Nutritional Management of Ketosis and Fatty Liver in Dairy Cows

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Clinical and Subclinical Ketosis

- **Subclinical**
  - Excess of ketones in the absence of clinical signs of disease (β-OH-butyrate > 14 mg/dL)

- **Clinical**
  - Elevated blood concentration of ketone bodies (> 27 mg/dl) in association with hypoglycemia (Glucose < 45 mg/dl) with clinical signs of disease
    - Anorexia, rumen atony, dry feces, decreased milk yield, nervous ketosis

Lactational Incidence and Prevalence

- Prevalent metabolic disorder in high producing dairy cows
- Lactational incidence in first 9 wks
  - 43% (BHBA ≥ 15 mg/dL)

Duffield et al. (2002)
Ketone bodies

CH₃-C-CH₃
Acetone

CH₃-C-CH₂-COO⁻
Acetoacetate

β-OH-butyrate

NAD⁺
OH

* β-OH-butyrate is incorrectly classified as a ketone body

Ketone bodies (β-OH-butyrate)

- Normally produced during β-oxidation of butyrate by rumen wall
- Supply energy
  - Adipose tissue synthesis
  - Milk fat synthesis
  - Brain during starvation
- Integral part of normal ruminant intermediary metabolism

Synthesis and Utilization of Ketones

Liver | Blood | Extra-hepatic tissues
--- | --- | ---
Acyl-CoA | FFA | Glucose, Acyl-CoA
Glucose, Ketones | Urine, Milk, Ketones | TCA, Acetyl-CoA, Ketones, TCA

Lungs
Causes

- Inadequate energy intake
- Increased triacylglycerol mobilization
- Excessive incomplete hepatic FA oxidation

Dry Matter Intake and Plasma NEFA

Fatty Liver or Hepatic Lipidosis

- Increased accumulation of triglycerides in the liver
- Diagnosed by liver biopsy
- No specific blood test
Classification of types of fatty liver

<table>
<thead>
<tr>
<th>Category</th>
<th>% Triglyceride by wet tissue weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal healthy</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Mild fatty liver</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Moderate fatty liver</td>
<td>5 - 10</td>
</tr>
<tr>
<td>Severe fatty liver</td>
<td>&gt;10</td>
</tr>
</tbody>
</table>

Gaal et al., 1983

Severe form is associated with serious effects on health and production.

Poor Transition Can Result in Metabolic Disorders

Fatty liver

Concentrations of Triglyceride and Glycogen in Hepatic Tissue of Transition Dairy Cows

Data from Underwood (2003)
## How prevalent is fatty liver?

<table>
<thead>
<tr>
<th></th>
<th>20%, 33%, 33%, 40%, 45%, 48%, 53%, 65%</th>
<th>5%, 5%, 11%, 14%, 15%, 15%, 20%, 24%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Moderate</strong></td>
<td><strong>Severe</strong></td>
<td><strong>May affect over half to two-thirds of lactating cows!</strong></td>
</tr>
</tbody>
</table>

Incidences reported from 9 studies around the world

Summary from Drackley (2006)

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### Fatty Liver Can Happen in Days

- Cow with NEFA concentration in plasma of 1.0 mM in the day of calving
  - Assuming that palmitic acid \((C_{16}H_{32}O_2)\) is the main NEFA in blood : \(1 \text{ mM} = 256 \text{ mg/L}\)
- Removal of NEFA depends upon its concentration in plasma and the blood flow to the liver
  - Hepatic blood flow of 1,000 L/h with 256 mg of NEFA/L = 256 x 1000 x 24 h = 6.1 kg of NEFA flowing through the liver in 24 h
  - 20 to 30% extraction efficiency
  - 1.2 to 1.8 kg of FA extracted by the liver in a single day for a cow with plasma NEFA of 1.0 mM
  - Bovine liver : 8 to 10 kg or 3 to 4 kg of dry weight
  - Liver triacylglycerol can increase in 5 to 10% units in a single day
- Therefore, hepatic lipidosis can occur in 1 to 2 days

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**Figure 1:** Metabolic pathways in dairy cows during peripartum fatty liver (adapted from Guffat et al., 1998)
Transition Period

- High energy requirements for milk synthesis
- Coordinated adaptations
  - Increased sensitivity of adipose tissue
  - Insulin resistance
  - High blood GH
  - Increased adrenergic receptors on the adipocyte cell membrane
  - Decreased hepatic glycogen and increased lipid content
  - Glycogenolysis associated with influx of NEFA
- High energy demands associated with low energy intake in presence of hormonal shifts → hepatic lipidosis
Hormones Trigger Mobilization of Stored Triacylglycerols

- Lipid droplets in adipocytes is coated with perilipins, preventing lipid mobilization.
- When [glucose] is low in blood, it triggers the release of glucagon, which binds its receptor in the adipocyte membrane, stimulating adenylyl cyclase, via a G protein, to produce cAMP.
- This activates PKA.
- PKA phosphorylates perilipin molecules on the surface of the lipid droplet.
- This allows HSL access to the surface of the lipid droplet.
- HSL hydrolyzes triacylglycerols to FFA.
- FAs leave the adipocyte, bind serum albumin in the blood, and are carried in the blood.
- Enter tissues via a specific fatty acid transporter.
- In tissues (liver, muscle), FA are oxidized to CO2, and the energy of oxidation is conserved in ATP.
Hepatic FA Metabolism

- Ruminant liver
  - Little hepatic lipase activity (LPL)
  - Low capacity to export VLDL
  - Oxidation of FA: main route for FA disposal
    - Ketogenesis becomes extremely important
      - Mitochondria and peroxisomes

Regulation of ketogenesis

- 3 levels
  - Adipose tissue level: lipolysis
  - FA entry into the mitochondria (inner membrane is not permeable to acyl CoA)
  - Acetyl CoA can undergo ketogenesis or complete FA oxidation: energy expenditures of the liver
**Fatty Acid Activation and Transport into Mitochondria (size dependent)**

- FA ≤ 12C cross the mitochondrial membrane without transporter protein.
- FA ≥ 14C use carnitine shuttle to enter mitochondria; carnitine acyltransferase is inhibited by [malonyl-CoA].
- FA is transiently attached to carnitine to form fatty acyl-carnitine catalyzed by CAT I in the outer mitochondrial membrane.
- Fatty acyl group is transferred from carnitine to intramitochondrial coenzyme A by CAT II.
- β-oxidation then proceeds.

**Ketogenesis**

- Hormone regulation:
  - Insulin/glucagon
  - NEFA

- Adipose Tissue

- NEFA
- Esterification - TAG
- VLDL

- Hepatocyte
  - Malonyl CoA
  - Acetyl CoA
  - β-OH-butyrate
  - Acetoacetate
  - Acetoacetate
  - CO₂
  - Acetone
  - β-OH-butyrate dehydrogenase
  - Carnitine transport
  - Esterification - TAG
  - VLDL
Why Ketogenesis vs Complete Oxidation?

- ATP synthesis is reduced (liver does not need to increase its energy and O₂ expenditure)
- Ketones can be exported from the liver and used as energy source by other tissues (muscle, brain, mammary gland, etc)
- Ketones are water-soluble (no need for albumin to transport). Albumin is low early postpartum
- Possible lack of OAA in the mitochondria (not demonstrated in ruminants) – gluconeogenic enzymes are upregulated in periods of low energy supply

When FFA Uptake is Extensive, Hepatocyte Increases Peroxisomal β-Oxidation

- Peroxisomal β-oxidation allows the tissue to dispose of excess of FA
- Generates less ATP per mol of FA oxidized
- First oxidative step, electron pass directly to O₂, generating H₂O₂ → catalase (heat) and the NADH formed in the second oxidative step are exported to the cytosol, eventually entering mitochondria
- Very long chain FA stimulate peroxisomal oxidation. High dietary fats induce the synthesis of the enzymes of peroxisomal β-oxidation in the liver.
- Liver peroxisomes do not contain the enzymes of the citric acid cycle → long-chain or branched FA are catabolized to shorter-chain products (hexanoyl-CoA), which are exported to mitochondria and completely oxidized.

Insulin Affects Tissues Differently

- Muscle
  - Uptake of glucose and immediate use (exercise) or storage as glycogen (exercising muscles can also take up glucose without insulin)
- Liver
  - Uptake of glucose and storage as glycogen
    - Inhibits glycogen phosphorylase
    - Activates glycogen synthase
    - Inhibits gluconeogenesis
    - Promotes re-esterification of FA to TAG (some excess glucose conversion to fatty acids in ruminants)
- Adipose Tissue
  - Promotes glucose uptake and conversion to glycerol for fat production
Insulin Control

- Gastrointestinal hormones
- Hormones

**Muscle**
- Glucose uptake
- Glycogen synthesis

**Adipose**
- Glucose uptake
- Triglyceride breakdown
- Triglyceride synthesis

**Liver**
- Glucose uptake
- Glycogen synthesis
- Fatty acid synthesis
- Glucose synthesis

**Brain**
- No effect

**Pancreas**
- Beta cells
- Insulin

**Feedback**

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Effects of Glucagon

- Prevents hypoglycemia
  - Stimulates glycogenolysis
  - Stimulates gluconeogenesis
- Increases with exercise/stress independent of blood glucose
- Exerts effects through cAMP second messenger system (phosphorylation of target enzymes)

---

Glucagon Control

**Adipose**
- Triglyceride breakdown
- Triglyceride storage

**Liver**
- Glucose breakdown
- Glucose synthesis
- Glucose release

**Brain**
- No effect

---

Effects of Glucagon

- Prevents hypoglycemia
- Stimulates glycogenolysis
- Stimulates gluconeogenesis
- Increases with exercise/stress independent of blood glucose
- Exerts effects through cAMP second messenger system (phosphorylation of target enzymes)
Hepatic lipidosis

- Multiparous cows > Primiparous
  * Greater TAG infiltration into the liver in multiparous
  * Although ketosis might not follow the same pattern

- Decreased ureagenesis:
  * TAG infiltration decreases ureagenesis independent of other metabolic changes during transition

- Decreased gluconeogenesis in some, but not all studies

Approaches to Minimize Ketosis and TAG Accumulation in the Liver

- Reduce TAG mobilization
  - Diets that promote propionate synthesis
  - Gluconeogenic precursors

- Increase FA oxidation by the liver
  - Carnitine and up-regulation of peroxissomal oxidation

- Increase VLDL export by the liver
  - Choline

Shorten the Dry Period:
Attempting to Put the Cow in a More Favorable Energy Status
1. Control (n=21)
   • 56 d dry period
   • 28 d low energy diet, 28 d mod. energy diet
2. Shortened Dry Period (n=23)
   • 28 d dry period
   • High energy diet
3. Continuously Milked (n=21)
   • 0 d dry period
   • High energy diet

(Rastani et al., 2005)
Effect of Propylene Glycol on Liver Lipids and TG

Studer et al. (1993)

% (DM basis)

Control PG 1L/d

% (DM basis)

Control PG 1L/d

MONENSIN

- Active against Gram + microorganisms (in excessive concentrations can also inhibit Gram -)
- Diverges C and H partition in the rumen
  - Reduces methanogenesis
  - Increases propionate production at the expense of C2 and C4
- Reduces CO2 and CH4 production
- Modifies rumen pH
  - Alters pattern of DM intake and concentrations of lactate
- Alters rumen N metabolism
  - Reduces proteolysis and deamination (reduces rumen N-NH3)

BHBA, mg/dL

P < 0.001

NEFA, µEq/L


P < 0.04

Control Monensin
Impact of Monensin CRC on Hepatic Composition (Triacylglycerol and Glycogen)


Cow Health - Ketosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk ratio (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson_A (1992)</td>
<td>1.98 (0.09, 15.87)</td>
<td>0.6</td>
</tr>
<tr>
<td>Wilson_B (1992)</td>
<td>0.32 (0.01, 7.88)</td>
<td>0.6</td>
</tr>
<tr>
<td>Beckett (1998)</td>
<td>0.96 (0.09, 15.29)</td>
<td>0.4</td>
</tr>
<tr>
<td>Duffield (1998)</td>
<td>0.50 (0.17, 1.48)</td>
<td>0.6</td>
</tr>
<tr>
<td>Valavanis_A (2001)</td>
<td>0.65 (0.18, 2.38)</td>
<td>1.7</td>
</tr>
<tr>
<td>Valavanis_B (2001)</td>
<td>0.36 (0.06, 1.03)</td>
<td>1.1</td>
</tr>
<tr>
<td>Duffield (2002)</td>
<td>0.64 (0.31, 1.39)</td>
<td>7.9</td>
</tr>
<tr>
<td>Green_A (2004)</td>
<td>0.74 (0.48, 1.15)</td>
<td>18.8</td>
</tr>
<tr>
<td>Green_B (2004)</td>
<td>0.71 (0.43, 1.19)</td>
<td>18.8</td>
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<tr>
<td>Green_C (2004)</td>
<td>0.86 (0.56, 1.32)</td>
<td>18.8</td>
</tr>
<tr>
<td>Green_D (2004)</td>
<td>0.65 (0.46, 0.99)</td>
<td>18.6</td>
</tr>
<tr>
<td>Green_E (2004)</td>
<td>1.13 (0.70, 1.82)</td>
<td>18.4</td>
</tr>
<tr>
<td>Green_F (2004)</td>
<td>0.80 (0.48, 1.38)</td>
<td>18.8</td>
</tr>
<tr>
<td>Zahra_A (2006)</td>
<td>0.36 (0.09, 1.47)</td>
<td>2.3</td>
</tr>
<tr>
<td>Petersson-Wolfe_A (1997)</td>
<td>0.96 (0.10, 1.07)</td>
<td>2.8</td>
</tr>
<tr>
<td>Petersson-Wolfe_B (1997)</td>
<td>2.00 (0.19, 21.28)</td>
<td>0.4</td>
</tr>
<tr>
<td>Petersson-Wolfe (2007)</td>
<td>1.00 (0.18, 5.83)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Overall (95% CI): 0.75 (0.63, 0.90)

Risk ratio: 0.13325

Ruminally Protected Amino Acids (Methionine)

- AA can be used as gluconeogenic precursors
- Might enhance oxidation of fatty acids by the hepatic tissue
- Might enhance VLDL synthesis and secretion (phospholipid synthesis and/or apolipoprotein synthesis)
- Might reduce ketogenesis
- Supply limiting amino acids for milk and milk protein synthesis
Effect of Supplemental Methionine Analog (Hydroxy Methyl Butanoic Acid) on Hepatic Metabolism

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hepatic TG, mg %</th>
<th>NEFA, mEq/L</th>
<th>Glucose, mg/dL</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>23.0</td>
<td>0.270</td>
<td>61.2</td>
<td>Bertics and Grummer, 1998</td>
</tr>
<tr>
<td>13 g Met</td>
<td>20.0</td>
<td>0.346</td>
<td>59.4</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>12.7</td>
<td>0.820</td>
<td>58.0**</td>
<td>Bertics and Grummer, 1997</td>
</tr>
<tr>
<td>13 g Met</td>
<td>15.4</td>
<td>1.078**</td>
<td>50.3</td>
<td></td>
</tr>
</tbody>
</table>

Effect of CP/RUP on Hepatic TG of Multiparous Transition Cows

<table>
<thead>
<tr>
<th>Treatment (Diet CP, %)</th>
<th>Hepatic TG, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.7 (26.5 % RUP)</td>
</tr>
<tr>
<td>Prepartum</td>
<td>0.55</td>
</tr>
<tr>
<td>Postpartum</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>Huyler et al. (1999)</td>
</tr>
</tbody>
</table>

Rumen-Protected Choline

- Choline is necessary for synthesis of the main phospholipids
  - Phosphatidyl choline (lecithin)
  - Lisophosphatidyl choline

- Lecithin is required for synthesis and secretion of hepatic VLDL and intestinal chylomicrons

- Deficiency can result in fatty liver
Impact of Rumen-Protected Choline on Fatty Liver Treatment

<table>
<thead>
<tr>
<th></th>
<th>Fatty liver</th>
<th>Control</th>
<th>Choline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEFA, µEq/L</td>
<td>703</td>
<td>562*</td>
<td></td>
</tr>
<tr>
<td>Hepatic TG µg/µg DNA</td>
<td>16.7</td>
<td>9.3*</td>
<td></td>
</tr>
<tr>
<td>Recovery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3, % of previous</td>
<td>60.4</td>
<td>52.2</td>
<td></td>
</tr>
<tr>
<td>Day 6, % of previous</td>
<td>48.5</td>
<td>29.9</td>
<td></td>
</tr>
</tbody>
</table>

* P < 0.05


Effect of RPC on clinical ketosis of Dairy Cows

- **Ketonuria**
  - Control: P = 0.001
  - RPC: P = 0.01

- **Clinical Relapses**
  - Control: P = 0.05


Effect of Feeding RPC on Hepatic Composition in Dairy Cows at 9 DIM

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
<th>RPC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>PRTP</td>
<td>PAR</td>
<td>TRT x PAR</td>
</tr>
<tr>
<td>DM, %</td>
<td>65.9±0.04</td>
<td>45.5±0.05</td>
<td>45.7±0.05</td>
<td>0.23 0.01 0.13</td>
</tr>
<tr>
<td>Glycogen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>As, %</td>
<td>0.95±0.20</td>
<td>0.92±0.23</td>
<td>1.15±0.22</td>
<td>1.13±0.25</td>
</tr>
<tr>
<td>DM, %</td>
<td>1.70±0.46</td>
<td>2.32±0.54</td>
<td>1.96±0.52</td>
<td>2.44±0.60</td>
</tr>
<tr>
<td>Triacylglycerol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>As, %</td>
<td>4.93±1.56</td>
<td>6.74±1.76</td>
<td>3.25±1.68</td>
<td>4.83±1.94</td>
</tr>
<tr>
<td>DM, %</td>
<td>8.10±2.9</td>
<td>12.69±2.59</td>
<td>4.87±2.48</td>
<td>7.17±2.85</td>
</tr>
<tr>
<td>Hepatic lipidosis, %</td>
<td>&gt;5% (4/14)</td>
<td>54.6 (9/11)</td>
<td>6.3 (1/12)</td>
<td>22.2 (2/9)</td>
</tr>
</tbody>
</table>

* Hepatic triacylglycerol >5% of wet tissue (Gaal et al., 1983).
Plasma Choline (mg/dL) on d 1 Postpartum and Hepatic Triacylglycerol (Log_{10} of % of wet weight) on d 9 Postpartum, Control (□, ------) and RPC (▲, ———)

Linear relationship (P < 0.001)
Control, \( \log_{10} \text{hepatic triacylglycerol} = 1.541 - 0.01133 \times \text{plasma choline (mg/dL)}, r^2 = 0.28 \)
RPC, \( \log_{10} \text{hepatic triacylglycerol} = 1.599 - 0.009576 \times \text{plasma choline (mg/dL)}, r^2 = 0.64 \)

Controlling caloric intake prepartum

Overfed Cows Consumed 56% more Calories Prepartum than Required based on NRC

Overfeeding During the Dry Period Increases Hepatic TG After Calving

Prepartum caloric intake of cows fed diets with differing Forage/NE\textsubscript{L} content

<table>
<thead>
<tr>
<th>Reference</th>
<th>Prepartum caloric intake, Mcal/d</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas et al. (2007)</td>
<td>11.6</td>
<td>16.2</td>
</tr>
<tr>
<td>Douglas et al. (2006)</td>
<td>11.5</td>
<td>22.0</td>
</tr>
<tr>
<td>Rabelo et al. (2003; 2005)</td>
<td>17.7</td>
<td>21.5</td>
</tr>
<tr>
<td>Doepel et al. (2002)</td>
<td>17.3</td>
<td>20.6</td>
</tr>
<tr>
<td>Hayirli et al. (2011)</td>
<td>15.1</td>
<td>20.5</td>
</tr>
<tr>
<td>Janovick and Drackley (2011)</td>
<td>14.3</td>
<td>19.1</td>
</tr>
<tr>
<td>Kanjanapruthipong et al. (2010)</td>
<td>14.7</td>
<td>18.8</td>
</tr>
</tbody>
</table>

Average 14.6 19.8

Effect of prepartum caloric intake on milk yield

<table>
<thead>
<tr>
<th>Reference</th>
<th>Milk Yield, kg/d</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas et al. (2007)</td>
<td>34.4</td>
<td>39.9</td>
</tr>
<tr>
<td>Douglas et al. (2006)</td>
<td>42.4</td>
<td>40.4</td>
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<tr>
<td>Rabelo et al. (2003; 2005)</td>
<td>38.0</td>
<td>37.3</td>
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<td>Doepel et al. (2002)</td>
<td>34.8</td>
<td>37.2</td>
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<tr>
<td>Hayirli et al. (2011)</td>
<td>34.8</td>
<td>34.4</td>
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<tr>
<td>Janovick and Drackley (2011)</td>
<td>29.9</td>
<td>33.2</td>
</tr>
<tr>
<td>Kanjanapruthipong et al. (2010)</td>
<td>26.3</td>
<td>29.0</td>
</tr>
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</table>

Average 34.4 35.9
### Effect of prepartum caloric intake on FCM yield

<table>
<thead>
<tr>
<th>Reference</th>
<th>Milk Yield, kg/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas et al. (2007)</td>
<td>35.6</td>
</tr>
<tr>
<td>Douglas et al. (2006)</td>
<td>40.8</td>
</tr>
<tr>
<td>Rabelo et al. (2003; 2005)</td>
<td>38.5</td>
</tr>
<tr>
<td>Doepel et al. (2002)</td>
<td>39.1</td>
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<tr>
<td>Hayrif. et al. (2011)</td>
<td>33.7</td>
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<tr>
<td>Janovick and Drackley (2011)</td>
<td>40.5</td>
</tr>
<tr>
<td>Kanjanapruthipong et al. (2010)</td>
<td>26.1</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>36.3</strong></td>
</tr>
</tbody>
</table>

### Effect of prepartum caloric intake on BHBA postpartum

<table>
<thead>
<tr>
<th>Reference</th>
<th>BHBA, mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas et al. (2007)</td>
<td>5.2</td>
</tr>
<tr>
<td>Douglas et al. (2006)</td>
<td>4.8</td>
</tr>
<tr>
<td>Rabelo et al. (2003; 2005)</td>
<td>5.4</td>
</tr>
<tr>
<td>Doepel et al. (2002)</td>
<td>-10</td>
</tr>
<tr>
<td>Hayrif. et al. (2011)</td>
<td>11.6</td>
</tr>
<tr>
<td>Janovick and Drackley (2011)</td>
<td>4.5</td>
</tr>
<tr>
<td>Kanjanapruthipong et al. (2010)</td>
<td>6.1</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>6.8</strong></td>
</tr>
</tbody>
</table>

### Far Off Cows

<table>
<thead>
<tr>
<th>Item</th>
<th>Multiparous</th>
<th>Primiparous</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW, kg</td>
<td>650</td>
<td>570</td>
</tr>
<tr>
<td>BW&lt;sup&gt;0.75&lt;/sup&gt;, kg</td>
<td>129</td>
<td>117</td>
</tr>
<tr>
<td>Net energy, Mcal/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>10.3</td>
<td>9.3</td>
</tr>
<tr>
<td>Growth</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Conceptus growth</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Weight gain at 0.2 kg/day</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Total, Mcal/day</td>
<td>15.8</td>
<td>15.3</td>
</tr>
<tr>
<td>Metabolizable protein, g/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>570</td>
<td>560</td>
</tr>
<tr>
<td>Growth</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>Conceptus</td>
<td>30</td>
<td>80</td>
</tr>
<tr>
<td>Total, g/day</td>
<td>840</td>
<td>880</td>
</tr>
<tr>
<td>DM intake, kg/day</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Diet NE&lt;sub&gt;j&lt;/sub&gt;, Mcal/kg DM</td>
<td>1.22</td>
<td>1.39</td>
</tr>
<tr>
<td>MP required, g/kg DM</td>
<td>64.6</td>
<td>80.0</td>
</tr>
<tr>
<td>Diet CP, % DM</td>
<td>10.8</td>
<td>13.3</td>
</tr>
</tbody>
</table>
Far Off Dry Cows

- Dry-off until ~ 255 d of gestation

- Ration considerations
  - NE\textsubscript{r} ~ 1.30 to 1.35 Mcal/kg for maintenance of BCS (15 to 17 Mcal/d)
  - Do not overfeed calories (dietary NDF ~ 50 to 55% to limit caloric density and feed intake)
  - Supply sufficient metabolizable protein (850 to 900 g/day)

- Evidence of increased insulin resistance during the immediate peripartum period with overfeeding during far-off period (Dann et al., 2003)
  - Trying to regain BCS can be a problem during this period of lactation

Effect of Fatness on DMI

Adapted from Hayirili, 1998

Correlations- Rabelo et al.(2003)

<table>
<thead>
<tr>
<th>Liver TG, d1</th>
<th>r</th>
<th>P &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake, final wk PP</td>
<td>.05</td>
<td>.70</td>
</tr>
<tr>
<td>Energy balance, final wk PP</td>
<td>.09</td>
<td>.47</td>
</tr>
<tr>
<td>Energy intake change, wk -4 vs d-1</td>
<td>.45</td>
<td>.0004</td>
</tr>
<tr>
<td>Energy balance change, wk -4 vs d-1</td>
<td>.45</td>
<td>.0004</td>
</tr>
<tr>
<td>Plasma NEFA change, final wk</td>
<td>.46</td>
<td>.0007</td>
</tr>
</tbody>
</table>
Summary

- Avoid obese cows at dry off — reproductive and dietary management during lactation
- Do not overfeed dry cows during the early dry period

- Maximize DM intake during the last 3 weeks of gestation and first 3 of lactation, but minimize drop in intake prepartum
  - Close up period
  - Group cows and heifers separately
  - Close up diets with moderate NFC (30 to 35%) and NDF (38 to 45%)
  - Add monensin at 300 mg prepartum and 24 ppm postpartum in the first 3 weeks of lactation
  - Use additives if necessary (300 mL of PPG and 15 g/d of rumen-protected choline)
  - Watch acidogenic salts in close up rations (urine pH & [Cl⁻] in the diet)

- Minimize early postpartum health problems
  - Catch and treat ill animals early (effective fresh cow protocols)