Immunity and Sub-Acute Ruminal Acidosis

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Outline

• Sub-acute ruminal acidosis (SARA) impact on the rumen
• Digestive mucosa response to SARA
• Systemic SARA responses
• Managing to reduce SARA impacts

Sub-Acute Rumen Acidosis (SARA)

Sub-Acute Rumen Acidosis

- ↑ Fermentable CHO
- ↑ Bacteria Growth Rate
- ↑ VFA
- ↓ pH (SARA)
- Shifts in Bacteria Populations
- ↑ Bacteria Toxins
- Damage to GI Epithelium
- Systemic Immune Response to SARA (Inflammation)

Rumen Epithelium Response to SARA

Healthy rumen papillus

Papillus following SARA challenge

Univ. of Guelph, Univ. of Manitoba, UNC
Rumen Microbiome Shifts with SARA

- ↓ microbial diversity → ↓ functionality
- ↓ fiber digesting bacteria
- ↑ virulent and pathogenic bacteria
- ↑ bacterial toxins

Papillae Adherent Bacteria Shifts during SARA

- Change in community structure
- ↓ diversity

Rumen Fluid Bacteria Shifts during SARA

- Alfalfa pellet-induced SARA
  - Prevotella (Bacteroidetes)
- Severe grain-induced SARA
  - E. coli (Proteobacteria)
- Mild grain-induced SARA
  - M. elsdenii (Firmicutes)
- Severe grain-induced SARA
  - S. bovis (Firmicutes)

Severity of SARA and degree of inflammation highly correlated with E. coli abundance.

University of Manitoba

Rumen Fluid Endotoxin (LPS)

- Manitoba work:
  - Study 1: Gozho et al. 2007. JDS 90:856; reverse log transformed
  - Study 2: Khafipour et al. 2009. JDS 92:1060; mean of 3 time points
  - Study 3: Li et al. 2012. JDS 95:294

Grain-Induced Increases in Other Bioactive Compounds

University of Alberta / Austria
Saleem et al. 2012. JDS 95:6606

Rumen Fluid Toxicity during Acute Acidosis
• Acute acidosis challenge in two cows (X9 and X10)

Nagaraja et al. 1978. JAS. 47:1329

Rumen Fluid Toxicity during Acute Acidosis

Rumen Structure

Nagaraja et al. 1978. JAS. 47:1329
Intestinal Structure

- Jejunum
- Ileum
- Large Intestine

Intestinal Protection

- Animals are protected from toxins and microbes in their intestines via:
  - Tight junctions between cells
  - Mucus layer
  - Cells specialized to protect animals from pathogenic microbes and their toxins
    - Goblet cells (mucus)
    - M cells
    - Paneth cells
    - Enteroendocrine cells
    - Tuft cells

Tight Junctions

- Tight junction proteins link intestinal mucosa cells
  - Block entry of pathogens and dietary antigens

Goblet Cells

- Goblet cells secrete mucins found in loose and adhered mucus that protects the intestinal epithelium

Suzuki 2013

Johansson et al. 2013
Other Cells with Immunoregulatory Activities

- Paneth cells secrete antimicrobial peptides
- M cells sample lumen for immune cells
- Enteroendocrine cells produce cytokines and hormones
- Tuft cells produce cytokines

Gut-Associated Lymphoid Tissue

- Gut-associated lymphoid tissue (GALT)
  - Microstructures of white blood cells that lie just beneath the epithelium in the lamina propria
  - Respond to gut contents by maintaining homeostasis (e.g. presence of commensal bacteria) or activating immune response (e.g. presence of pathogenic organisms)
  - Regulate cell cycles of epithelial cells and “tightness” of tight junctions
Immunoglobulin A

- Immunoglobulin A (IgA) is produced by activated B cells (plasma cells)
  - Can bind and deactivate bacteria and antigens
  - B cells produce many different IgA that are specific to a single organism or antigen

Response to Dysbiosis

- Commensal bacteria in gut suppress inflammation
- Dysbiosis or pathogenic organism challenge results in:
  - Inflammation
  - Activation and recruitment of immune cells
  - Damage to epithelium
  - Passage of organisms and pathogens to sub-mucosal space

Findings from Monogastric Studies

• Crosstalk between microbes, intestinal cells, and GALT cells is essential for healthy epithelium
• A “healthy” mix of commensal microbes promotes mucin production and suppresses inflammation
• An “unhealthy” mix of gut microbes reduces mucin production and tight junction integrity, promotes systemic and local inflammation, and can induce sickness in healthy animals
• Chronic inflammatory disease states are associated with dysbiosis

SARA Impacts on the Intestines

• Excessive carbohydrate fermentation in the rumen mirrored by changes in the intestines
• Fecal indicators of SARA
  – Diarrhea, frothy feces, increased fecal particle size, mucin casts

Fecal Bacteria Shifts During SARA


LPS in the Large Intestine

SARA feeding challenge

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Grain-Induced SARA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rumen LPS (EU/mL)</td>
<td>10,405</td>
<td>118,522</td>
</tr>
<tr>
<td>Feces LPS (EU/g)</td>
<td>12,832</td>
<td>93,154</td>
</tr>
</tbody>
</table>

Li et al. 2012. JDS 95:294

Abomasal oligofructose (OL) or starch (ST) challenge

<table>
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<tr>
<th></th>
<th>Control</th>
<th>OL</th>
<th>ST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feces LPS (EU/g), average over 42 h</td>
<td>2,445</td>
<td>21,345</td>
<td>5,324</td>
</tr>
</tbody>
</table>

Gresley et al. 2016. JAS 94:284
Rumen Epithelium Response to SARA

Univ. of Guelph, Univ. of Manitoba, UNC

Colon Epithelium Response to SARA

Nanjing Agricultural University, Goat study

35% Concentrate 65% Concentrate

Inflammatory Response to SARA

Liver Acute Phase Proteins
• Main ones are α-1 acid glycoprotein, haptoglobin (Hp), LPS-binding protein (LBP), and serum amyloid A (SAA)
  – Produced by liver and other tissues in response to an inflammatory trigger
• They moderate the inflammatory response, recovery, and tissue repair
• Produced in response to grain-induced SARA, indicating grain-induced SARA causes inflammation

Liver release of acute phase proteins and inflammatory cytokines generates systemic inflammation
If liver is damaged, bacteria or antigens can enter systemic circulation

Liver

Remum
Intestines
Heart

Bacteria or antigens that penetrate mucosa flow to liver
Lameness and SARA

- Laminitis is subsequent to gut damage and liver inflammatory response
- In the horse, properties of endogenous and exogenous compounds produced following gut damage result in changes in the hoof:
  - Dilation of arterioles
  - Constriction of venules
  - Inflammation of the corium
  - Death of corium cells
  - Hypoxia
  - Reduced cell adhesion
  - Disrupted growth factor signaling

Reducing Risks of SARA

- Animal management
  - Adequate bunk space
  - Avoid empty bunk / long periods away from feed
- Ration composition
  - Adequate NDF, particle size, and effective fiber
  - Proper starch inclusion level
  - Proper starch fermentability
  - Adequate moisture
### Reducing Risks of SARA

- **Monitor feces particle size**
  - Fiber >1 cm suggests poor digestibility
    - Mary Beth Hall
  - >10% on top screen suggests SARA or other digestibility problem
    - Cotanch and Darrah
- **Watch for mucin plugs, foamy or frothy feces**

### Reducing Risks of SARA

- **Provide exogenous buffers**
  - 0.5-0.75% sodium bicarbonate (Beauchemin and Penner)
  - DCAD > 300 mEq/kg (Erdman)
  - Increase with heat stress

### Reducing Risks of SARA

- **Supplements**
  - Stabilize rumen environment
    - Live yeast, yeast products, direct fed microbials
  - Increase mucosa integrity / reduce mucosa inflammation
    - Live yeast, yeast products, biotin, zinc, thiamin
  - Reduce systemic inflammatory response
    - Omega-3 fatty acid sources, OmniGen-AF

### Summary

- In healthy animals, gut structures and the gut microbiome interact to suppress inflammation and maintain animal health
- During SARA, dysbiosis combined with reduced epithelial integrity allows systemic entry of gut toxins
- Localized tissue damage and systemic inflammation resulting from SARA lead to reduced performance
Thank you!
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