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SMALL AIRWAY DISEASE AND EQUINE RESPIRATORY HEALTH

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The focus of this article is lower airway disease and its relationship to poor air quality. We will take a journey through the horse's lungs and examine their various challenges. There have been several exciting developments recently which have changed our understanding of and approaches to dealing with respiratory problems in horses. On the broader front, there is a clear emergence in veterinary and indeed human medicine which sees a change away from treating disease to maintaining health. This approach focuses on providing knowledge which will empower those involved in the day-to-day care of horses to maintain their horse's health. In the context of the respiratory system, this approach can also have direct benefits for people who care for horses.

This article begins with a description of the journey air takes to reach the lungs. The costs and demands placed on the lung are then reviewed, followed by a description of the most common problems of airways. Practical husbandry and management procedures which can help maintain the horse's respiratory health are then described. Finally there is a description of some of the pharmacological approaches your veterinarian may use in treating a respiratory problem.

The respiratory system

Air enters the nostrils and is warmed and humidified by the turbinates (blood rich scrolls of bone) prior to entering the trachea. Larger particles in the air are also trapped by the turbinates as a first line of defence of the lungs. From the trachea, the air travels along an ever increasing number of initially larger airways (bronchi) to small airways (bronchioles). In the horse, the airways are lined by cilia which act as an escalator to move mucus and particles up from the lungs. As well as cilia, there are mucus-producing cells in the linings of the airways. Indeed, the cilia normally beat in a thin layer of mucus which is moved up the airways. However, in disease states, such as with infection, the nature of the mucus can become tenacious. This is an important consideration later in the section on pharmaceuticals. Groups of lymphoid cells are scattered throughout the airways. They form and maintain the lung's immunity to many infectious agents.

The inward journey of air through the airways comes to an end at the alveolar sacs. It is within these sacs and across a very fine membrane, known as the alveolar membrane, that gas exchange occurs. Oxygen passes across the membrane into the red blood cells and carbon dioxide passes back across the other way. Oxygen is necessary for the survival of the tissues and carbon dioxide is a by-product of energy production. The journey of this stale air back out of the lungs then commences as the horse exhales.

A final defence barrier exists in the alveoli. Tiny inhaled particles which get passed through the turbinates and airways land in the air sacs and are cleaned up by cells called macrophages. These cells engulf material ranging from tiny particles of dust to bacteria. However, they can be overloaded. For example, heavy burdens of dust can decrease the ability of those cells to fight infectious agents such as bacteria. A horse in a dusty environment will therefore be more prone to infection than a horse in a cleaner environment.

The lung evolved to deal with air. To maintain a healthy lung, it is important to minimize pollutants it is exposed to.

THE COSTS AND DEMANDS OF RESPIRATORY FUNCTION

Athletic performance puts extra demands on the respiratory system. At rest, an average horse takes in approximately five litres of air with each breath. It takes 12 breaths per minute and has a heart rate of approximately 32 beats per minute. Therefore, at rest, our average horse will inhale and exhale approximately 60 litres of air per minute. However, during competition, the horse will increase the volume of air per breath to between 12 and 15 litres taking over 150 breaths per minute. The lungs now have to move over 2,250 litres of air per minute, with less than half a second for each breath. The breathing patterns of equine athletes are closely linked with locomotion. The cantering and galloping horse has respiration and locomotion locked into a 1:1 phase. With each stride the horse will be taking a breath. This action aids in respiration, as it allows the large body mass of the abdominal organs to act like a piston. The galloping horse takes over 150 breaths per minute. This is in contrast to a Standardbred which takes upwards of 70 breaths per minute with between 20 and 25 litres of air per breath. Thus, the galloping horse takes shallower and more frequent breaths than the Standardbred. However, both athletes have to move large volumes of air efficiently to compete successfully. The equine athlete has to move large volumes of air in a very short period of time. Even a small increase in the amounts of mucus in the airways and minor degrees of airway spasm or thickening of the lining of the airways will adversely affect performance.

The demands of athletic exertion are not without their costs on the horse's lungs. Training, strenuous exercise and the stress of transport affect one of the lungs' main defence mechanisms, i.e. macrophages (clean up cells). Such changes are believed

to be important in explaining the increased incidence of respiratory diseases in horses exposed to these conditions. Air quality is a concern for air transport. Research by Dr. Des Leadon has shown that one of the most critical factors is the time the airplane spends on the ground. This is when the level of airborne pathogens can be highest. Hence, it is important to minimize the time it takes to load and unload horses and avoid delays at take off and sitting on the tarmac.

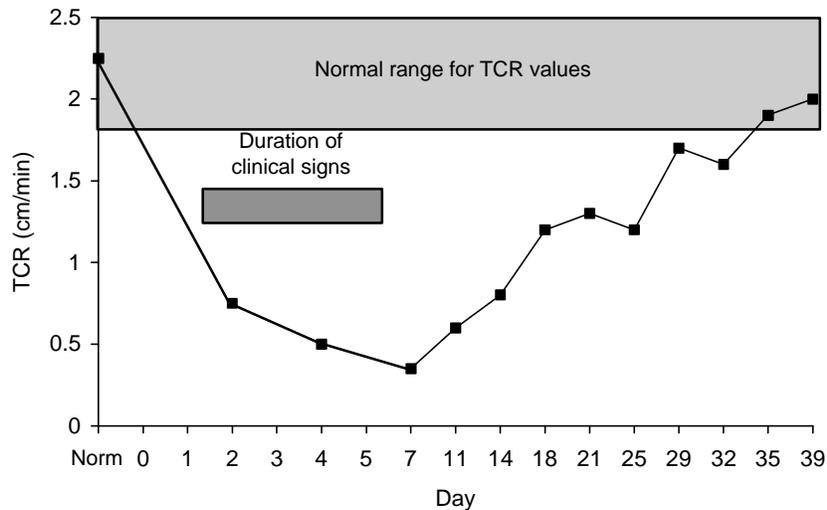


Figure 1: Summary of the average tracheal clearance rate (TCR) that occurred in seven horses before and following experimental infection with equine influenza (flu) virus on Day 0. The stippled area of the graph represents the normal range for TCR. For the 32 days between the pre-exposure (NORM) TCR to a return of TCR to the normal range at Day 35, the TCR values were significantly decreased. Note that the overall average TCR remained significantly decreased for more than four weeks after clinical signs had disappeared. (Willoughby *et al.*, 1990).

Horses involved in most forms of athletic exertion suffer exercise-induced pulmonary hemorrhage (EIPH). While only a small percentage of horses show blood at the nostrils, a much higher percentage will have a small amount of blood present in the airways after their competition. This hemorrhage originates from the upper back corner of the horse's lung. Previously, it was believed that underlying airway disease (inflammation) led to EIPH. However, it has also been shown that blood in the lung causes inflammation. This new knowledge will change our approaches to tackling EIPH. The latest research focus has been on the vascular system and blood pressure changes during exercise. Although the cause is not clear, on a day-to-day management basis we must remember that this hemorrhage occurs commonly and the site of hemorrhage makes an ideal location for secondary infection.

Inflammation of the small airways

The focus of this article is on small airway disease in horses. The best known is Chronic Obstructive Pulmonary Disease (COPD or “heaves”). This is a full-blown allergic disease. Horses suffering from COPD show obvious symptoms while at rest. These include a chronic cough, flared nostrils and forced abdominal breathing. This characteristic abdominal breathing occurs as the horse contracts its stomach muscles to force air through obstructed airways. The obstruction is caused by inflammation, increased mucus production and bronchospasm. COPD arises from what is believed to be a full-blown allergic response, usually to dust from the horse’s feed and bedding. It is comparable to a person with severe asthma. A horse suffering with this condition would not be capable of moderate exercise without becoming severely distressed. COPD can manifest in many degrees of severity.

At the other end of the scale is a lower airway disease described as Lower Respiratory Tract Inflammation (LRTI) or Small Airway Disease (SAD). While it is not a full blown allergy as in the case of heaves, it is an inflammatory process. It usually becomes apparent when the horse is put under extreme exertion. This inflammation may not become apparent in the horse that is used for pleasure although the disease can become more severe with time until even light exercise becomes distressing.

The question arises: “Is small airway disease significant to the apparently healthy athlete?” The answer is, unfortunately, a resounding “yes!”. Minor degrees of airway inflammation and small increases in mucus production quickly take their toll on the equine athlete attempting to take 150 breaths per minute, as is the case with horses in competition. Another complicating factor is that horses do not have a sensitive cough reflex. There can be quite a lot of mucus in the horse’s airways without it coughing. This is in sharp contrast to humans and dogs. An endoscopic examination of the airways can reveal large amounts of mucus in a horse with no history of coughing. A horse with respiratory disease does not necessarily cough.

If a sample of mucus material is collected from the lungs, large numbers of neutrophils (pus cells) are usually found. Significant bacterial infections can be found when the samples are taken to the microbiology laboratory. These bacteria can be the primary cause of the problem, or they can be a secondary complicating issue following a viral infection. These secondary infections can increase the horse’s recovery time.

COMMON CAUSES OF SMALL AIRWAY DISEASE

There are three common causes of small airway disease:

1. Infectious agents (including bacteria and viruses).

2. Airborne dust. Mould spores are the most common constituents and causes for concern in the air of stables. When inhaled in large enough numbers, these spores can cause inflammation and irritation of the small airways in horses which do not suffer allergy.
3. Noxious gases. The most common is ammonia.

It should always be highlighted that the above causes can interact in many ways. For example, dust can increase a horse's susceptibility to infection. Equally, a horse suffering a respiratory tract infection in a dusty environment will take a lot longer to recover than if it was breathing fresher air.

Another way these factors can interact has been demonstrated using nuclear medicine studies at the Equine Research Centre. These studies showed that it takes a month for the cilia lining the airways to recover their function following a bout of influenza. So, while the horse looks sick for only a few days, its lungs will take up to a month to recover (Figure 1). At this time, the lungs will also be very sensitive to the inhalation of airborne pollutants.

With the motto of "prevention being the best cure," emphasis should be placed on providing fresh air. Both the provision of fresh air, and therapeutic agents, will be discussed in this article as the latter can be particularly beneficial to getting horses back to full health and fitness to meet their true athletic potential.

Environment

The successful environmental control of disease involves maintaining the horse's level of exposure to irritants below that which induces disease. This critical level is called the Threshold Limiting Value (TLV). Unfortunately, the TLV for stable irritants is unknown. The level of irritants which can affect horses varies within and between individuals. The best approach lies in minimizing the horse's exposure to such contaminants at all times. The simplest management method is to turn the horse out for as many hours in the day as possible. This can be facilitated by use of a run-in shed. When horses cannot be turned out in this way managing the indoor air quality becomes critical. There are two main sources of dust in the stable: the first is the horse's feed and the second is the bedding.

Forage

Hay is the single most common source of mould spores for the horse. All hay will have some mould spores present. There are many types of mould living on the hay as it grows in the field. These spores come from what are typically referred to as "field

fungi” and are usually large and do not have a good chance of getting into the lower airways. The dust spores that are more dangerous are small (respirable). The highest exposures to dust are associated with hay that has been baled damp, as can happen after a rainy summer. The high moisture content influences the microflora in the bales and metabolic activity of the organisms causes the bales to heat. The moulds that thrive in this high moisture and heat are very prolific. The spores from these moulds are very small and when inhaled can reach deep into the lungs.

The soaking of hay is a time-proven method of minimizing the horse’s exposure to mould spores. However, feeding soaked, poor quality hay to horses cannot be condoned. As hay which falls to the floor dries, the spores can again become airborne to be inhaled by the horse. Furthermore, even though the spores are not inhaled from soaked hay, they are still ingested along with any toxins present. Moulds produce secondary metabolites called mycotoxins which if present in large enough amounts can cause health problems. Mycotoxins may contribute to reproductive, immunological, respiratory, gastrointestinal and other disorders in livestock, including the horse. Preliminary studies at the Equine Research Centre have shown the presence of potentially significant levels of mycotoxins in hay being fed to horses. This was in hay that owners were happy with, based on visual inspection. In addition, in heavily moulded hay the nutritional content can be changed.

Alternatives to hay such as alfalfa cubes or haylage can be fed whenever the hay quality is in question (Figure 2). Silage and haylages are increasingly being successfully used as alternatives to hay. Haylage is mature grass or legume that is baled with a high moisture content but sealed in airtight plastic bags. As fermentation occurs the pH becomes lower. These acidic conditions inhibit mould growth. As long as the bags are airtight then there should be no mould growth. When the bags are opened to feed, they should be fed within two to three days as this product moulds very quickly once it has been exposed to air. Broken or damaged bags should not be used. There have been some deaths due to botulism associated primarily with big-bale silage. In this context, silage which smells of ammonia or contains dirt should be avoided.

Treated chaffed hay and straw and complete cubed diets also offer alternatives to feeding hay. These products are convenient and usually effective in minimizing respiratory disease.

Mycotoxins

“Mouldy” forage can contribute to a range of disorders in the horse. Inhaled fungal and actinomycete spores can cause primary allergic and inflammatory respiratory disease, as well as influencing the incidence, severity and duration of episodes of infectious respiratory disease. However, moulds may also produce toxic secondary metabolites called mycotoxins. Mycotoxins may contribute to reproductive, immunological, respiratory, gastrointestinal and other disorders in livestock including

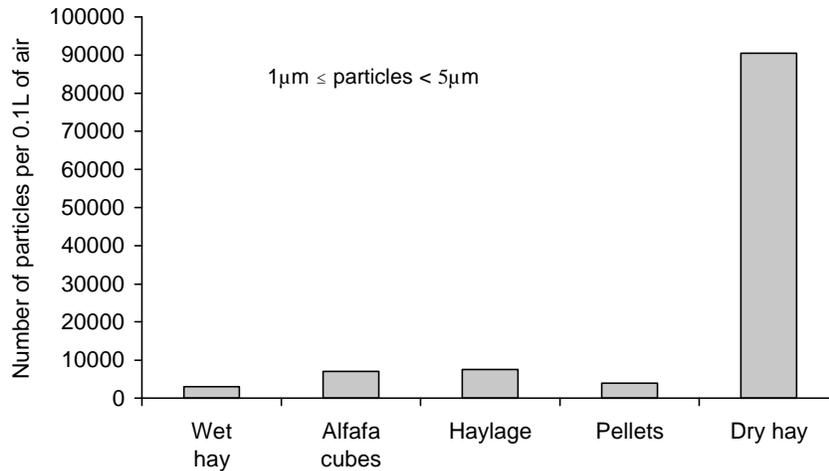


Figure 2. Dust particles associated with five forage products during feeding

the horse. Mycotoxins can behave as immunosuppressants thus having the possibility to contribute to secondary disorders. Mould and subsequent mycotoxin contamination of a forage can increase in extreme environmental conditions such as droughts or rain, followed by cold weather, or from mechanical damage to the forage.

Fusarium mycotoxins include vomitoxin (deoxynivalenol or DON), zearalenone, fumonisins, moniliformin and fusarin C. There is evidence of synergism between mycotoxins, one example being between vomitoxin and fusaric acid (a phytotoxin). Symptoms are induced at much lower levels of exposure when these two toxins are ingested together than when ingested separately.

Fumonisin B1 is associated with mouldy corn poisoning in horses (ELEM or Equine leukoencephalomalacia). Animals must consume a feed which contains at least 10 ppm fumonisin B1 for ELEM to occur. Fumonisin B1 can also cause liver damage and pulmonary edema in horses and swine. Combined levels of fumonisin B1 and fumonisin B2 as low as 5 ppm have been associated with ELEM whereas swine were unaffected at those levels. Zearalenone is an estrogenic toxin. Toxicity can lead to reproductive problems including hyperestrogenism. Disorders seen in swine and horses include uterine enlargement and inflammation and atrophy of the ovaries. It has not been shown to cause abortions. Vomitoxin belongs to a group of mycotoxins called tricothecenes which have been associated with loss of appetite, vomiting, lesions of the intestinal tract, immunosuppression, lethargy and ataxia in domestic animals and man.

Preliminary studies at the Equine Research Centre have shown the presence of potentially significant levels of vomitoxin in hay being fed to horses. This was in hay that owners were happy with, based on visual inspection. Vomitoxin is among the most frequent tricothecene contaminant found on cereal crops in the United States. FDA levels of concern for vomitoxin for wheat are 2 ppm for wheat entering the

milling process for humans and 1 ppm for the finished product for humans. The level for wheat for livestock is 4 ppm. As a comparison, the levels found in this study could potentially have an influence on the health of horses consuming such hay. The threshold of significant biological activity is unknown for the horse; however, chronic exposure to lower levels rather than acute exposure to high levels may contribute to a wide range of disorders.

Bedding

Even the cleanest of straw contains significantly more small, respirable fungal spores than alternative beddings, such as wood shavings, paper, peat or the new synthetic beddings. However, in poorly ventilated stables or where deep litter is allowed to accumulate, significant moulding of the plant-based beddings can occur. Deep litter management systems have the added disadvantage of allowing build-ups of bacteria, the larvae of gastro-intestinal parasites and noxious gases such as ammonia.

Ammonia

Ammonia is a recognized concern of stable management. The source of ammonia is the horse's urine and feces. Ammonia is released by the action of bacteria that degrade organic matter. Ammonia inhibits the movement of the cilia in the airways, consequently affecting these defence mechanisms' ability to remove particles from the lung. Ammonia can also increase mucus production. Aerial ammonia is highly soluble in water so much of it is absorbed in the upper airways. Ammonia can also be absorbed by hygroscopic dust particles. The ammonia can be released from these particles in the lung. Ammonia can be particularly high when stalls are being mucked out (Figure 3). If the horse is left in the stall during mucking, it will be subjected to high levels of ammonia and high levels of dust.

Management practises will affect the levels of ammonia that are found in a horse barn. Ammonia is water soluble so manure pits, wooden walls, bedding with high moisture contents and humid air can hold ammonia. Ammonia levels in barns increase with increasing temperatures and humidities. Methods which lower ammonia levels include a well drained floor, high ventilation rate, frequent mucking out and dry bedding with some commercially available control products.

Ventilation

A well-ventilated stable will help to minimize the horse's exposure to a wide range of environmental contaminants. These include fungal spores, bacteria, and noxious gases.

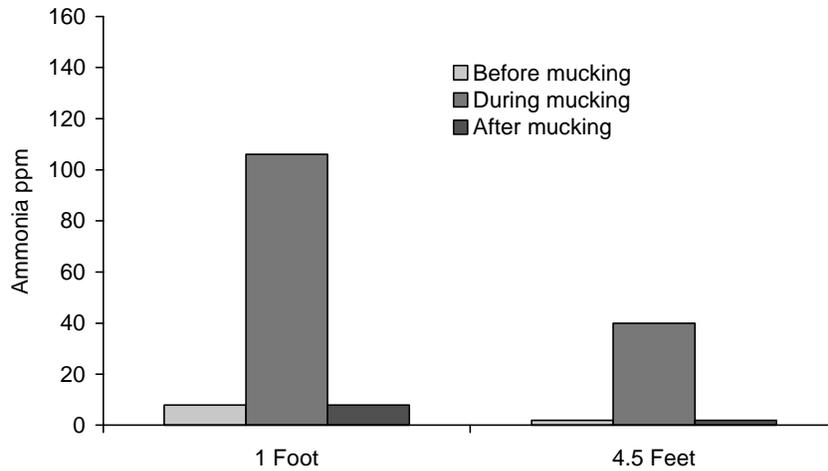


Figure 3. Ammonia levels measured at two heights above floor level in stalls with straw bedding

However, significant levels of fungal spores can be inhaled in well-ventilated stables when contaminated feeds and beddings are present. The horse is inquisitive; it sniffs at its bedding. When the horse lies down, its nostrils are positioned for maximum uptake of spores released from its bedding. Indeed, a horse given mouldy hay in the field (the ultimate of natural ventilation) can still come down with airway problems.

The importance of ventilation in stalls even where clean feeds or beddings are used cannot be over-emphasized (Figure 4). Ventilation will help to overcome condensation, prevent moulding of bedding material *in situ* and minimize the levels of all airborne contaminants to which the horse may be exposed.

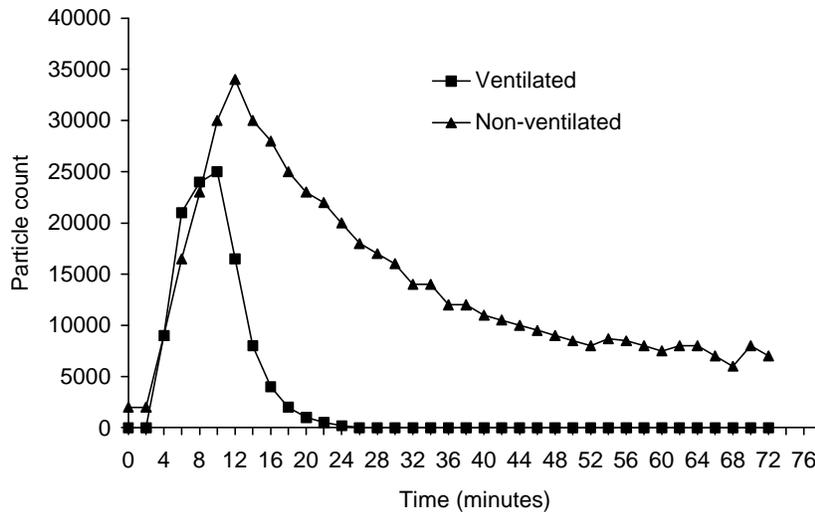


Figure 4. The effects of ventilation on dust levels in a stable after mucking out. Dust levels quickly drop in the well-ventilated stable

To ensure adequate ventilation when designing new or altering existing horse accommodation, openings must be positioned or mechanical ventilators used to allow six to eight air changes per hour. Proper mixing of air throughout the whole building is critical, the latter being particularly important with barns. Louvres or Netlon can be used to prevent draughts at horse height. In warmer weather, barn doors and windows are usually left open. Ventilation systems should be designed to achieve sufficient air changes in the barn in colder weather when these openings are closed. The ideal ventilation system must provide adequate fresh air and distribute it uniformly without causing drafts.

Horses have a wide temperature tolerance, with an ideal temperature range being between 10-30°C. In a cold barn without drafts the only horses likely to experience cold stress are young foals. It is better to put a blanket on your horse and to allow some air flow than to shut the barn up tight. If extra heat is needed there are a number of infrared heaters on the market that are very suitable for stables.

Insulation

During the winter many people make the mistake of trying to keep the barn warm by severely reducing ventilation. The result is that moisture cannot escape and a cold, clammy, damp environment is produced. Insulation allows you to maintain a tolerable temperature inside the stable, even though a constant air exchange is occurring. In the winter insulation conserves heat and reduces condensation and in the summer it helps to keep the barn cooler. In the spring and fall, insulation helps to maintain a stable environment inside while there are temperature fluctuations outside caused by warm days and cold nights. The vents in a well insulated barn can be smaller than in a non-insulated barn.

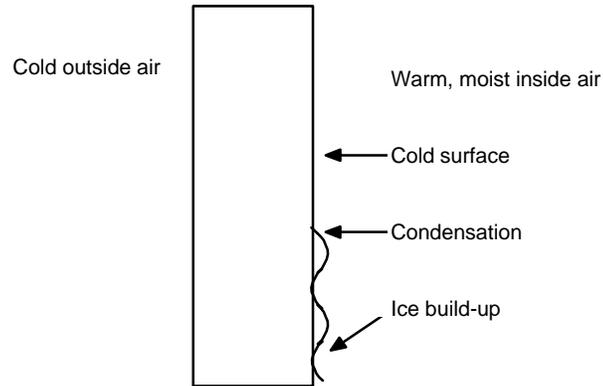
Condensation occurs when warm moist air contacts a cold inside wall (Figure 5). If the surface temperature of the inside wall is below the dew point (55°F or 13°C), air next to the surface becomes saturated and moisture condenses to water. When the surface temperature is below freezing, frost occurs. Water stains on the ceiling of a barn or stable are tell-tale signs of moisture and/or ventilation problems.

If the inside wall is warmer than the outside wall (close to 55°F or 13°C, the dewpoint) then condensation will not occur (Figure 6). However, the air will cool as it passes between the two walls and condense on the outside wall. To solve this problem, a vapour barrier on the warm wall can also help prevent condensation in the insulation. Wet insulation is not as effective and condensation could lead to rotting of the barn structure.

Sunlight

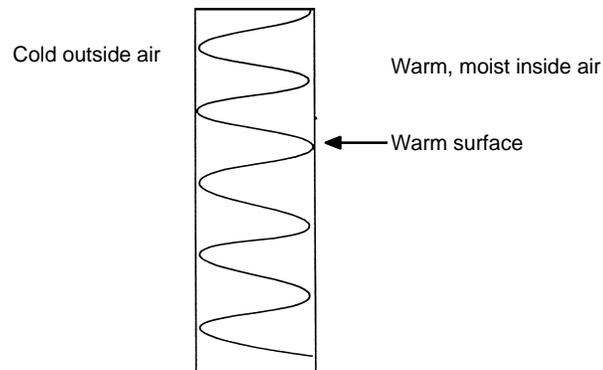
Sunlight is one useful natural resource often overlooked with horse housing. A skylight of clear perspex in the roof allows light, including the UV rays, into the stable. The

UV rays are a strong and inexpensive natural killer of bacteria and viruses. A general guide is 10% of the roof area used for skylights.



Inside surface temperature is below dew point (13°C)

Figure 5. No insulation



Inside surface temperature is above dew point (13°C)

Figure 6. Insulation

Prophylactic and therapeutic approaches to non-infectious lower respiratory tract diseases

An overview of prophylactic and therapeutic approaches to LRTI and COPD will be provided in this section. These conditions share some common pathophysiological changes. However, there are facets of both conditions that are unique in terms of therapeutic approaches and some situations where pharmaceuticals used in treating one condition are inappropriate when dealing with the other. Even more seriously pharmaceuticals appropriate for the treatment of one condition could be life threatening in the other.

Figure 7 presents a step-wise progression up a pyramid for the treatment and alleviation of COPD. Therapy starts at the bottom of the pyramid and if symptoms persist or worsen each tier is added in turn until satisfactory control occurs. Once the horse is stabilized, the pyramid can be descended as tiers are progressively removed.

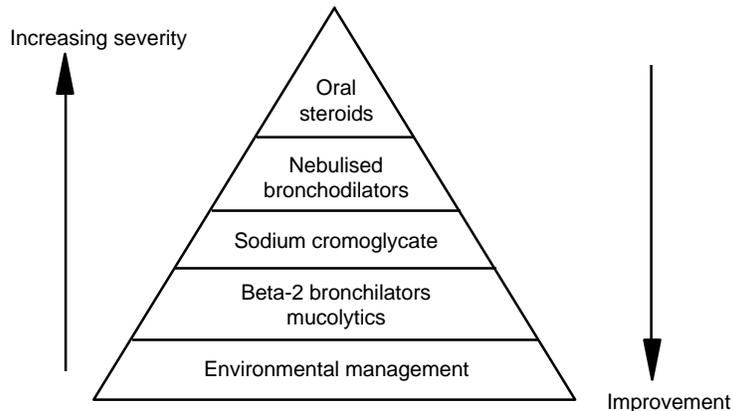


Figure 7. COPD therapy objectives (Clarke, *et al.*, 1995)

STEP 1: ENVIRONMENTAL MANAGEMENT

This is the most important component of treating and preventing COPD. Failure to properly attend to air hygiene is the primary reason for failure of therapeutic regimens. Poor air quality is also an important causative factor associated with LRTI. Inhaled mould spores can induce a primary inflammatory response without an allergic reaction occurring. However, it must also be remembered that infectious agents including viruses, bacteria and mycoplasmas are involved in many episodes of LRTI. Even when these pathogens are involved, attention to air hygiene is important in decreasing the severity of symptoms in individual cases and also in hastening the recovery from an infection.

The principles involved in the environmental management in relation to air hygiene of stables have been reviewed previously in this article. The critical factors include:

- a) the provision of adequate ventilation and appropriate drainage within stables,
- b) the use of alternatives to straw for bedding,
- c) the avoidance of deep litter bedding and
- d) the provision of forage using the than traditionally made hay.

STEP 2: BRONCHODILATORS AND MUCOLYTICS

Bronchodilators, mucus accumulation and the increased production of thick tenacious mucus are common pathophysiological changes associated with diseases of the lower airways. The B₂-agonist clenbuterol (Ventipulmin, Boehringer Ingelheim) is the most widely used bronchodilator in equine practice. Anticholinergics e.g. atropine though effective as bronchodilators can have unwanted systemic side effects. Xanthene derivatives including theophylline and aminophylline are bronchodilators, but have short durations of action and side effects including tachycardia and sweating which are frequently seen due to their narrow therapeutic margin. The mucolytic agent dembrexine is often used in combination with a beta₂-agonist to alleviate symptoms associated with accumulators of mucus. Mucolytic agents help to decrease the viscosity of thick tenacious mucus while the beta₂ agonist will stimulate mucociliary clearance enhancing the removal of mucus from the lungs.

STEP 3: SODIUM CROMOGLYCATE

The administration of sodium cromoglycate by nebulizer one a day for 5 days can provide up to 1 month of prophylaxis to asymptomatic COPD horses exposed to poor air hygiene. There does appear to be individual variation in responsiveness to sodium cromoglycate. Sodium cromoglycate is known as a mast cell stabilizer. There may be another mechanism by which it induces protection to inhaled allergens.

STEP 4: NEBULIZED BRONCHODILATORS

Nebulization of clenbuterol has been shown to be effective in inducing bronchodilation in horses which are non-responsive to intravenous or oral clenbuterol. Ipratropium bromide is an atropinic agent which induces bronchodilation when administered by nebulization. One advantage of nebulization is that it can be used to avoid unwanted side effects associated with systemic administration of pharmaceuticals; however, there is added inconvenience and cost associated with the use of nebulization. While there are unlikely to be a lot of new drugs to treat respiratory disease in the future, there will be new technologies such as inhalers which will facilitate the delivery of pharmaceuticals directly into the lung.

STEP 5: ORAL CORTICOSTEROIDS

Corticosteroids are used to treat COPD a lot more frequently in North America than in Great Britain. Laminitis is one steroid-induced side effect that is cause for

concern. Care should also be taken in administering corticosteroids to horses which may have a respiratory tract infection. These risks can be minimized by careful choice of dose and frequency of administration. Dosage should be decreased as the horse's condition improves. Another strategy involves the simultaneous use of a corticosteroid with a beta2-agonist.

Conclusion

Considerable short and long term demands are placed on the equine athlete's lungs. Special attention must be paid to the quality of the air which our horses breathe. Respiratory tract infections are practically unavoidable with competing athletes, even with the most up-to-date vaccines. Pharmaceuticals will continue to have an important role in these and in other respiratory problems of horses. As to respiratory disease of horses, the two main messages suggested are firstly, that prevention is better than cure, and secondly, the earlier treatment is commenced, the sooner the horse will recover.

FOR CONSIDERATION IN EVERYDAY STABLE MANAGEMENT:

- wet all hay that is fed indoors and feed it on ground level
- sprinkle the barn aisle with water when sweeping
- remove the horse from the barn when the stalls are being mucked or swept
- turnout for as long as possible
- use a low dust bedding with a daily mucking out
- consider ventilation during all seasons
- up to date vaccination program
- exercise horses regularly

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