New Insights into health of dairy calves during the pre-weaning period

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OUTLINE

- Introduction
- Common health issues
  - *BRD and diarrhea*
  - *Metagenomic studies*
- On going research at TTU
GROWTH DURING PRE-WEEKING PERIOD HAS LONG TERM IMPACT ON PERFORMANCE

Hulbert and Moisa, J Dairy Sci, 2016
FEEDING CALVES

Restricted  Ad libitum

Goals:
• Deep, clean and dry bedding
• Good ventilation / air quality

COMMON HOUSING SYSTEMS

Individual pens  Group pens

Curtis et al. Veterinary Record, 2018
INDIVIDUAL HOUSING

- Pros:
  - Isolated animals
  - Decreased disease / pathogens transmission
  - Easy to monitor milk consumption and health

- Cons:
  - Feeding is labor intensive (ad libitum systems often not practical)
  - Cleaning is hard and labor intensive
  - Welfare / socialization / public perception

GROUP HOUSING

- Pros:
  - Easy to clean
  - Easy to adopt ad libitum feeding systems
  - Socialization and public perception

- Cons:
  - Transmission of pathogens
  - Difficult to monitor intake
  - Difficult to detect sick animals
DIFFERENT HOUSING SYSTEMS – DIFFERENT CHALLENGES

- Lower incidences of disease
- Difficult to feed
- Higher incidences of disease
- Higher feed intakes

COMMON HEALTH ISSUES

- Diarrhea – Scours
- Bovine respiratory disease
  - *Pneumonia – Otitis*

nasopharynx is connected to the middle ear via the Eustachian tube
MULTIFACTORIAL DISEASES

METAGENOMICS – SCOURS

Birth

Weekly collection of fecal samples

Weaning

DNA extraction from fecal samples

Amplification of the 16S rRNA gene / Purification of amplicons/sequencing

Ribosomal Database Project (RDP) pipeline initial processor

Removal of chimeric sequences (DECIPHER)

RDP classifier / genera prevalence in each different sample

Estimation of Chao1 index / rarefaction curves

Discriminant analysis

Weekly Chao1 estimates were analyzed with multivariable models. Chao1 index estimates were trusted as repeated measurements

Genera significant for the discriminant analysis models were further analyzed with the use of multivariable models

Oikonomou et. al, PLOS ONE, 2013
Discriminant analysis of fecal microbiomes by week of life

Discriminant analysis of fecal microbiomes for the first week of calf life and for calves that suffered or not from diarrhea

Oikonomou et al., PLOS ONE, 2013

Adjusted means of body weight by week of life as well as adjusted means of diarrhea incidence for different Faecalibacterium spp. terciles

Oikonomou et al., PLOS ONE, 2013
Oral Administration of *Faecalibacterium prausnitzii*

**Incidence of severe diarrhea (%)**

- CONTROL: N = 296
- FPTRT: N = 258

**Days from birth until diarrhea**

**Mortality due to severe diarrhea**

- **A**
  - P ≤ 0.05
  - Survival probability (%) vs Days from birth until death or weaning

- **B**
  - P = 0.17
  - Survival probability (%) vs Days from birth until death or weaning

Overall mortality

**Oral Administration of *Faecalibacterium prausnitzii***

- Mortality due to severe diarrhea
- Overall mortality

Foditsch et al., PLOS ONE, 2015
Oral Administration of *Faecalibacterium prausnitzii*

![Graph showing ADG (kg) for Control and FPTRT](image)

*Fodisch et al., PLOS ONE, 2015*

**METAGENOMICS – BRD**

- 174 calves
- Nasal swabs collected at 3, 14, 28, and 35 days of life
- 16s rRNA gene sequencing

*Fodisch et al., PLOS ONE, 2015*

*Lima et al., Scientific Reports, 2016*
METAGENOMICS – BRD

Lima et al, Scientific Reports, 2016

METAPHYLAXIS – BRD

- CTR = untreated
- M1 = one tildipirosin injection administered at 10 days of life
- M2 = two tildipirosin injections at 10 days and 35 days of life

<table>
<thead>
<tr>
<th>Mortality</th>
<th>CTR</th>
<th>Reference</th>
<th>Hazard ratio (95% confidence limit)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td></td>
<td></td>
<td>0.53 (0.30–1.33)</td>
<td>0.11</td>
</tr>
<tr>
<td>M2</td>
<td></td>
<td></td>
<td>0.62 (0.29–1.39)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BRD</th>
<th>CTR</th>
<th>Reference</th>
<th>Hazard ratio (95% confidence limit)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td></td>
<td></td>
<td>0.06 (0.47–0.87)</td>
<td>0.07</td>
</tr>
<tr>
<td>M2</td>
<td></td>
<td></td>
<td>0.70 (0.49–1.04)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Otitis</th>
<th>CTR</th>
<th>Reference</th>
<th>Hazard ratio (95% confidence limit)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td></td>
<td></td>
<td>6.35 (3.67–12.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>M2</td>
<td></td>
<td></td>
<td>0.40 (0.18–1.3)</td>
<td>0.30</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>BRD and/or Otitis</th>
<th>CTR</th>
<th>Reference</th>
<th>Hazard ratio (95% confidence limit)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td></td>
<td></td>
<td>0.70 (0.19–2.55)</td>
<td>0.009</td>
</tr>
<tr>
<td>M2</td>
<td></td>
<td></td>
<td>0.73 (0.46–1.18)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

TRADITIONAL CALF RAISING MANAGEMENT

TRANSPORTATION CHALLENGES – HIGH RISK FOR BRD
MANAGEMENT OF HIGH RISK CALVES

Total n of animals enrolled = 1,360

Active ingredient is mycobacterium cell wall fraction (MCWF) of *Mycobacterium phlei*, a non-pathogenic, soil-borne bacterium

<table>
<thead>
<tr>
<th>Item</th>
<th>Enrolled (%)</th>
<th>Treated (%)</th>
<th>Dead (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calves</td>
<td>1,360</td>
<td>155 (11.3)</td>
<td>16 (1.2)</td>
</tr>
<tr>
<td>CON</td>
<td>458</td>
<td>60 (13.1)</td>
<td>6 (1.3)</td>
</tr>
<tr>
<td>BTIS</td>
<td>449</td>
<td>44 (9.8)</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>ATIS</td>
<td>453</td>
<td>51 (11.4)</td>
<td>5 (1.1)</td>
</tr>
</tbody>
</table>

CON: control; BTIS: before transport; ATIS: after transport

Disease treatment events were lower than the national average

Courtesy of Luciano Caixeta
No difference in hazard of treatment within first month of life

<table>
<thead>
<tr>
<th>Group</th>
<th>Adjusted Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>Ref.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BTIS</td>
<td>0.74</td>
<td>0.50 – 1.09</td>
<td>0.14</td>
</tr>
<tr>
<td>ATIS</td>
<td>0.84</td>
<td>0.57 – 1.2</td>
<td>0.35</td>
</tr>
</tbody>
</table>

CON: control; BTIS: before transport; ATIS: after transport

BTIS reduced hazard of treatment for pneumonia but not for scours within first month of life

<table>
<thead>
<tr>
<th>Group</th>
<th>Pneumonia</th>
<th>Scours</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>CON</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>BTIS</td>
<td>0.54</td>
<td>0.31 – 0.94</td>
</tr>
<tr>
<td>ATIS</td>
<td>0.88</td>
<td>0.55 – 1.42</td>
</tr>
</tbody>
</table>

CON: control; BTIS: before transport; ATIS: after transport

Courtesy of Luciano Caixeta
SERUM BIOMARKERS OF STRESS AND INFLAMMATION AFTER TRANSPORTATION OF NEWBORN CALVES

- 168 calves
  - Control (untreated) group
- Biomarkers measured
  - Haptoglobin
  - Cortisol
  - L-lactate

Correlation between biomarkers

- Haptoglobin
  - 67.9 μg/ml
- Cortisol
  - 17.36 ng/ml
- L-lactate
  - 6.5 mM
Association between biomarkers and BRD

![Graph showing BRD incidence for different biomarkers](image1)

Association between Hp and BRD

![Graph showing proportion not treated for BRD](image2)
Association between biomarkers and weight gain

![Graph showing the association between biomarkers and weight gain](image)

- **Hp**: Average Daily Gain (kg/d)
- **Cortisol**: Average Daily Gain (kg/d)
- **L-lactate**: Average Daily Gain (kg/d)

**P-values**:
- **P < 0.01**
- **P = 0.14**
- **P = 0.18**

**PHYSIOLOGIC VS PATHOLOGIC LEVELS OF HAPTOGLOBIN**

![Graph showing physiologic vs pathologic levels of haptoglobin](image)

*D.L. Godson et al./Veterinary Immunology and Immunopathology 51 (1996) 277–292*
LEVELS OF HAPTOGLOBIN IS ASSOCIATED WITH IMMUNE SYSTEM ACTIVATION

CONTINUING CALF RESEARCH