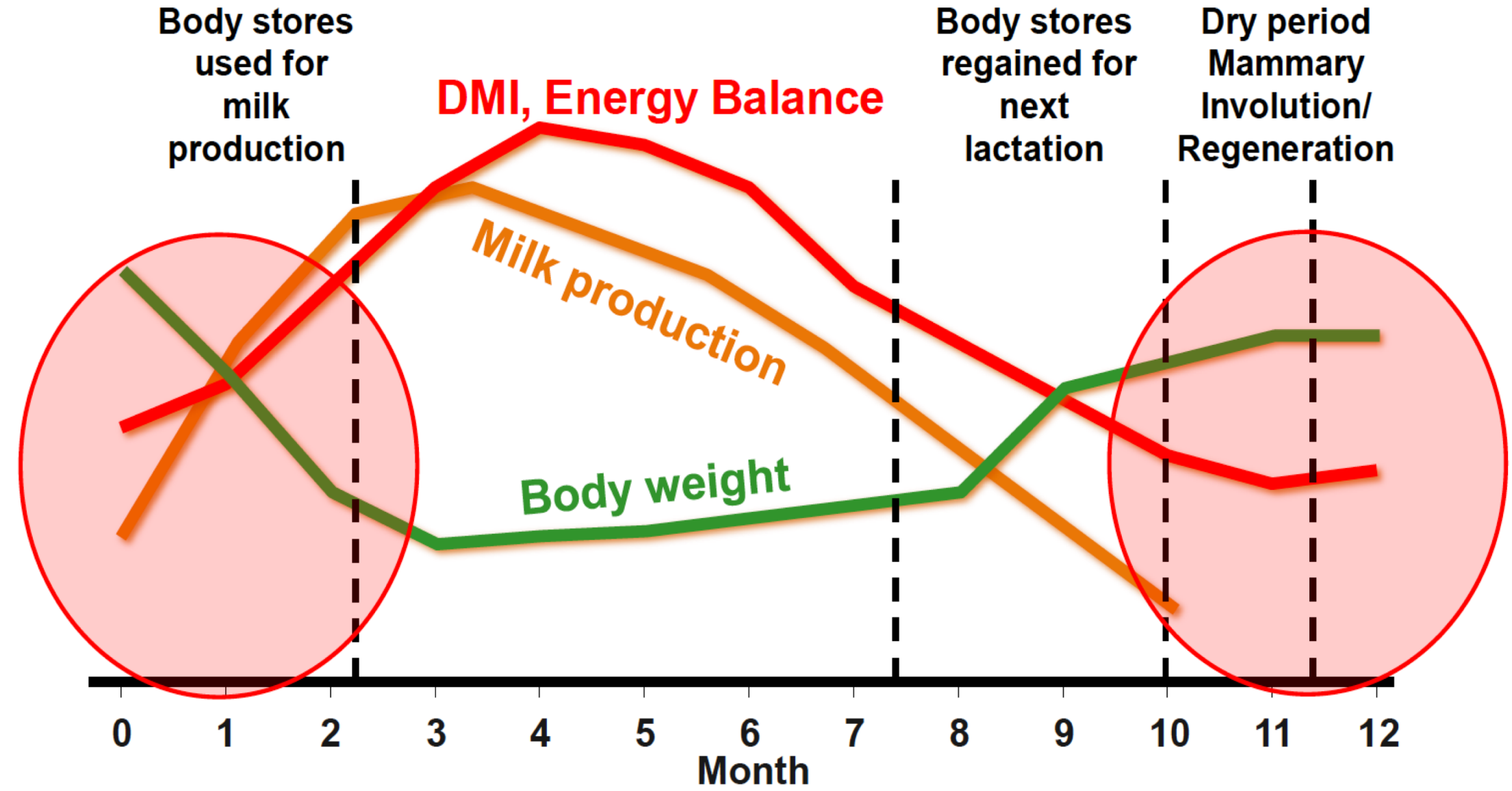
KETOSIS

DOÇ. DR. ALİ ÇALIK

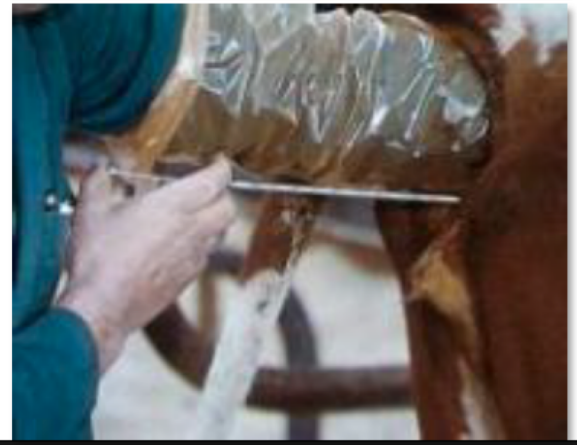
Typical Gestation-Lactation Cycle for Dairy Cattle



Transition Period

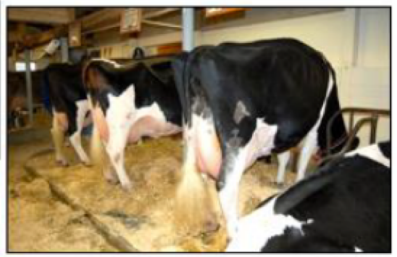
Periparturient Period

Reproduction



Parturition

Lactation



Dry Period

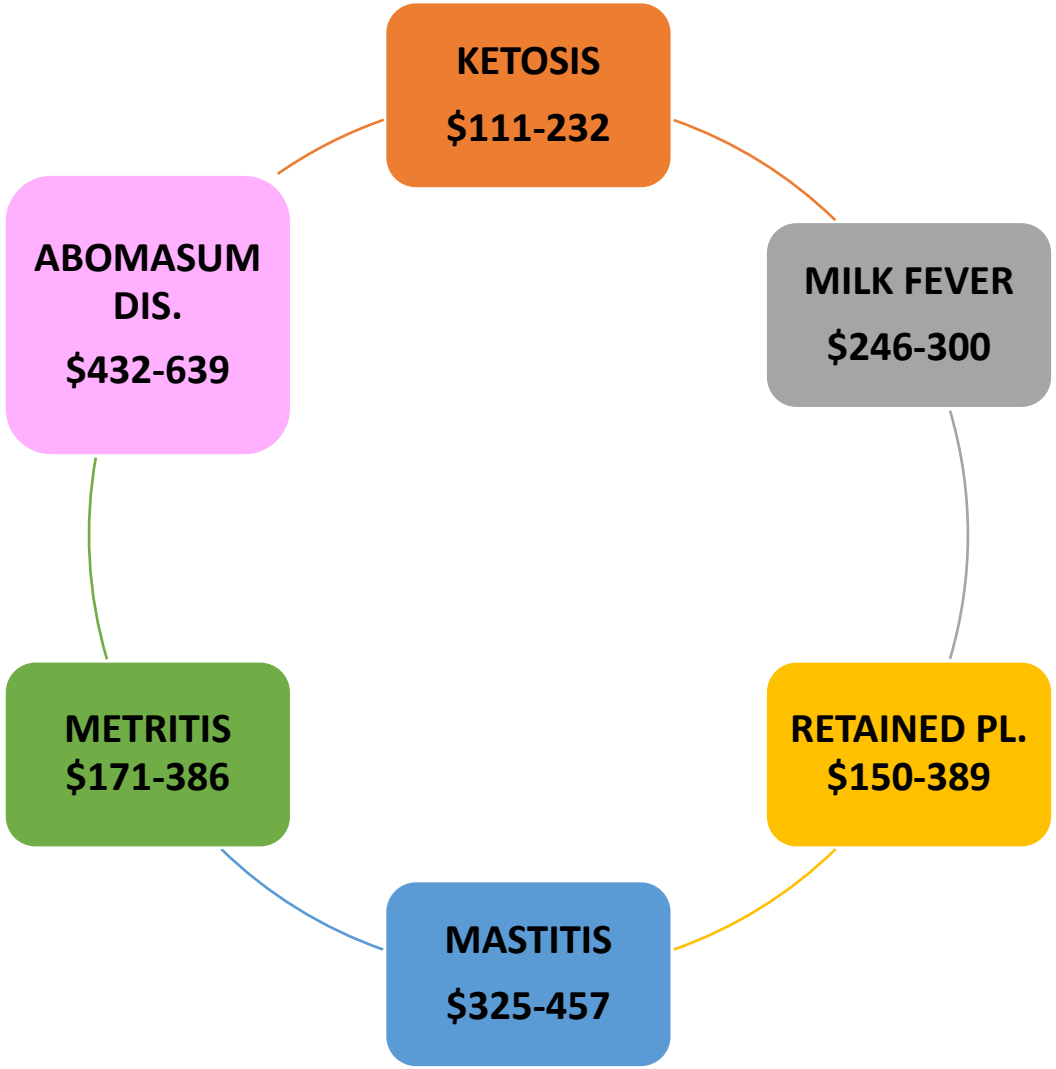
-60 -21 0 21

Transition period

Gestating, non-lactating state → Non-pregnant, lactating

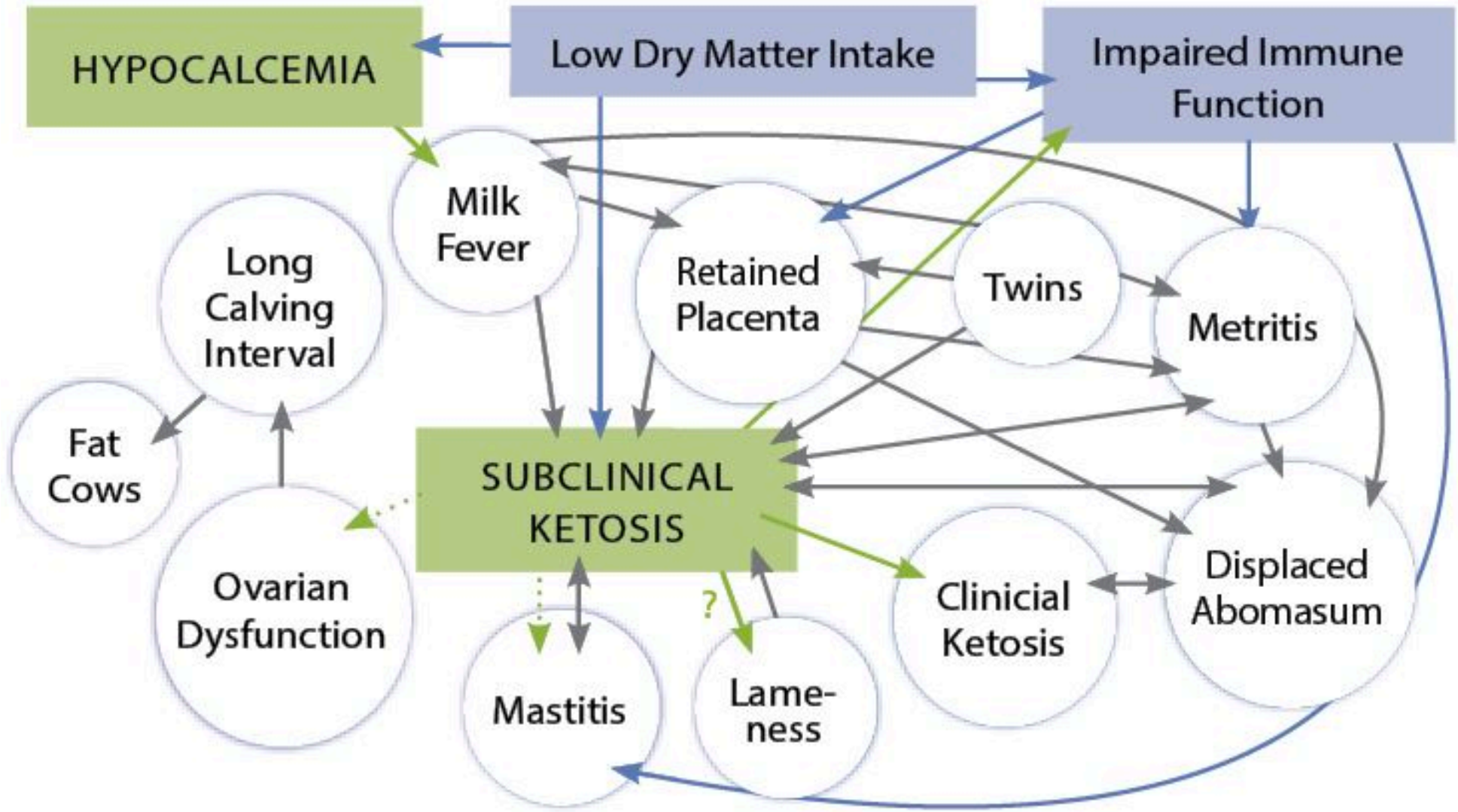
Gestating, lactating state

TRANSITION PERIOD DISEASES



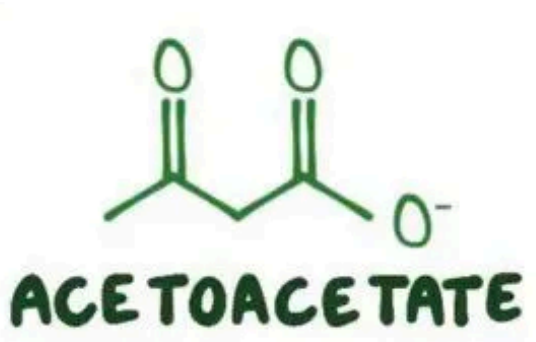
Transition Cow Disease?

The causes and effects of subclinical ketosis bear warning.

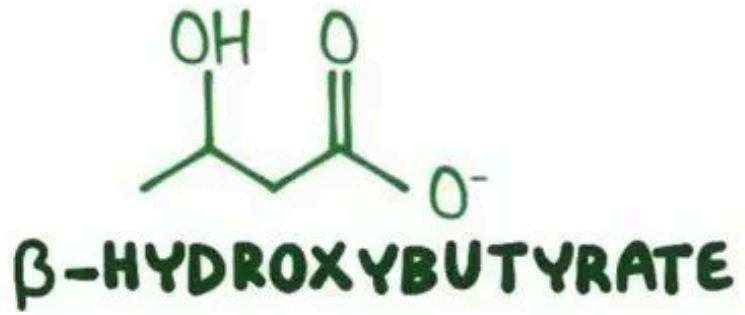


SOURCE: TODD DUFFIELD, GERARD CRAMER, UNIVERSITY OF MINNESOTA

KETOSIS - ACETONEMIA



- High milk production cow
- Occurs during early lactation
  - 10 days to 6 wks
  - Generaly aroud 3rd wk

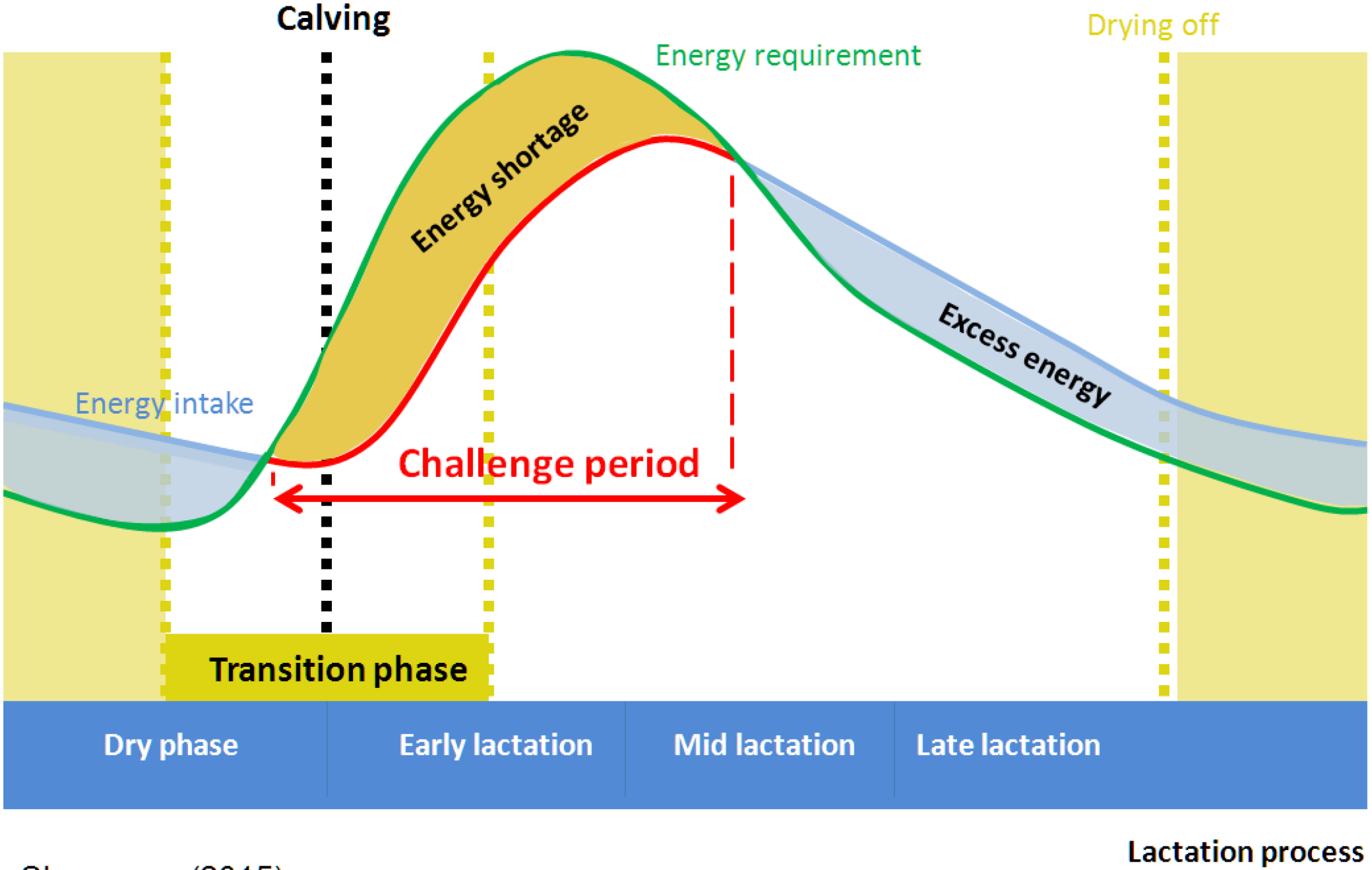


- Ketosis is an elevated concentration of ketone bodies (acetone, acetoacetate, beta-hydroxybutyrate) in all body fluids

KETOSIS

- **CHARACTERIZED BY:**
  - Low blood glucose,
  - Excess ketone bodies in blood and urine,
  - Lack of appetite,
  - weight loss, depressed milk production
  - in cases of severe ketosis, incoordination and neurologic signs.

- **INCIDENCE**
- clinical ketosis can range from 2 to 15%
- subclinical ketosis from 9 to 34 %



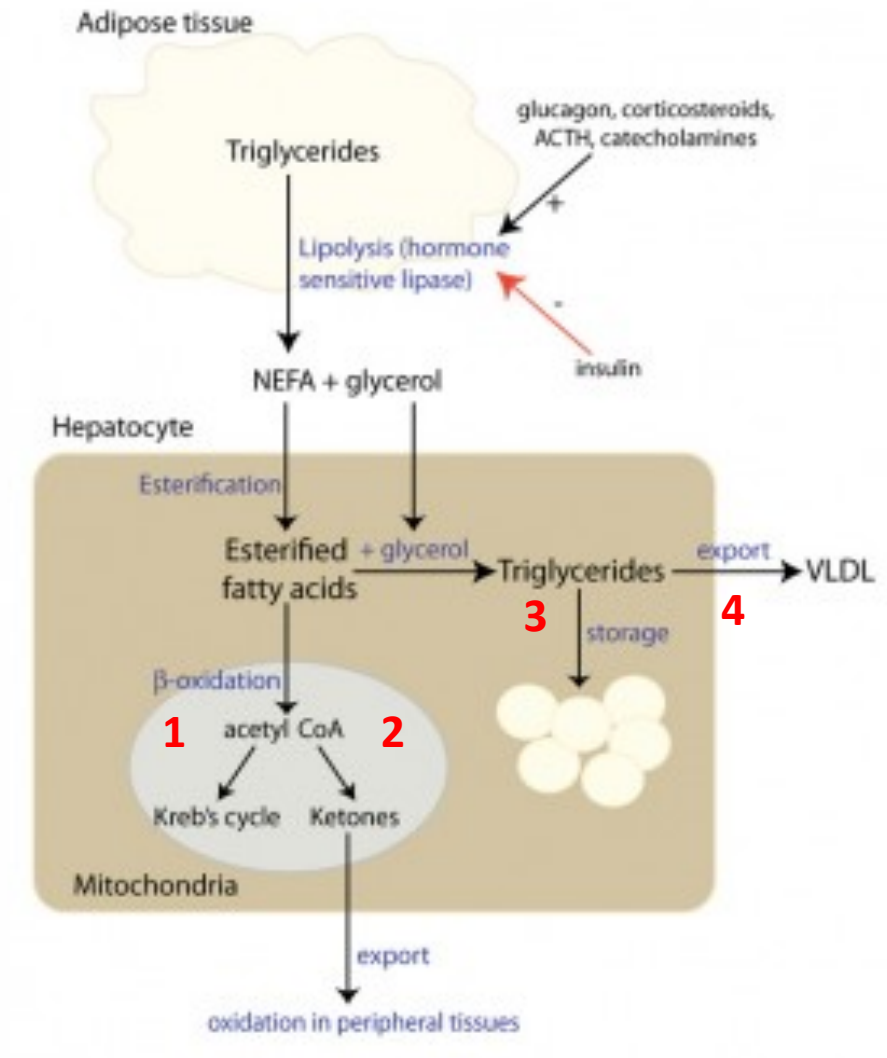
Shaumann (2015)

ETHIOLOGY

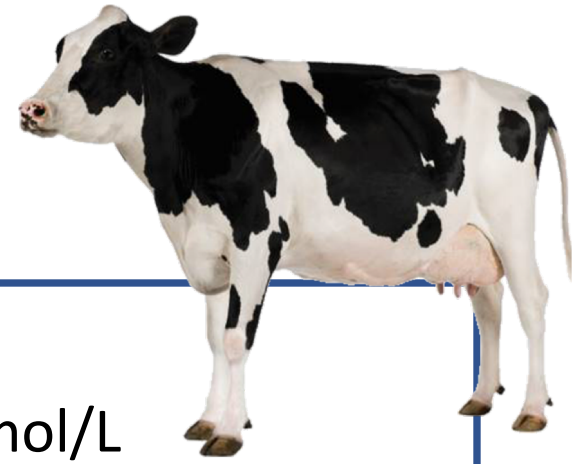
- Combination of intense adipose mobilization and a high glucose demand.
- Both of these conditions are present in early lactation, at which time negative energy balance leads to adipose mobilization, and milk synthesis creates a high glucose demand.
- Adipose mobilization is accompanied by high serum concentrations of nonesterified fatty acids (NEFAs). During periods of intense gluconeogenesis, a large portion of serum NEFAs is directed to ketone body synthesis in the liver.
- Thus, the clinicopathologic characterization of ketosis includes **high** serum concentrations of NEFAs and ketone bodies and **low** concentrations of **glucose**.

Fatty acids follow four pathways in the liver:

- (1) complete oxidation via the tricarboxylic acid cycle to generate H2O, CO2, and energy;
- (2) incomplete oxidation resulting in the release of ketone bodies and less energy; (**KETOSİS**)
- (3) esterification of non-esterified fatty acids (NEFA) to triacylglycerols (TAG) and accumulation within the hepatocytes (**FATTY LIV**ER)
- (4) exported out of the liver as part of VLDL; and



CLASSIFICATION OF KETOSIS



- **subclinical ketosis (SCK)**
  - beta-hydroxybutyrate in the serum between 1200 to1400 umol/L
- **clinical ketosis (CK) –**
  - **hyperketonemia, hypoglycemia, clinical symptoms including lower appetite, loss of body weight, decreased milk production, and dry manure**
  - beta-hydroxybutyrate above 2600 to 3000 umol/L

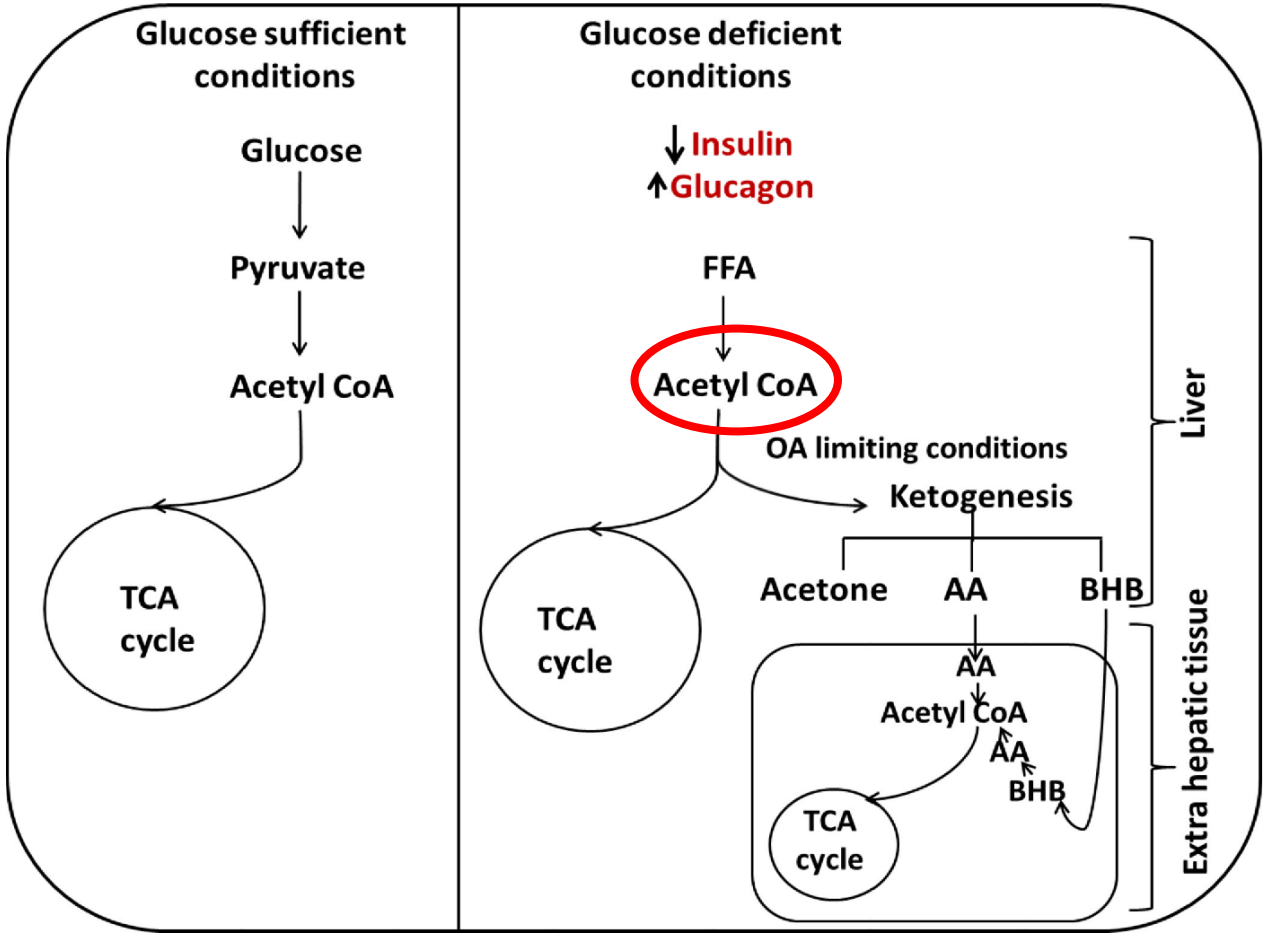
- **1. TYPE I (Primary Ketosis)**
- **2. TYPE II (Secondary Ketosis)**
- **3. BUTYRIC ACID SILAGE KETOSIS**

TYPE I (Primary Ketosis)

- classic form of ketosis
- occurs between 3 and 6 weeks postpartum when milk energy outflow reaches its peak
- type I ketosis - type I diabetes mellitus

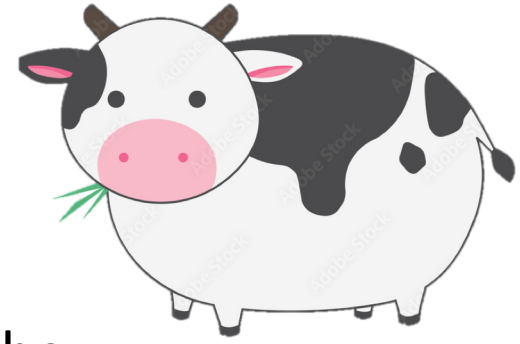
TYPE I (Primary Ketosis)

- hypoinsulinemia due to a shortage of glucose precursors for milk production.
- Gluconeogenesis (Glucagon ↑)
  - Propionate (VFA)
  - Muscle proteins
    - limited due to host protection of muscle proteins
- Lipoysis



TYPE II (Secondary Ketosis)

- usually occurs immediately after calving and is concurrent with other diseases such as fatty liver
- type II ketosis—type II diabetes mellitus
  - Insulin resistance may also exist = OBESITY
- FAT COW – MORE RISK
  - Obesity and overfeeding during the dry period are critical for the development of this type of ketosis.
  - Fat cows are prone to dry matter intake depression – less energy



TYPE II (Secondary Ketosis)

- Insulin resistance may also exist = OBESITY
- Obese cows are also prone to increased adipose sensitivity, which is the tendency to mobilize body fat very rapidly under conditions of stress or negative energy balance.
- Blood ketone concentrations are not as high in type II ketosis as for type I.
  - However treatment is not easy – fat infiltration

BUTYRIC ACID SILAGE KETOSIS

- Attributed to intake of feed high in ketogenic precursors (i.e., butyric acid)
  - **Butyric acid is precursor of Acetyl CoA**
- Silage rich in Butyric acid (Clostridium sp. - unwanted)
- Cows can metabolize the butyrate produced by ruminal fermentation (about 750 g/day), mostly by using it as metabolic fuel for the rumen tissue
- **SCK** : 50-100 g BA Silage
- **CK**: Over 200 g BA Silage

CLINICAL FINDINGS

Reduced feed intake
Reduced milk production
Acetone – Breath

Body temperature
Rumen Motality
Dry Manure

Nervous signs
Licking itself/objects
Agression

DIAGNOSIS

- URINE TESTS:
  - Evaluate acetoacetone
  - Works good when clinical signs are present
  - Not recommended for herd prevelance control
- MILK TESTS
  - Assessing Acetoacetate: poor sensivity
  - Assessing BHB: Good sensibility and specificity
- BLOOD TEST:
  - BHB
  - Works perfect

SCK: 1200 to1400 umol/L BHB
CK: above 2600 to 3000 umol/L BHB

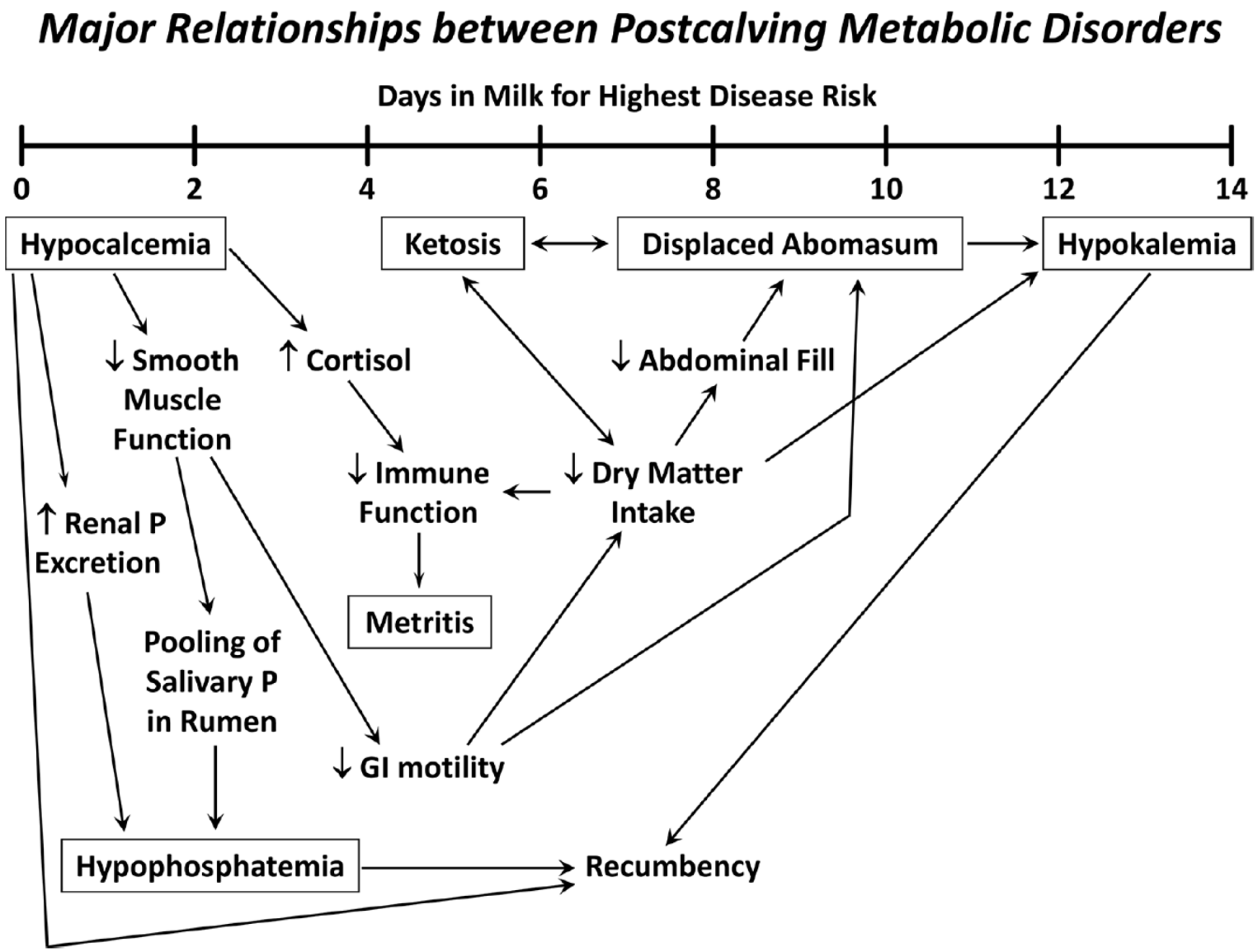
TREATMENT

- **GOAL: increase blood glucuse level ASAP!**
- IV administration of 500 mL of 40% dextrose solution
- Administration of glucocorticoids, including dexamethasone or isoflupredone acetate at 5–20 mg/dose
- Propylene glycol administered orally (250–400 g/dose) once per day acts as a glucose precursor and is effective as ketosis therapy.
- Choline, Niacine, Vit B12, Metiyonine

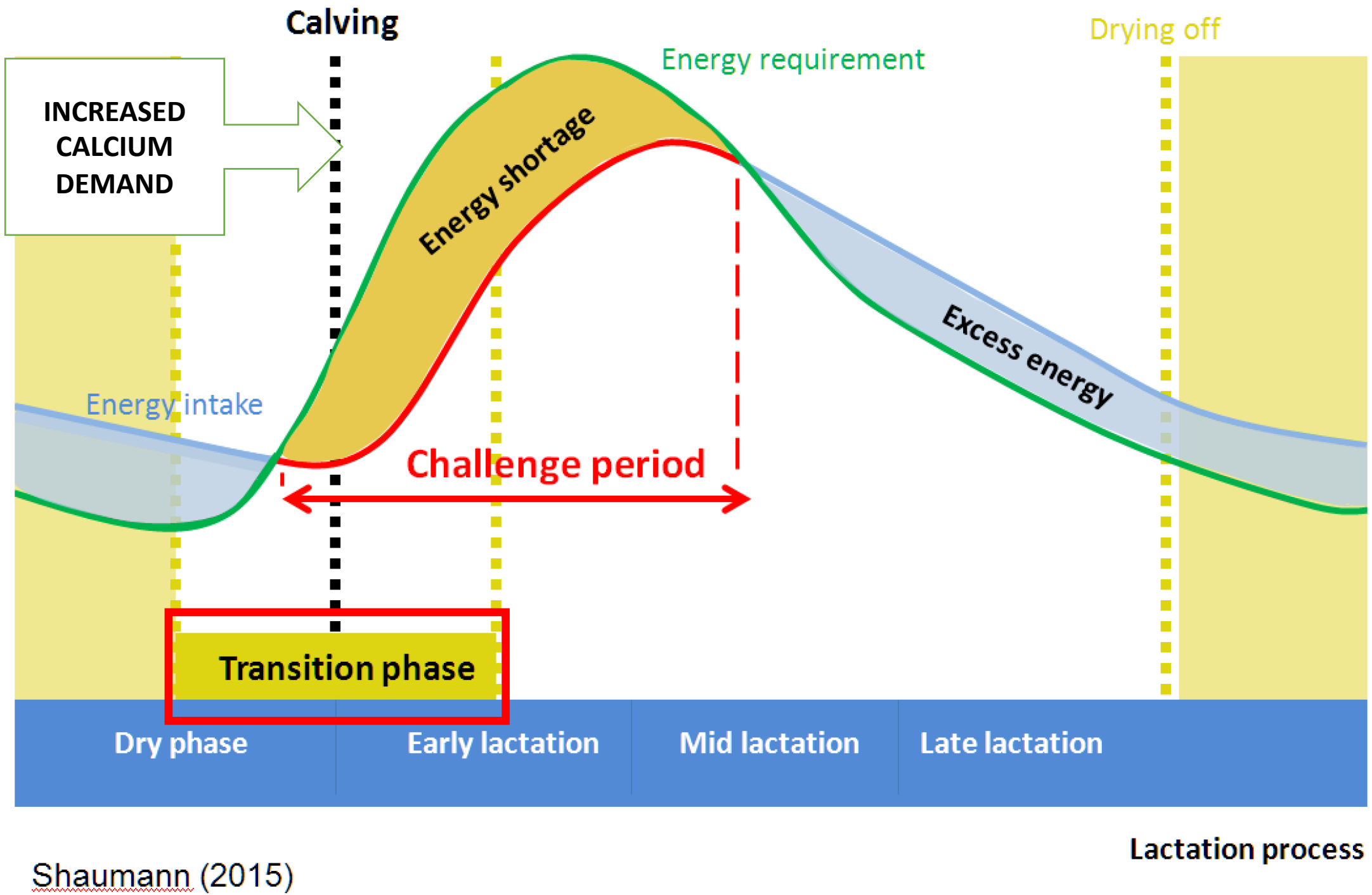
Outcome	Type I	Type II	Type III. Butyric Acid Silage Ketosis
Highest risk period	3 to 6 weeks after calving	1 to 2 weeks after calving	Very high or high
Description	Spontaneous, underfeeding	Fat cows, fatty liver	Normal or High
Blood BHB	Very high	High	Variable
Blood glucose	Low	Low (may be high initially)	Variable
Blood insulin	Low	Low (may be high initially)	Variable
Body condition	Probably thin	Often fat (or lost fat)	Variable
Fate of NEFA	Ketone bodies	Liver triglycerides initially, then ketone bodies	Variable
Liver gluconeogenesis	High	Low	Variable
Liver pathology	None	Fatty liver	Variable
Prognosis	None	Poor	Good
Key diagnostic test	Post-fresh BHB	Pre-fresh NEFA	Silage analysis
Key intervention	Post-fresh management and nutrition	Pre-fresh management and nutrition	Destroy, dilute or divert the silage

MILK FEVER
HYPOCALCEMIA

DOÇ. DR. ALİ ÇALIK



CONSEQUENCES OF POOR NUTRITION and MANAGEMENT



Shaumann (2015)

MILK FEVER / HYPOCALCEMIA

Normal blood Ca concentration
2.0 - 2.5 mM/L
(8.5 to 10.4 mg/dL)

- Characterized by lower **blood Ca level**
- Blood Ca is maintained within a narrow range **(2.0 - 2.5 mM/L)**
- Milk Secretion = calcium levels to decline from a normal ranges
-  When bone Ca release not enough
- Clinical (less than **1.4 mM** blood Ca)
- Subclinical (between **1.4 – 2.0 mM**) – No sign

MILK FEVER / HYPOCALCEMIA

MAIN REASON

DIETARY ANION-CATION BALANCE (DCAD)

DCAD = (**Na^+** + **K^+**) – (**Cl^-** + **S^-**)

enter the blood with nearly 100% efficiency

LACTATION: +250-350 mEq/kg diet

DRY PERIOD: between 0 to -100 mEq/kg diet

A highly positive DCAD in prepartum (Dry Period)

Cause postpartum **hypocalcemia / milk fever**

PREPARTUM DIET
positive DCAD
HIGH Na and K

Forages are generally high in cations, such as K and Ca

Blood pH will increase
ALKOLOSIS

The kidneys keep the alkalosis from becoming life threatening by excreting the extra K+ into the urine. The high cation content of the urine produces an alkaline urine.
Cow urine will usually have a pH between 7.8 and 8.4.

positive DCAD Diet = High Urine pH

Calcium is cationic ione (Positive charge)

- Cationic diets (High Na and K), interferes with the ability of parathyroid hormone to interact with its receptors on bone and kidney tissues, upsetting Ca homeostasis.
- **POST-PARTUM**:The cow is unable to compensate for the flow of blood Ca into the mammary gland for colostrum and milk production and ***develops severe hypocalcemia***

STAGE 1: show signs of hypersensitivity and excitability. Cows may be mildly ataxic, have fine tremors over the flanks .Cows may appear restless. If calcium therapy is not instituted, cows will likely progress to the second, more severe stage.

STAGE 2: unable to stand but can maintain sternal recumbency. subnormal body temperature, and cold extremities. Smooth muscle paralysis leads to GI stasis, which can manifest as bloat, failure to defecate, and loss of anal sphincter tone. Cows often tuck their heads into their flanks, or if the head is extended, an S-shaped curve to the neck may be noted.

STAGE 3: cows lose consciousness progressively to the point of coma. They are unable to maintain sternal recumbency, have complete muscle flaccidity, are unresponsive to stimuli, and can suffer severe bloat. As cardiac output worsens, heart rate can approach 120 bpm, and peripheral pulses may be undetectable. If untreated, cows in stage 3 may survive only a few hours.

PREVENTION

- There are 2 main approaches to prevention of hypocalcemia
  - dietary manipulation (During Dry Period)
  - strategic oral Ca supplementation

Dietary Approaches to Reduce Hypocalcemia

- **GOAL: USE ANIONIC DIETS**
- Diets relatively high in Na or K increase the risk for hypocalcemia, whereas diets relatively high in chlorine or sulfur reduce the risk
- Low DCAD diets cause metabolic acidosis and reduce the risk of milk fever.
  - DRY PERIOD: between 0 to -100 mEq/kg diet
- Using anionic salts in DRY PERIOD is important in prevention
  - ammonium chloride, ammonium sulfate, calcium chloride, magnesium sulfate
  - 150g
- CHECK URINE pH: 6-6.5
  - IF LOWER 6 = reduce anionic salts / cause renal failure

Oral Calcium Supplementation to Reduce Hypocalcemia

- Oral Ca supplementation results in rapid absorption of substantial amounts of Ca into the bloodstream
- 50 g of Ca orally (as $CaCl_2$) with water
- Calcium carbonate, calcium oxide, and calcium hydroxide are generally regarded as ***insoluble*** and are therefore unsuitable for use as oral Ca supplements
- Strategies for giving oral Ca supplements around calving should include at least two doses, one at calving and a second dose the next day.

TREATMENT

- Restoring normal serum calcium levels as soon as possible
- Recommended treatment is IV injection of a calcium gluconate salt
  - 400-500 ml 25% calcium gluconate
  - administered slowly = cardiotoxic effects
  - cardiac auscultation / STOP if dysrhythmias
- SC calcium alone may not be adequately absorbed because of poor peripheral perfusion and should not be the sole route of therapy

TREATMENT

- Approximately 75% of cows stand within 2 hr of treatment
- Cows that respond initially, 25%–30% relapse (reappear) within 24–48 hr and require additional therapy
  - Oral Ca supplementation