# Current Therapy and Herd Monitoring for Ketosis in Dairy Cows

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Senior Seminar Paper
Cornell University College of Veterinary Medicine
March 31, 2010

**Abstract**

A 25 month old Holstein first calf heifer on a small New York State dairy farm presented to the Cornell University Ambulatory service for a complaint of inappetance of approximately 24 hours. The heifer's problem list included ketosis, left displaced abomasum, metritis, inappetance, weakness, poor body condition, dehydration and Strongyle infestation. Treatments for the heifer included toggle pin fixation of the displaced abomasum, hypertonic saline, dextrose, dexamethasone, B-vitamins, calcium and antibiotic therapy. The heifer was reported to be doing well approximately 2 weeks after treatment.

Ketosis, primary or secondary, is one of the most common metabolic diseases seen on modern commercial dairy herds. Excessive negative energy balance resulting in ketosis can have many adverse effects on the lactating cow, and successful prevention and treatment of this disease is vital to the success of commercial dairies. This discussion will focus on current ketosis treatments, procedures veterinarians can use to help producers solve a ketosis problem, and pros and cons of varying ketosis monitoring techniques.

**Case History and Signalment**

A 25 month old Holstein first calf heifer presented to the Cornell University Ambulatory service for a primary complaint of inappetance of approximately 24 hours. The heifer had calved nine days prior to the date of presentation, and a large, dead calf was delivered by the Cornell Ambulatory service via fetotomy. The heifer was noted to be standing and eating before the clinicians left the farm, and the owner gave Procaine

Penicillin G (PPG) to the heifer for 2 days (instructions were to give for 5 days post-calving). The heifer lives on a small, stanchion herd located in central New York which milks approximately 30 cows, and animals are turned out to pasture when conditions allow. The cows (milking and dry) are fed hay, corn silage, and 1 scoop of grain mix twice per day throughout the year. No individual milk records were available, so the heifer's milk production level is unknown, although the herd average is around 30lbs/cow/day. The only other history known about the heifer is that she was treated for chronic diarrhea at 3 months of age, and a Giardia infection was confirmed on fecal exam.

**Clinical Findings**

On presentation, the heifer was able to ambulate, but was weak when attempting to stand and walk. She was enophthalmic and 8-10% dehydrated, with drooping ears (not cold to the touch) indicative of depression, and very thin (body condition score 1.5/5). Temperature, pulse rate and respiration rate were all within normal limits, and no evidence of mastitis was noted. A left-sided abdominal ping was ausculted, and the rumen was weakly contracting once or twice each minute. A rectal examination revealed a small amount of normal manure, a small rumen, and a slightly enlarged fluid filled uterus. On manipulation of the uterus a moderate amount of foul smelling, brown to red discharge was expressed externally. A urine sample was obtained from the heifer which tested positive for a large amount of ketones. A small amount of blood was obtained from the coccygeal vein and tested for B-hydroxybutyric acid (BHBA) levels, yielding a result of 2.6mmol/L.

The heifer's problem list included ketosis, left displaced abomasum (LDA), metritis, inappetance, weakness, poor body condition, dehydration and Strongyle infestation diagnosed by fecal examination at Cornell.

**Differential Diagnosis for Ketosis**

It is important to note the difference between the two different types of ketosis common to the dairy cow: Primary vs. Secondary.

Primary ketosis is simply the presence of excess ketones in the blood in the absence of any other disease process occurring in the cow at the same time. These cows have insufficient energy intake which results in increased mobilization of adipose tissue stores. Treatments used to treat ketosis in these animals will typically result in positive outcomes.

Secondary ketosis is the presence of ketones in the blood as a result of a disease (displaced abomasums, metritis, mastitis) causing decreased appetite. Because the cow feels ill and does not want to eat, her body begins to mobilize adipose tissue to meet her energy demands. Treatments aimed at correcting ketosis in these cases will not be effective unless the underlying disease is corrected.

In our heifer's case, secondary ketosis is the most likely scenario, although it is impossible to be sure whether her ketosis developed before her other disease processes (LDA, metritis) or vice versa.

**Treatment**

A roll and toggle pin fixation technique was used to correct the heifer's LDA. No sedation was needed to roll the cow due to her weak and depressed state. While restrained, a 14 gauge needed was inserted into her right jugular vein and she was given 1L of hypertonic saline, 250mL 50% dextrose plus 8mL dexamethasone and 10mL B-complex vitamins, and 250mL 23% calcium intravenously. Within a few minutes of treatment the heifer was standing and eating hay. No immediate complications of the procedures were noted before the Ambulatory service left the farm. The owner was instructed to give PPG to the heifer for 5-7 days to address the metritis.

**Prognosis**

Prognosis for a dairy cow with presumed secondary ketosis with more than one primary disease process (LDA, metritis), in poor body condition, and infested with worms is guarded to poor. When greater than one round of treatment is necessary to address ketosis in the dairy cow, prognosis will further decline.

Approximately 2 weeks after treatment the farmer was phoned and reported that the heifer was doing well, although she still seemed to be "weak in her legs". No further information was available at the time of follow up.

**Discussion**

Negative energy balance (NEB) is a physiologic state experienced by every post-partum cow to some degree. Dairy cows simply cannot consume enough energy to meet the demands placed on their metabolism by the mammary gland in early lactation.[2] This state of NEB causes increased mobilization of adipose tissue stores, and increased blood

levels of non-esterified fatty acids (NEFA). These NEFA initially provide a source of milk fat for the mammary gland, and a source of energy for liver gluconeogenesis. The liver eventually reaches its' capacity to completely oxidize the NEFA, and the resulting incomplete oxidation cycle produces ketone bodies (acetone, aceto-acetic acid, and BHBA). Another side effect of the liver becoming overwhelmed with NEFA is the increased storage of triglycerides resulting in the condition known as "fatty liver". It is important to remember, however, that while every cow experiences the state of NEB, not every cow will mobilize excessive amounts of body fat and develop clinical or sub-clinical ketosis.

Clinical ketosis can be divided in to two broad categories for practical purposes: Classical and Periparturient (also referred to as Type 1 and Type 2 ketosis).[1] In classical ketosis, the peak incidence is around the period of peak milk production (approximately 3-6 weeks after freshening). Often these cows experienced no troubles during late pregnancy and calve without serious complication. Problems develop because of a lack of glucose precursors in the diet, resulting in a hypoglycemic state. Cows in this category of ketosis normally respond well to standard treatments for ketosis (steroids, dextrose, propylene glycol). Periparturient ketosis is a problem many modern farms are currently dealing with, and can be much more frustrating for the farmer than classical ketosis. Cows in this category typically enter a state of reduced feed intake and NEB during the late dry period, usually from some stressor such as pen overcrowding, social anxiety, or many others. Periparturient ketosis (often referred to as "fat cow syndrome") results from very fast mobilization of adipose stores in response to this stress. These cows show clinical signs about 1-2 weeks after freshening, and are in a hyperglycemic and immune

suppressed state. There is extensive triglyceride accumulation in the liver, and neutrophil and hepatic macrophage function is impaired resulting in increased susceptibility to infection.[2] Because these animals are already hyperglycemic, standard ketosis treatments may not only be ineffective, but may cause further damage to the cows' already fragile metabolic state. There is also evidence that cows with fatty infiltration of the liver have a blunted response to insulin, which may further impair the cows' ability to respond to standard treatments.[7]

Sub-clinical ketosis (SCK) is a disease in which the cow has a normal appetite and milk production, along with elevated blood ketone levels. Because cows with SCK are asymptomatic, some farmers may not know or care about the disease, as they may feel that it isn't hurting their bottom line as long as the cows remain at their normal milk production level. Recent research out of Cornell has shown that, in fact, SCK can and does cause significant financial loss on modern dairies.[10] Cows with evidence of SCK have up to 19% reduced risk of becoming pregnant, and may lose up to 1500lbs of ME305 milk during a lactation. They also have a 3-4x higher risk of developing displaced abomasum, and 2.5x higher risk of metritis. All of these factors together constitute a significant increase in culling rate, milk loss, and financial cost to the dairy.

Because SCK can be so costly to the dairy, it is a very valuable skill for the veterinarian to effectively test for the disease in order to assist the farm in instituting changes to control the problem. In the case of testing for SCK, the three choices of fluids to test are blood (serum), urine, and milk. I will not discuss each possible test on the market today, but will focus on serum NEFA/BHBA testing and urine testing using the

Ketostix test strip. Milk testing for ketosis often suffers from very poor sensitivity and will not be discussed here other than to mention its existence.[6]

The Ketostix urine test strip for detecting ketosis (urine aceto-acetic acid) is probably the most widely known test in use today, and is used by many herdsman and veterinarians to confirm suspicion of ketosis in an individual animal. The problem with using these strips to test/monitor for SCK is the variable sensitivity (Se) and specificity (Sp). Many different studies have been done to test Se and Sp of the Ketostix, and results are usually Se>60% and Sp>80%.[6] The importance of this information lies in the fact that if a veterinarian uses these strips to test for SCK, there will be a rather high number of false negatives (cows that actually have SCK but do not show positive on the test strip). These results will give an inaccurate picture of what is actually occurring on the farm.

Serum NEFA/BHBA testing is considered the gold standard test for SCK, and has been for some time. Testing NEFA or BHBA gives quantitative data with which to make decisions, and gives the veterinarian hard data to show the farmer. It has been proven that testing for SCK using pre/post-partum NEFA or post-partum BHBA are each reliable predictors of clinical disease in the future, with pre-partum NEFA being the best predictor. Critical threshold values have been established as follows: Pre-partum NEFA>0.29mEq/L; Post-partum NEFA>0.57mEq/L; Post-partum BHBA>10mg/dL (0.97mmol/L). Values above these thresholds resulted in significant increase in risk of developing displaced abomasum, clinical ketosis, metritis, or retained placenta.[9]

Problems do exist with using serum NEFA/BHBA for SCK testing, however. While BHBA is quite stable in sampling tubes, NEFA tubes can be hard to handle and prone to give inaccurate laboratory results if not stored/shipped properly.[14] The time

taken to get a result is also a downside to laboratory testing, as typically 1-2 days will pass before results can be known. Lastly, and probably most importantly, the testing for serum NEFA/BHBA is quite expensive, with one test costing around $8 (price from NYS Diagnostic Laboratory). Compared to the pennies that it costs to use a Ketostix strip, many farmers will most likely have a hard time justifying the added costs. The Precision Xtra Meter, however, has recently shown that an affordable, accurate test for SCK can be run cow-side. This human glucometer/ketometer measures BHBA levels from a few drops of whole blood and gives results in about 10 seconds. The quick results make the meter ideal for on-farm testing and decision making. The cost of the meter itself is about $15-20 currently, and each strip is about $1. The Se and Sp of this meter were shown to be higher than Ketostix and Ketolac test strips.[13]

As nearly every herd can benefit from periodic SCK screening, it is important for a veterinarian to know how to appropriately perform a herd-based test. In many cases, a herd vet does not need to have 95% certainty in order to make a decision. A confidence level of 75% is usually enough evidence to make a management change, although this fact needs to be accurately communicated to the herd manger/owner.[6] For testing a herd for SCK, the cows who are at risk for the disease are transition cows, or those cows +/- 14 days from calving (excluding those cows within 48 hours before or after calving). A minimum of 12 animals must be tested to obtain the desired 75% confidence level. If there are not enough cows on the farm in the at risk period, the only way to accurately test for SCK is to wait for more cows to enter the transition period.[6] Multiple studies have been done to determine the alarm level for SCK, which is the prevalence at which a

management change will be made. The alarm level is usually between 10-15% for SCK depending on the study.[6]

Once SCK has been determined to be a problem on a farm, there are many strategies that can be employed to prevent the disease in the future. Prophylactic treatment of SCK is a strategy that has been employed on some dairies, meaning any cow with a positive urine test for SCK is automatically treated as if she had clinical signs (even if she is eating/milking normally). This can be effective, but also has downfalls such as increased labor and treatment costs, increased stress for the cow (especially with multiple days of treatment) and decreased lying time for the cow as they are in head locks for longer periods waiting to be treated. Cows that have a decrease in overall resting time have been shown to be at a higher risk for developing not only SCK, but many other diseases (most important being lameness).[4] The preferred method for monitoring fresh cows for SCK is to note that the cow had evidence of SCK, but not to treat until the cow develops clinical signs.[11] This allows the majority of cows to recover spontaneously without the additional stresses and costs associated with treatment.

Other areas to focus on with transition cow management include evaluating transition cow housing and maternity pen management. It is very important that dry cows are not overcrowded in their pens and are provided with properly sized stalls to rest in.[5] Ignoring these facts will lead to a decrease in dry matter intake and possible development of periparturient ketosis. Ensuring the maternity pen (if one is present on the farm) is managed appropriately is also vital to the success of healthy transition cows. Pen moves 2-10 days before calving must be minimized, as animals stressed at this time will be much more likely to develop clinical disease post-calving.[5]

Monitoring pre-partum feeding behavior has also been shown to be an effective strategy for detecting cows with SCK.[3] Cows were monitored from 3 weeks before calving to 3 weeks after calving, and the research showed that for every 10 minute decrease in average daily feeding time, the risk of SCK increased by nearly 2 times. This monitoring strategy can be employed in a simpler manner by noting which cows in the barn still have larger piles of feed during the morning check. The cows with larger piles can be targeted for more targeted testing if necessary.

Certain feedstuffs have been shown to be effective in preventing SCK in the dairy cow. Monensin, an ionophore antibiotic, will alter the ruminal volatile fatty acid production in favor of proprionate, which is the precursor to glucose in the ruminant liver. Monensin can be added to the ration, or given as a controlled release capsule. The capsule, when given 3 weeks pre-partum, was shown to decrease the risk of SCK by 30%.[8] Propylene glycol, one of the common treatments for clinical ketosis, has also been shown to effectively prevent SCK.[12] Propylene glycol is metabolized to proprionate in rumen or absorbed unchanged and enters directly in to gluconeogenesis resulting in more energy available to the cow. Unfortunately, propylene glycol must be given orally each day, as adding it to a ration causes a decrease in dry matter intake because of poor palatability, but it remains a viable option to prevent SCK nonetheless.

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