KETOSIS

Dr. Naqa Saleh

OVERVIEW

- Its an important metabolic disease of cattle and sheep, caused by impairment metabolism of carbohydrate and volatile fatty acid
- Biochemically it characterized by: hypoglycemia, ketonemia, ketonuria, and ketolacia and low levels of hepatic glycogen
- Clinically: acetonemia in cattle / pregnancy toxemia in sheep

Etiology

- The main function of glucose in the body is regulation of energy metabolism
- Glucose metabolism in ruminants:
- The ruminant absorbs very little dietary carbohydrate as hexose sugar because dietary carbohydrates are fermented in the rumen to short chain fatty acids:

1. Acetate 70%: to peripheral tissues and mammary glands → storage as lipids / secretion as milk fat / energy (oxaloacetate helps the cycle of energy production; in its absence ketone bodies will accumulate)
2. Propionate 20%: most important glucose precursor(glycogenic); produced from starch, fiber and proteins and converts them to Glu & Lac
3. Butyrate 10%: ketogenic precursor produce ketone bodies after ruminal digestion

- Ketone formation sources: Butyric acid in rumen; mobilization of fat
- Glucose needs in ruminants must largely be met by gluconeogenesis

Etiology

- ➢ Negative Energy balance
- ✓ Highest dry matter intake 8-10 weeks after calving
- ✓ Peak milk production 4-6 weeks after calving

→ negative energy balance → mobilization of adipose tissue → NEFA, BHBA → Gluconeogenesis, ketogenesis

- ✓ Cows will reduce milk production in response to a reduction of energy intake, but this does not happen in early lactation because hormonal stimuli for milk production overcome the effects of reduced food intake and glucose metabolism . Under these circumstances, lowered blood glucose levels result in a lowered blood insulin thus Long chain fatty acids are released from fat stores under the influence of both a low insulin and this leads to increased ketogenesis

- Role of insulin and glucagon
- Controlling energy metabolism
- Insulin: stimulates glucose use by tissues, decreases hepatic gluconeogenesis, prevents lipolysis
- Glucagon: counter-regulatory hormone to insulin
- Cows in early lactation have low insulin: glucagon ratios and are in a catabolic stat
- Elevated ketones may stimulate insulin production and may act as a negative feedback
- Hepatic insufficiency :

1. Type I: 'spontaneous‘ ketosis Gluconeogenic pathways maximally stimulated, demand › capacity
2. Type II: ‘fatty liver’ Gluconeogenic pathways not maximally stimulated → TG formation (TG transport low) → accumulation → fatty liver → liver more suppressed

- Predisposing Factors are those that:
- Decrease the energy supply
- Increase the demand for glucose
- Increase the utilization of body fat as an energy source

are likely to increase ketone production and ketonemia

- Adrenal gland dysfunction and hypothyroidism

TYPES OF BOVINE KETOSIS

1. Primary ketosis (production ketosis): Cows in good BC + high production potential = negative energy balance
2. Secondary ketosis: other dis. lower food intake
3. Alimentary ketosis: high butyrate in silage (subclinical mostly)
4. Starvation ketosis: poor BC + poor feedstuffs (def in propionate and protein causes less gluconeogenesis)
5. Ketosis due to specific nutritional deficiency: cobalt & possibly phosphorus (failure to metabolize propionic acid)

EPIDEMIOLOGY

- ***Housed*** *animals in* ***winter*** *&* ***spring***
- ***Immediate post-parturient period*** *with 90% of cases occurring in the first 60 days of lactation*
- ***Age***: any age, more incidence at the peak of production (4^{th})
- ***Herd dif***: heritable predisposition minimal, feeding frequency (ad libitum < twice a day)
- ***BCS***: no relation to fat, but BC loss during the dry period increases ketosis for following lactation

Decreased milk production

Increased risk for delayed estrus

Lower 1^{st} service conception rate

Metritis, Mastitis, ….

PATHOGENESIS

- hypoglycemia and ketonemia affect the clinical syndrome
- Immunosuppression
- Degree of hypoglycemia # severity of clinical signs + rapid response to glucose →Glu ↓ (predominant factor)
- The ***nervous signs*** which occur in some cases of bovine ketosis are thought to be caused by the production of isopropyl alcohol, a breakdown product of acetoacetic acid in the rumen, although the requirement of nervous tissue for glucose to maintain normal function (reversible encephalopathy)
- ***Spontaneous ketosis*** in cattle is usually reversible by treatment

CLINICAL FINDINGS

- ***The wasting form:***
- Most common form
- Decreased appetite & milk yield over 2-4 days
- Fast weight loss
- Normal Temperature, pulse, respiratory rate
- characteristic odor of ketones is detectable on the breath and often in the milk
- Very few die, but without treatment milk yield will never be restored regardless of spontaneous recovery within a month (25%)

- ***The nervous form:***
- Sudden bizarre signs (short episodes of 1 - 2 h and may recur at intervals of 8-12 h)
- Walking in circles
- Head pushing
- Blindness
- Aimless movements and wandering
- Vigorous licking & chewing
- Hyperesthesia, tremor or tetany

This cow with Acetonaemia shows loss of Appetite with poor Abdominal fill, a drop in milk yield and weight loss

This cow with nervous Acetonaemia is head pressing, circling, Aimlessly Wandering and licking at self and Inanimate objects, as seen here

CLINICAL PATHOLOGY

- Glucose: decreased, 20-40 mg/dl (normal 50)
- Blood ketones: increased, BHBA 1400 µmol/L<

(normal <1000 µmol/L): expensive test

- Milk cowside test (Best for screening):

✓ inexpensive + immediate result : cowside

✓ Less variable + easy to collect + few false neg.: milk

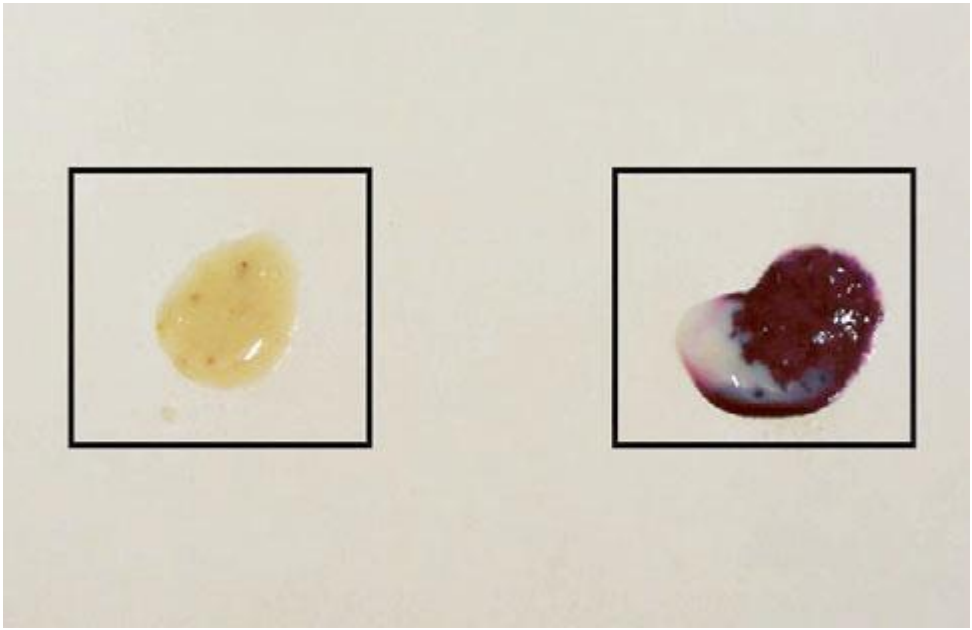
✓ Several commercial test powders or strips to detect BHBA (not sensitive enough for subclinical cases)

- Urine cowside test:

✓ Nitroprusside urine strip

- Milk fat/Pr >1.5 in day one teat milk indicates lack of energy

The Rothera’s reagent has turned purple after being mixed with milk from a ketotic cow. This confirms the diagnosis of acetonaemia



CLINICAL PATHOLOGY

- Clinical chemistry and hematology
- Liver enzymes: elevated
- Liver function tests: normal
- Liver biopsy: degree of liver damage
- Liver glycogen: decreased
- No specific hematologic change

Differential diagnosis

The clinical picture is usually too indefinite, especially in cattle, to enable a diagnosis to be made solely on clinical grounds. General consideration of the h istory, with particular reference to the time of calving, the duration of pregnancy in ewes and the feeding program, and biochemical examination to detect the p resence of hypoglycemia, ketonemia, and ketonuria are necessary to establish a diagnosis.

Wasting form

- Abomasal displacement
- Traumatic reticulitis
- Primary indigestion
- Cystitis and pyelonephritis
- Diabetes mellitus

Nervous form

- Rabies
- Hypomagnesemia
- Bovine spongiform encephalopathy.

TREATMENT

1. Replacement therapy

- Glucose (dextrose):

✓ IV injection of 500 mL of a 50% solution of glucose → transient hyperglycemia, increased insulin and decreased glucagon secretion, and reduced plasma concentration of NEFA → marked improvement (repeated medications necessary)

✓ SC inj. → prolonged response, discomfort, swellings prone to infection

✓ IP inj. (20%) → risk of infection

TREATMENT

- Propylene glycol and glycerine/glycerol

✓ Propylene glycol (200-700 g daily), or salts of propionic acid, can be administered in the feed and give good results

2. Hormonal therapy

- Glucocorticoids:

✓ Hyperglycemia occurs within 24 h of administration and appears to result from a repartitioning of glucose in the body rather than from gluconeogenesis

✓ Dexamethasone sodium phosphate (40 mg)

- Insulin:

✓ facilitates cellular uptake of glucose, suppresses fatty acid metabolism and stimulates hepatic gluconeogenesis

✓ protamine zinc insulin is 200-300 IU per animal, SC every 24-48 h as required

3. Vit B12 & cobalt

Response of cows with primary ketosis to treatment with corticosteroids and IV glucose is superior, with fewer relapses, than therapy with corticosteroids or glucose alone

Control

- Adequate nutrition of the cow in the dry and lactating period
- Cows should neither be starved nor be over fat at calving
- More frequency feeding
- Energy supplements:

1. propylene glycol is given to cattle in early lactation at 350 to 1000 mL daily for 10 days after calving;
2. glycerol can be substituted for propylene glycol at equivalent dose rates (only for nypoglycemic cows)
3. Propionic acid and its salts for 3 weeks prepartum and 3 weeks post partum are beneficial

Control

- Herd monitoring

✓ Blood glucose estimations on a sample of cows in their second week of lactation (<35)

✓ Testing for ketones in urine or milk of cows in their first or second week of lactation