1. What is ketosis?
Ketosis is a common metabolic disorder in high yielding dairy cows. Negative energy balance in early lactation, fat mobilization in the absence of sufficient energy (glucose) supply or reduced energy uptake from the feed ration will be followed by elevations in ketone body concentrations (Acetone, Aceto-acetate and Beta-Hydroxy Butyrate (BHB)). The disease is reported with herd incidences ranging from 2-20% (Ingvartsen, 2003). However, evidence from the literature points to a vast underreporting of the disease (see section 2).

In the past, ketosis was diagnosed by clinical signs of reduced feed intake, dehydration, an “empty” appearance of the abdomen, and sometimes nervous signs. Upon physical examination the diagnosis can be verified by the detection of elevated concentrations of ketone bodies in urine or milk. The typical time of diagnosis is 25-30 days in lactation (Rajala-Schultz et al., 1999), although concentrations of ketone bodies have been elevated long before (Nielsen et al, 2005).

Ketosis can either be a primary condition (due to an incapacitation of the liver to produce glucose) or a secondary condition, due to diseases and disorders followed by a reduced feed intake (Ingvartsen, 2003).

Ketosis is followed by a reduced milk yield, reduced reproductive performance, metritis and displaced abomasums, and therefore the disease is very costly to the dairy industry. Economic analyses point to an average loss per case of approximately 135€.

2. What is subclinical ketosis?
In later years research has shown that in many herds, cows suffer from ketosis without showing clinical signs, and this condition is called subclinical ketosis. Ketosis is characterized by elevated concentrations of ketone bodies, e.g. BHB, in blood, urine and milk in the absence of clinical signs (Duffield et al., 1997). For cow-side tests of milk, the threshold of BHB is typically 1.5 mMol/L. Cows that suffer from subclinical ketosis will have a lower food intake and reduced milk yield. The peak prevalence of subclinical ketosis occurs in the first 2 weeks of lactation (Duffield et al., 1997) and can be prevalent in 8-80% of newly calved cows, depending on the management of the herd. Research in Canada determined that herd prevalence for subclinical ketosis is approximately 41% for the first 9 weeks of lactation (Duffield, 2001). A recent study in Denmark shows that approximately 20% of Danish cows suffer from subclinical or clinical ketosis, based on cow-side screening of more than 70,000 post partum cows (Sloth and Trinderup, 2010).

Table 1. Relations between ketosis types and their causes

<table>
<thead>
<tr>
<th></th>
<th>Type I ketosis</th>
<th>Type II ketosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary ketosis</strong></td>
<td>Lack of energy in the feed ration in early lactation</td>
<td>Decreased feed intake due to fatty liver or severe body condition loss during the dry period</td>
</tr>
<tr>
<td><strong>Secondary ketosis</strong></td>
<td>Deprivation of feed due to e.g. claw disorders, metritis, left displaced abomasums</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Relations between ketosis types and their causes
3. Herd Navigator™ and detection of ketosis

The Herd Navigator™ concept differs considerably from traditional ketosis detection, where the diagnosis is either based on clinical signs or detection of elevated concentrations in urine or milk. Typically, only one test for ketone bodies will be performed in the periparturient period, and insensitive to the use of urine or milk for the test, results can be somewhat misleading due to sensitivity and specificity issues related to the cow-side test sticks (Carrier et al, 2004). See also section 6.

Herd Navigator™ will take milk samples for BHB-analyses every day from the first milking day, and hence build a so-called time series of analyses. The biometric and biological model (figure 1) will assess the development in BHB-concentrations for each cow, and compute the risk of ketosis on a daily basis. Once the risk has reached the threshold level for ketosis, an alarm will appear on the user interface. As each cow will have her own reference value of BHB based on the first few samples, differences in baseline values reflecting differences in BHB concentrations will be accounted for.

In the literature, poor correlations of blood and milk BHB concentrations in relation to other ketone bodies have been reported (Enjalbert et al, 2004, Larsen et al, 2009). In contrast, a studies made in Switzerland and Denmark (Gutzwiller 1995, Ingvartsen et al, 2003) showed a very good correlation. We are of the opinion that repeated measurements of BHB will account for the assumed lack of correlation to blood parameters, and the reported good response of ketosis alarm cows to treatment further underline the validity of milk BHB measurements.

There are other means of detecting ketosis in-line and real-time, for example by use of fat to protein ratio, but this method has a much lower accuracy than measurements of milk ketone bodies (Knagel et al., 2010, Sloth & Trinderup, 2010). Further, a recent Danish study of the use of the chewing index as an indicator of ketosis did not show promising results (Pedersen, 2010).

Typically, ketosis alarms appear 10-15 days post partum (Figure 3), and field testing in Denmark revealed that this alarm type is typical for Type I ketosis (energy deficiency). People able to smell Acetone will be able to verify the diagnosis.

In some cows, the alarm will appear before day 10 in lactation, and this is typical for Type II ketosis (obese cows and fatty liver, or weight loss during the dry period). These cows cannot be detected by smell of acetone, and hence stay undetected until they show clinical signs many days later, and with a marked reduction in milk yield.

Based on the distribution of Type I and II ketosis alarms, the focus on ketosis management in the herd can be directed to feeding management or dry cow management.

4. Yield losses associated with clinical and subclinical ketosis

Cows that suffer from ketosis are typically individuals that are genetically disposed for high milk yields, and hence they have a very steep incline in milk yield in the early lactation period.

There are several reports showing a milk yield loss of 400-600 kg per lactation in cows diagnosed with clinical ketosis (Rajala-Schultz et al, 1999). The data are based on differences in milk yield from healthy cows and cows treated for clinical ketosis.

On the contrary, experience from Herd Navigator™ test herds in Denmark show that cows that are diagnosed early in the lactation and treated for ketosis can maintain their potential for higher yields than the average cows in the herd, thus changing a milk yield loss to a milk yield gain (Figure 4).

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5. Treatment of ketosis with Herd Navigator™

Cows with ketosis have traditionally been treated in order to reestablish normoglycemia and reduce serum ketone body concentrations. Administration of 50% dextrose solution intravenously or oral administration of propylene glycol, combined with glucocorticoids is common practice. Experience from the testing of Herd Navigator™ showed that Type I ketosis can effectively be cured by oral dosing of propylene glycol (400 g/dose) for three days. In case of Type II ketosis, the propylene glycol administration must be accompanied by injection of long acting glucocorticoids.

As ketosis cases occurring before day 10 in the lactation (Type II ketosis due to fatty liver) can be refractory to treatment, causes of these must be carefully scrutinized, and errors in dry cow management corrected. Based on the literature, a long-acting insulin preparation (IM injection, 150-200 IU/day) can be beneficial (Sakai et al., 1993).

6. Herd Navigator™ compared to cow-side tests

Cow-side tests for ketosis are common practice in herd health programs, either to point to cows suffering from ketosis or to assess the prevalence of subclinical ketosis. In Denmark, cow-side testing for BHB in the first week of lactation is part of the Danish “New-Health Advisory program”. One of the Danish Herd Navigator™ test herds participated in this herd health program for a couple of years, and therefore the performance of Herd Navigator™ could be compared to the cow-side test. The BHB testing was performed on urine samples using Ketostix measurements (Bayer Animal Health, Copenhagen, Denmark). Data for the comparison were retrieved from the Danish National Cattle Database. The veterinarian performing the cow-side test is a very skilled person, and we may assume that his classification of test results were very accurate.

A first screening of the data showed that ketostix results below 1.5 mMol/L (readings 1 and 2) never resulted in ketosis alarms, and hence the threshold value for comparison was set to ketostix values higher than this value (Ketostix readings 3, 4 and 5). The threshold for a Herd Navigator™ ketosis alarm was set to a risk of 55%, based on prior testing of the system. To assess the validity of the Herd Navigator™ alarms, the milk yield of alarms cows was used. A true diagnosis was characterized by a significant drop in milk yield or lack of increase in milk yield in the days around the alarm.

A total of 216 calvings and subsequent cow-side tests and Herd Navigator™ monitoring were analyzed, covering the period January 1st, 2009 to July 15th, 2010. Three cows were omitted from the dataset because of lack of comparative data, leaving 213 calvings for the analysis.

In table 2 below the cow-side test is compared to Herd Navigator™. As can be seen from the data, the sensitivity of the cow-side test was 39 %, with a specificity of 97%. The sensitivity is the ability for the cowside test to detect true cases of ketosis, whereas the specificity of the test to avoid false positive tests. The major reason for the low sensitivity is the fact that can clearly be seen from the data, that a one time test in early lactation is inferior to the build of a time-series of data with Herd Navigator™, also showing that increased values of blood, urine and milk BHB can appear later than week one in lactation.

In conclusion, the use of Herd Navigator™ for monitoring ketosis in newly calved cows is an improvement as compared to cow-side tests, as approximately 67% of the ketosis cases in this herd were detected by Herd Navigator™ in the absence of a positive cow-side test.

Table 2. Comparison of Ketostix tests to Herd Navigator™ ketosis alarms (assumed to be gold standard) in a Danish Herd Navigator™ test herd

<table>
<thead>
<tr>
<th></th>
<th>Herd Navigator™ alarm</th>
<th>No Herd Navigator™ alarm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Ketostix test</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Secondary ketosis</td>
<td>20</td>
<td>174</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>180</td>
</tr>
</tbody>
</table>

Sensitivity of the cow-side test compared to Herd Navigator™:

\[
\frac{13}{13+20} = 39\% 
\]

Specificity of the cow-side test compared to Herd Navigator™:

\[
\frac{174}{174+6} = 97\% 
\]