Inflammatory Airway Disease

Outline

• What is IAD
• Review of Heaves
• Criteria for IAD
• Exclusion
• Types of horses affected
• Clinical signs
• Diagnosis
• Treatment options

Minimum Criteria for IAD\(^1\)

• Seen in horses of any age
• Poor performance
• Exercise intolerance
• Coughing
• With or without excess tracheal mucus

\(^1\)Coulet et al JVIM 2007
IAD is NOT HEAVES

Old Disease

- “Heaves are produced upon the diaphragm by too much food in the stomach and bowels and is cured by lessening the quantity of food to occupy the same space. After the horse is turned out to grass a few days, the heaves will usually disappear, from the fact that the bowels are generally relaxed by exercise and pure air” ... 1903 D. Magner

Review of RAO

- NO LONGER CALLED COPD
- Not similar to the human form of COPD
- Similar to human asthma
- Seen mostly in horses > 7 years of age
- Most common exacerbation is winter and spring
- No gender or breed predilection, though females seem to be more prone.

2B Rush ACVIM 2006
Review of RAO

- 12% of mature horses have some degree of environmental-induced lower airway disease
- 50% of horses that present for evaluation of respiratory disease have heaves
- Heritable component
  - 10% incidence in horses with healthy parents
  - 44% incidence in horses with 2 affected parents
  - Intermediate incidence in horses with one parent affected

Etiology of Heaves/RAO

- Hypersensitivity reaction
- Primary allergens thought to be
  - Aspergillus fumigatus,
  - Thermoactinomyces vulgaris,
  - Faenia rectivirgula

Pathophysiology of Heaves

- Delayed hypersensitivity reaction
- Natural defense mechanisms are hyper-reactive
- Inflammation occurs in excess
- Massive infiltration of neutrophils
- Proliferation of mucosal cells
- Leads to thickening in the airway walls and obstruction of normal air flow during breathing
**Bronchoconstriction**

- Mucosa is thickened by inflammation
- Increase in mucous secretion
- Acetylcholine causes constriction of smooth muscle

Thus... **BRONCHOCONSTRICTION**

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**Inflammation & Bronchoconstriction**

**Leads to...**

- Hypoxemia
- Hypoxemia severe enough to drive ventilation in dyspneic horses
- Increased dead space ventilation (74%)
- High V/Q ratios >10

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**Inflammation & Bronchoconstriction**

**Leads to...**

- Pulmonary hypertensions is consistent finding
  
  – Due to hypoxic vasoconstriction and alveolar hyperinflation

- Horses with end stage heaves have **increased right heart size**
Diagnosis

- Usually based on clinical history and signs
- Heave line, increased respiratory effort at rest.
- Bronchoalveolar lavage
- Presence of neutrophils
- Can be as high as 50-70% neutrophils
- Horses with >20% neutrophils will likely have impaired lung function

Bronchoalveolar Lavage Fluid

Normal horse
<5% Neutrophils

Heavy horse
>20% Neutrophils

Inflammatory Airway Disease
Inflammatory Airway Disease

- Not Recurrent Airway Obstruction
- Heterogeneous population of horses with low-grade to severe pulmonary inflammation
- Impaired performance
- Interruption of training of young performance and race horses

Review Airway of Horses

Obligate Nasal Breathers

- Exposure to ammonia
- Irritant material such as endotoxin in organic dust
- Upper respiratory tract filters out much of inhaled particulate
- Minimizes exposure of lungs to the particulate matter
- Filtration system not perfect
Filtration System

• Very small particulate matter
• < 5-10 microns in diameter
• Gaseous materials pass freely down the airways and reach small airways an alveoli

Response

• Initiate a nonspecific immune response
• Culminates in neutrophil, eosinophil, and or mast cell migration to alveolar and airway lumen
• Increased production of mucus
• Activation of irritant receptors
• Trigger of reflex bronchoconstriction and cough
• Eventually results in impairment of pulmonary function

Response

• Presence of inflammatory response
• Tissue inflammation
• Edema
• Exudation
• Decreasing size of functional airway diameter
• Over time
• Lower airway inflammation may cause permanent tissue damage and impairment of pulmonary function
Response

• Prolonged antigenic exposure
• May lead to development of allergic airway disease
• IAD may still be in some animal a preliminary stage in the development of RAO
• This relationship however is still often a huge debate!!

Inflammatory Airway Disease

• Affects horses of any age
• Subtle clinical signs
• Poor performance
• Exercise intolerance
• Plus or minus coughing
• With or without excess tracheal mucus

Prevalence

• Guessing game
• 55% of 2-year old thoroughbreds in training could be classified as having lower airway disease on the basis of mucus in the trachea on endoscopy and inflammation on examination of TTW
• 37% of horses from abattoir studies have histological evidence of airway inflammation
Exclusion criteria for IAD

• Evidence of systemic signs of infection
  – Fever
  – Hematologic abnormalities comparable to infection
  – Increased respiratory effort at rest (RAO)

Definition of IAD

• Non-septic inflammation detected by
  – Cytology of bronchoalveolar lavage fluid (BALF)
  – Pulmonary dysfunction
    • Evidence of lower airway obstruction
    • Airway hyper-responsiveness
    • Impaired blood gas exchange at rest or during exercise

Clinical Signs

• Chronic intermittent cough
• Cough occurs at rest or during exercise
• Increased mucoid secretions
• Serous to mucopurulent nasal discharge
Clinical signs continued

- +/- subtle wheezes or ↑ breath sounds
- Severe IAD may have ↑ RR and abdominal contraction on expiration
- No pleural pressure changes as with heaves

Clinical Signs continued

- Poor performance
- Delayed recovery of respiratory rate after exercise
- Exaggerated respiratory effort during work
- All above signs are non-specific!

- In non-race horses can persist for months to years

Pathogenesis

- Poorly defined
- Variety of etiological agents
- Contribution of agents to development of IAD varies among horse populations
  - AND...
  - Feeding
  - Housing
  - Preventive medicine practices
  - Distribution of infectious agents
  - Genetic influences
Pathogenesis

- Non-infectious agents thought to be key
- Exposure to high burdens of aerosolized particles and gases in an cumulative manner
- Respirable fraction may contain variety of organic and inorganic particles including
  - Endotoxin,
  - Ultrafine particles,
  - Mites,
  - Microorganisms,
  - Inorganic dust and noxious gases

Pathogenesis

- All from being stabled
- Exact contribution is unknown
- Can either be allergens or infectious agents or both

How Do You Diagnosis IAD?
Diagnosis

- Tracheal inflammation NOT SUFFICIENT to characterize IAD
- Discordance between TTW and BALF cytology
- Association between tracheal wash inflammation (neutrophils) and cough is known

- TTW is deemed insufficient for diagnosis in the absence of BALF or pulmonary function testing

Bronchoalveolar Lavage Fluid

- Test of choice for IAD and RAO
- Most commonly encountered cytology is:
  - Increased nucleated cell count
  - Lymphocytosis,
  - Monocytosis
  - Mild neutrophilia.

- 2 other profiles seen:
  - Increased mast cell >2%
  - Increase eosinophils >0.1%
- Abnormal BALF has been associated with non-race horses and race horses
Pulmonary Function Testing

• Especially if horse has a hx of poor performance,
• Pulmonary function testing can help if impaired lung mechanics are the cause of the poor performance
• Plethysmographic method is adapted to use in the field
• Has been available since 2001
• Open Pleth™, Ambulatory monitoring Inc, Ardsley NY
• Easy to transport, not invasive, well tolerated

Open Pleth

www.ambulatory-monitoring.inc

Open Pleth

www.ambulatory-monitoring.inc
Pulmonary Function Testing

- Not invasive
- Tight fitting mask on the nose
- Two elastic bands over the thorax and abdomen
- Performed on the horse under light sedation
- Duration of test about 30 minutes

Pulmonary Function Testing

- Based on flowmetric comparison of two different techniques
- Respiratory inductance plethysmography and pneumotachography
- The device measures the “breathing pump” by measuring the thoracic and abdominal action during breathing through the inductance coils within the core of the two elastic bands placed around the chest and abdomen of the patient

Pulmonary Function Testing

- At the same time measurements of tidal volume, minute ventilation and peak inspiratory and expiratory flows are registered at the nose by the pneumotachograph
- The plethysmographic and pneumotachographic flowmetric data are compared during simultaneous recordings
- Discordance of the two techniques is indicative of airway obstruction
Pulmonary Function Testing

• Open plethysmograph has been validated in horses to assess for presence or absence of airway hyper-reactivity
• This tends to be very helpful when horses are mildly affected or are in a period of remittance of clinical signs
• Yet still have abnormal airway reactivity that responds to marked bronchoconstriction, inflammation and mucus production when exposed to triggering factors

Pulmonary Function Testing

• Assessment of airway hyper-reactivity starts with measurement of baseline function
• If normal, the horse is exposed to initially very low increasing concentrations of histamine
• Pulmonary assessment is re-assessed after each nebulization
• Test is stopped after a set threshold of pulmonary resistance is reached

Just A Note

• Pulmonary function testing may have a value during pre-purchase examination
• Helps evaluate the presence or absence of airway hyper-reactivity in horses
• Such as those in remission of clinical signs of RAO, seasonal pasture associated RAO or IAD
Radiographs

- Non-specific findings...
- Insufficient for diagnosis of IAD
- Can rule out other potential differential diagnoses

Ultrasound

- Also non specific for IAD
- Can help rule out other disease

Differential Diagnoses

- IAD has many non-specific findings shared with multiple other respiratory conditions
  - RAO:
  - Hay challenge
  - Lack of labored breathing or severe exercise intolerance helps distinguish.
  - BALF fluid of IAD less neutrophilia and more basophils, eosinophils and mast cells
Differential Diagnoses

- Upper Respiratory Disease
  - Variety conditions lead to static and dynamic airway obstruction
  - Presence of abnormal breathing sounds at rest or during exercise
  - Absence of serous or mucoid nasal discharge
  - Absence of lower airway inflammation rule out IAD

Differential Diagnoses

- Bronchopneumonia
  - Severe infection, fever, depression
  - Weight loss, decreased appetite
  - Signs of systemic disease not IAD
  - Tracheal wash may differentiate IAD and pulmonary infection
  - IAD horses may have septic tracheal wash but WILL NOT be systemically ill

Differential Diagnoses

- Exercise Induced Pulmonary Hemorrhage
  - Common cause of poor performance
  - Diagnosis made by finding blood upon tracheoscopy or
  - Increased hemosiderin in alveolar macrophages
EIPH

– Controversial:
– Link between EIPH and IAD?

– Several studies found no significant correlation between hemosiderophage and neutrophil counts in BALF of horses with IAD.¹²

¹ Sanchez et al JVIM 2005
² Clark Aust Vet J 1995

Differential Diagnoses

• Viral Infection
  • Usually display more severe signs of illness
  • Fever, lethargy, cough and nasal discharge

• Lung Worm
  • Dictyocaulus arnfieldii
  • Similar clinical signs to IAD
  • Coughing, abnormal respiratory noise, mildly increased respiratory effort
Lung Worm

- Eosinophilic BALF
- TTW may reveal presence of larvae
- Resolution of signs with parasiticidal drugs rules out IAD

Treatment

Goals of Treatment

- Must be clear so client, patient and veterinarian are satisfied
- Entails team approach
- Client education is key!
- Goals:
  - Eliminate cough and bronchoconstriction that impair performance
  - Reduce mucus production and airway plugging
  - Reduce airway reactivity
  - Prevent recurrences
Treatment

- Important to get a baseline assessment of patient prior to start of therapy
- Includes ideally
  - Auscultation with and without rebreathing bag
  - Careful physical examination
  - Observation during exercise
  - Baseline pulmonary function testing
  - Measure of airway reactivity
    BAL cytology

Treatment

- Combination of environmental modification and anti-inflammatory drugs SHOULD help with IAD
- However...limited evidence based data regarding the efficacy of the therapy

Environmental management

- Use feedstuff and bedding that are low in dust and endotoxin concentrations
- Increase removal of airborne particles and noxious gases by improving ventilation
- Use cardboard or shavings for bedding
- Use pelleted feed instead of hay
- Decrease dust exposure during cleaning and feeding time
Control Airway Inflammation

- For those horses with IAD that have a neutrophilic BAL, aerosolized corticosteroids seem to work well
- Can use systemic corticosteroids as well
- Need to dose for 2-4 weeks
- Doesn’t always work

Anti-Inflammatories

- Dexamethasone 0.03-0.1 mg/kg q 24 hours
- Prednisolone 1-2.2 mg/kg a 24 hours
- Inhaled
  - Fluticasone 2000-2500 ug q 12-24 hours
  - Beclomethasone 2500-3750 ug q 12-24 hours

Mast cell stabilizers

- Sodium Cromoglycate improves clinical signs and decrease hyper-responsiveness
- Good response in horses with BALF with high mast cell counts
- This is an aerosolized drug
Sodium Chromoglycate

• 0.02% solution for nebulization
• 200 mg q 12 to 24 hours

Inteferon-alpha

• Oral administration of low dose interferon-α (50 U q 24 hours for 5-7 days, wait 10 days repeat the same dose)
• Decreases airway inflammation
• Reduction of BALF immunoglobulins and inflammatory mediators
• Higher doses don’t work
• Does not affect mast cell or eosinophil counts

Bronchodilators

• Unknown if they truly work. Extrapolated from RAO studies
• Most likely best to use with corticosteroids as well RAO.
• Usually takes 2 weeks for resolution of signs
Bronchodilators

- Systemic: Clenbuterol 0.8-3.2 ug/kg a 12-24 hours
- Teofylline 0.5-1 mg/kg q 2-8 hours
- Inhaled
  - Ipatropium bromide 360-470 ug/kg a 6-12 hours
  - Albuterol 360-720 ug q 3-12 hours

HOW LONG???

- Treatment should be given for 2-4 weeks in all cases
- Since many times clinical signs are subclinical
- If the treatment doesn’t seem like its made an improvement after that time frame, may need to switch some of the drugs around
- Each horse seems to respond differently to treatment

Repeat BALF

- Since IAD is many times a subclinical disease
- Prior to horses going back into full training
- Should repeat BALF to make sure decrease in inflammation and pulmonary function testing if possible
Much more work needs to be done

- Determine prevalence of IAD in different horse populations
- Investigate relationship of IAD and syndrome of tracheal inflammation and excess mucous as studied in many race horses
- Relationship between viral and bacterial infection and development of IAD
- Evaluate effect of bronchodilators and anti-inflammatory drugs for tx of IAD

Take Home Message

- Not Recurrent Airway Obstruction
- Heterogeneous population of horses with low-grade to severe pulmonary inflammation
- Impaired performance
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Take Home Message

- Clinical Signs
- Chronic intermittent cough
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- No pleural pressure changes as with heaves
Take Home Message

- Diagnosis
- Thorough Physical Examination
- Rebreathing Examination
- BAL
- Pulmonary Function Testing
- Treatment
- 2-4 weeks
- Varies with the horse
- Recheck before allowing horse to go back to work

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