Ketosis (Acetonemia, Post-Parturient Dyspepsia of cattle)

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Definition

- It is a disease of ruminants caused by impaired metabolism of **carbohydrate and volatile fatty acids**.
- Biochemically, it is characterized by **ketonemia**, **ketonuria, hypoglycemia** and **low level of hepatic glycogen**.
- Clinically

➢ acetonemia in cattle

➢ pregnancy toxemia in ewes.

- **Incidence**

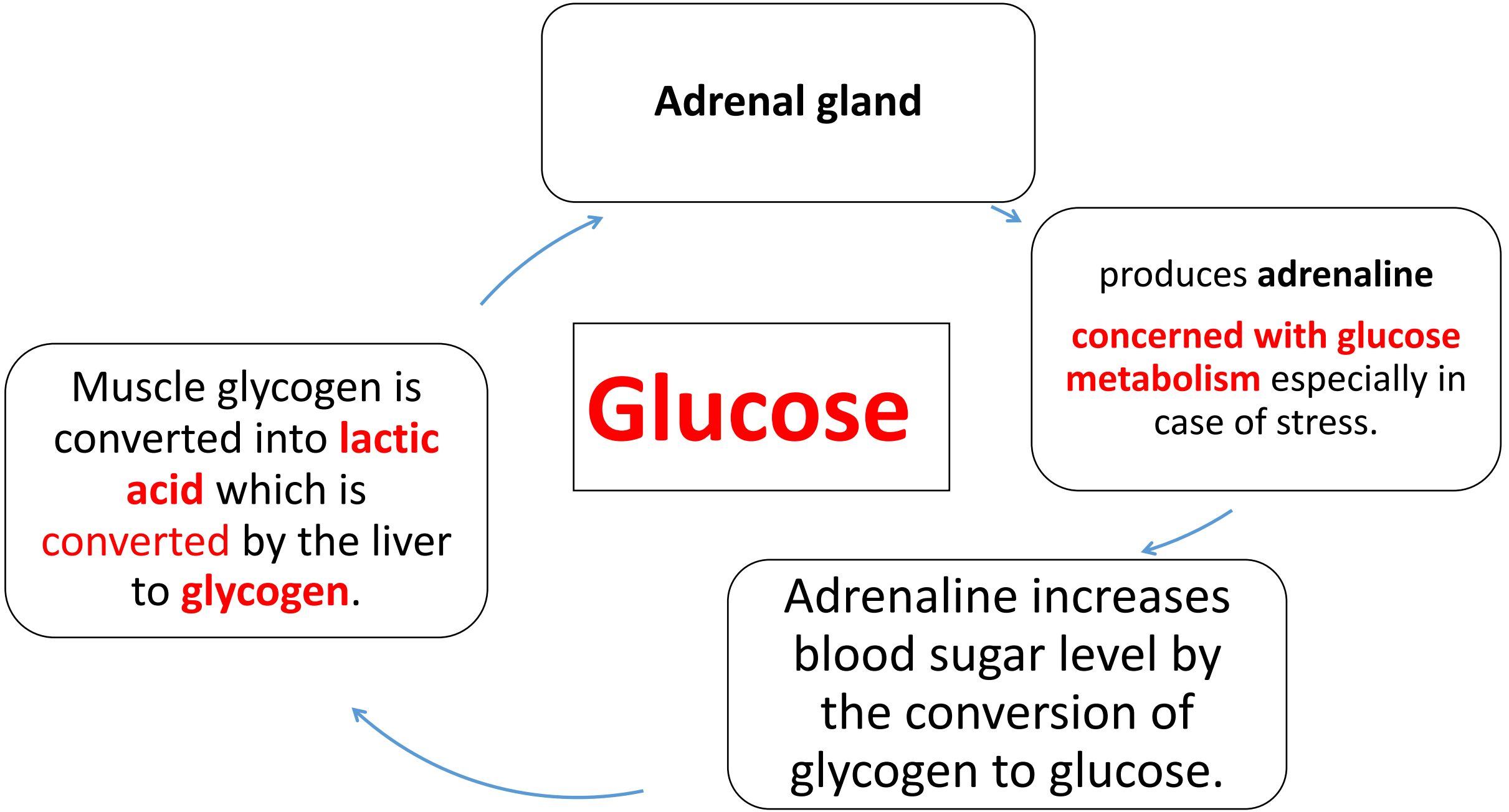
(1) Ketosis is a disease of dairy cattle and high milkers buffaloes.

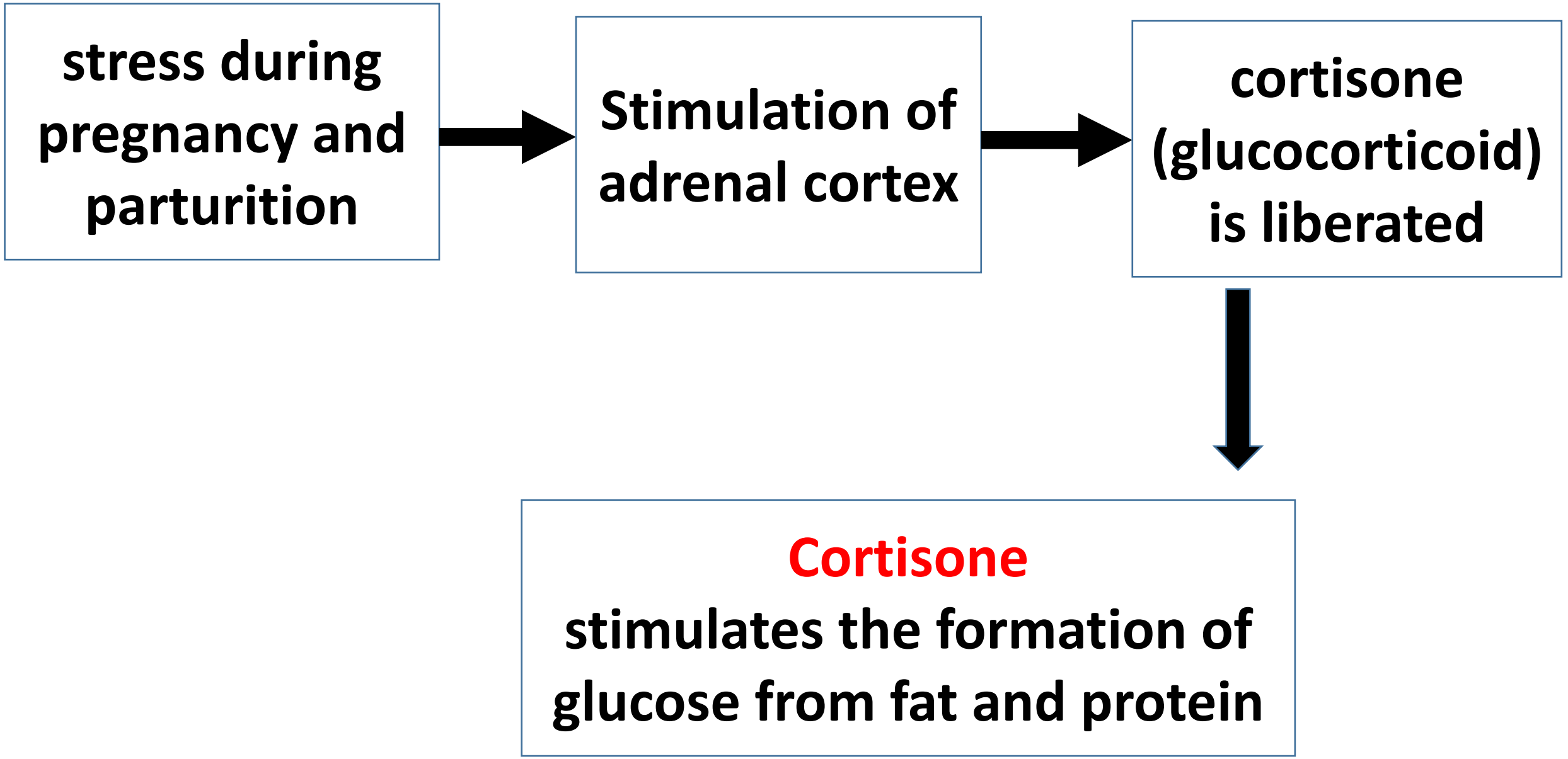
(2) It occurs mainly in animals housed or pastured during the winter.

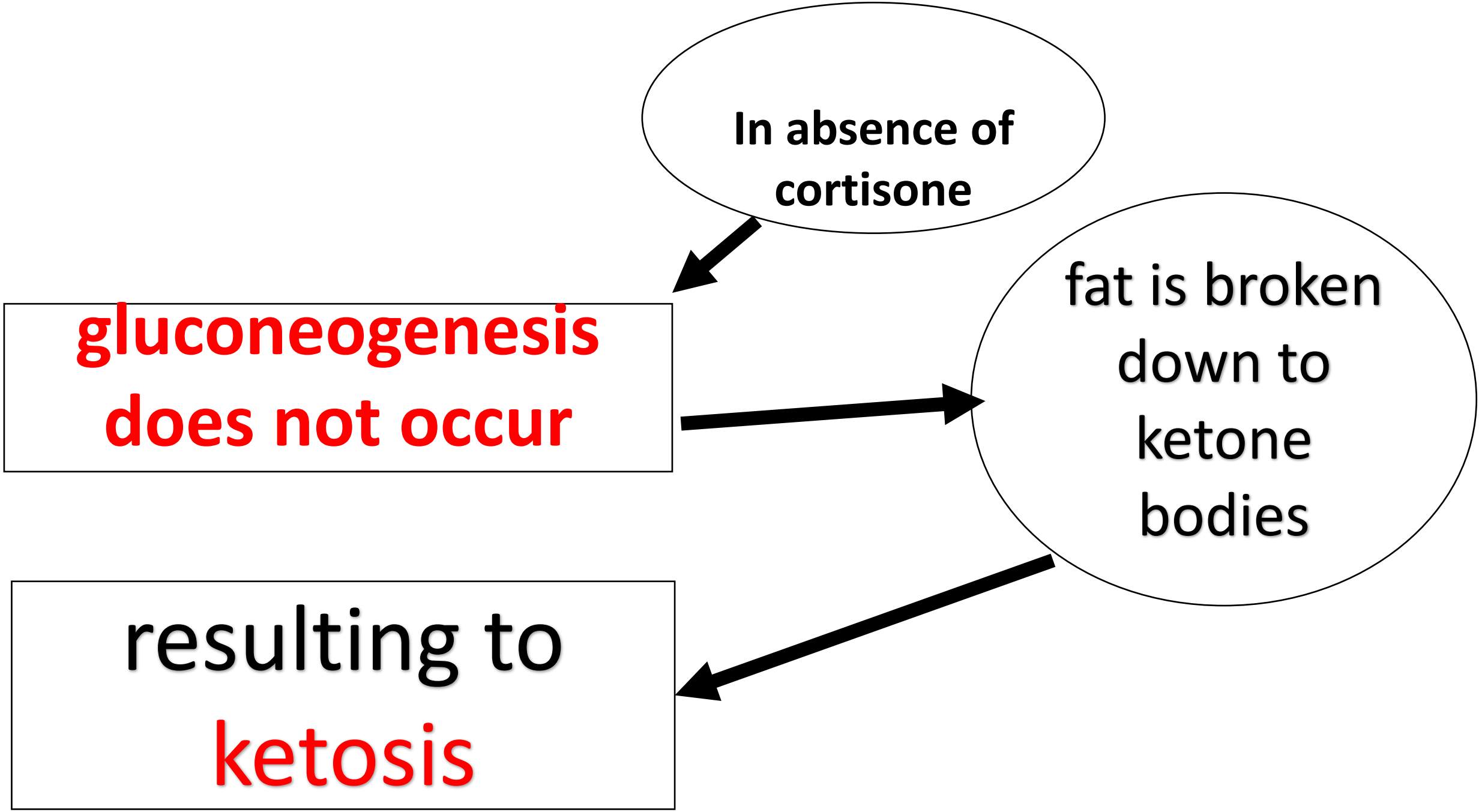
(3) It causes major losses to dairy farmers and highly fetal in pregnancy toxemia (Ewes).

Predisposing causes

1. Endocrine gland disturbances (Adrenocortical insufficiency):


Adrenal gland
produces **adrenaline**
concerned with glucose metabolism especially in case of stress.
Adrenaline increases blood sugar level by the conversion of glycogen to glucose.
Muscle glycogen is converted into **lactic acid** which is converted by the liver to **glycogen**.
Glucose


stress during pregnancy and parturition
Stimulation of adrenal cortex
cortisone (glucocorticoid) is liberated
Cortisone
stimulates the formation of glucose from fat and protein


In absence of cortisone
gluconeogenesis does not occur
fat is broken down to ketone bodies
resulting to ketosis

2) Hypothyroidism (because some cases respond to thyroxine therapy): Thyroid hormone maintains basic metabolic rate and gluconeogenesis and thus has a role in glucose formation.

3) Role of insulin: insulin helps in the **peripheral utilization of glucose**. In diabetic patient, glucose isn't permeable to cells due to decrease level of insulin in blood.

Cells don't get glucose as a result of which fat break down to ketone bodies. This referred as diabetes keto-acidosis.

(4) Hepatic insufficiency due to inability of the liver to produce enough glucose to satisfy the requirements of the mammary gland.

(5) Deficiency of cobalt because vitamin B12 cannot be synthesized and so **epinephrine isn't formed** so that gluconeogenesis does not occur and **hypoglycemia** results then fat is broken down to ketone bodies.

Pathogenesis

A. Normally, the **ingested carbohydrate** is converted into

1. ketogenic acid (70% acetic acid& butyric acid)
2. glucogenic acid (10% propionic acid)

a ratio of about 4:1

B. When dietary **fiber increases** the ketogenic acid increase & fat % of milk increases.

C. When soluble dietary **carbohydrate (starch)** increases, the propionic acid increases.

The utilized propionic acid by liver depends on **synthesis of vitamin B12** which require cobalt in ruminant digestion.

If glucose supply in tissue is normal, the propionic acid is converted **to oxaloacetate in the liver.**

- **Glucose is formed in liver to be enter the blood from:**

➢ ***Oxaloacetate***

➢ ***Glucogenic amino acid.***

➢ ***Glycerol from fat.***

- If milk production is **low**, the mammary gland extract about 40% of glucose which **enter the blood to be lactose**, this ratio increased by increased milk production e.g. the cow that secrets **30 kg milk daily** loss about **3 pounds** of sugar glucose.

- The ketogenic fatty acid need glucose to completely oxidized to $CO_2+H_2O+Energy$ (in krebs cycle)
- so glucose deficiency results in accumulation **of ketogenic fatty acids, ketonemia & ketonuria (Figure.2).**

- IF glucose metabolism is going on, the acetic acid & butyric acid will form the activated acetate which:
- *1) Converted to fat or*
- *2) Utilized for energy*
- In **absence of oxaloacetate the activated acetate** converted to **ketone bodies** including:

1) Acetoactic acid

2) Beta hydroxy butyric acid

3) Isopropyl alcohol (which resulted from breakdown of acetoacetic acid in the rumen) causing nervous from of ketosis.

ketotic cows is characterized by:

(1) Presence of hypoglycemia, low level of hepatic glycogen and ketonemia which exert an effect on the clinical syndrome.

(2) Hypoglycemic encephalopathy (any disorder of the brain) and depression of cerebral metabolism due to decrease in glucose utilization.

(3) Increase of ketone bodies in the blood specially acetoacetic acid which is toxic and may result in terminal coma.

Ingested Carbohydrate in ruminants

Ketogenic acid (4 amounts)

- Acetic acid (70%)
- Butyric acid (20%)

→ Activated acetate

- In the absence of oxaloacetate converted to
  1. acetoacetic acid which is breakdown to Isopropyl alcohol causing nervous ketosis.
  2. Beta hydroxy butyric acid causes
     A. Ketonemia
     B. ketonuria
- In normal glucose metabolism converted into
  1. Fat ⟶ Body or milk fat
  2. Energy + CO_2 + H_2O
  3. Oxaloacetate.

Glucogenic acid (1 amounts)

- Propionic acid (10%)
  - + cobalt
  - + Vitamin B12: From Rumen
- Oxaloaetate
- Also Glucogenic amino acid
  Glucose (in Liver) ⟶
  Blood glucose ⟶ Lactose

Symptoms of bovine ketosis

There are five forms of bovine ketosis

Weight loss in ketosis

[1] **Subclinical form**

- urine and blood contain ketone bodies in excess amount
- there is no obvious symptoms of ketosis

[2] **Wasting or digestive form**

It is the most common form. It is manifested by:

(1) Gradual but moderate decrease in appetite and milk production over a period of 2-4 days.

(2) Body weight is lost rapidly, from the decrease in appetite.

(3) Cows become woody (Woody cow) due to the apparent wasting and loss of cutaneous elasticity.

(4) The feces are firm and dry due to ruminal atony.

(5) The cow is moderately depressed and disinclined to move or eat may be due to abdominal pain.

(6) Temperature, pulse and respiration are normal.

(7) Ketone smell in breath, milk, sweat, urine and stable.

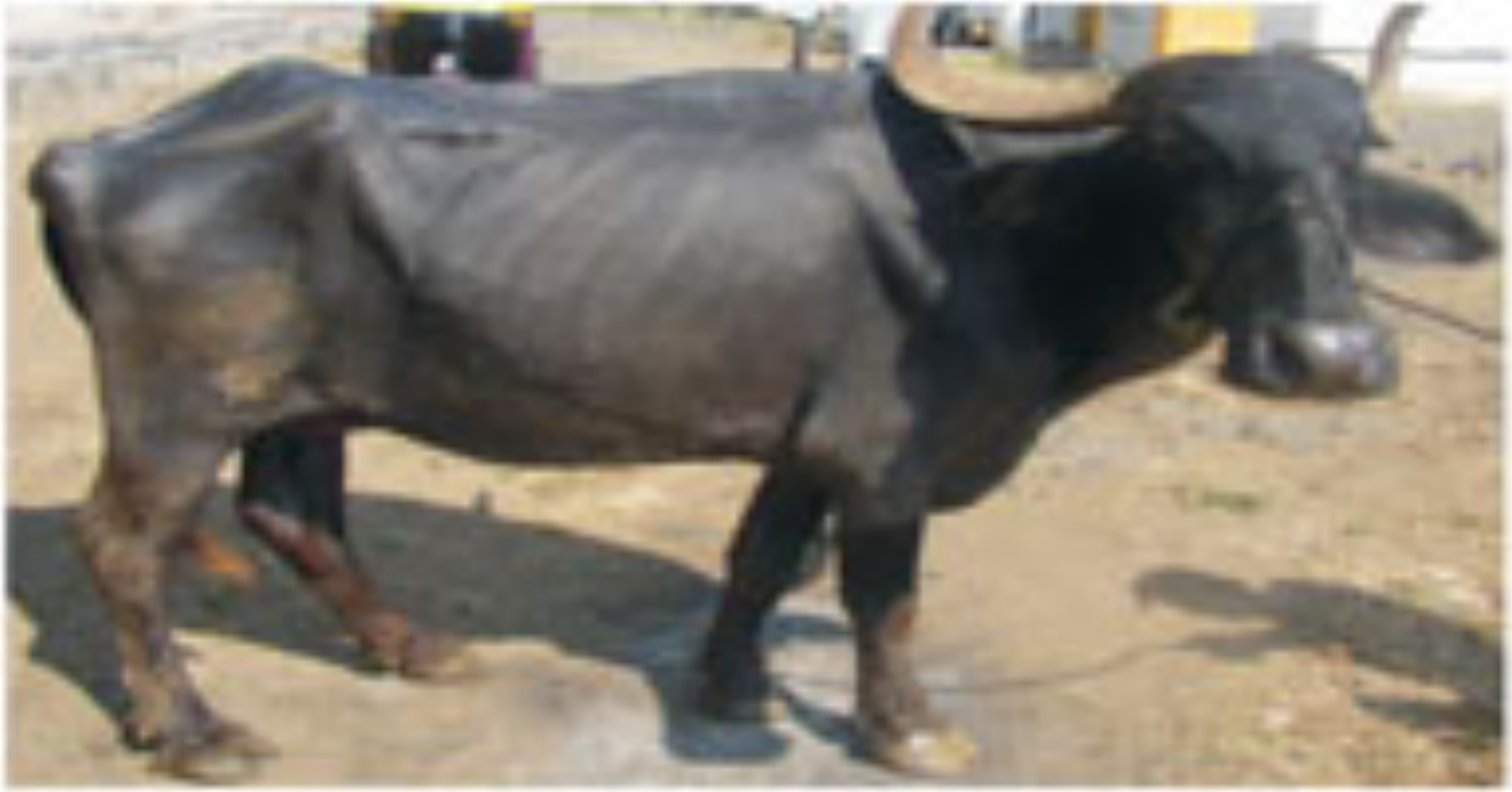


Fig. 8: Local buffalo suffering from ketosis showing characteristic loss of body weight

3. Nervous form

- Suddenly appear walking in circles, head pushing or leaning onto stanchion, apparent blindness, aimless movements, wandering, vigorous licking of the skin and inanimate objects.
- Depraved appetite
- Chewing movement with salivation
- Hyper aesthetic- bellowing on pinching or stocking .
- Moderate tremor and tetany
- Gait is usually staggering
- Nervous sign usually occur in short episodes which last for I or 2 hrs and may recur at intervals of about 8 to 12 hrs.
- Affexcted cows may injure themselves during the nervous episodes.

[4] Mixed form of wasting and nervous forms

[5] Milk fever like form

It resembles milk fever disease but the muscular twitching and hypersensation are constant symptoms.

This form responds to treatment with calcium and glucose therapy due to presence of hypoglycemia and hypocalcemia.

Diagnosis of bovine ketosis

(1)History of calving or late pregnancy and winter season.

(2) Clinical symptoms of ketone odor, wasting and or nervous form.

(3) Biochemical abnormality.

Ruther's test for detection of ketone bodies: (For urine): To 5 ml urine add ammonium sulfate to saturation (about 1 gm) and 2 or 3 drops of **sodium nitropursside solution**; mix and cover with strong ammonium hydroxide**. A reddish purple ring is positive.**

- A positive test is considered as warming rather than a sign of disease.

(For serum): Put 2 drops of plasma or serum in a test tube and supersaturate with ammonium sulfate crystals by shaking. Add 2 drops of approximately 5% sodium nitropursside solution and shake. Let stand 3 minutes.

- A permanganate color indicates a trace;
- a light blue, a moderate amount;
- a deep blue, a large amount of ketone bodies

Items	Cow		Ewes	
	Healthy	Ketotic	Healthy	Diseased
Blood glucose mg%	45-75	40 or less	50-80	23 or less
Blood ketone mg%	5-15	10-100	7-40	Increased more than 40
Blood acetoacetic acid mg%	0.1.1	Up to 7	0.24-0.34	Up to 25
Blood beta hydroxyl butyric acid mg% (β-hydroxybutyrate (BHBA)	8.00 (Less than 1000 lmol/L)	Up to 30 (subclinical ketosis greater than 1400 lmol/L, (clinical ketosis , in excess of 2500 lmol/L).		excess of 3000 mmol/L,
Ketone bodies in urine mg%	Absent	80-1300		
Ketone bodies in milk mg%	rare	Up to 40		
Plasma free fatty acids mcq/l	0.90	Up to 28	0.1-0. 4	1.0
Blood urea nitrogen mg%	6-27	increase	25-30	Up to

Necropsy finding

(1) **Yellowish friable enlarged liver.**

(2) Enlargement and hyperemia of adrenal cortex.

(3) Fatty changes in kidney and heart.

(4) Pneumonic lungs due to hypostatic congestion.

Differential diagnosis

(1) Wasting form

1) Traumatic reticulitis (no relation to calving and pain < is positive, normal serum glucose).

2) Vagus indigestion (marked stasis of alimentary with bloat).

3) Abomasal displacement (marked abomasal sounds absence of ruminal sounds)

(2) Nervous form

1) Rabies (mania and ascending paralysis)

2) Hypomagnesemia.

3) Hypocalcemia.

4) Bovine spongiform encephalopathy.

5) Lead poisoning are closely resemble nervous form in addition to blindness, convulsion history.

Treatment

- **Hygienic treatment**

(1) Complete rest of the animal in ample space.

(2) Clean water supply and keep bowl open.

(3) Avoid cold stress, under nutrition, or sudden change in ration.

➢ Medical treatment

(1) Sources of glucose:

1) IV injection of dextrose **25-40% 500ml for cattle** (in ewes 150-250 ml) IV, twice daily for 3-5 successive days causing temporary hyperglycemia.

2) Oral hyperglycemic agents: **Glycerol or glycerin 100 mg or propylene glycol 110 mg** (mix with food or as a drench, twice daily for 2-4 days) or sodium propionate (100-200 gm once daily for 3 day).

Action of Glycerol or propylene glycol are **glucogenic** and thus produce glucose.

NB: IV glucose and oral glycerol give the best result as they depress the fat content of milk.

(2) Calcium gluconate 20% (250 ml IV and 250 SC) to correct the milk fever form with IV glucose.

(3) Hormonal therapy (One of the following)

1) Glucocorticoids: Such as **dexamethazone** 10 ml (30 mg)

I/M one or two doses for cattle (to induce gluconeogenesis, increases the blood sugar level, reduces ketone bodies formation by utilization of acetyl coenzyme A).

2) **Adrenocorical hormone** 400-500 IU.

Insulin or protamine zinc 200 IU/SC (to facilitate transport of glucose into cells).

3). Thyroxine 250 -300 mg/day for five days I/M (to induce glucogenesis so increase blood sugar).

(5) **Cobalt sulfate 5 mg** in cattle and 1 mg in sheep orally with water. Vitamin B J2 100- 300 mg IM every week.

(6) **Transmission of fresh ruminal juice 1-3 liters.**

(7) **Chloral hydrate** (for nervous and wasting forms): Initial dose of 30 gm followed by 8gm twice daily for several days. It is given per os in a capsule or as drenches in molasses and water by stomach tube (to overcome motor irritation in nervous form, it also **breaks down the starch in rumen** and **stimulate the production and absorption of glucose**.

It also influence on rumen fermentation in direction of increased production of propionate so that blood glucose level increased).

Prevention

(1) Avoid overrating during pregnant period, under starvation and malnutrition.

(2) Supply the diet with copper, cobalt and phosphorus.

(3) Preservation containing nicotinic acid, yeast powder, sodium hydrogen phosphate may be given daily.

(4) Ground maize may be incorporated in the ration because maize is easily digested and thus help in rapid rise of Wood glucose level.

(5) Monensin hydrochloride may be fed as it increases **propionate level** over acetate level.