers usually involve a mask and a powered device. The MDIs come ready to use in a canister, are procured from the human market, and are delivered using a specialized chamber.31 The soft mist is the most recent technology approved to treat severe asthma using a specialized delivery system.32 The size distribution of the droplets varies between nebulizers and affects the amount of medication reaching the deep small airways; the respirable particulates reaching the alveoli/gas exchange area of the lungs should ideally be <4 microns diameter. However, particulates of much smaller size stay aerosolized in the lungs and are expired back outside.

Mechanical Nebulization: Dexamethasone (Sodium Phosphate)
Dexamethasone sodium phosphate was found to have a low bioavailability when nebulized with a mechanical device,31 and although it did not induce adrenal suppression in a study on healthy horses, it did induce some adrenal suppression on a small number of horses with severe asthma in which only 5 mg of dexamethasone was nebulized.32 Although this low dose of nebulized dexamethasone was not reported to improve the lung function of horses with severe asthma, more studies are necessary to optimize the dosage for severe asthma cases. Higher doses have been shown to affect the bacterial composition of the upper airways of horses with mild asthma, but the treatment did not have as much effect on the composition of the fungal population in the airways as the environment did.33 The adrenal suppression induced with higher doses of nebulized dexamethasone (unpublished) decreases the potential benefits of this approach.

Metered Dose Inhalers (MDIs): Fluticasone Propionate, Beclomethasone Dipropionate, Budesonide
When comparing efficacy between studies using MDIs, it should be noted that there were some changes in the type of propellant used over the years, which affects the lung distribution and therefore dosage equivalence. The first controlled studies reporting treatments of equine severe asthma with MDIs used beclomethasone dipropionate.14,15 Several dosage regimens have been proposed and showed some overall efficacy to improve the lung function of horses with severe asthma.5,34 However, adrenal suppression was also reported, even when using the lowest doses of beclomethasone dipropionate.34 Fluticasone propionate has a greater affinity for the glucocorticoid receptor and may be slightly more potent than beclomethasone dipropionate. The earliest studies have tested its use in horses with severe asthma over a relatively short period of time,11,35,36 whereas the more recent studies have assessed its effects on lung tissues when used over a very long period of time (up to 1 year of treatment).37–39 During short-term treatment periods, fluticasone showed efficacy inferior to that obtained with systemic dexamethasone in horses with severe lung obstruction.11 As with fluticasone, inhaled budesonide improved lung function in horses with severe asthma, but it was also associated with some adrenal suppression effect.18

Soft Mist Inhaler (SMI): Ciclesonide (des-Ciclesonide)
Ciclesonide is a pro-drug with a low affinity for the glucocorticoid receptor, low bioavailability, and a high first-pass metabolism. This means that the small amount of parent drug (ciclesonide) that would be swallowed during inhalation would mostly stay in the digestive system or undergo hepatic metabolism without reaching the systemic circulation. Ciclesonide is metabolized by esterases in the lung epithelium into desiclesonide, which increases its potency by 100-fold.40

The effects of various doses and inhalation devices on the blood cortisol concentrations in 8 horses with severe asthma maintained in a dusty environment and using dexamethasone as a reference have been recently reported.5 The results showed no decrease in blood cortisol (indicating no adrenal suppression), even when the highest dose of ciclesonide was used. Contrary to dexamethasone, the serum total protein level did not decrease with ciclesonide therapy. The clinical efficacy of inhaled ciclesonide
on horses with severe asthma was also demonstrated in this study at the dosage of 2700 mcg twice daily and 3712.5 mcg once daily. The lung mechanics and clinical scores were significantly improved by day 7 at the 2700 mcg twice daily dosage, whereas they were improved by day 14 at the 3712.5 mcg once daily dosage. The number of horses reaching complete resolution of lung airflow obstruction with the ciclesonide treatment was similar to the results obtained after administration of a potent bronchodilator control treatment (N-butylscopolamine) in these horses. Recently, a large-scale randomized, controlled, and blinded field study used clinical scoring as a measured outcome to test the efficacy of inhaled ciclesonide (vs. placebo; 2744 mcg twice daily for 5 days followed by 4116 mcg once daily for 5 days) in 224 horses with severe asthma. By design, environmental and treatment conditions were not strictly controlled, and a large number of horse owners and equine practitioners were included, which may explain how > 40% of the placebo horses improved. However, the response rate and improvement in clinical score were much greater in the treatment group with > 73% responders and score decreasing from a mean of 15.3 to 7.2. Interestingly, some horses were diagnosed and treated for pituitary pars intermedia dysfunction but did not show signs of laminitis with the ciclesonide treatment. The blood cytology and chemistry analysis also confirmed the safety of the treatment as it did not show any effect of the ciclesonide therapy.

Additional Therapies Targeting Lung Inflammation

Because of the side effects associated with corticosteroid treatment (other than ciclesonide delivered via SMI), other therapeutic options have been investigated targeting lung inflammation in horses with severe equine asthma.

Dietary Fatty Acid (Omega-3)

The absorption of polyunsaturated fatty acids that are precursors of omega-3 series of polyunsaturated fatty acids decrease the substrate available to produce proinflammatory eicosanoids and inflammatory cytokines. A controlled crossover study evaluating the effect of increased free fatty acid diet content in 9 horses with severe equine asthma using sunflower or seal blubber oil showed an absorption and integration of the fatty acids into the airways’ leukocytes membranes. Although the lung inflammatory cell count from BALF decreased with treatment, there was no improvement in the horses’ clinical response measured by histamine challenge hyperreactivity. Another randomized controlled study evaluated the effect of dietary supplementation of omega-3 polyunsaturated fatty acid for 8 weeks in conjunction with a switch to a complete pelleted diet in 35 client horses with mild/moderate or severe equine asthma. The visual clinical score improved in all horses (including placebo), supporting the benefits of a pelleted diet in horses with equine asthma; however, the clinical score improved to a greater degree for horses on the high fatty acid diet, showing some added benefits of this diet over simple management measures. Interestingly, the BALF neutrophilia decreased in the fatty acid diet group but not in the placebo group. This study shows that the dietary omega-3 fatty acid approach would only be recommended in combination with a low-dust pelleted diet over a long period of time.

Cytosine-Phosphate-Guanine-Oligodeoxynucleotides Nanoparticles

Cytosine-phosphate-guanine-oligodeoxynucleotides nanoparticles are single-stranded synthetic DNA molecules that have an immunomodulatory effect and can direct the immune system reaction away from the allergic Th2 pathway, for example. They have been shown to decrease allergen-induced airway neutrophilia in the lungs, and administration improved clinical signs in horses with severe asthma when delivered by inhalation using an equine nasal chamber device and a mechanical nebulizer. Although not available commercially yet, this may be a therapeutic approach that could have the potential to control horses’ airway neutrophilia in the future.

Tamoxifen

Tamoxifen is a nonsteroidal estrogen receptor modulator that was tested in vitro on equine neutrophils. It affects growth and survival of equine neutrophils and decreases the production of oxidative chemicals, which are favorable properties to control the neutrophilic lung inflammatory cascade observed in severe equine asthma. However, a blinded study evaluating tamoxifen treatment in horses with severe equine asthma did not report any changes in BALF neutrophilia and mucus severity and reported only a slight decrease in the lung resistance.

Hydrosoluble Curcumin

A modified hydrosoluble curcumin derivate, modified for inhalation delivery, has been tested in horses with severe equine asthma either when kept in a dusty environment or after induction of lung inflammation with lipopolysaccharide (LPS) nebulization. The curcumin derivative decreased BALF cellularity in the horses with severe equine asthma kept in the dusty environment, but not after the LPS challenge. The production of reactive oxygen products was nevertheless decreased in the latter case. Further studies are necessary to assess the value of this compound in the treatment of equine asthma.

Bronchodilators

It is important to not rely solely on bronchodilation when implementing a therapeutic plan for equine asthma since this approach has been shown to wor-
sen asthma control and increase mortality in people.51 Indeed, the use of bronchodilators without decreasing exposure to dust has the potential to increase the number of organic particles reaching the lower airways, triggering an increased inflammatory response.52 One study evaluating horses with severe equine asthma treated only with an inhaled bronchodilator (salmeterol) for 3 months while kept indoors reported that horses experienced disease exacerbations after 8 weeks of treatment.52 Bronchodilators should be used as a third therapeutic line after environmental changes and corticosteroids. The author only uses bronchodilators in combination with corticosteroids and only as a short-term rescue approach to relieve respiratory symptoms in the most severe equine asthma cases. Research trials assessing bronchodilators in equine medicine have primarily evaluated both relief of the bronchoconstriction and the duration of these effects. The beta-2 adrenergic agonists are available as short- or long-acting products and have been reported to have a rapid onset of action, whereas the muscarinic cholinergic antagonists have a slow onset of action (up to 1 hour). This manuscript will focus on bronchodilators relevant to equine practice and not cover the medications that are used in research or are not easily available.

Beta-2 Adrenergic Agonists

The most-studied systemic beta-2 adrenergic agonist in horses is clenbuterol. Its beta-2 adrenergic bronchodilatory effect was first shown in ponies with severe equine asthma, which was then confirmed using a clinical scoring in a large field study of horses with severe equine asthma treated with oral clenbuterol (0.8-3.2 µg/kg twice daily).54 Systemic administration can be associated with side effects that are dose dependent and include sweating, tachycardia, and anxiety.55 Furthermore, the internalization of beta-2 adrenoreceptors decreases its bronchodilator efficacy over time.66 However, this down-regulation effect is reduced when dexamethasone is added to the treatment protocol in conjunction with clenbuterol.56 Oral administration of clenbuterol does not have the ideal pharmacokinetics to be used in horses with respiratory distress since it has a delayed onset of action. It is currently recommended that clenbuterol therapy be used for a short period of time in combination with corticosteroids and in conjunction with appropriate environmental management aimed at reducing aerosolized allergens. Short-acting beta-2 adrenergic agonists used in equine medicine primarily include albuterol and/or salbutamol. The duration of the bronchodilatory effects of these drugs are only 30 to 60 minutes.57,58 However, because of their rapid onset of action ( maximal bronchodilation within 5 minutes),58,59 these drugs are effective for clinical cases in respiratory distress where a quick relief is indicated. Administration of albuterol using an MDI and two different devices has been shown to have a quite similar bronchodilatory response.59 Currently, it is recommended to use a commercially available delivery device (nasal application with a chamber”) for delivery of albuterol using an MDI as this tends to have a better efficacy as reflected by the reduced number of “puffs” to reach 50% maximal bronchodilation level.59 Using this commercially available device and an MDI with hydrofluoroalkane propellant, the dose necessary to obtain maximal bronchodilation is 540 mcg (6 puffs) on average. Levalbuterol is the R-enantiomer of the racemic albuterol and does not have the potential adverse effects of the S-enantiomer (at least in vitro), while providing a duration of effect of 120 minutes in horses with severe equine asthma.57 This is still a much shorter duration of effect than in humans, where bronchodilation lasts for 6 hours, and is still too short to be practical as the sole medical treatment for horses with severe equine asthma. Salmeterol is a long-acting beta-2 adrenergic agonist that showed some effective bronchodilation in horses with severe equine asthma for approximately 6 hours.60 However, the onset of action is slow, taking up to 60 minutes for effects to occur,60 making salmeterol less practical of an emergency treatment option for horses in respiratory distress.

Muscarinic Cholinergic Antagonists

The flagship of muscarinic cholinergic antagonists is atropine. However, because of the many side effects associated with systemic administration of this drug, inhaled formulations of modified atropine compounds are used instead. The only muscarinic cholinergic antagonist recommended for use in horses is ipratropium, which is available as an MDI. Commercially available options for human use include bare ipratropium solutions, MDIs, dry powder, and SFIs. Most of the studies on horses with severe equine asthma used the dry powder formulation, and it was quickly effective as a bronchodilator at rest. It did not provide any beneficial effect during exercise.61 This was also the case for healthy horses treated with this drug, likely because the horses were already at maximal exercise-induced bronchodilation and did not benefit from the ipratropium intervention.61-63 Some side effects (decreased gastrointestinal sounds and oral dryness) can be expected in horses after nebulization of ipratropium solution.64 This may not be the case when administration is done with MDIs, but it remains to be confirmed. The duration of action of ipratropium in horses with severe equine asthma has been reported to be between 4 and 6 hours, varying a great deal between horses.64 It is interesting to note that ipratropium seems to have a greater bronchodilatory effect on the larger airways than on the small peripheral airways.64 Revatropate is another muscarinic cholinergic antagonist that has been evaluated in horses with severe equine asthma with the aim to decrease the potential side effects associated with ipratropium solution nebulization.64 The improvements in lung function obtained with revatropate and an
ipratropium solution were similar, but the revatropate induced further clinical scoring improvement probably because it induced some more peripheral airways’ bronchodilation.64 Revatropate, however, is not commercially available.

3. Medical Treatment of Mild/Moderate Equine Asthma

As mentioned above, because few technologies are sensitive enough to objectively measure the lung function of horses with mild/moderate asthma, clinical trials evaluating medical therapy for this disease process are scarce. Most of the information described above for severe equine asthma is used empirically in mild/moderate equine asthma clinical cases. There are, however, a few exceptions, and a few controlled studies have addressed the clinical efficacy of some medications in mild/moderate equine asthma horses. Sodium cromoglycate, a mast cell stabilizer, improved the clinical signs in a controlled study with 12 racehorses assessed for poor performance and abnormal respiratory signs at a high dose of 200 mg nebulized twice daily.65 The effect of this treatment on the performance of those horses was not reported, but the study showed a potential beneficial effect for horses with increased mast cells in the BALF. It may be indicated in cases where a proportion of mast cells is seen degranulating at the BALF cytological analysis. Airway hypersensitivity and hyperresponsiveness are hallmarks of asthma and can be objectively documented using the response to standardized bronchoprovocative challenges (such as with increasing doses of histamine). One study using a randomized crossover design in 8 horses found that dexamethasone IM and inhaled fluticasone propionate both decreased airway hypersensitivity and hyperresponsiveness after 1 week of treatment, but without effect on BALF cytology.20 This confirmed that corticosteroids therapy has some value in the treatment of mild/moderate equine asthma. In another study, horses with moderate equine asthma that were kept in a dusty environment had an allergic immunological signature (shown by an increase in IL-17 expression in the BALF). As expected, systemic dexamethasone therapy effectively decreased the cytokine expression of lung cells from the horses; the BALF cytology, however, was not significantly affected.57 This shows that similar to severe equine asthma, a dusty environment impedes the clearance of inflammatory cells in the lungs of horses with mild/moderate equine asthma, even when treated with corticosteroids. The benefit of bronchodilators over corticosteroids as treatment for horses with mild/moderate equine asthma was not reported when measuring the horses’ aerobic capacity assessed by measuring peak oxygen consumption during exercise to fatigue (VO2peak).16 It therefore appears that once horses have improved the lung inflammation by environmental and corticosteroids therapy, bronchodilators would not add to their aerobic capacity, similar to what has been found in healthy horses.16,62

4. Environmental Measures

Organic dust plays a key role in the pathogenesis of equine asthma (see in-depth manuscript from Dr. Couetil in this AAEP session). Clinical re-response to a moldy hay challenge has been used for decades and is included in the definition criteria that assist in distinguishing mild/moderate from severe equine asthma.66 Horses with severe equine asthma will show some bronchoconstriction, sometimes within hours, after exposure to moldy hay, which translates into clinical signs of labored breathing at rest.66 When a moldy hay challenge is repeated in horses with severe equine asthma, their lung function deteriorates in a predictable manner after each challenge,67 contributing to the wide use of the moldy hay challenge as a model in research for severe equine asthma. Horses with mild/moderate equine asthma will present with abnormal respiratory tract clinical signs at rest but with no increase in respiratory effort after the challenge. Environmental air quality, however, seems to be equally important for mild/moderate equine asthma.66 It has been known for a long time that bringing horses indoors in an environment without measures to limit dust exposure will trigger an influx of neutrophils in both healthy and severe equine asthma horses; the inflammatory response can reach extreme levels in research horses known to have consistently severe equine asthma (>71% BALF neutrophils as compared to >27% BALF neutrophils in healthy horses).68 Improvement in air quality has an overriding effect over treatments with corticosteroids in horses with mild/moderate equine asthma,66 as well as in horses with severe equine asthma.69 Keeping horses with severe equine asthma indoors, but combined with measures to decrease exposure to hay and bedding dust, improves clinical signs in horses with severe equine asthma within 3 days.69 There is a strong agreement in the literature, however, that except for the particular case of pasture-associated severe equine asthma,70,71 several weeks of pasture will provide the lowest level of lung airway obstruction and inflammation.69,72–75 In areas where pasture-associated severe equine asthma is prevalent, horses pastured are also susceptible to have seasonal moderate and severe lung inflammation, with up to 87% of horses in a teaching herd having at least some mild lung inflammation during the winter.76 Assessing air quality is usually performed with measurements of airborne particulates, with particular attention to those of a size that can reach the lower airways (i.e., respirable dust). Aerosols can be divided into 3 categories regarding their deposition in the respiratory system, and based on human data, it is accepted that 50% of the particulates in each category will achieve the following distributions: the inhalable, the thoracic, and the respirable fraction. Fifty percent of the particulates with 100 microns diameter will be inhalable (deposit in the respiratory tract, extra-thoracic), 50% with 10 microns diameter will be thoracic (deposit in
conducting airways), and 50% with 4 microns diameter will be respirable (deposit in the gas exchange/alveoli of the lung). It was recognized early on that activities such as mucking or sweeping alleys in barns contribute to the concentration of total and respirable dust.\textsuperscript{77} It is important, however, to note that breathing zone concentration for particulates is more relevant than barn concentration\textsuperscript{78,79} and that there is no correlation between the two zones’ dust concentration.\textsuperscript{80} This is also emphasized since there is a great variability between horses’ exposure to dust when stabled\textsuperscript{80} as some horses may be pacing in their stall or have other habits that favor dust aerosolization. In addition to airborne dust concentration, attention should be paid to the composition of the dust and in particular its concentration of endotoxins and beta-glucan.\textsuperscript{81–86} Standardized hay dust suspension has been used to challenge horses, and although it triggered a lung neutrophilia in horses with severe equine asthma (and a significantly lower response in healthy horses), the challenge did not induce clinical signs associated with bronchoconstriction.\textsuperscript{84} Importantly, all dusts are not equal,\textsuperscript{85} and there is a synergistic effect between organic dust concentration, endotoxin,\textsuperscript{83} and beta glucan content.\textsuperscript{82} A longitudinal study in a racing barn with moderate levels of airborne dust found that the concentrations in beta-glucans and endotoxins were not proportional to the total dust concentration; furthermore, there was an opposite seasonal increase between the two components as the beta-glucans were greater in the winter and the endotoxins were greater in the summer.\textsuperscript{81} Therefore, variability in those three critical dust components cannot be considered to be correlated. There is a clear agreement between studies that improving hay and bedding conditions will have a dramatic effect to reduce airborne dust. For example, when horses were switched from a conventional management with straw bedding and hay to a low-dust management with wood shavings and pelleted diet, not only did the area respirable particulates decrease by 50%, but more importantly, the breathing zone respirable fraction also had only 3% of the dust measured with the conventional management.\textsuperscript{78} However, between the hay and the bedding, the forage has a greater impact on the respirable dust and endotoxin concentrations in the breathing zone of horses than the bedding.\textsuperscript{78,87–89}

**Hay**

Fungi are found in hay and bedding and play a critical role in the pathophysiology of severe equine asthma; challenges with mold antigens (\textit{Micropolyspora faeni, Aspergillus fumigatus,} and \textit{Thermoactinomyces vulgaris}) were done almost 30 years ago to assess the bronchoconstrictive response of horses with severe equine asthma.\textsuperscript{80} A European retrospective study showed that horses were 2 times more likely to have mild/moderate equine asthma when fungal elements were observed in the transtracheal wash cytology.\textsuperscript{91} As mentioned above, endotoxins are also important, and haylage is an effective method to decrease endotoxin concentration in the air.\textsuperscript{87} However, it is not practical for all areas, and when hay is used, the type of forage and the timing of its harvest and storage conditions are also important; late-harvest, second-cut hay stored in a dry environment is recommended to decrease the dust and fungi content.\textsuperscript{92} In any case, hay nets should also be avoided as they have been shown to increase exposure to dust in racing stables,\textsuperscript{80} and respirable dust exposure is associated with lung eosinophilia.\textsuperscript{93} Many hay options have been tested regarding hay handling in barns, all aimed at decreasing the respiratory risk associated with feeding unprocessed hay. Simply immersing hay in water resulted in a 60% decrease in respirable dust concentration, but it seems that soaking hay for 30 minutes may be the most beneficial approach with a reduction by 90%.\textsuperscript{88,94} However, a detailed analysis of the dust composition was not provided in those studies. There is a clear consensus among studies that steaming hay decreases bacterial and mold content,\textsuperscript{95,96} however, its effect on endotoxin exposure has not yet been described. Steamed hay is appetent and increases the dry matter intake of the horses.\textsuperscript{97} There are few data on the clinical efficacy of hay steaming in severe equine asthma horses. A study using a very small group of horses with severe equine asthma reported some benefits on mucus scoring, inhaled fraction, and exposure to endotoxins;\textsuperscript{95} however, the study did not have enough power to definitely conclude that steamed hay improved clinical signs in severe equine asthma. Pelleted hay has been used as a reference in clinical trials, with an oil-mixed hay system shown to have equivalent efficacy.\textsuperscript{98} Lung mechanics were improved after only 6 days and remained improved for the 93 days of the study, while mucus score improved after 13 days and airway neutrophilia improved after 65 days of the oil-mixed hay system diet.

**Bedding**

Many studies have also assessed a variety of beddings to decrease ambient and breathing zone particulates in horses. It is usually accepted that wood shavings are a practical and effective method to decrease ambient dust in barns,\textsuperscript{78} however, it should be kept in mind that excellent quality straw can have similar benefits.\textsuperscript{99} Wood shavings are often more practical and easier to obtain than the best-quality straw. Wood shavings combined with grass haylage are effective at maintaining horses with severe equine asthma free of symptoms even when kept indoors.\textsuperscript{100} Newspaper and cardboard bedding have been proposed as horse bedding options.\textsuperscript{101,102} Cardboard bedding was effective at maintaining horses with severe equine asthma in remission while kept indoors on grass silage.\textsuperscript{102}
Ambient Temperature

Heat (25°C) in the barns may worsen severe equine asthma as compared to warm temperature (18°C), supporting the possibility that cold temperature could be considered to help with uncontrolled severe equine asthma cases. 103

5. Conclusion

In conclusion, environmental management of dust is important to successfully maintain horses with severe equine asthma free of symptoms and free of lung inflammation. Although it may be difficult to convince horse owners that these environmental measures are more important than medication, such discussions are worth the veterinarian’s time since owners who try to apply some measures do perceive a clear improvement in clinical signs. 14

Antigen avoidance measures alone have also been shown to be beneficial over the long term as not only do they control lung inflammation, but they also decrease bronchial smooth muscle mass. 18 Unfortunately, it is sometimes discouraging to see that re-exposure to dust affects lung mechanics within only a few days of exposure, so dust-free management should be an all-year-long, long-term commitment. 100

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Declaration of Ethics

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

Conflict of Interest

Dr. Léguillette has been remunerated by Boehringer-Ingelheim for a presentation on equine asthma.

References and Footnotes


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*Aservo Equihaler™, Boehringer Ingelheim Vetmedica GmbH, Germany.*