Characterizing Feed Restriction’s Impact on Biomarkers of Leaky Gut

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Insufficient Nutrient Intake

- Variety of occasions in animal agriculture when feed intake is naturally or intentionally inadequate to meet to requirements
  - Gestating sows
  - Off-feed events
  - Transition period of dairy cows
  - Heat stress
  - Overcrowding
  - Drought
Intestinal Histology

Does inadequate feed intake cause leaky gut?

Pearce et al., 2011
LPS/LBP Complex

 ↑ Inflammatory response

 ↑ Acute Phase Proteins:
   • Serum Amyloid A
   • Haptoglobin
   • LBP
Intentionally Induced-Leaky Gut Preliminary Data

Gamma-secretase inhibitor (GSI: causes leaky gut in laboratory animals)
**Dry Matter Intake**

Day: $P < 0.01$

**LBP**

Day: $P < 0.01$

**Serum Amyloid A**

Day: $P < 0.01$

**Haptoglobin**

Day: $P < 0.01$
Hypothesis

Feed restriction increases biomarkers of leaky gut
Materials and Methods

- 28 lactating Holstein cows (157 ± 45 DIM; 713 ± 54 kg BW)
  - Parity ranging from 2 to 4
- Period 1 all cows individually fed total mixed ration (TMR)
- Period 2 each cow assigned one of 5 feed treatments
  - 100% of ad libitum feed intake
  - 80% of ad libitum feed intake
  - 60% of ad libitum feed intake
  - 40% of ad libitum feed intake
  - 20% of ad libitum feed intake
- Feed was administered 3 times daily
Materials and Methods

- Day 1
- Day 2
- Day 3

Acclimation Period
- Fed TMR and Body weight

Period 1
- Began Receiving Different Treatments

Period 2
- Body weight and sacrificed AL and AL40 treatments
Daily Measurements

- Blood serum and plasma
  - CBC obtained on P1D2 and P2D4
- Vitals (x2; 0700 and 1900 h)
  - Heart rate (HR), Respiration rate (RR), Rectal temperature (Tr)
- Milk yield (x2; 0600 and 1800 h)
- Feed intake
  - P1 (0800 h)
  - P2 (0800, 1200, 1800 h)
Within a cow, each specific variable’s period 1 value (when available) served as a covariate.

PROC MIXED SAS 9.4 (SAS Institute Inc., Cary, NC)
- Fixed effects: replicate, treatment
- Preplanned orthogonal contrasts (linear, quadratic, cubic)

Data reported as LSmeans:
- Significant: $P \leq 0.05$
- Tendency: $0.05 < P \leq 0.10$
**Dry Matter Intake**

- Treatment: $P<0.01$
- Linear: $P<0.01$

**Milk Yield**

- Treatment: $P<0.01$
- Linear: $P<0.01$
Insulin

- Treatment: $P<0.01$
- Linear: $P<0.01$

BHBA

- Linear: $P=0.07$

NEFA

- Treatment: $P<0.01$
- Linear: $P<0.01$

Glucose

- Treatment: $P<0.01$
Insulin: Dry Matter Intake

Treatment: $P=0.04$
Quadratic: $P<0.01$

P2D5

- AL
- AL80
- AL60
- AL40
- AL20

Bars labeled with 'a' or 'ab' indicate significant differences.
**Haptoglobin**

- Treatment: $P=0.06$
- Cubic: $P=0.02$

**Serum Amyloid A**

- Linear: $P=0.10$

**LBP**

- Linear: $P=0.09$

**Lymphocytes**

- Linear: $P=0.04$
Feed Restriction’s Impact on the Ileum

Cows Fed 100% of Ad-Libitum Feed Intake

Cows Fed 40% of Ad-Libitum Feed Intake
Conclusions

- Increasing feed restriction increases the circulating levels of acute phase proteins
- Feed restriction alters intestinal villi morphology
- The insulin to feed intake ratio did not differ between ad libitum controls and the most severely restricted treatments

We conclude that feed restriction impacts intestinal permeability and increases biomarkers of inflammation.
Summary

The negative consequences of inadequate nutrient intake on agriculture productivity may in part be due to leaky gut.
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