Zuku Review FlashNotes™

KETOSIS

Extended Version

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

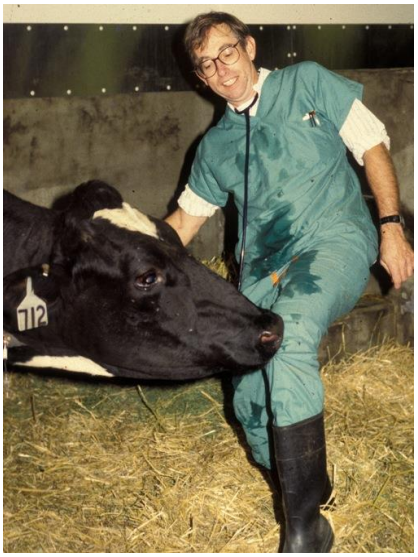
COMMON, COMMON, COMMON

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)

    AND
  - High level of **fat mobilization** are **BOTH** required



Pica (abnormal appetite) secondary to nervous ketosis

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

Cause of CNS signs uncertain – ↓ glucose, ↑ ammonia?

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)

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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

Urine - Ketostix® - very sensitive

- **acetoacetate** – 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 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

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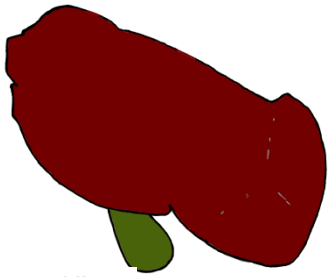
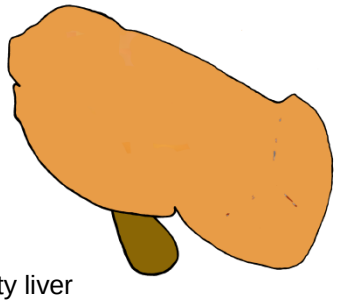
Prognosis:

Good with treatment for mild clinical cases;
Guarded to poor for cows with **fatty liver**



Normal liver



Fatty liver

Fatty liver + severe ketosis can = dead cow

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 proprionic 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

Refs: Pasquini's Guide to Bovine Clinics 4th ed., pg 32-3, Divers and Peek, Rebhun's Diseases of Dairy Cattle, 2nd ed., pp. 590-6, and the Merck Veterinary Manual Online Edition Bovine Ketosis (acetonemia), Hepatic Lipidosis, (fatty liver disease), Pregnancy toxemia of ewes and Pregnancy toxemia of cows. Image courtesy, Dr. Lisle George

For more details of basic ruminant nutrition as it relates to ketosis, see the following pages

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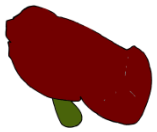
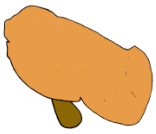
If your brain is not too full……..

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, proprionic, butyric acids)
  - And some non-esterified fatty acids (NEFAs).
  - These **VFAs** are absorbed and **used for energy production** by tissues
    - **Proprionic** 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 <u>lacks</u> 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:

	Rumen			Liver	
NORMAL	CARBS converted to VFAs via microbes: continuously produced and absorbed	**VFAs:** ACETIC PROPRIONIC BUTYRIC --- **NEFAs**	Used directly by tissues, and/or → ≈ 100% uptake by liver Most converted to BHB in rumen epithelial cells, tissues use directly --- Low levels seen	converted to Acetyl CoA lipids Used for gluconeogenesis; major Kreb's cycle substrate --- Esterified, then oxidized to Acetyl CoA , go into Kreb's cycle or to ketones / VLDLs	 **NORMAL LIVER**
KETOSIS	↓ Carbs/VFAs due to lack of intake +/or increased demand = **NEG Energy balance**	↑ Lipolysis >> release of NEFAs ↑production of ketones	**KETONES** NEFAs → Acetoacetate(AA) ↓ ß-hydroxybutyrate (BHB) ↓ Acetone	AA - primary ketone produced Reduction in mitochondria Spontaneous decarboxylation in cytoplasm	 **FATTY LIVER**

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		**Diagnosis**	**Treatment**
Late pregnancy	Unable to eat enough in late preg (lack of room!); esp with twins; = pregnancy toxemia in sheep	Clinical signs Acetone breath ↑ NEFAs, BHB in milk, urine, and blood	Increase intake, increase glucose: -Force feeding -Propylene glycol drenches -IV Dextrose -Glucocorticoids -↓mild prod by reduced milking times
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	Usually corrects with resolution of problem	Preg cows/fatty liver – require intensive therapy
Subclinical	May only see loss of condition/weight loss; +/- 2° Ds.	BHB > 1400 µmoles/L	**Prevention** Increase nutrition 2 wks pre-calving; increase intake post –calving Daily exercise
Clinical	See weight loss, loss of condition, drop in milk prod., change in appetite – concentrate intake ↓s	BHB > 3000 µmoles/L	

Nervous Ketosis	Weight loss/decreased condition/milk production Bizarre behavior – licking, chewing, pica, bellowing, aggression; Circling, staggering, trembling	May require sedation + ketosis therapy; chloral hydrate also provides glucose	Problem herds: Monitor ketones Propylene glycol