OVERVIEW OF EIPH, PREVALENCE AND IMPACT ON HORSE HEALTH

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The Groundwork
Pascoe and coworkers: University of California Davis
Hinchcliff and coworkers: University of Melbourne
Erickson and coworkers: Kansas State University
Exercise-induced pulmonary hemorrhage
Exercise Induced Pulmonary Hemorrhage in Other Species
History of EIPH

Bartlett’s Childers
Aka “Bleeding” Childers

Flying Childers
b. 1716
“The first truly great racehorse”
Clinical Presentation of EIPH

- Nose bleed
  - Epistaxis
- 0.15% of horses
  - Takahashi et al., 2001
- Only diagnostic method before the flexible endoscope
- Source of blood?
Endoscopy

Many horses have blood in their air passages

Obvious that blood originates in the lungs

A large percentage of horses bleed

(Pascoe et al, 1981)

http://www.tufts.edu/vet/sports/performance.html
Grading the Severity of Bleeding
Grade 2 or greater reduces performance

(Hinchcliff et al, 2005)
Clinical Presentation of EIPH

- Hemosiderophages
- Macrophages that have “eaten” old blood
- Very common
- 90% of racing horses bleed

(Sweeney et al, 1992; McKane et al, 1993)
A problem of horses that exercise intensely
- 26 – 77% of Standardbreds
- 62% of Quarter horses
- 75.4% of Thoroughbreds (Raphel and Soma, 1982)
  - Prevalence increases with repeated endoscopic examination of each horse (Birks et al., 2002)
  - More likely to spot “a bleed”
Severity of EIPH in 744 Thoroughbreds (Melbourne, Aus.)

(Hinchcliff et al., JAVMA 227:768, 2005)
The incidence of EIPH increases with:
- Age (lifetime starts)
- Speed
- Distance
- More prevalent on hard going
- Colder days
Effect of EIPH on performance
(744 Thoroughbreds, Melbourne, Aus.)

(Hinchcliff et al., JAVMA 227:768, 2005)
Are the Majority of Horses with EIPH Systemically Sick?

- No fever
- Eat well
- No signs of pain
- In a few horses, bleeding is a consequence of a heart arrhythmia (easily detectable by physical examination)
- Radiographic changes may be evident in lungs of some severe bleeders
- Ultrasound examination less useful
The only horses that have been examined are those whose career has been ended by severe repeated bleeding

In 1987, UC Davis examined 26 horses in Hong Kong

In 2007, we obtained tissue from 7 horses from the Singapore Turf Club

In 2011, we obtained 10 horses from midwestern USA tracks
Horse lung terminology

Dorsal

Caudal

Dorso-caudal

Cranial

Ventral

Cranio-ventral
Distribution of lesions is caudo-dorsal
Affects left and right lungs equally
EIPH: pathology

Hemosiderin
Fibrosis
Angiogenesis
  (new blood vessels)
Bronchiolitis

O'Callaghan et. al. 1987
Re-examine the EIPH lesions Singapore Turf Club and Midwestern Racetracks

Horses that were retired because of repeated bleeds
Pathological Consequences of Severe EIPH (epistaxis)
Lung slices

Control

A few lesions

Many lesions
Lesion scoring

- Scored lesions
  - Hemosiderin
  - Interstitial fibrosis
  - Pleural/septal thickening
  - Vein wall thickness
  - New blood vessels

Derksen et al., Eq Vet J 41:586, 2009
Thoracic Radiograph of Severe EIPH Horse
Oxygen consumption: 19 gallons/min
Heart rate: 220 beats/min
Volume of blood/beat: 3 pints
Blood flow thru lungs: 75 plus gallons/min
Anatomy of the pulmonary circulation

- Arteries, veins
Latex cast of human airway (white), arterial tree (red), and venous tree (blue) provided with permission from Ewald Weibel.
Alveoli where gas exchange takes place
Blood capillaries

Air

Air
Lung capillary

- The wall of the capillary is 3/10000 mm thick
- Exposed to high pressure during exercise
- Capillary stress failure
Blood pressure in the lung during exercise
Pulmonary arterial pressure increases with speed

Manohar 1993

Rest  EX:8 m/s  EX:10 m/s  EX:13 m/s

Mean pulmonary artery pressure (mm of Hg)

Control  4 Hours after Furosemide
Blood pressure in the lung during exercise

95 mm Hg (80)

Right heart

Left heart
Blood pressure in the lung during exercise:

- Right heart: 95 mm Hg (80)
- Left heart: 55 mm Hg (45)
Blood pressure in the lung during exercise

Right heart: 95 mm Hg (80)
Left heart: 75 mm Hg (65)

55 mm Hg (45)
Capillary stress failure

Erickson and Poole, IVIS
Capillary stress failure during exercise (3 horses)

West et al., J Appl Physiol 75:1097, 1993
Raising capillary pressure from 25 to 100 mm Hg causes leakage of red blood cells

<table>
<thead>
<tr>
<th>Animal</th>
<th>Pressure at which capillaries break</th>
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<tbody>
<tr>
<td>Horse</td>
<td>92 mm Hg</td>
</tr>
<tr>
<td>Dog</td>
<td>66 mm Hg</td>
</tr>
<tr>
<td>Rabbit</td>
<td>37 mm Hg</td>
</tr>
</tbody>
</table>
Raising capillary pressure from 25 to 100 mm Hg causes leakage of red blood cells

Birks E K et al. J Appl Physiol 1997;82:1584-1592
Raising arterial transmural pressure above 95 mm Hg causes leakage of red blood cells
Red blood cells leaked from capillaries

Erickson and Poole, IVIS
What is the consequence of bleeding into the lungs?
Single instillation of blood into the air passages is cleared rapidly

Control

7 d

6 h

14 d

Derksen et al., Eq Vet J 39:334, 2007
Multiple weekly instillations of blood cause very little disease

Williams et al., Eq Vet J 43:354, 2011

Normal

Autologous blood
5 instillations

Very occasional bronchiolitis obliterans
Lesions of EIPH are unlike those caused by blood instillation.
Equine Pulmonary Vein Anatomy

Normal lung

Intra-lobular Vein
Venocclusive remodeling

- 1) Venous wall remodeling
- 2) Hemosiderin
- 3) Interstitial fibrosis
- 4) Pleural and septal fibrosis
- 5) Neovascularization

Normal

Williams et al., Vet Pathol 45:316, 2008

Severe EIPH

Verhoeff-van Gieson stain
Venocclusive Remodeling will Raise Capillary Pressure Even Higher

EIPH occluded vein

Occluded vein
Pulmonary capillaries
Pulmonary vascular remodeling: a response to

- Mechanical stimuli
  - Increased intravascular pressure
  - Shear stress
- Chemical stimuli
  - Hypoxia
  - Inflammation – role in remodeling (Hassoun et al, 2009)
    - Pressure is proinflammatory in lung venules (Kuebler et al, 1999)

Pulmonary venous remodeling
- Understudied!
- Response to sustained pulmonary hypertension (Johnson et al, 1997)
Blood flow is greatest in the dorso-caudal lung region

Bernard et al., J Appl Physiol
81:1062, 1996

Hlastala et al., J Appl Physiol
81:1051, 1996
Hemosiderin causes fibrosis
  - Buschman and Ballard, Chest:104:293, 1993
  - Eagan et al., Resp Med 90:547, 1996
Pathogenesis of EIPH
Venous remodeling and furosemide

- Furosemide has direct effects on pulmonary veins
  - Greenberg et al, JPET 42:228, 1994
- Relaxes venous smooth muscle
- This should decrease capillary pressure
  - Reduce severity of bleeding
Sudden death and pulmonary hemorrhage

- 6 centers
- 268 cases
- Circa 69% pulmonary hemorrhage
- Cause of death or a complication

Lyle et al., Eq Vet J 43:324, 2011