

# **Ketosis**

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Lesson - I

# Defenition, Importance of Keosis, Etiology of Ketosis







Unit : Ketosis Lesson : 1

# Defenition, Importance of Keosis, Etiology of Ketosis

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#### **Ketosis - Defenition**

- It is defined as a multifactorial disorder of energy metabolism
- A basic metabolic disturbance resulting from negative energy balance during lactation, a reduction of glucose in the blood and liver and an increased fat mobilization that results in elevated ketone body accumulations
- Characterized by abnormally elevated concentrations of the ketone bodies and hypoglycemia
- Ketone bodies include acetoacetic acid, acetone and  $\beta$  hydroxybutyrate









# **Importance of Ketosis**

Selection of milch animals for high milk yield results in elevated milk production during early lactation

Increase in milk production exceeds the capacity of the animal to ingest sufficient feed to meet requirements for energy

Net result is negative energy balance – mobilization of body fat and protein – TG and amino acid – gluconeogenesis and ketogenesis









# **Importance of Ketosis**

Certain degree of ketosis is a natural state in ruminants

Cows partition nutrients during pregnancy and lactation and are in a lypolytic stage in early lactation and are at risk for ketosis during this period

Ketosis becomes a disease condition when the absorption and production of ketone bodies exceeds their use by the ruminant as an energy source resulting in elevated blood ketones free or nonesterified fatty acids (FFAs) and NEFAs









#### **Glucose Metabolism**

Maintenance of adequate concentration of glucose in the plasma is critical for regulation of energy metabolism.

Ruminants absorbs very little carbohydrate as hexose sugars as carbohydrates are fermented in the rumen to short chain fatty acids - acetate (20%), propionate (20%) and butyrate (10%). Hence glucose requirement is largely met by gluconeogenesis.

Propionate and amino acids are the major precursors for gluconeogenesis.

Glycerol and lactate are of less importance.







#### **Glucose Metabolism**

**Propionate** 

Most important glucose precursor produced in the rumen from starch fiber and proteins Enters the portal circulation and is efficiently removed by the liver Production is favoured by inclusion of high grain in the diet

**Amino Acids** 

#### Glucogenic

Important precursor for gluconeogenesis

Dietary protein is the most important quantitative source

Labile pool of body protein particularly skeletal muscle is also an important source

Contribute for energy synthesis, milk lactone synthesis and milk protein synthesis







### **Energy Metabolism**



High producing dairy cows are in negative energy balance in the first few weeks of lactation

Highest dry matter intake does not occur until 8 to 10 weeks after calving

But peak lactation is at 4-6 weeks. Hence the energy intake may not keep up with the demand



In response to negative energy balance and low serum glucose concentration (consequently low serum insulin)

Cows will mobilize adipose tissue with consequent increase sin nonesterified fatty acids (NEFA)

Subsequent increases in serum concentrations of  $\beta$  - hydroxybutyrate (BHB), acetoacetate and acetone

Hepatic mitochondrial metabolism of fatty acids promotes both gluconeogenesis and ketogenesis







#### **Ketone Formation**

**Butyrate in rumen** 

Rumen fermentation of the diet converted to β-hydroxybutyrate in the rumen epithelium and absorbed as such

**Mobilization of fat** 

Mobilized fat transported to the liver, oxidized to acetyl CoA and NADH







#### **Ketone Formation**

Acetyl Co A is oxidized via TCA cycle

Oxidation requires adequate supply of oxaloacetate from the precursor propionate

Metabolized to acetoacetyl Co A

Propionate deficiency- oxaloacetate deficiencylimited oxidation of acetyl CoA – metabolized to acetoacetyl CoA – acetoacetate and BHBA







# Hepatic Insufficiency and Types of Ketosis

- Uptake of fatty acids by the liver leads to fatty liver - hepatic insufficiency
- Occurs in cows predisposed to ketosis by overfeeding during dry period









# **Types of Ketosis**

Type I ketosis or spontaneous ketosis

Little conversion of NEFAs to triglycerides. Hence little fat accumulation in the liver

Gluconeogenic pathways are maximally stimulated

Rapid entry of NEFAs into hepatic mitochondria Results in high rates of ketogenesis High plasma / serum ketone concentration

Ketosis occurs when the demand for glucose outstrips the capacity of the liver for gluconeogenesis due to insufficient glucose precursors







#### TYPE II

Gluconeogenic
pathways are not
maximally
stimulated
So NEFA uptake is
not active

- NEFAs become esterified in the cytosol forming triglyceride
- Capacity of cattle to transport triglyceride from the liver is low
- Resulting in accumulation and fatty liver
   Fatty liver further depresses gluconeogenesis









# Type iii Ketosis

**Animals fed with** high butyrate producing diet

 As excess butyrate is produced directly in the rumen

E.g. Maize







# Role of Insulin and Glucagon

- Insulin and glucagon regulates the energy metabolism in ruminants
- Counteracting effects play a role in the homeostatic control of glucose
- Low insulin glucagon ratio stimulates lipolysis adipose tissue and ketogenesis in the liver
- Cows in early lactation have low insulin and glucagon ratio









#### **Subclinical Ketosis**

- Elevated concentration of blood ketones without clinical disease
- More common than clinical ketosis
- Significant economic loss
- Common in high producing dairy cows 2-7 weeks postpartum
- Small additional nutritional or metabolic insult develop clinical ketosis









# Thank you