**KETOSIS**

**Classic case:** Early / peak lactation dairy cow, OFF FEED, +/- depressed, weight loss, acetone breath

**COMMON, COMMON, COMMON**

**Presentation:**

"ADR" - Ain’t Doin’ Right - depression, partial anorexia in early lactation

- Ketosis occurs when energy intake is inadequate for output.
  - High **glucose demand** (lactation +/- or pregnancy)
  - High level of **fat mobilization** are BOTH required

**Forms of Ketosis:**

1.) Wasting disease/loss of condition in early/peak lactation

- **Primary ketosis** – no other diseases present
  - **Subclinical** - cows in good condition at calving
    - Still eating and producing
    - Some herds, 30-50% of cows
    - If chronic, will see fatty infiltration of liver
  - **Clinical** - cows +/- good condition at calving
    - Off feed, especially concentrates
    - ↓ milk production
    - Fatter cows – “sicker quicker” severe hepatic lipidosis possible, can be fatal

- **Secondary ketosis** – often transient
  - Periparturient disease present - ↓ appetite = Neg energy balance
    - DAs, hypoCa, retained placenta, metritis, mastitis, lameness

- **Pregnancy toxemia**
  - Late pregnant cows – cause unknown; rare but serious-intensive Rx, possible C-section
  - Late pregnant sheep with TWINS= pregnancy toxemia of ewes (rare in goats)

2.) “Nervous” ketosis: CNS signs seen include:

- Circling, staggering, bellowing
- Licking, chewing, pica
- Trembling, Aggression

**Differential Dx:**

Must evaluate cow for any underlying illness that can contribute to being off-feed
Fat cow syndrome (liver failure)
Diseases with CNS signs -Listeriosis (CNS signs not transient), Rabies (FATAL)

**Cause of CNS signs uncertain – ↓ glucose, ↑ ammonia?**
Test(s) of choice:
  History and clinical signs, risk factors, acetone smell on breath

A little background:
- **Metabolism of FAT** produces KETONES
- Volatile fatty acids (VFAs) & non-esterified fatty acids (NEFAs) = major component of fat.
- Three major ketones we measure
  - β-hydroxybutyrate (BHB)
  - Acetone
  - Acetoacetate.

Screening tests for ketones:
- Individual cows or herd testing
- **Ketonuria precedes ketonemia**
- Use fresh samples/fresh strips
  - acetoacetate – purple color
  - hydration affects results
  - trace/pale color - subclinical dz

**Urine - Ketostix®** - very sensitive
- acetoacetate

**Milk - Acetest®**
- Good *specificity* (trust a *pos.* result)
- Acetone/acetoacetate

**BHB testing**
- Most *sensitive* test (trust a *neg.* result)
- Positive = clinical disease

Blood work abnormalities:
- +/- Hypoglycemia, metabolic acidosis
- **Ketonemia**
  - BHB > 1400 μmoles/L – subclinical
  - BHB > 3000 μmoles/L – clinical
- Liver enzymes ↑ with hepatic lipidosis (variable)
  - AST, GGT, SDH

↑ **NEFAs** – best for herd testing
- Indicates lipolysis is occurring
- Prepartum > 0.30 mEq/L
- Postpartum > 0.70 mEq/L
- Some ↑ NEFAs is normal immediately post-calving

Rx of Choice:
- Restore normoglycemia + ↓ serum ketone bodies – provide glucose/precursors
  - IV Glucose – 50% dextrose
  - If NOT pregnant, glucocorticoids – dexamethasone or isoflupredone acetate
  - Propylene glycol drenches
  - Force feeding
  - Decrease milk production – reduce milking duration for days (only if mastitis ruled out)

Restore to full nutrition
Don’t stop supplementation till after cow is normal several days
Pregnant cows may require intensive therapy, may need C-section; = pregnancy toxemia
Cows with fatty liver also require intensive therapy that may take weeks to resolve

Prevention:
- Nutritional management
  - Increased plane of nutrition 2 wks prior to calving
  - Increase energy intake after parturition
  - Adequate vitamins and minerals
- Daily exercise – prevent overconditioning
- Problem herds
  - Monitor ketone levels in urine and milk
  - Propylene glycol supplement
**Prognosis:**
- **Good** with treatment for mild clinical cases;
- **Guarded to poor** for cows with fatty liver

**Pearls:**
- Some level of ketosis probably occurs in ALL high producing dairy cows in early lactation.
- High ketones also affect appetite
  - Cows refuse concentrate, necessary for propionic acid production
  - Propionic acid = primary glucose precursor in ruminants.
- **RISK Factors:**
  - Excessively thin or excessively fat cows
  - Subclinical ketosis contribute to decreased overall productivity premature culling
  - Increased incidence of DAs in herds with ketosis problems


For more details of basic ruminant nutrition as it relates to ketosis, see the following pages
BASIC RUMINANT NUTRITION review:

- Glucose absorbed directly only in the small intestine (SI)
- Rumen microorganisms use dietary carbohydrates (CHOs)
  - Produce volatile fatty acids (VFAs - acetic, propionic, butyric acids)
  - And some non-esterified fatty acids (NEFAs).
  - These VFAs are absorbed and used for energy production by tissues

- **Propionic** VFA is a primary glucose precursor used by liver
  - Almost 100% absorbed from portal vein
  - Enters the Kreb’s cycle

- **Butyric** VFA converted to β-hydroxybutyrate (BHB) in rumen epithelium
- **Acetic** VFA converted to Acetyl CoA and/or lipids

- When a cow lacks carbohydrates/VFAs (glucose precursors)
  - Rumen metabolism becomes inadequate
  - see increase in lipolysis for energy needs
  - ↑ release of NEFA’s from adipose tissues
  - **NEFAs are converted to ketones** - acetoacetate, beta-hydroxybutarate, and acetone
  - NEFAs are used directly for energy
  - or converted to very-low-density lipoprotein (VLDLs).

- What ketosis does:
  - Depresses appetite
  - Decreases release of VLDLs from liver
  - Inhibits VLDL utilization by tissues
  - So VLDLs build up in liver
  - In chronic or severe ketosis cases, cow eventually develops fatty liver

My Notes:
<table>
<thead>
<tr>
<th>Rumen</th>
<th>Liver</th>
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<tbody>
<tr>
<td><strong>NORMAL</strong></td>
<td><strong>NORMALLY LIVER</strong></td>
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<tr>
<td><strong>NO</strong> CARBS converted to VFAs via microbes: continuously produced and absorbed</td>
<td>converted to Acetyl CoA lipids</td>
</tr>
<tr>
<td>VFAs:</td>
<td>Used for gluconeogenesis; major Kreb’s cycle substrate</td>
</tr>
<tr>
<td>ACETIC</td>
<td></td>
</tr>
<tr>
<td>PROPIONIC</td>
<td>Esterified, then oxidized to Acetyl CoA, go into Kreb’s cycle or to ketones / VLDLs</td>
</tr>
<tr>
<td>BUTYRIC</td>
<td></td>
</tr>
<tr>
<td><strong>NEFAs</strong></td>
<td>Low levels seen</td>
</tr>
<tr>
<td><strong>KETOSIS</strong></td>
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<tr>
<td>↓ Carbs/VFAs due to lack of intake +/- increased demand = NEG Energy balance</td>
<td>AA - primary ketone produced</td>
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<tr>
<td>↑ Lipolysis &gt;&gt; release of NEFAs</td>
<td>Reduction in mitochondria</td>
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<tr>
<td>↑ production of ketones</td>
<td>Spontaneous decarboxylation in cytoplasm</td>
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**KETONES**
- NEFAs → Acetoacetate (AA)
- \(\beta\)-hydroxybutyrate (BHB)
- Acetone

**Ketones** can be used directly for energy production in tissues + incorporated into milk fat

**BUT**

When N energy balance continues, VLDLs build up in liver as ketone levels increase AND mechanisms for tissue utilization and release into plasma are inhibited = fatty liver

Some ketone production is inevitable in high producing cows; most cows gradually overcome this; with high levels of subclinical ketosis herds – see INCR incidence of parturient disease, affects economics significantly

**Primary Ketosis**
- **Late pregnancy**
  - Unable to eat enough in late preg (lack of room!); esp with twins; = pregnancy toxemia in sheep
- **Early lactation**
  - Takes time to adapt to lactation diet; May develop fatty liver and become ill if not treated
- **Peak lactation**
  - Usually self-limiting; occurs b/c glucose demand overwhelms supply; milk production drops, ketones decrease

**Secondary Ketosis**
- Intake decreases b/c of concurrent disease, eg., mastitis, metritis, DA, retained placenta

**Diagnosis**
- Clinical signs
- Acetone breath
- ↑ NEFAs, BHB in milk, urine, and blood

**Treatment**
- Increase intake, increase glucose:
  - Force feeding
  - Propylene glycol drenches
  - IV Dextrose
  - Glucocorticoids
  - mild prod by reduced milking times
- Preg cows/fatty liver – require intensive therapy

**Prevention**
- Increase nutrition 2 wks pre-calving; increase intake post-calving
- Daily exercise

<table>
<thead>
<tr>
<th>Subclinical</th>
<th>Clinical</th>
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<tr>
<td><strong>May only see loss of condition/weight loss; +/- 2° Ds.</strong></td>
<td><strong>See weight loss, loss of condition, drop in milk prod., change in appetite – concentrate intake ↓s</strong></td>
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<tr>
<td>BHB &gt; 1400 μmoles/L</td>
<td>BHB &gt; 3000 μmoles/L</td>
</tr>
<tr>
<td>Nervous Ketosis</td>
<td>Weight loss/decreased condition/milk production</td>
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