1. OBJECTIVES OF MONITORING PROGRAMS

There are two main reasons for monitoring transition dairy cows in general, and running metabolic tests in particular. The objectives overlap, but are distinct and should be clear before embarking on testing. The objectives are:

- herd or group level: to monitor the success of current management with the goal of early detection of problems or deviation from the management program,
- individual level: to identify cows at high risk for disease with the goal of intervention for these individuals to prevent or mitigate clinical disease.

This paper reviews the importance of energy metabolism in transition dairy cows, its associations with disease and reproduction, and strategies for monitoring cows during this critical time.

2. METABOLITES TO MEASURE ENERGY STATUS IN TRANSITION COWS

Circulating concentrations of non-esterified fatty acid (NEFA) and β-hydroxybutyrate (BHB) measure the success of adaptation to negative energy balance. NEFA reflects the magnitude of mobilization of fat from storage. BHB reflects the completeness of oxidization (“burning”) of fat in the liver. Ketone bodies (BHB, acetone and acetoacetate) are the intermediate metabolites of oxidation of fatty acids, specifically resulting from the incomplete oxidation of fatty acids. As the supply of NEFA to the liver exceeds the ability of liver to completely oxidize the fatty acids to supply energy, the amount of ketone production increases (Figure 1). Ketone bodies can be used by muscle as an alternative fuel source to glucose, sparing glucose for milk production (Herdt, 2000a). However, ketone production does not result in as much net energy release as does complete oxidation of fatty acids. Additionally, increasing concentrations of ketones are thought to suppress feed intake.

Glucose is the primary metabolic fuel, and is absolutely required for vital organ function, fetal growth, and milk production. In dairy cows, the massive energy demand to support milk production
is partly met through gluconeogenesis. Glucose concentrations are under tight homeostatic control. Therefore, although glucose has a central role in metabolism, it is a poor analyte for monitoring or investigating herd problems (Herdt, 2000b).
Figure 1. Schematic summary of fat and energy metabolism in peripartum dairy cows that are not successfully adapting to negative energy balance

Large amounts of fat are mobilized and delivered to the liver as NEFA. A lack of dietary energy intake results in a lack of gluconeogenesis and in turn, a lack of glucose to allow for complete oxidation of NEFA. Rather, production of excessive amounts of ketone bodies occurs.

The key associations of NEFA and BHB with health and performance in transition dairy cows are:

- high NEFA in the 2 weeks before calving is associated with,
- 2 to 4 times increased risk of LDA (Cameron et al. 1998; LeBlanc et al. 2005),
- 1.8 times increased risk of retained placenta (RP) (LeBlanc et al 2004),
- 2 times increased of culling before 60 days in milk (DIM) and 1.5 times increased risk of culling over the whole lactation (Duffield et al. 2005),
- subclinical ketosis (BHB > 1200-1400 μmol/l) in early lactation is associated with,
- 4 to 8 times increased risk of LDA (Geishauser et al. 2000b; LeBlance et al 2005),
- decreased probability of pregnancy at first AI (Walsh et al. 2004),
- decreased milk production (Duffield, 2000),
- increased duration and severity of mastitis (Suriyasathaporn, 2000).

3. SUBCLINICAL KETOSIS

In a field study of 1010 cows in 25 herds in Ontario, the peak incidence (first diagnosis of new cases) of subclinical ketosis was 30% and occurred in the first week after calving, with few new cases beyond the third week postpartum (Duffield, 2000). The cumulative incidence to 9 weeks
postpartum was 43%. The mean incidence varied among the 25 herds from 8 to 80%. In the same study, the peak prevalence (proportion of cows testing positive at a given time point) of subclinical ketosis was approximately 33% and occurred in week 2 after calving (Duffield, 2000). Therefore, the first two weeks postpartum are the optimal time to test for subclinical ketosis. The median overall prevalence in the first two weeks was approximately 20%. It is noteworthy that in these data there was little correlation between the incidences of clinical and subclinical ketosis. Diagnosis rates of clinical ketosis are commonly a reflection of the diagnostic criteria used (which may not be valid) and the intensity and consistency of efforts to apply these criteria. Accordingly, treatment rates for clinical ketosis often do not reflect the true incidence of ketosis (Duffield, 2000; Oetzel, 2004).

Oetzel (2004) recommends including cows that are 5 to 50 DIM in testing for subclinical ketosis. He suggests that, combined with a comprehensive investigation including disease and culling records and overall assessment of nutritional and management practices, the distribution of the time postpartum at which subclinical ketosis occurs, may give direction to further investigation and a working diagnosis. Specifically, he suggests that “Type I” ketosis (low blood glucose due to lack of precursors for gluconeogenesis, but no fatty liver) occurs at 3 to 6 weeks postpartum, whereas “Type II” ketosis (associated with fatty liver just before or at calving) occurs at 5 to 15 DIM. An increased number of samples would be required to attempt to discern these syndromes. Practically, recognition of when ketosis is occurring should give direction to preventive efforts. When ketosis is detected primarily in the first two weeks postpartum, emphasis should be placed on bringing cows to the close-up dry period in moderate body condition (BCS = 3.5) and particularly on measures to enhance feed intake in the last few weeks before, and through the calving period. Further investigation of an elevated prevalence of ketosis in early lactation may be aided by NEFA testing of cows in the 10 days before expected calving.

If there is little evidence of ketosis in the first two weeks postpartum, but an increased incidence 3 to 6 weeks postpartum, that suggests that preventive measures should be emphasize enhancing feed intake in post-fresh period. It should be noted that the data from Duffield (2000) suggest that the vast majority of subclinical ketosis occurs within the first two weeks postpartum, with few new cases thereafter. Such ketosis is associated with management in the pre-fresh, maternity and early post-fresh periods. It is not clear whether other patterns of ketosis are more common under different management systems than those in the herds studied by Duffield et al. Further research to describe the occurrence of subclinical ketosis under different management conditions is warranted. Until such data are available, present evidence indicates that most subclinical ketosis occurs in the first two weeks after calving.

Testing programs with the objective of monitoring the prevalence of subclinical ketosis should focus on the first two weeks after calving. Used with knowledge of their test characteristics to inform interpretation, serum BHB, milk BHB measured with Keto-Test®, or Ketostix® in urine (when read after 5 seconds and using the “small” cut-point as described by Carrier et al. (2004) are valid diagnostic tests for subclinical ketosis. These two cowside tests are economical, practical and sufficiently accurate relative to laboratory analysis of serum for use in the field. Selection of the 100 or 200 μmol/l cut-point for classification of the Keto-Test® will depend on the objective of the testing. If the objective is group-level monitoring for early detection of increased prevalence of ketosis (as a reflection of the general success of transition management), then greater sensitivity is desirable and the 100 μmol/l should be used. If the objective is to select individual cows for treatment with the goal of preventing clinical disease, then fewer false positives may be desirable and the 200 μmol/l cut-point would be appropriate.

Based on clinical experience, Oetzel (2004) suggests an “alarm” threshold of 10% prevalence of subclinical ketosis, based on serum BHB. Published reports indicate a typical prevalence of
subclinical ketosis of around 15% (Oetzel, 2004); studies in Ontario have found average prevalence of over 20% (Duffield et al. 1998; Duffield et al. 2003). Adjusting for cowside test performance, a threshold of 10% true prevalence of subclinical ketosis corresponds to an apparent prevalence (proportion of tests that are positive) of 25% when using the Keto-Test® with a 100 μmol/l cut-point, or 11% at the 200 μmol/l cut-point (Oetzel, 2004).

4. SELECTION AND TIMING OF TESTS

4.1 Number of samples

In a close-up or fresh cow group of up to 50 to 1000 cows, assuming that detection of a prevalence of subclinical disease of 10% is the threshold of interest, to have 75% confidence of detecting the problem, 13 samples are required (Dohoo et al. 2003). Oetzel (2004) proposes using 12 samples for simplicity of interpretation.

Each of the three main ketones is present in blood, milk and urine and can be measured, but acetoacetate is volatile and unstable, and relatively difficult to measure, and is therefore not commonly used in the field to measure ketosis. BHB is the predominant ketone body in blood, where it is stable. There is some variation of BHB concentrations diurnally and with feeding. Ketones are excreted in urine, resulting in higher concentrations in urine than in blood. Therefore, other things being equal, urine tests for ketones tend to lack specificity relative to serum. BHB concentrations in milk reflect concentration in serum, but are only 10 to 15% as high (Duffield, 2000). NEFA concentrations peak just before feeding (Herdt, 2000b). Practically, it is not terribly important to time collection of blood samples for NEFA or BHB testing relative to feeding. Indeed, feed should be freely available to peripartum cows for > 20 hours a day. However, for monitoring over time, samples should be collected at approximately the same time of day to avoid confounding of the results by diurnal or postprandial variations.

5. TEST PERFORMANCE FOR DETECTION OF SUBCLINICAL KETOSIS

5.1 Urine (relative to serum BHB ≥ 1400 μmol/l)

Ketostix® in urine - when read after 5 seconds and interpreted at the level of “small” positive: sensitivity = 79% and specificity = 96% (Carrier et al. 2004).

Acetest® tablet sensitivity = 100% but specificity = 59% (Nielen et al. 1994). The lack of specificity (too many false positives) makes this test unsuitable for monitoring for ketosis.

5.2 Milk

Bioketone® powder (relative to serum BHB ≥ 1200 μmol/l): sensitivity = 28% and specificity = 100% (Geishauser et al. 2000a). The lack of sensitivity (too many false negatives) makes this test unsuitable for monitoring programs.

Keto-Test® (relative to serum BHB ≥ 1400 μmol/l).

Oetzel (2004) summarized reported test performance from 4 published studies as well as his own field experience:

- at 100 μmol/l sensitivity = 83% and specificity = 82%
- at 200 μmol/l sensitivity = 54% and specificity = 94%
Test characteristics varied somewhat among studies, apparently largely as a function of the prevalence of subclinical ketosis among the cows being tested. As the prevalence increases, the sensitivity is generally greater, and the specificity lower.

6. SAMPLE HANDLING

Serum (red top tube) or plasma (purple top tube) is acceptable for BHB and NEFA testing. BHB will be falsely elevated by hemolysis in the sample (Duffield, 2000); although there is no published data in cattle, it is probable that the same would be true for NEFA. NEFA concentrations could be slightly falsely elevated if serum were not separated within 12-24 h of blood collection, or if samples were not kept chilled (Stokol & Nydam, 2004). Serum can be kept frozen for at least 1 month without affecting NEFA results.

Samples should be collected from the tail vein (not the milk vein) and ideally chilled, separated within a few hours, and then frozen or shipped chilled for receipt at the laboratory within 1 to 2 days. However, delay of up to 24 hours for separation, and maintenance at room temperature for 1 day or refrigerated for < 3 days does not substantially affect results (Stokol & Nydam, 2004).

7. PREDICTIVE VALUE OF NEFA AND BHB FOR CLINICAL DISEASE AND REPRODUCTION

7.1 Displaced abomasum

7.1.1 Background

Displacement of the abomasum is a common and economically important problem of dairy cattle. In addition to the costs of treatment, affected cows produce less milk in the short term and have a higher culling risk. There are numerous risk factors for left displaced abomasum (LDA) (Cameron et al. 1998; Shaver, 1997), but significant gaps remain in understanding its pathogenesis.

Geishauser et al. (2000b) summarized research on the association of various metabolites with the risk of subsequent LDA. Subclinical ketosis and serum aspartate aminotransferase activity in the first two weeks postpartum were associated with increased risk of LDA. There is experimental evidence that severe hypocalcemia is associated with decreased abomasal motility, but it is not clear whether this can be generalized to either clinical milk fever or subclinical hypocalcemia. Several authors suggest that a lack of rumen fill and abomasal atony are elements in the pathogenesis of LDA, but there is little direct evidence to support these hypotheses.

The objective of the study summarized here (LeBlanc et al. 2005) was to identify metabolites and potential cut-points associated with increased risk of subsequent LDA for practical application in monitoring transition cows.

7.1.2 Materials & Methods

The cows were all Holsteins in commercial dairy herds (30 to 130 milking cows, with average production of approximately 9000 kg of milk per cow in 305 days). A technician visited each of 20 farms weekly on the same day, at approximately the same time, within 2 h of the morning feeding. Starting 4 to 10 d before expected calving, and at each weekly visit up to and including the first week postpartum, a blood sample was taken for analyses of serum concentrations of β-hydroxybutyrate (BHBA), non-esterified fatty acids (NEFA), cholesterol, glucose, urea, calcium, and phosphorus. A sample of milk was collected between 1 and 7 DIM for measurement of BHBA using a validated test strip (Keto-Test). Disease events (twins, dystocia, retained placenta, milk
fever, systemic metritis) were recorded. LDA was diagnosed by a veterinarian and was generally confirmed during surgical correction. Determinants of risk of LDA before 30 DIM were modelled with multivariable logistic regression in SAS, accounting for clustering of cows within herds.

Three sampling time periods were modelled: 1 week (4 to 10 d) before expected calving, n = 1132; the week before actual calving, n = 1044; and 1 to 7 days postpartum, n = 1063. In each period, each cow was sampled only once. Because serum NEFA concentration normally begins to rise in the last few days before calving, it has been suggested to exclude samples taken in the last 2 d before calving (Oetzel, 2004). We examined the effect of excluding such samples. Samples taken after diagnosis of LDA were excluded and disease events that occurred before diagnosis of LDA were offered to the models. For metabolites that remained in the final models, a range of cutpoints of the test result was tested, and sensitivity, specificity and likelihood ratios (LR) were calculated.

### 7.1.3 Results

There were 53 cases of LDA (incidence risk = 5.1%) and the median time of diagnosis was 11 DIM. In cows with LDA, mean NEFA concentrations began to diverge from the mean in cows without LDA 14 d before calving (Figure 2), whereas mean serum BHBA concentrations did not diverge until the day of calving (Figure 3).

![Figure 2](image-url)

**Figure 2.** Serum non-esterified fatty acids (NEFA) concentrations (mean and SE) in Holstein dairy cattle that were and were not subsequently diagnosed with left displaced abomasum within 30 d after calving.

Each cow was sampled once weekly from one week before expected calving until the first week postpartum. The data are pooled into 2-d increments relative to the actual day of calving (from LeBlanc et al. 2005).
Figure 3. Serum $\beta$-hydroxybutyrate (BHB) concentrations (mean and SE) in Holstein dairy cattle that were and were not subsequently diagnosed with left displaced abomasum within 30 d after calving

Each cow was sampled once weekly from one week before expected calving until the first week postpartum. The data are pooled into 2-d increments relative to the actual day of calving (from LeBlanc et al. 2005).

Prepartum, considering all metabolites, parity and body condition, only NEFA concentration was associated with risk of subsequent LDA. Between 0 and 6 d before calving, cows with NEFA concentration $\geq 0.5$ mEq/l were 3.6 times more likely to develop LDA after calving (Table I). For prospective application, among samples taken 4 to 10 days before expected calving, the optimum NEFA cut-point remained 0.5 mEq/l. The sensitivity, specificity and LR were 46%, 82%, and 2.6, respectively. The optimum cut-point did not change and the LR was 3.3 if samples taken within 2 days before calving were excluded, making this exclusion unnecessary. Between 1 and 7 d postpartum, retained placenta, metritis, and increasing serum concentrations of BHBA and NEFA were associated with increased risk of subsequent LDA. However, considered separately, postpartum, serum BHBA was a more sensitive and specific test than NEFA concentration. The odds of LDA were 8 times greater in cows with serum BHBA $\geq 1200$ $\mu$mol/l (Table II). Cows with milk BHBA concentration $\geq 200$ $\mu$mol/l were 3.4 times more likely to develop LDA. Serum calcium concentration and milk fever were not associated with LDA (Figure 4).
Days from calving

-20 -15 -10 -5 0 5 10

Serum calcium (mmol/l)

Cows without DA (n = 1078)
Cows with DA (n = 53)

Figure 4. Serum calcium concentrations (mean and SE) in Holstein dairy cattle that were and were not subsequently diagnosed with left displaced abomasum within 30 d after calving.

Each cow was sampled once weekly from one week before expected calving until the first week postpartum. The data are pooled into 2-d increments relative to the actual day of calving (from LeBlanc et al. 2005).

Table I. Simple associations of prepartum serum non-esterified fatty acids (NEFA) concentrations with the risk of subsequent left displaced abomasum (LDA) within 30 d after calving in Holstein dairy cattle (from LeBlanc et al. 2005)

<table>
<thead>
<tr>
<th>Cutpoint (mEq/l)</th>
<th>Cows at/above cutpoint (%)</th>
<th>Risk of LDA at/above cutpoint (%)</th>
<th>Risk of LDA below cutpoint (%)</th>
<th>OR¹</th>
<th>95% CI¹²</th>
<th>P¹</th>
<th>Se³</th>
<th>Sp⁴</th>
<th>LR⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured in the last week before calving (n = 1044)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 0.3</td>
<td>63.4</td>
<td>6.2</td>
<td>3.1</td>
<td>2.0</td>
<td>0.9 to 4.6</td>
<td>0.11</td>
<td>77.4</td>
<td>37.3</td>
<td>1.2</td>
</tr>
<tr>
<td>≥ 0.4</td>
<td>47.2</td>
<td>7.5</td>
<td>2.9</td>
<td>2.6</td>
<td>1.2 to 5.9</td>
<td>0.02</td>
<td>69.8</td>
<td>54.0</td>
<td>1.5</td>
</tr>
<tr>
<td>≥ 0.5</td>
<td>35.2</td>
<td>9.2</td>
<td>2.8</td>
<td>3.6</td>
<td>1.9 to 7.0</td>
<td>0.0001</td>
<td>64.2</td>
<td>66.3</td>
<td>1.9</td>
</tr>
<tr>
<td>≥ 0.6</td>
<td>25.5</td>
<td>9.8</td>
<td>3.5</td>
<td>2.9</td>
<td>1.8 to 4.7</td>
<td>&lt; 0.0001</td>
<td>49.1</td>
<td>75.8</td>
<td>2.0</td>
</tr>
<tr>
<td>≥ 0.8</td>
<td>15.5</td>
<td>10.5</td>
<td>4.1</td>
<td>2.6</td>
<td>1.4 to 4.9</td>
<td>0.003</td>
<td>32.1</td>
<td>85.4</td>
<td>2.2</td>
</tr>
<tr>
<td>≥ 1.0</td>
<td>9.2</td>
<td>12.5</td>
<td>4.3</td>
<td>3.1</td>
<td>1.3 to 7.1</td>
<td>0.01</td>
<td>22.6</td>
<td>91.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Measured 4 to 10 days before expected calving (n = 1131)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 0.3</td>
<td>45.1</td>
<td>6.7</td>
<td>3.2</td>
<td>2.3</td>
<td>1.4 to 3.9</td>
<td>0.002</td>
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<td>≥ 0.4</td>
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<td>3.4</td>
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<td>72.2</td>
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<td>≥ 0.5</td>
<td>19.0</td>
<td>11.6</td>
<td>3.2</td>
<td>4.1</td>
<td>2.5 to 6.9</td>
<td>&lt; 0.0001</td>
<td>46.3</td>
<td>82.4</td>
<td>2.6</td>
</tr>
<tr>
<td>≥ 0.6</td>
<td>12.4</td>
<td>11.4</td>
<td>3.8</td>
<td>3.0</td>
<td>1.7 to 5.4</td>
<td>0.0001</td>
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<td>88.5</td>
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</tr>
<tr>
<td>≥ 0.8</td>
<td>7.1</td>
<td>11.3</td>
<td>4.3</td>
<td>2.6</td>
<td>1.3 to 5.2</td>
<td>0.007</td>
<td>16.7</td>
<td>93.4</td>
<td>2.5</td>
</tr>
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<td>≥ 1.0</td>
<td>4.4</td>
<td>16.0</td>
<td>4.3</td>
<td>4.1</td>
<td>1.8 to 9.1</td>
<td>0.0006</td>
<td>14.8</td>
<td>96.1</td>
<td>3.8</td>
</tr>
</tbody>
</table>

¹ From logistic regression models accounting for the correlation of cows within herds. OR = odds ratio
² 95% confidence interval around the odds ratio
³ Epidemiologic sensitivity
⁴ Epidemiologic specificity
⁵ Likelihood Ratio
Table II. Simple associations of metabolites measured 1 to 7 d after calving that were significantly associated with the risk of subsequent left displaced abomasum (LDA) within 30 d after calving in Holstein dairy cattle (from LeBlanc et al. 2005)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cutpoint</th>
<th>At/above cutpoint (%)</th>
<th>Risk of LDA at/above cutpoint (%)</th>
<th>Risk of LDA below cutpoint (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
<th>Se (%)</th>
<th>Sp (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum NEFA (mEq/l) n = 1063</td>
<td>≥ 0.4</td>
<td>81.1</td>
<td>5.3</td>
<td>2.0</td>
<td>2.7</td>
<td>0.7 to 9.8</td>
<td>0.13</td>
<td>92.0</td>
<td>19.4</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>≥ 0.5</td>
<td>69.3</td>
<td>6.1</td>
<td>1.5</td>
<td>4.1</td>
<td>1.6 to 10.6</td>
<td>0.004</td>
<td>90.0</td>
<td>31.7</td>
<td>1.3</td>
</tr>
<tr>
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<td>≥ 0.6</td>
<td>58.1</td>
<td>7.0</td>
<td>1.6</td>
<td>4.8</td>
<td>2.2 to 10.6</td>
<td>&lt; 0.0001</td>
<td>86.0</td>
<td>43.2</td>
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<tr>
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<td>≥ 0.8</td>
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<td>8.5</td>
<td>2.4</td>
<td>3.9</td>
<td>1.9 to 7.7</td>
<td>0.0001</td>
<td>68.0</td>
<td>64.0</td>
<td>1.9</td>
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<td>≥ 1.0</td>
<td>23.1</td>
<td>11.4</td>
<td>2.7</td>
<td>4.8</td>
<td>2.6 to 8.9</td>
<td>&lt; 0.0001</td>
<td>56.0</td>
<td>78.5</td>
<td>2.6</td>
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<td>12.8</td>
<td>2.9</td>
<td>5.1</td>
<td>2.6 to 10.2</td>
<td>&lt; 0.0001</td>
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<td>13.9</td>
<td>14.9</td>
<td>3.1</td>
<td>5.7</td>
<td>2.6 to 12.8</td>
<td>&lt; 0.0001</td>
<td>44.0</td>
<td>87.6</td>
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<td>8.4</td>
<td>18.0</td>
<td>3.5</td>
<td>6.1</td>
<td>2.5 to 14.8</td>
<td>&lt; 0.0001</td>
<td>32.0</td>
<td>92.8</td>
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<td>≥ 1.5</td>
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<td>21.5</td>
<td>3.6</td>
<td>7.4</td>
<td>3.1 to 17.2</td>
<td>&lt; 0.0001</td>
<td>28.0</td>
<td>95.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Serum BHBA (µmol/l) n = 1063</td>
<td>≥ 600</td>
<td>69.1</td>
<td>6.4</td>
<td>1.2</td>
<td>5.4</td>
<td>1.7 to 16.8</td>
<td>0.004</td>
<td>92.2</td>
<td>32.1</td>
<td>1.4</td>
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<td>≥ 800</td>
<td>44.6</td>
<td>8.8</td>
<td>1.5</td>
<td>6.4</td>
<td>3.4 to 12.2</td>
<td>&lt; 0.0001</td>
<td>82.4</td>
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<td>11.7</td>
<td>2.1</td>
<td>6.3</td>
<td>3.3 to 12.2</td>
<td>&lt; 0.0001</td>
<td>68.6</td>
<td>73.9</td>
<td>2.6</td>
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<td>2.2</td>
<td>8.0</td>
<td>4.2 to 15.1</td>
<td>&lt; 0.0001</td>
<td>62.7</td>
<td>82.2</td>
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<td>≥ 1400</td>
<td>14.3</td>
<td>17.8</td>
<td>2.6</td>
<td>8.0</td>
<td>4.7 to 13.7</td>
<td>&lt; 0.0001</td>
<td>52.9</td>
<td>87.7</td>
<td>4.3</td>
</tr>
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<td>≥ 1600</td>
<td>10.6</td>
<td>21.2</td>
<td>2.8</td>
<td>9.3</td>
<td>6.3 to 13.7</td>
<td>&lt; 0.0001</td>
<td>47.1</td>
<td>91.2</td>
<td>5.4</td>
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<td>3.9 to 17.7</td>
<td>&lt; 0.0001</td>
<td>35.3</td>
<td>93.8</td>
<td>5.7</td>
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<td></td>
<td>≥ 2000</td>
<td>6.1</td>
<td>21.5</td>
<td>3.7</td>
<td>7.0</td>
<td>2.7 to 18.1</td>
<td>&lt; 0.0001</td>
<td>27.5</td>
<td>95.0</td>
<td>5.5</td>
</tr>
<tr>
<td>Milk BHBA (µmol/l) n = 768</td>
<td>≥ 50</td>
<td>60.2</td>
<td>7.6</td>
<td>2.3</td>
<td>3.4</td>
<td>1.4 to 8.5</td>
<td>0.008</td>
<td>83.8</td>
<td>41.2</td>
<td>1.4</td>
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<td>≥ 100</td>
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<td>8.9</td>
<td>3.2</td>
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<td>1.2 to 6.6</td>
<td>0.02</td>
<td>64.3</td>
<td>61.8</td>
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<td>21.7</td>
<td>12.0</td>
<td>3.7</td>
<td>3.4</td>
<td>1.8 to 6.6</td>
<td>0.0002</td>
<td>47.6</td>
<td>79.8</td>
<td>2.4</td>
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<tr>
<td></td>
<td>≥ 500</td>
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<td>22.5</td>
<td>4.5</td>
<td>5.9</td>
<td>3.8 to 9.0</td>
<td>&lt; 0.0001</td>
<td>21.4</td>
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<td>7.1 to 605</td>
<td>0.0002</td>
<td>7.1</td>
<td>99.9</td>
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1. From logistic regression models accounting for correlation of cows within herds but not for covariates. OR = odds ratio
2. 95% confidence interval around the odds ratio
3. Epidemiologic sensitivity
4. Epidemiologic specificity
5. Likelihood Ratio

7.1.4 Discussion

NEFA and BHBA are both indirect measures of the magnitude of negative energy balance and the success of the cow’s adaptation to it. BCS was not associated with the risk of LDA, indicating that NEFA and BHB provide better insight into metabolic function with respect to development of LDA. The present results confirm a previous large field study (Cameron et al. 1998) showing that the severity of peripartum negative energy balance, reflected by NEFA concentration, is a key element in the etiology of LDA. A considerable proportion of the variability in these metabolites was likely attributable to differences in feed intake, which is influenced by many aspects of management. Programs to monitor transition cows may have the objective of group-level monitoring of the adequacy of the management program, or early detection of individuals with metabolic problems with the goal of intervention. The present results were analyzed and should be interpreted at the individual-cow level. A major challenge for implementation of prepartum metabolic testing is the inability to know precisely when cows will calve. For samples taken approximately one week before expected calving, it is not necessary to wait to submit samples for analysis in order to exclude those from cows within 2 d before calving.

Unfortunately, there is presently little evidence to inform choices of intervention in response to elevated NEFA or BHBA. Administration of propylene glycol, insulin, or corticosteroids might be...
beneficial, but further research is needed on treatment regimes that might be effective at reducing the risk of LDA.

7.2 Associations of metabolic health in the transition period with uterine health and reproductive performance

It is increasingly recognized that clinical and subclinical health in the transition period is associated with uterine health and subsequent reproductive performance. Retained placenta is fundamentally a disease of immune function in the two weeks before calving which is associated with both antioxidant and energy status (LeBlanc et al. 2004), among other factors. Essentially all cows experience bacterial contamination of the uterus in the first 2 to 3 weeks postpartum (Sheldon, 2004; Sheldon et al. 2006; Hammon et al. 2005), but the development of acute (within 10 DIM, metritis) or chronic (between 21 and 60 DIM, clinical and subclinical endometritis) uterine disease is largely dependent on immune function in the first 3 weeks postpartum (Hammon et al. 2004).

Energy status in the transition period is associated with reproductive success 2 to 4 months later. It is now well established that approximately 20% of cows are anovulatory at approximately 60 DIM. It has recently been shown that, controlling for other factors, cows that were subclinically ketotic in the first week of lactation were 50% more likely to be anovulatory at 60 DIM (Walsh, 2006). NEFA concentrations prepartum have also been associated with the probability of anovulatory (McCarthy et al. 2005). Subclinical ketosis in the second week of lactation is associated with a 50% reduction in the probability of pregnancy at first insemination (Walsh et al. 2004). Similarly, others have reported that NEFA concentrations at 3 DIM were inversely associated with pregnancy at first breeding (Burkhart et al. 2005).

8. CONCLUSIONS

Subclinical ketosis is a prevalent and important disease, which is associated with increased risk of LDA, decreased milk production, and decreased reproductive performance. Measurement of the prevalence of subclinical ketosis is useful for investigation of herd problems of transition cow health and performance, and for routine monitoring. The response to peripartum negative energy balance is one key aspect in the pathogenesis of LDA. The timing and magnitude of peripartum increases in circulating concentrations of NEFA and BHBA are associated with the risk of eventual abomasal displacement. Programs to monitor management of the transition period in general and risk of LDA in particular should focus on NEFA concentrations in the week before expected calving and on BHBA concentration in the first week after calving. These metabolites are also associated with uterine health and reproductive performance from 1 through 20 weeks later. A key link among diseases is feed intake. Peripartum energy metabolism and immune function will be favoured when cows eat as much as possible through the transition period. Proactive management and investigation of problems should focus on minimizing nutritional, housing, social, and environmental factors that may reduce feed consumption.

9. SUMMARY

Veterinarians can provide a valuable service to clients by implementing proactive monitoring programs for early detection of problems in the transition period. One large element of such programs is monitoring energy metabolism. Cows at risk of retained placenta, displaced abomasum, uterine disease, and anestrus can be identified weeks before the conditions became clinical. Measurement of NEFA in the week before expected calving and BHB in the first 2 weeks after calving are useful elements of a monitoring program.
10. KEY WORDS
Dairy, transition period, monitoring, ketosis, NEFA, displaced abomasum.

11. RÉSUMÉ
Les vétérinaires peuvent rendre un service à leurs clients en implantant des programmes proactifs de suivi de la période peripartum, dont un élément important est le statut du métabolisme énergétique. Les vaches qui sont à risque élevé de rétention placentaire, déplacement de caillette, maladies utérines, et anoestrus peuvent être identifiées des semaines avant que ces problèmes ne se manifestent cliniquement. Les AGNE dans la semaine avant le vêlage prévu et le BHB dans les 2 semaines après le vêlage sont des éléments utiles dans un programme de suivi préventif.

12. MOTS CLÉS
Laitier, période de transition, suivi, acétonémie, AGNE, déplacement de caillette.

13. ZUSAMMENFASSUNG

14. SCHLÜSSELWÖRTER
Milchkuh, Uebergangszeitraum, Ueberwachung, Ketose, Unveresterte, Fettsaeuren, Labmagenverlagerung.

15. RESÚMEN
Los médicos veterinarios pueden proveer un servicio valioso a los clientes implementando programas de monitoreo para detección temprana de problemas en el periodo de transición. Un elemento importante en dichos programas es el monitoreo del metabolismo energético. Vacas con riesgo de retención placentaria, desplazamiento de abomaso, enfermedad uterina y anestro pueden ser identificadas varias semanas antes de que presenten condiciones clínicas. La medición de los ácidos grasos en la semana previa a la fecha probable de parto y el BHB en las primeras 2 semanas después del parto son elementos útiles en un programa de monitoreo.

16. PALABRAS CLAVES
Lechera, periodo de transición, monitoreo, cetosis, ácidos grasos, desplazamiento de abomaso.

17. REFERENCES


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