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)
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
  - \( \beta \)-hydroxybutyrate (BHB)
  - Acetone
  - Acetoacetate.

Screening tests for ketones:
- Individual cows or herd testing
- **Ketonuria precedes ketonemia**
- Use fresh samples/fresh strips
  - **Urine - Ketostix®** - very sensitive
    - acetocetate – purple color
    - hydration affects results
    - trace/pale color - subclinical dz
- **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 \( \mu \)moles/L – subclinical
  - BHB > 3000 \( \mu \)moles/L – clinical
- Liver enzymes \( \uparrow \) 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 \( \uparrow \) NEFAs is normal immediately post-calving

Rx of Choice:
- Restore normoglycemia + \( \downarrow \) 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*

![Normal liver](image1) ![Fatty liver](image2)

**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

**Images and links** worth a look:
- [Chronic Hepatic lipidosis](https://example.com), from Cornell University, [Dr. John King’s Necropsy Show and Tell](https://example.com)
- [Abnormal liver images](https://example.com), including fatty liver, [Normal liver images](https://example.com), other [bovine necropsy images](https://example.com) from Colorado State University, [Cattle Necropsy manual](https://example.com)

  **β-hydroxybutyrate (BHB)** and **Non-esterified fatty acids (NEFAs)** role in ketosis, tests from Cornell University, [Clinical Chemistry Basics](https://example.com)

  [Pregnancy Toxemia in Sheep](https://example.com) (good image, very pregnant sheep, probably with twins) from the [Maryland Small Ruminant Page](https://example.com) information sheets including,


**For more details** of basic ruminant nutrition as it relates ketosis, see the following pages (but if your brain is full, you can stop here....)
If your brain is not too full……..

**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:**
### KETOSIS IN RUMINANTS

<table>
<thead>
<tr>
<th>Rumen</th>
<th>Liver</th>
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</thead>
<tbody>
<tr>
<td><strong>NORMAL</strong></td>
<td></td>
</tr>
<tr>
<td>CARBS converted to VFAs via microbes: continuously produced and absorbed</td>
<td>VFAs: ACETIC PROPRIONIC BUTYRIC</td>
</tr>
<tr>
<td>NEFAs</td>
<td>= 100% uptake by liver</td>
</tr>
<tr>
<td></td>
<td>Most converted to BHB in rumen epithelial cells, tissues use directly</td>
</tr>
<tr>
<td></td>
<td>Low levels seen</td>
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</tbody>
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#### KETOSIS

| Carbs/VFAs due to lack of intake +/- increased demand = NEG Energy balance | Lipolysis ➔ release of NEFAs | Production of ketones | KETONES | NEFAs ➔ Acetoacetate(AA) | β-hydroxybutyrate (BHB) | Acetone | AA - primary ketone produced | Reduction in mitochondria | Spontaneous decarboxylation in cytoplasm |
|---|---|---|---|---|---|---|---|
| | | | | | | | | | |

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

### Subclinical Ketosis

- **Clinical**: May only see loss of condition/weight loss; +/- 2° Ds. / See weight loss, loss of condition, drop in milk prod., change in appetite – concentrate intake ↓

### Nervous Ketosis

- Weight loss/decreased condition/milk production
  - Bizarre behavior – licking, chewing, pica, bellowing, aggression;
  - Circling, staggering, trembling

### 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
- Problem herds:
  - Monitor ketones
  - Propylene glycol

### BHB

- > 1400 μmoles/L
- > 3000 μmoles/L