Clinical Diagnosis and Treatment of Ketosis

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Abstract

Ketosis afflicts lactating dairy cattle of all ages, increasing during peak production years. It may occur two to three weeks prepartum to four months postpartum. Common symptoms are diminished appetite, decreased milk, nervousness, profuse salivation, unnatural gait, licking themselves, grasping hard objects and damaging mouth, becoming explosively excited and unmanageable. Clinically, animals reveal lack of alertness, eyes lack luster, rumen is hard and partially empty and noisy, feces are abnormally firm, and urine is clear, showing characteristic color responses to the Ross modification of the Rothera test. Stress factors may cause ketosis such as high production, indigestion, milk fever, partial starvation, metritis, mastitis, and ovarian cysts.

Treatment for ketotic animals varies depending on conditions. Intravenous injection of dextrose is the author's standard treatment. Orally administered propylene glycol after initial use of dextrose or glucocorticoids has given excellent results. Intravenous or intramuscular cortisone has given extremely variable results. Intravenous or intramuscular adrenocorticotropic hormone, in prolonged ketosis, preceded by glucocorticoids. Dramatic recoveries have resulted from chloral hydrate for animals suffering from primary ketosis.

Introduction

If one is to consider in detail the factors contributing and leading to a correct and positive clinical diagnosis of ketosis in the dairy cow, several direct or indirect considerations immediately come to mind. These may include the age of the animal, stage of lactation, signs observed by the dairyman (history), and finally the actual clinical examination of the patient by the veterinarian. In addition, the veterinarian should attempt to ascertain whether the case presented is, in the broad sense, one of "primary ketosis" or the relatively commonly occurring "secondary ketosis." In the latter, treatments, regardless of their relative merits, are doomed to failure unless the inciting cause is recognized and alleviated.

Age of the animal. I still continue to be amazed at the number of experienced and well-established dairymen who, while keenly capable of recognizing the earliest signs of ketosis in their highest producing animals at the peak of their productive life (average 5 to 8 years of age), fail to recognize the early signs of ketosis in first-calf heifers. I conclude from this that either ketosis in cattle as 2-year-olds is relatively rare in some herds in contrast to the overall incidence, or that these dairymen confuse the thumb rule of first calf heifers "never having milk fever" (hypocalcemia; post parturient paresis) and proceed to apply this rule to ketosis also. In actuality, however, ketosis in all recognized forms can and does occur in dairy cattle of all ages though I feel it is safe to assume that most veterinarians would agree that the incidence increases directly in proportion to the peak of production years, i.e., age 5 through 8 in the average herd.

Stage of lactation. It has been my experience that ketosis may occur during the period of from 2 to 3 weeks prepartum to as long as 4 months postpartum. In our clinic we are initially called to treat the majority of cases 10 days to 4 weeks postpartum. I might digress here just a moment to take issue with various physiologists whom I understand can demonstrate "starvation ketosis" in their laboratories almost at will regardless of the stage of lactation of the dairy cow. I, on the other hand, can unequivocally state that I have never been able to demonstrate the abundance of ketone bodies in a patient's urine (using the standard Ross modification of the Rothera test) which is in any stage of the gestation period except the aforementioned 2 to 3 week prepartum to 4 months postpartum period. This span of time has had included both cases of actual starvation (27 out of 53 adult cattle actually died in one herd) as well as "self-imposed starvation" (complete anorexia) in various diseases extending for as long as 9 to 12 days in extreme cases. Therefore, and in summation regarding stage of lactation, I wish to reiterate that I have seen cases only during the 2 to 3 week prepartum to 4 months postpartum periods!
**Signs observed by the dairyman (history).** I should first like to portray the most typical form which we encounter in the northeastern U.S. A dairyman who is inexperienced with ketosis but an astute observer first notes that the animal “leaves some of her grain” and, in fact, at the end of about 3 days eats little of it. Similarly, average quality silage will be increasingly refused over the next 3 days and average quality hay over the following 3. Finally, and with few exceptions, the dairyman reports that the cow turns her head and prefers to eat the bedding (if straw or very poor quality or moldy hay) to anything else which may be offered to her. I can summarize this rather lengthy example by simply stating that if allowed to develop long enough, ketosis will force the animal to demonstrate a perverted appetite or pica. At the same time, I do not wish to leave the wrong impression that all cases are allowed to extend through all these stages. On the contrary, the experienced dairyman seeks help at the onset, i.e., when the cow first leaves a small quantity of her grain, or, if fed in a milking parlor, does not consume the normal amount ravenously in a short period of time.

Changes in milk production are quite variable but in general either the cow drops 2 to 5 pounds (0.9 to 2.2 kg) per milking, or in many early subclinical cases the farmer simply reports that the cow “is not producing what she should be.” In any event the relatively slight drop in production in early ketosis is in direct contrast to most other conditions causing partial or complete anorexia near or following parturition such as metritis, mastitis, traumatic reticulitis (hardware), etc. which are accompanied by nervous signs. These are extended (especially the forearms), grasping the side of the drinking cup with their mouths to the extent of inflicting injury to their tongue, lips, and dental pad and even loosening or breaking off several incisor teeth, and even demonstrate intermittently signs of mania. An example of the latter would be the usual calm and quiet animal suddenly “exploding” when the milking machine is being put on with resultant removal of same as well as the milker! Such individuals “mule kick” beautifully with both rear limbs in exact rhythm as well as jumping with the forelimbs and frequently bellowing. The eyes sparkle and the “wild expression” is obvious.

**Clinical examination.** I was taught the art of clinical examination and physical diagnosis by Dr. W. J. Gibbons (now of Auburn, Alabama) 26 years ago and for the past 23 years have been teaching this art to junior veterinary students at the New York State Veterinary College at Cornell University, Ithaca, New York, and, therefore, I recognize the danger of pursuing my “forte” into a detailed, comprehensive and somewhat boring and unnecessary depth inappropriate to this symposium. I shall sincerely endeavor to describe only the salient features of the assigned topic but wish to emphasize that we routinely examine all of the systems of the patient in every case lest something be overlooked.

In the typical uncomplicated case some of the following features may be observed: The cow’s expression is slightly altered and may be described as bordering upon dullness or lack of alertness. The eyes lack normal luster, and more than one experienced clinician can “at a glance” diagnose ketosis based upon this observation alone with remarkable accuracy. The temperature, pulse, and respiratory rates are within the normal ranges. Auscultation of the thorax and abdomen reveals no abnormal findings with the exception that the rumen most often is hyperactive and described best as “in a state of almost continual rumbling” in contrast to the normal intermittent and more full contractions at the rate of 2 per 1 to 1.5 minutes. At this time it may also be noted that the rumen is not quite as full and its content is a little more firm upon palpation from without in the region of the upper left paralumbar fossa as compared with the rumens of normal stable-mates. Similarly, the feces of the ketotic cow will be slightly to definitely more firm than is considered normal for the particular diet which is being fed. The urine frequently (though not always) is clear (“water colored”) rather than the light amber color characteristic of normal cow’s urine. Approximately 50% of our dairymen and practitioners can accurately identify ketosis by the odor of acetone on the cow’s breath, milk, or urine. One scientist challenges this and states that “the odor more closely resembles the smell of methyl sulfide; indeed, familiarity with the smell of acetone might mislead a person from recognizing the characteristic odor of a cow with acetonemia (1).” Since I am not among the 50% of practitioners endowed with this talented olfactory apparatus and since I would not know what methyl sulfide...
smelled like unless I read the label and broke the bottle, I shall refrain from further comment along these lines!

Finally, the Ross modification of the Rothera test is run on the patient's urine. The reagent consists of 99 g of ammonium sulfate mixed with 1 g of sodium nitroprusside. Approximately 1 g of this mixture is added to 5 to 7 ml of urine in a standard test tube or 10 cc blood vial and, after dissolving, 1 ml of ammonium hydroxide solution or a flake of sodium hydroxide is added. After standing for 3 to 5 min, the test is read:

No color change, (negative)
Slight lavender, 1+
Deep lavender, 2+
Beet red or purple, 3+
Deep beet red or purple and opaque, 4+ (strongly positive)

If urine is difficult or impractical to obtain, milk may be substituted. However, the color changes will never be as distinct. On the other hand there are those who maintain that milk is more accurate in the detection of true ketosis than is the urine. I do not share this view, not from challenging our scientists who support this belief but rather from the repeated impression that if the animal showing a negative milk reaction and only a slight urine reaction is not treated for ketosis, ketosis will shortly develop in most cases while if she receives a standard initial treatment, a full-blown case of ketosis will not usually develop.

In the 10% of the cases we see accompanied by nervous signs (described in the history) we note upon closer examination a degree of hyperesthesia in most all cases. Typically the patient will "cringe" or "scootch" away from even the light touch of one's hand. This is readily observed when the head of the stethoscope is placed over the forward part of the rib cage. Upon completion of the examination and if I am still not certain of the diagnosis of "nervous ketosis", I prefer to have the cow walked. At least 90% of them will demonstrate a "sidewinders gait" in which they "walk crooked" or, in actuality, the hind feet, either to the right or left, tend to "get ahead of the front feet." In many cases this may be observed in the standing animal by a marked curvature of the back (spinal column) with an abnormal lateral bend. Needless to say, the cow which has progressed to the maniacal state, is not released for this part of the examination! Finally, muscle trembling may be noted in some few cases being particularly evident in the lower shoulder (elbow) and mid-flank regions.

**Other Health Factors That May Cause Ketosis**

Frankly and simply stated (whether right or wrong) I believe that any factor which may act as a stress to the cow during this stage of gestation may predispose to ketosis. Arbitrarily I classify this as "secondary ketosis." I do not believe that this is the time or place to discuss the differential diagnosis of cases of primary ketosis from all the possible predisposing causes of secondary ketosis since, in essence, this is only accomplished by a course in most veterinary colleges designated as Large Animal Medicine and generally encompasses courses beginning in the first term of the junior year and ending just prior to graduation. However, I feel compelled to list a few of the more common offenders encountered in our area to exemplify the wide variation of factors:

- Simple indigestion: becoming more common in our area yearly especially in the heaviest and best conditioned cows that are afforded little or no exercise during winter (stanchion or tie stall) confinement during the last 2 to 3 weeks prepartum. The indigestion accompanied by partial and then complete anorexia predisposes to the secondary ketosis.
- Indigestion from any other cause: overeating, spoiled or damaged feed, etc.
- Prolonged cases of milk fever: the "crawler" or the down cow for a prolonged period (3 to 5 days "plus") if accompanied by partial or complete anorexia.
- Starvation or semi-starvation: cases which are heavy milkers and obviously are not being fed enough to maintain both production and body condition.
- Metritis: most cases are accompanied by difficult birth or retained placenta and a "bad odor" and are obvious. Some cases must be detected by a complete examination, however. Anorexia, again.
- Abomasal distention and displacement with or without torsion: a major stress involving a most important part of the digestive system. Partial to complete anorexia.

In addition to these obvious "stress causes" there is one condition which has become increasingly popular (apparently) in the past 10 years in the chronic or repeat case of primary ketosis which responds only transiently to treatment. Rectal examination reveals a medium-sized cyst on one ovary, but the cow never shows any of the classical signs of cystic ovaries. Removal of this cyst by expression or tapping is
accompanied by complete remission of signs of ketosis. Perhaps only an endocrinologist knows why!

The final points I wish to imply and reiterate in regard to secondary ketosis would be two:

1. It is of utmost importance, for proficiency and economies, to identify the causative factors in secondary ketosis. In so doing, one may rightfully eliminate the possibility of primary ketosis and proceed to deal with the true inciting phenomenon which, if unrecognized or disregarded, will continue to predispose to ketosis.

2. I am also a firm believer, in addition, in treating the secondary ketosis in any one of the standard methods employed in treating primary ketosis. Some others maintain (and rightfully so, I suppose) that "if the predisposing cause is removed, the ketosis will disappear spontaneously." I believe that in this regard there is no valid contraindication to the "double barrelled" approach which, in my hands, affords the most prompt and complete recovery.

Treatment of Ketosis

Since I am but a clinician and as such not a research scientist it would seem most improper for me to plagiarize someone else's work and report the results to you or even to suggest that I am personally experienced with more than a few of them! Nonetheless, I shall fulfill this part of my assignment by first listing, together with the appropriate reference (1) a number of drugs or procedures or both which have been demonstrated by some one person (or several) to be of therapeutic value in the medical treatment of ketosis. They include glucose, fructose, ammonium lactate, calcium lactate, sodium lactate, sodium acetate, sodium propionate, glycercol, propylene glycol, glucocorticoids, ACTH, insulin, choline chloride, cysteamine hydrochloride, L-methionine, hydroxy analogue, acetilmethionine, cyanocobalamin, cobalt, thiamine hydrochloride, nicotinic acid, vitamin A, vitamin E, potassium chloride, chloral hydrate, udder inflation, fasting.

I shall comment on chemicals and drugs which I have used or am using in treating cases of ketosis:

Dextrose 40%. Give intravenously 500 ml. This is still my standard treatment. I am aware that as long ago as 1943 when I was a veterinary student in chemical physiology my professor (the late Dr. C. E. Hayden) made the statement that "80% of 500 cc of 40% dextrose is eliminated in the urine within two hours after administration." My answer then (kept to myself, however) was the same as it is now: "In many cases either that 80% does a considerable amount of good while going through, or the other 20% is tremendously powerful!"

Many cases are alleviated by this one treatment but, admittedly many others need more treatment, such as up to 1,500 cc initially, 500 cc daily (or every other day) for 2 to 5 to 7 times, or 2,000 cc given slowly by intravenous drip.

Fructose. One-half gram per kilogram as 50% solution, intravenously. I have used this sporadically for the past 10 years but have failed to observe clinical response superior to that obtained with 40% dextrose.

Sodium propionate. Give 4 to 8 ounces (114 to 228 g) orally twice daily up to 10 days. Used as a preventive or as a "follow up" after initial intravenous injection of 500 ml of 40% dextrose. Good results but exerts destructive action on lung tissue if inhaled. Abandoned with the advent of propylene glycol.

Propylene glycol. Give 6 to 12 ounces (171 to 342 g) daily and orally preferably in two divided doses. Used as a preventive or as a "follow up" after initial use of dextrose or glucocorticoids or both. Excellent results.

Glucocorticoids. Give dose equivalent to 1 g of cortisol intramuscularly or intravenously. Extremely variable from excellent to poor results.

Adrenocorticotropin. Give 200 to 800 units intramuscularly. Excellent results particularly in the prolonged or intermittent case and following the use of glucocorticoids previously (2 to 3 days).

Cobalt. Give excess of 100 mg per day (as sulfate or chloride).

Chloral hydrate. Give one ounce (28.5 g) twice daily for 3 to 5 days. (In nervous cases, sometimes necessary to give intravenously to be effective).

Comments and summation regarding treatments. I routinely administer 500 cc of 40% dextrose intravenously on the initial call and drench the animal with 8 ounces (228 g) propylene glycol containing cobalt. If the owner is physically capable of drenching the animal, I dispense one gallon (3.78 liters) of the propylene glycol-cobalt mixture and recommend that he repeat giving 3 to 6 ounces (85.5 to 171 g) twice daily until the cow is completely normal or until the gallon is used. It is not completely clear to me why cobalt is as beneficial as it frequently appears to be. I started using it over 20 years ago (in conjunction with dextrose) because the late Dr. C. E. Hayden stated that "apparently the gluconeogenic organisms in the rumen thrive in an abundance of cobalt."
More recently, cobalt and its relationship to vitamin B₁₂ has been demonstrated and more people are “pushing its use” for this reason.

I rarely use glucocorticoids in our area for two reasons. 1) When they were first introduced I used them experimentally as recommended and rarely was able to approach the anticipated results or the results others experienced in areas 25 and 45 miles away, respectively. I concluded in this regard and with absolutely no scientific basis that cases in certain areas respond dramatically following their use while in other areas the response is disappointing and poor. 2) The administration of glucocorticoids is definitely contraindicated in many conditions predisposing to secondary ketosis.

I most commonly employ adrenocorticotropin in cases on consultation which have been repeatedly treated with glucocorticoids. I feel that the direct stimulation of the “by-passed” adrenals often brings rewarding results in these cases.

Chloral hydrate, while logically employed in cases of the nervous type of ketosis, also in some herds brings about somewhat dramatic recoveries in primary ketosis. I have known of three herds in which the herdsman only wanted the cow examined and if the diagnosis was ketosis, they would assume the responsibility of treatment and would administer by capsule 28.5 g of chloral hydrate twice daily for 3 to 5 days with excellent results.

I would be remiss if I did not mention supportive husbandry recommendations which I routinely employ in the treatment of a ketotic cow. I recommend to the dairyman that his primary responsibility is “to get the cow back on full feed as quickly as possible.” To this end, I recommend that he try first cutting legume hay or timothy hay rather than the best quality second or third cutting alfalfa; try whole oats, calf feed, coarsely ground horse feed, potato parings, sliced apples or “anything” to “trick” this cow with the perverted appetite into resumption of eating. As soon as he finds the feed she likes, start mixing the conventional feed with it in increasing proportions until after 5 to 7 days, “she is back on full feed on the normal diet.”

Also may I prevail upon your endurance to mention a couple of my thoughts on prevention?

1. We have a few herds with previously high incidence of ketosis in which the owner purchases propylene glycol by the 55 gallon drum. Beginning approximately 2 weeks prepartum and extending 3 weeks “plus” post partum each cow is “fed” 6–8 ounces (171 to 228 g) of propylene glycol daily. This is started in a reasonable manner of one tablespoonful of propylene glycol on the silage the first day, 2 tablespoonfuls the next, and so on until the cow becomes accustomed to it. In each herd, the dairyman has been well satisfied.

2. I believe that it is important that the diet of the cow not be abruptly changed at the time of parturition. I think it is relatively unimportant as to which way this is achieved, i.e., either maintain the cow on the standard 12% dry and fitting ration up to two weeks postpartum and then gradually change to the milking ration or change the cow to the milking ration at least 2 weeks prepartum so that no further change will be necessary at parturition. While the “lead feeding” advocates would favor only the latter, I have not witnessed the anticipated superior results that the proponents of this method have advocated! I feel that the abrupt change at the time of parturition is the important thing to guard against presumably because of the role it may play in predisposing to simple indigestion—anorexia—ketosis.

In conclusion, may I really digress from my specific assignment and challenge the members of this organization with a bold and shocking statement? “I do not know nor has anyone ever told me what actually constitutes the inciting cause of primary ketosis at the farm level!” There are many cows in many herds which, in spite of the best management and nutritional practices partially “go off feed” just before, at, or shortly after parturition and then proceed (apparently because of this) to develop ketosis. If the answer to this is determined (be it an excess or deficiency of some element, vitamin, trace mineral, endocrinal influence or “what not”) there will no longer be a need for a symposium on ketosis!

Reference