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Ketosis الخلونمية

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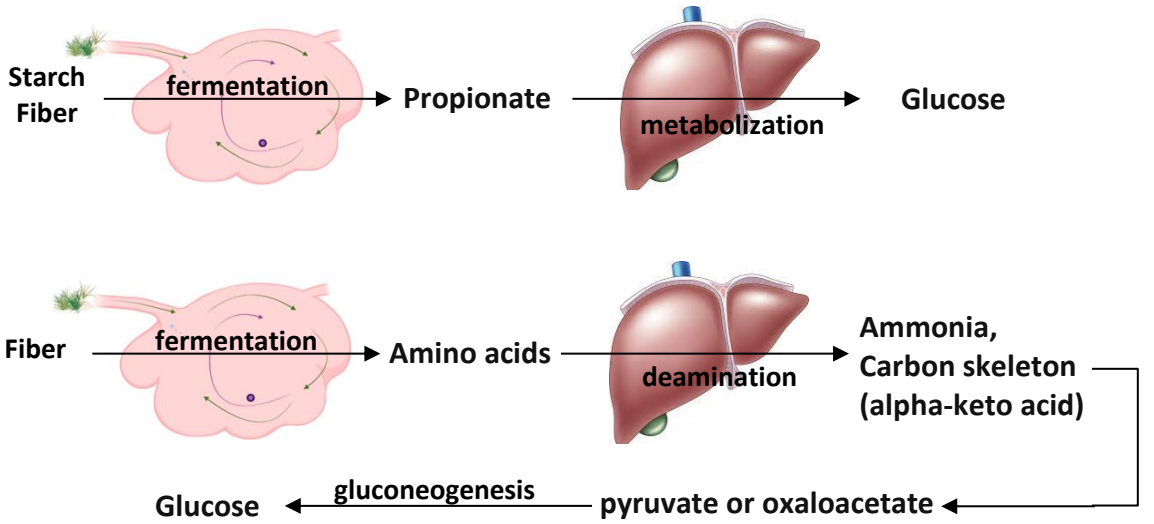
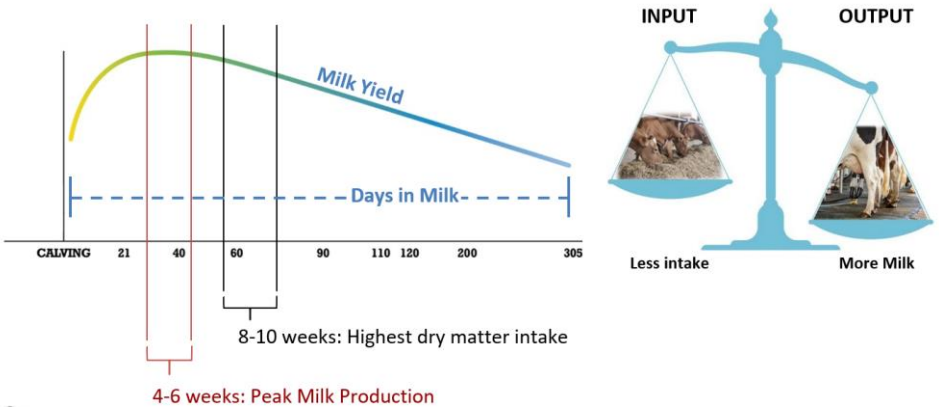
Summary:

- Glucose needs in cattle must largely be met by gluconeogenesis.
  - Ruminants absorb very little dietary carbohydrate because they are fermented in the rumen to short-chain fatty acids, including acetate (70%), propionate (20%), and butyrate (10%).
  - Propionate and amino acids are the major precursors for gluconeogenesis.



Energy Balance

- High-producing dairy cows always have negative energy balance in the first few weeks of lactation (low serum concentrations of glucose).



Response to a negative energy balance

- Cows mobilize adipose tissue, with consequent increases in serum concentrations of nonesterified fatty acids (NEFA) and subsequent increases in serum concentrations of β-hydroxybutyrate (BHB), acetoacetate, and acetone.
- Hepatic mitochondrial metabolism of fatty acids promotes both gluconeogenesis and ketogenesis.

Ketone Formation

- Ketones arise from two major sources: butyrate in the rumen and mobilization of fat.
  - A large proportion of butyrate is converted to BHB in the rumen epithelium.
  - Free fatty acids produced from the mobilization of fat are transported to the liver and oxidized to produce acetyl-CoA.
    - In case of decreased propionate and oxaloacetate:

      acetyl-CoA $\xrightarrow{\text{metabolized}}$ acetoacetyl-CoA $\xrightarrow{\text{metabolized}}$ acetoacetate and BHB

    - BHB and acetoacetate can be utilized as energy sources.

Etiology

- Glucose is essential for tissue metabolism, particularly the formation of milk-associated lactose.
- The utilization of volatile fatty acids for energy purposes is dependent on a supply of glucose.
  - Periparturient cows will reduce milk production in response to a reduction of energy intake, but this does not follow automatically nor proportionately in early lactation because hormonal stimuli for milk production overcome the effects of reduced food intake.
- Lowered plasma glucose concentrations result in lowered plasma insulin concentrations.
- Long-chain fatty acids are released from fat stores under the influence of both a low plasma insulin : glucagon ratio and the influence of high somatotropin concentration, and this leads to increased ketogenesis.

Types of Bovine Ketosis

- Based on the cause, biochemical, and hormonal pathogenesis of ketosis, in addition to the importance of predisposing factors, ketosis can be classified into:
  - Primary ketosis (production ketosis): clinical or subclinical ketosis (hyperketonemia).
  - Secondary ketosis: secondary to other disease due to decreased food intake.
  - Alimentary ketosis: due to excessive amounts of butyrate in silage.
  - Starvation ketosis: occurs in poor body condition and that are fed poor quality feedstuffs.
  - Ketosis resulting from a specific nutritional deficiency: cobalt and possibly phosphorus.

Epidemiology

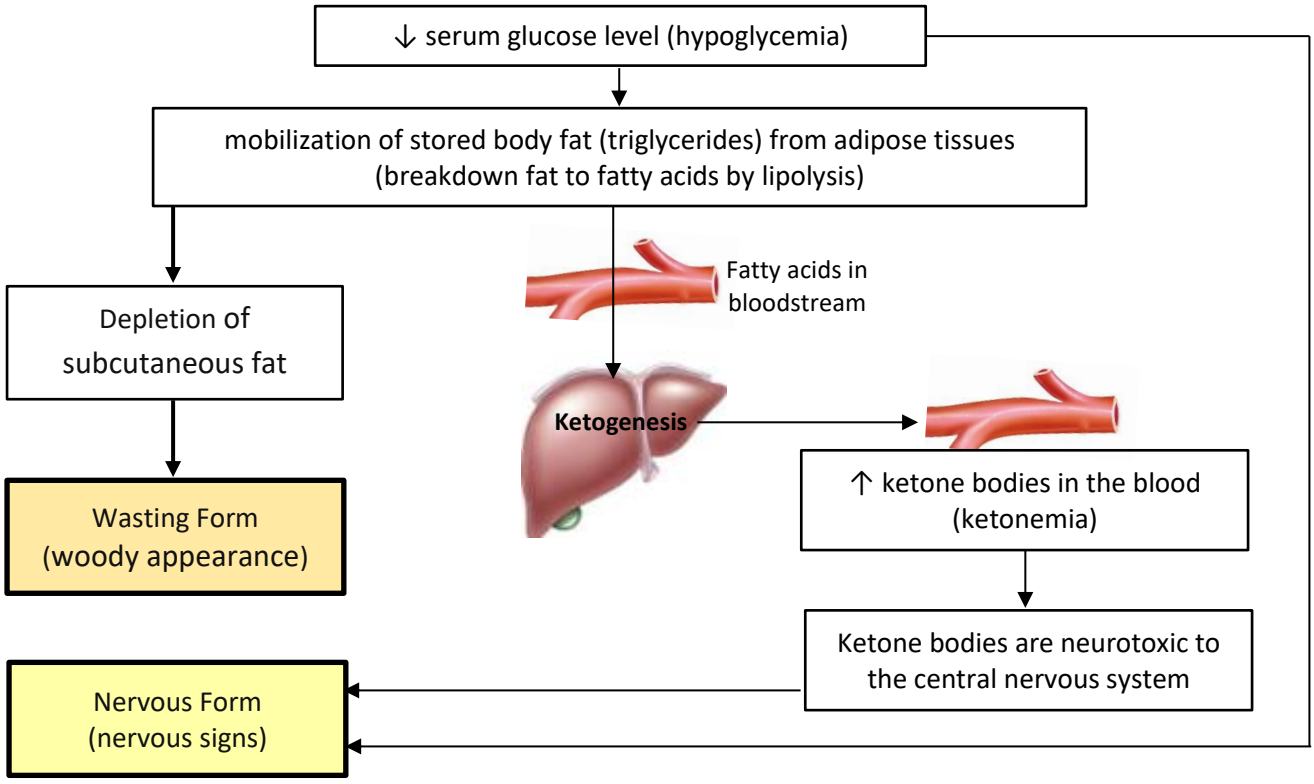
- Very common in lactating dairy cattle in most countries with intensive farming.
- The occurrence is very much dependent on management and nutrition.
- Occurs in the immediate postparturient period (90% of cases occur in the first 60 d of lactation).
- Body-condition loss during the dry period increases risk for ketosis in the following lactation.

Economic Significance

- Decreased milk yields.
- Lower milk protein and milk lactose.
- Increased risk for delayed estrus and lower first-service conception rates.
- Lower pregnancy rates and increased inter-calving intervals.
- Increased risk of cystic ovarian disease, metritis, and mastitis.
- Increased involuntary culling.

Pathogenesis

- Cows in ketosis rely on body fat and, to a lesser extent, body protein to meet energy demands.



- **Note:** In severe cases of negative energy balance, the cow may also break down muscle protein to release amino acids that can be converted into glucose through the gluconeogenesis, providing some additional energy.

Clinical Findings

- Two major clinical forms of bovine ketosis: wasting and nervous, but these are the two extremes.
- **Wasting form** (the most common form):
  - Gradual but moderate decrease in appetite and milk yield over 2 to 4 days.
  - Body weight is lost rapidly (farmers describe affected cows as having a "woody" appearance).
  - The feces are firm and dry.
  - The cow is moderately depressed and is quieter than usual.
  - The ruminal movements may be decreased in amplitude and number.
  - The characteristic sweet odor of ketones is detectable on the breath and often in the milk.
  - Very few affected animals die.
- **Nervous form (nervous ketosis):**
  - Walking in circles, straddling or crossing of the legs.
  - Head pushing or leaning into the stanchion.
  - Apparent blindness, aimless movements and wandering
  - Depraved appetite with vigorous licking of the skin and inanimate objects.
  - Chewing movements with salivation
  - Hyperesthesia may be evident, with the animal bellowing on being pinched or stroked.
  - Moderate tremor and tetany may be present.
- **Subclinical Ketosis (Hyperketonemia):**
  - Increase in blood/plasma/serum BHB above the normal reference range or ketonuria in a cow without detectable clinical signs of disease (The clinical diagnosis is not effective).
  - Cows may have depression in milk yield and a reduction in fertility.

Clinical pathology

- Hypoglycemia, ketonemia, ketonuria, or elevated ketones in milk.

Necropsy Findings

- The disease is not usually fatal in cattle, but fatty degeneration of the liver.

Differential Diagnosis

- **Wasting form:**
  - Abomasal displacement
  - Traumatic reticulitis
  - Primary indigestion
  - Cystitis and pyelonephritis
- **Nervous form:**
  - Rabies
  - Hypomagnesemia
  - Bovine spongiform encephalopathy

Treatment

- The disease responds readily to treatment in cattle with mild hepatic lipidosis.
- Treatment options:
  - Glucose solutions:
    - Dextrose (500 mL of 50% dextrose once, IV).
    - Propylene glycol (300 to 500 mL daily for 5 days, PO).
  - Parenteral corticosteroid (to provides support for gluconeogenesis)
    - Dexamethasone, dexamethasone-21-isonicotinate or flumethasone, IM.
  - Cyanocobalamin (vitamin B12, 1 to 4 mg IV, daily for 2 to 6 treatments).

Control

- Correction of energy imbalance.
- Herd biochemical monitoring coupled with condition scoring.
- Daily monensin administration to late-gestation and early-lactation dairy cows.

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References:

- Constable PD, Hinchcliff KW, Done SH, et al. (2017). Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. 11th ed. Elsevier, St. Louis, Missouri, USA. P: 1708.