Milk Biosynthesis and ejection

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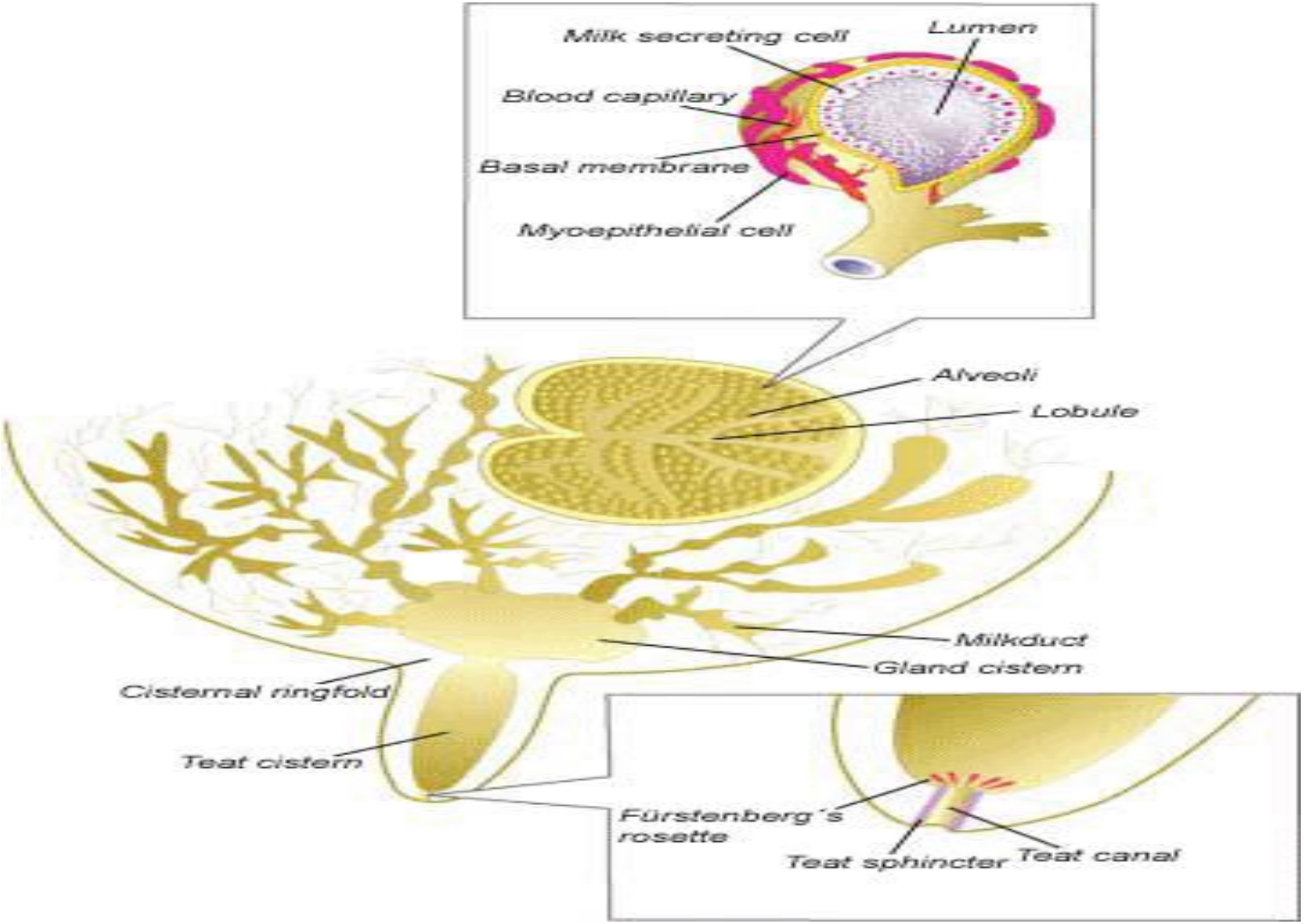
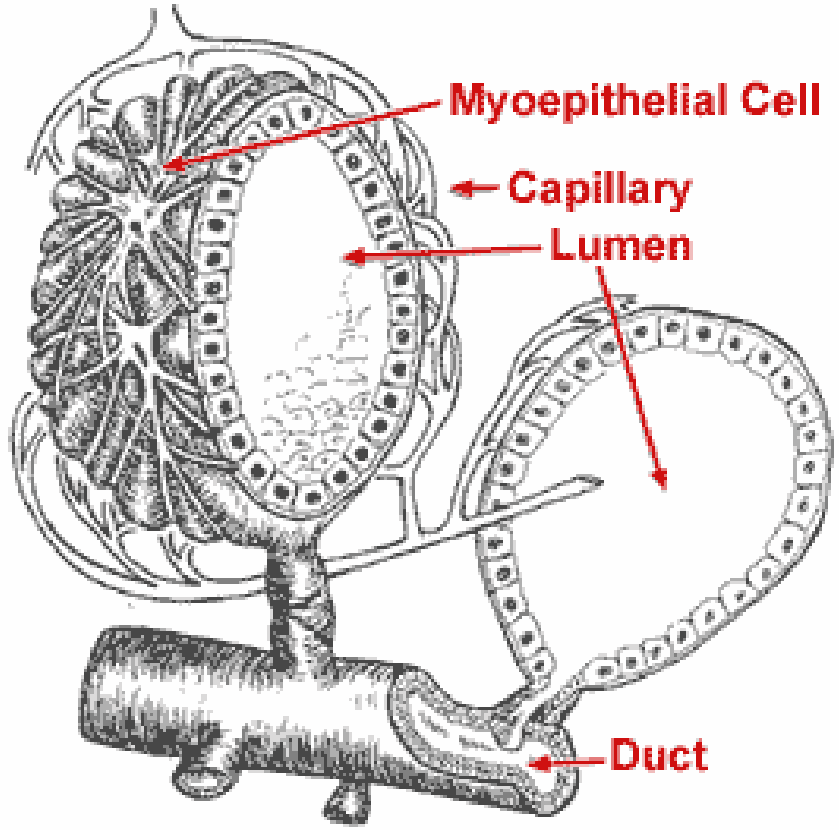
Milk is synthesized in the mammary gland (the udder). The udder consists of four milk quarters each with its own teat. Each udder quarter is separate from the others. At the lower end of the teat is a teat canal surrounded by a strong teat-closing sphincter muscle that controls the flow of the milk. This muscle prevents leakage of milk between milkings. Inside the teat is a cavity called the teat cistern (holds about 473 ml of milk).Above this cavity and in the actual udder quarter lies the udder cistern. These two cisterns are separated by more or less well- defined folds. The inner walls of the cisterns consist of thin mucous membranes .These are very sensitive and can easily be injured, by incorrect milking.


Milk secreting cell
Lumen
Blood capillary
Basal membrane
Myoepithelial cell
Alveoli
Lobule
Milkduct
Gland cistern
Cisternal ringfold
Teat cistern
Fürstenberg´s rosette
Teat sphincter
Teat canal

Gland Cistern

The gland cistern joins to the teat cistern at the base of the udder. The gland cistern, which can vary greatly in capacity, functions as a collecting vessel for milk from the major milk ducts that flow into it. The gland cistern fills rapidly during milk letdown.

Alveoli



-grape-like clusters

-Each alveolus is composed of a single layer of epithelial cells surrounding a central cavity.

-These cells absorb nutrients from the blood, transform them into milk and discharge the milk into the cavity of the alveolus.

-Each alveolus is also surrounded by specialized muscle cells known as myoepithelial cells that are responsible for milk ejection during letdown.

The alveolus contains a single layer of epithelial secretory cells surrounding a central storage area called the lumen which is connected to a duct system. The secretory cells are ,in turn surrounded by a layer of myoepithelial cells and blood capillaries. The raw materials for milk production are transported via the blood stream to the secretory cells. It takes 400-800 liters of blood to deliver components for one liter of milk. The alveoli are very small and are grouped in clusters. Their density can reach 75000/Cm^3.The number is greatest in newly calved or peak- milking cows and normally decreases during the latter half of the lactation period. Incorrect milking causes this decrease to accelerate, resulting in lower total production. The walls of the alveoli contain branching, muscle-like cells which play an important part in the emptying of the udder.

Biosynthesis of Milk Components

Biosynthesis of milk components occurs in the mammary epithelial cell

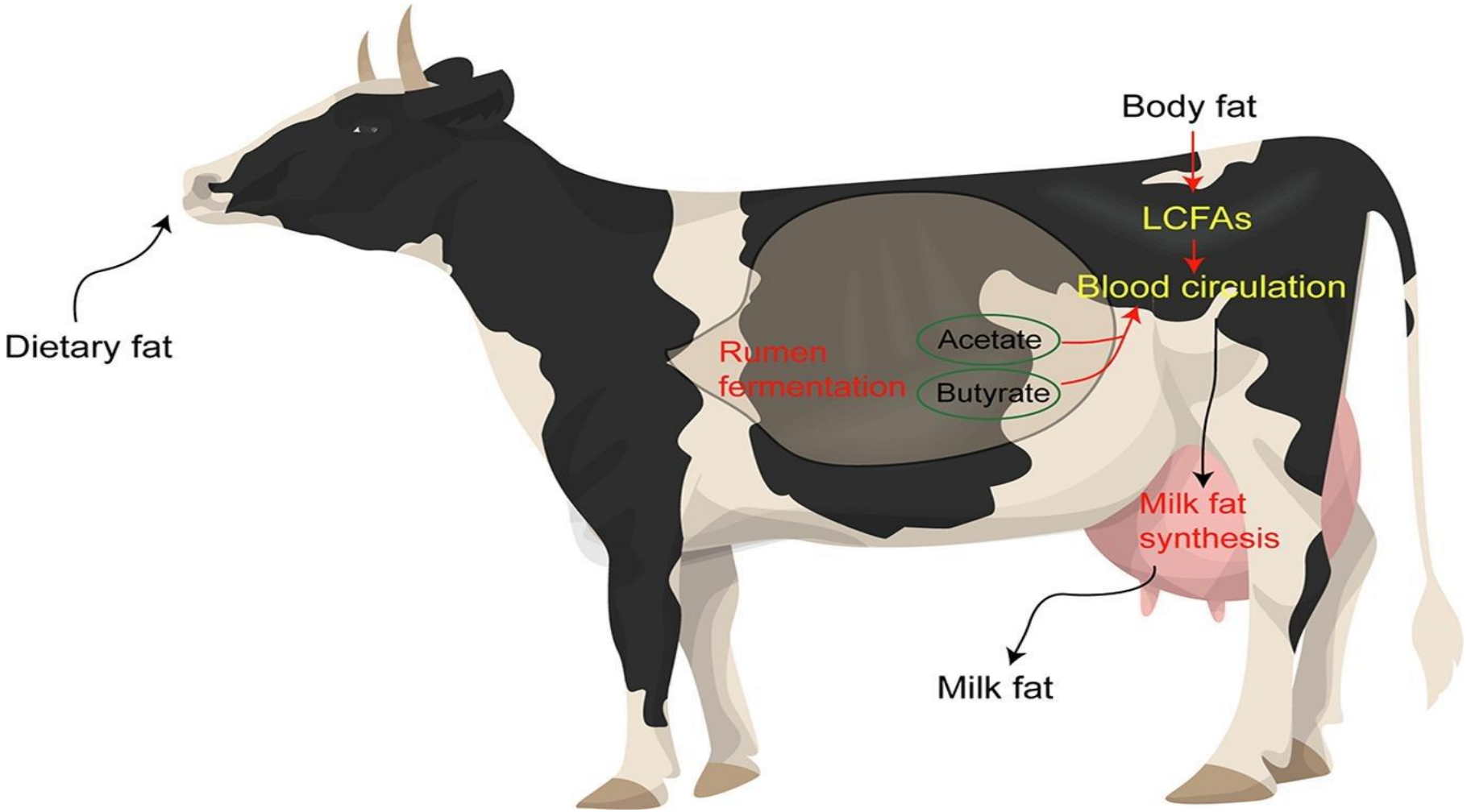
- Precursors from blood
- One liter of milk requires 500 L of blood
- Fat biosynthesis
- Protein biosynthesis
- Lactose biosynthesis

Biosynthesis of milk fat

- In mammals, fat are produced in milk-secreting mammary gland cells in the form of milk fat globules , which are surrounded by a milk fat globular membrane (MFGM).
- The globular membrane of milk fat is composed mainly of polar lipids include phospholipids (PL) ,They serve as bioactive ingredients with processing functions, although they represent only a small proportion of total milk lipids

Anabolism of Milk Fat

- Milk fat biosynthesis is primarily achieved through the synthesis of triglycerides (TGs) from glycerol and fatty acids.
- fatty acids can be classified as short-, medium-, or long-chain fatty acids, each stemming from different sources.
- short- and medium-chain FAs are primarily produced through de novo synthesis in mammary epithelial cells,
- LCFAs are mostly derived from non-esterified fatty acids present in the plasma.
- The first step in the de novo synthesis of FAs in ruminants involves the fermentation of carbohydrates in the rumen.
- Fatty acid synthesis is the process of producing de novo fatty acids from carbohydrate and amino acid-derived carbon sources.
- Fatty acid synthase (FASN) performs the majority of enzymatic steps , Palmitic acid is the primary product of FASN, accounting for ~90% .


Body fat
LCFAs
Blood circulation
Dietary fat
Rumen fermentation
Acetate
Butyrate
Milk fat synthesis
Milk fat

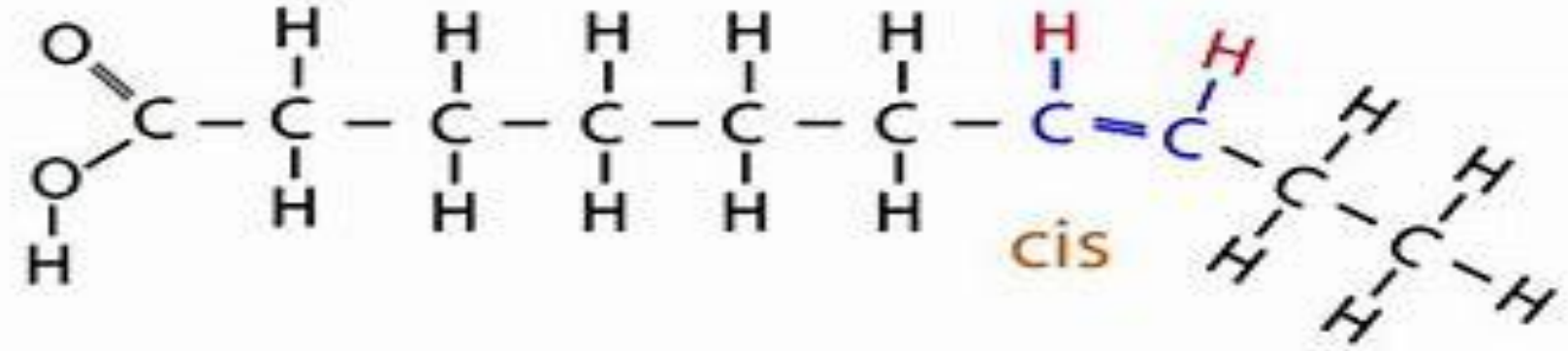
- More than 95% of milk fat is composed of triglycerides (TAGs), and the remainder is composed of a small proportion of diacylglycerol, phospholipids, and free fatty acids, such as conjugated linoleic acid, sphingomyelin, and butyric acid
- triglycerides is formed by the esterification of fatty acids to glycerol-3-phosphate.
- TAG synthesis is based on two mechanisms:
- de novo synthesis in mammary epithelial cells and absorption from circulating blood
- All short- and medium-chain fatty acids (C4-C14) and approximately one-half of C16 fatty acids are synthesized de novo from acetyl-coenzyme A (CoA) in mammary epithelial cells, and the remaining half of C16 fatty acids and all long-chain fatty acids (LCFAs) longer than C18 are absorbed from circulating blood.

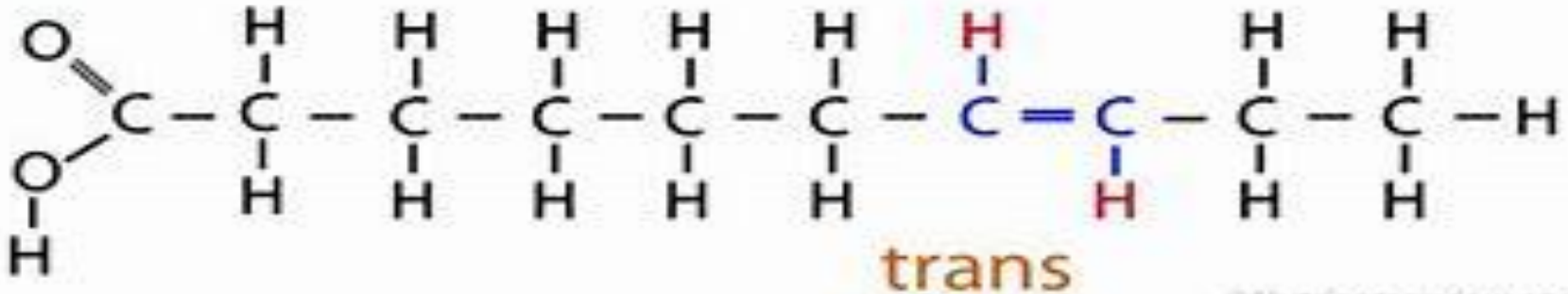
- Uptake, transport, and activation of FAs occurs
- Mammary cells are responsible for the uptake of FAs from the blood, after which these fatty acids are hydrolyzed by the action of the very low-density lipoprotein receptor (VLDLR) and lipoprotein lipase (LPL).
- The hydrolyzed FAs then enter mammary epithelial cells through free diffusion or active transport.
- Inside the cells, fatty acids undergo activation via attachment to long-chain acyl-CoA synthetase (ACSL), which is bound to fatty acid binding protein 3 (FABP3) and are then conveyed to the site where they are used

- Phospholipids have a beneficial effect on health in that they may be involved in
- regulation of various inflammatory responses or may have a chemo-preventive and chemotherapeutic effect on certain types of cancer. Then reduce the side effects of some medicines. The positive effect of PL on various diseases due their high efficacy in delivering their fatty acid residues for incorporation into cell membranes .
- Monounsaturated fatty acids have a positive effect on the concentration of high-density lipoproteins (HDL) while reducing the concentration of low-density lipoproteins (LDL), which are stored in blood vessels throughout the body.

- Another important constituent in milk are fatty acids (FA) They are present in the form of triglycerides, phospholipids, or free fatty acids.
- Fatty acids are classified according to the length and degree of unsaturation of the hydrocarbon chain
- Milk fat contains several unique fatty acids which have biological importance.
- The most characteristic fatty acids for cow‘s milk fat are fatty acids with an odd number of carbon atoms, conjugated linoleic acid and butyric acid .
- Polyunsaturated fatty acids (PUFA) with 18 carbon atoms consist mainly of the group of (cis or trans) isomers of conjugated double bond linoleic acid.

Cis- and Trans-Fatty Acids

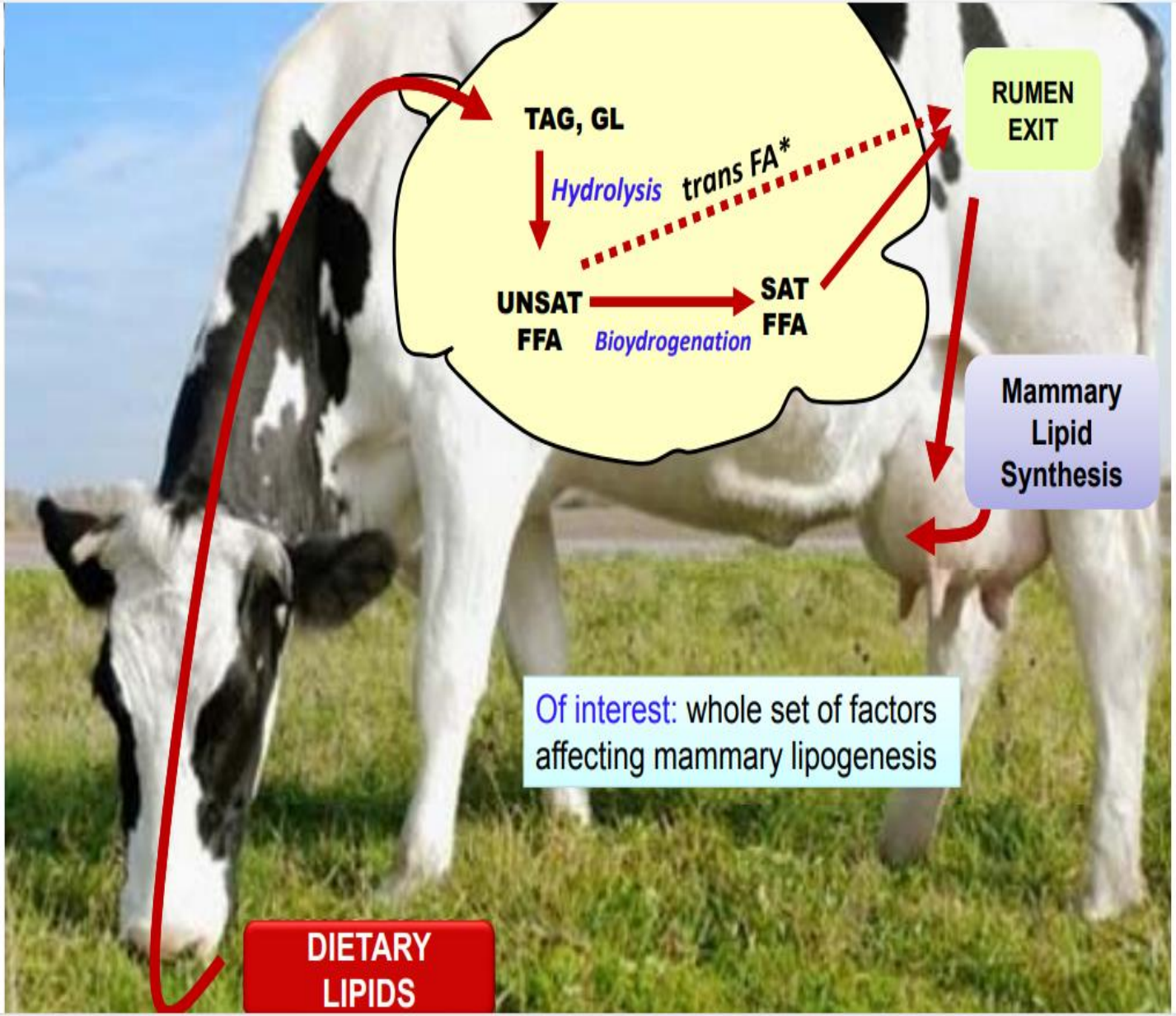


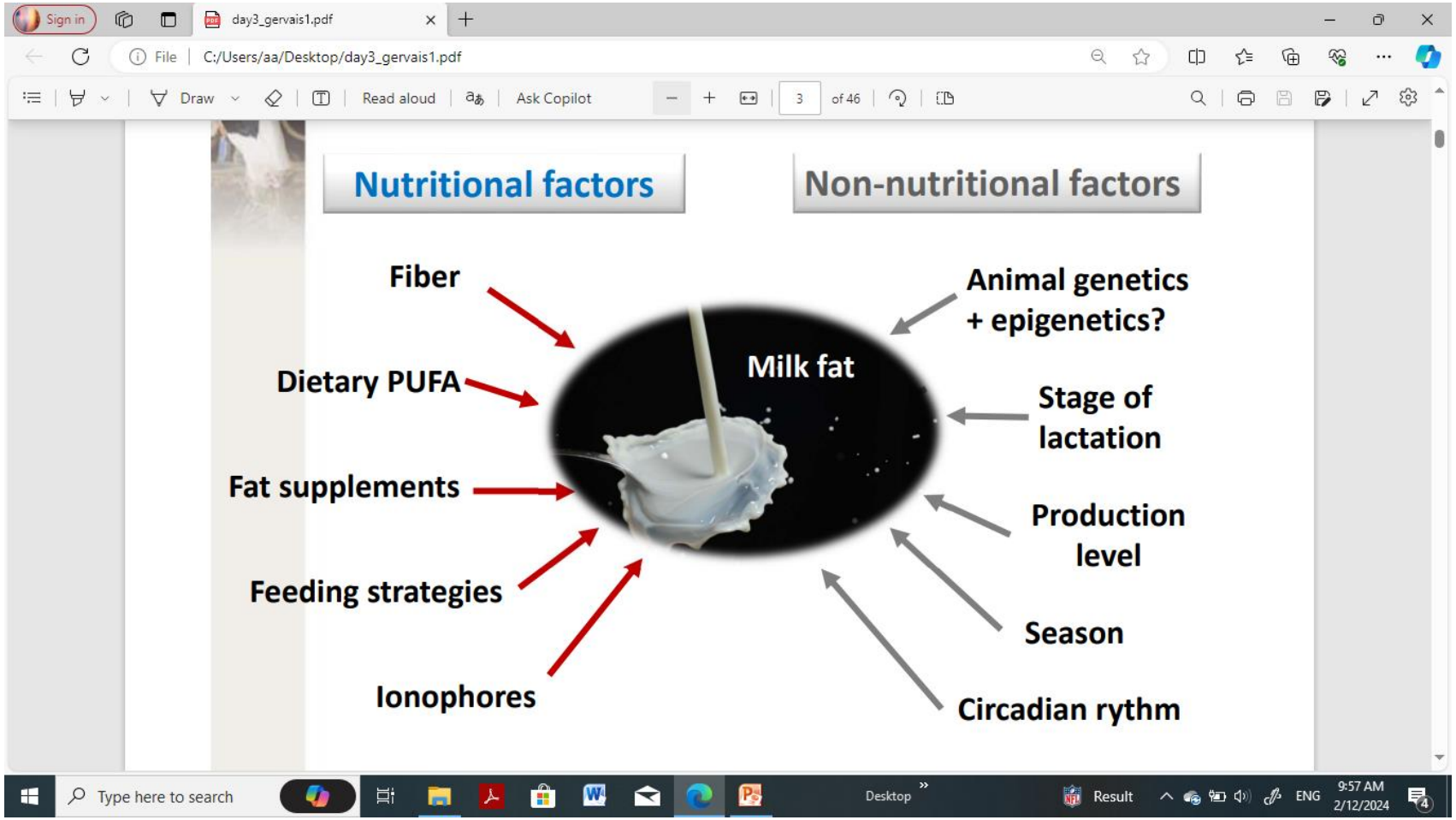


- trans Fatty acids are unsaturated fatty acids that contain 1 or more unconjugated double bond in the trans configuration.
- The term trans fats is used to describe triglycerides that are rich in trans fatty acids. Although some trans fatty acids are produced during fermentation in the rumen of ruminant animals,
- most trans fatty acids are generated during industrial processing through partial hydrogenation of vegetable oils.

- Examination of a large number of candidate genes has allowed the identification of DNA polymorphisms associated with properties important for milk production that can be used to improve selection for milk fat production and milk fat components .
- This provides opportunities to change the composition of milk fats through a genetic approach ,Milk fat synthesis is regulated by several important enzymes.
- The stearoyl-CoA desaturase (SCD) gene encodes a key enzyme in the cell biosynthesis of monounsaturated

- Oleic acid as the second major FA in milk fat.
- Phospholipids show good emulsifying properties and can be used as a delivery system for fat-soluble components which offers extraordinary potential, especially for the encapsulation of bioactive substances because milk PL vesicles show unique stability
- Liposome-encapsulated n-3 PUFAs target specific inflammatory sites such as lesions associated with inflammatory bowel disease or tumors.


TAG, GL
Hydrolysis
trans FA*
RUMEN EXIT
UNSAT FFA
Bioydrogenation
SAT FFA
Mammary Lipid Synthesis
Of interest: whole set of factors affecting mammary lipogenesis
DIETARY LIPIDS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File | C:/Users/aa/Desktop/day3_gervais1.pdf
Draw | Read aloud | Ask Copilot | 3 of 46
Nutritional factors
Non-nutritional factors
Fiber
Dietary PUFA
Fat supplements
Feeding strategies
Ionophores
Milk fat
Animal genetics + epigenetics?
Stage of lactation
Production level
Season
Circadian rythm
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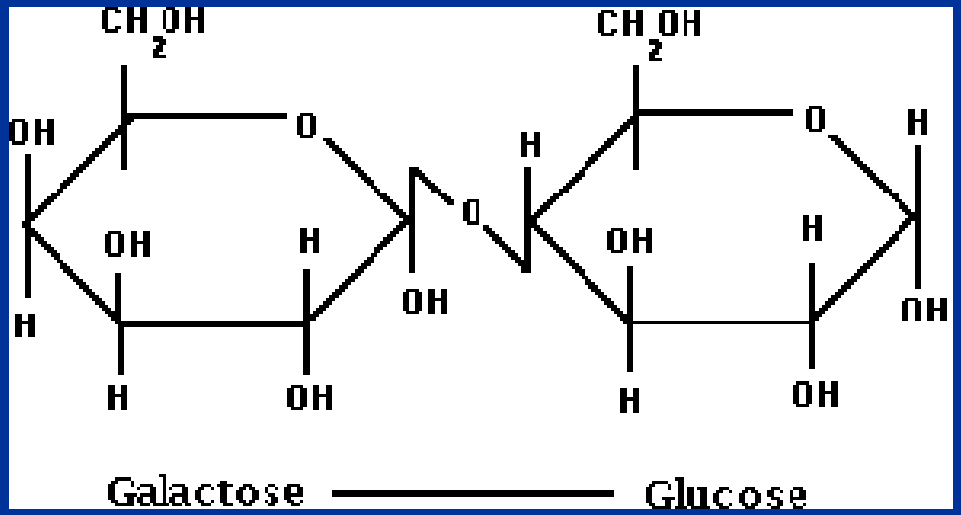
ionophore

- compound that facilitates transmission of an ion (as of calcium) across a lipid barrier (as in a cell membrane) by combining with the ion or by increasing the permeability of the barrier to it

Milk Protein Biosynthesis

- Milk protein are synthesized from amino acids in the ribosome (rough endoplasmic reticulum)
- There are 18 amino acids in milk
- Milk contains more essential amino acids than any other natural food

Lactose Biosynthesis



- Glucose is ***absolutely essential*** for lactose biosynthesis
- Blood glucose level in ruminants is 1/2 that in non ruminants
- 45-60% of blood glucose in ruminants from *Gluconeogenesis*

- Lactose is synthesized in the udder from blood glucose absorbed by the basal membrane of mammary epithelial cells (. Around 20% of the circulating blood glucose of a dairy cow is converted
- into lactose during lactation Together with some minerals (Na, K, and Cl), lactose contributes to the equilibrium of the blood–milk barrier, being the main osmotic regulator between the blood and alveolar lumen. In fact, lactose determines the amount of absorbed water in the alveoli, and thus, the volume of produced milk, soon as lactose is synthesized by the Golgi, it is packed into secretory vesicles. Here, LP determines a strong osmotic pressure, because this disaccharide cannot pass through the vesicle membrane; water is required to get into the secretory vesicles and re-establish equilibrium.
- The uptake of the precursor (glucose) from the circulatory system is regulated by facilitative glucose transporters, whose genetic expression also directly affects milk synthesis .

Milk Ejection or Milk Let-Down

Neurohormonal process that result in movement of the milk from the lumina of the alveoli into the major ducts and then to the bottom part of the udder.

Milk Let-Down

- Neuro-hormonal reflex
- The suckling stimulus or massaging of the udder stimulates somatic nerves in the teat, which send a signal to the **posterior pituitary** gland and causes the release of the hormone **oxytocin**.
- Oxytocin causes the myoepithelial (muscle) cells around the alveoli to contract.
- For efficient milking, there are several important factors to remember.
  - Stimulate 1 min before milk let-down
  - The maximal effect of oxytocin occurs during tfirst 2 to 3 minutes of milk let-down.
  - Stress during cow preparation or during milking will inhibit oxytocin release.
  - Inhibition of oxytocin release

Cows have different types of release reflexes:

Reflexes which relax the muscle in the duct system of the udder and sphincter of the teat to let the the milk to pass down, these reflexes are triggered by nerve impulses arising from a stimulus that the cow associates with suckling by calf or milking.

The following preparations for milking that can act as the stimulus for milk ejection:

1-Washing of the cow´s udder.

2-The application of the teat cups.

3- The feeding of the concentrates.

4-The sight and sound of the milking machine (sound of the vacuum

pump).

5- The noise of the milker pails.

6-The massage of the udder and teats.

The nerve impulse travels to the brain which causes the pituitary gland to release oxytoxin and prolactin into the blood and then via the blood to the milk glands to begin the process of milk let- down.

B-Reflexes triggered by the hormone of oxytocin which cause the alveoli to contract and so press out the milk (i.e. the muscles begin to compress the alveoli).

The effect of the oxytocin hormone lasts about 5 to 7 minutes. Milking must completed in that time to remove most of milk from the udder. Fear and excitement interfere with milk ejection because if the cow is frightened the oxytocin may be completely blocked by adrenalin hormone, so the cow must feel safe and in good hands, otherwise insufficient oxytocin will be secreted, in other words, the milking routine should always be regular, undisturbed and the machine must operate correctly to increase the milk yield. Initiation of lactation at the time of parturition is under the control of prolactin.

About 80 percent of the milk is removed from the udder at each milking. If too much milk is left in the udder, the pressure builds up quiker. This causes the cow to dry up sooner.

The major components of milk such as lactose, proteins especially casein and fat are mainly synthesized within the alveolar cells of the mammary gland from materials extracted from the blood. The water, vitamins and minerals content of milk is transferred by the filtration process from the blood to the lumen of the alveolus and the epithelial cells combine some of the minerals with the organic compounds. For example 75% of the calcium in milk is in chemical or physical combination with casein, phosphate and citrate and more than one–half of the phosphorus in milk is combined with casein. The Vitamins molecules in milk are transferred unchanged from the blood.

Milking Quality

The production of high-quality milk requires good management practices. The characteristics of high-quality milk include:

1-It is free of dirty and other sediment.

2-It has a low bacteria count.

3-It has no chemical contamination.

4-It has low somatic cells.

5-No water has been added.

6-It has a good flavor.