

Mammary gland : physiology and anatomy

E-learning course from ESA

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Mammary gland

Learning objectives :

The objective of this distance learning course is to understand the basis of mammary gland: physiology and anatomy. A healthy mammary gland is one the basis to product commercialisable dairy products, in terms of quality and quantity. Also calves, the futures heifers, are depending of the mammary gland, via the colostrum and milk. To understand the basis of the working of mammary gland is essential to a good performance of dairy farmers.

Basic knowledge in physiology of mammary gland will aim the development the students' capacity to dialogue with farmers, veterinarian and others professionals of dairy sector.

The content of this brick is:

- Anatomy of mammary gland;
- Neural system of the mammary gland;
- Blood supply;
- Galactopoiesis;
- Lactation curve;
- Dry Period.

The contents of this distance learning course were adapted from: “*Principles of dairy science*” (Schmidt, Van Vleck and Hutjens, 1988), “*The lactation Biology*” (Hurley, 2010).

1. Anatomy of mammary gland

The development of the mammary gland starts early in the fetal life. Already in the second month of gestation teat formation starts and the development continues up to the sixth month of gestation. When the calf fetus is six months, the udder is almost fully developed with four separate glands and a medial ligament, teat and gland cisterns.

The development of milk ducts and the milk secreting tissue take place between puberty and parturition. The udder continues to increase in cell size and cell numbers throughout the first five lactations of the cow, and the milk production capacity increases correspondingly.

To begin studying the anatomy of mammary gland, some anatomical landmarks in the inguinal region must be identified; including the teats, four mammary quarters (two fore and two rear), mammary groove, and fore and rear quarter attachments (suspensory system).

A strong udder suspensory system is required to maintain proper attachments of the gland to the body. The mammary gland is a skin gland, and is external to the body cavity. A Holstein cow may have 50 kg of weight hanging from her body when she walks into the milking parlor to be milked. So the system of ligaments and other tissues which attach the udder to the cow are critical for successful lactation.

There are seven different tissues that provide support for the udder:

1. **The skin covering the gland**, most superficial tissue, is a minor support (Figure 1);
2. **The superficial fascia**, or areolar subcutaneous tissue, attaches the skin to underlying the tissue and is another minor support for the cow's udder;
3. **The coarse areolar**, or cordlike tissue, forms a loose bond between the dorsal surface of the front quarters and abdominal wall. Weakening of these causes the udder to break away from abdominal wall. This is part of what is referred to as the fore quarter attachments when evaluating dairy cattle conformation. These are important for keeping the fore quarters closely attached to

the body wall; however are not the major supports of the udder.

4. **The subpelvic tendon** is not actually part of the suspensory apparatus, but gives rise to the superficial and the deep lateral suspensory ligaments. It is not a continuous tissue sheet but is attached to the pelvic bone at several points. This tendon does not support the udder directly, however it gives rise to the lateral suspensory ligaments.
5. **The lateral suspensory ligament** are mostly composed of fibrous tissue (with some elastic tissue), arising from the subpelvic tendon. They extend downward and forward from the pubic are. When it reaches the udder it spreads out, continuing downward over the external udder surface beneath the skin and attaching to the areolar tissue (Figure 1).
6. **The deep lateral suspensory ligament (lamellae)** is an inner part of the lateral suspensory ligament also arises from the subpelvic tendon, however is thicker than the superficial layer, mostly fibrous tissue. It extends down over the udder and almost enveloping it. The ligament attaches to the convex lateral surfaces of the udder by numerous lamellae which pass into the gland and become continuous with the interstitial framework of the udder. Collectively, the lateral suspensory ligaments provide substantial support for the udder. The left and right lateral suspensory ligaments do not join under the bottom of the udder, and the fibrous nature of these ligaments means that they do not stretch as the gland fills with milk. So, the center of the udder tends to pull away from the body as the gland fills (Figure 1).
7. **The median suspensory ligament** is the most important part of the suspensory system in cows. It is composed of two adjacent heavy yellow elastic sheets of tissue that arise from the abdominal wall and that attach to the medial flat surfaces of the two udder halves. The median suspensory ligament has great tensile strength. It is able to stretch somewhat as the gland fills with milk to allow for the increased weight of the gland. It is located at the center of gravity of the udder to give balanced suspension, so that even if rest of the layers are cut away except for the median suspensory ligament, the gland stays balanced under the cow (Figure 1).

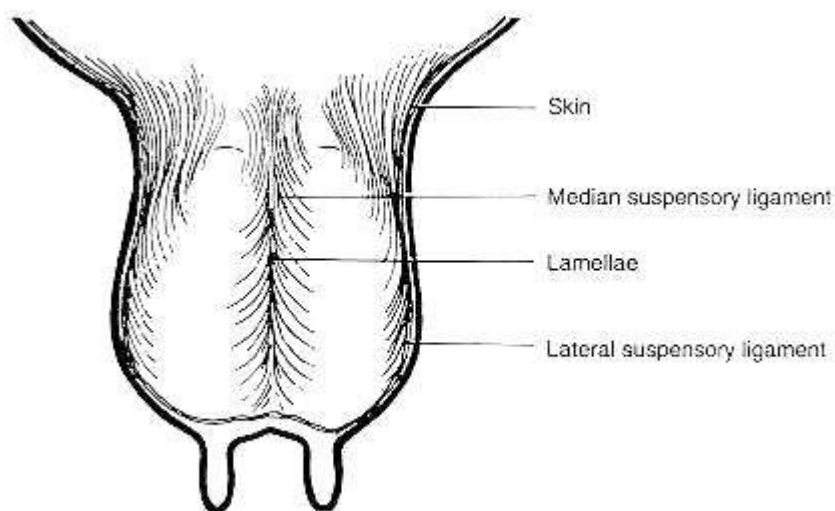


Figure 1 - Diagram of a cross section of the supporting structures of the mammary glands of the cow as viewed from the rear.

1.1. Teats

The only exit for the secretion from the mammary gland and the only means for the calf to receive milk are the teats. Teat size and shape are independent of the size, shape or milk production of the udder. Average size for the fore teats is about 6.6 cm long and 2.9 cm (in diameter), and for the rear teats is 5.2 cm long and 2.6 cm in diameter (Figure 2).

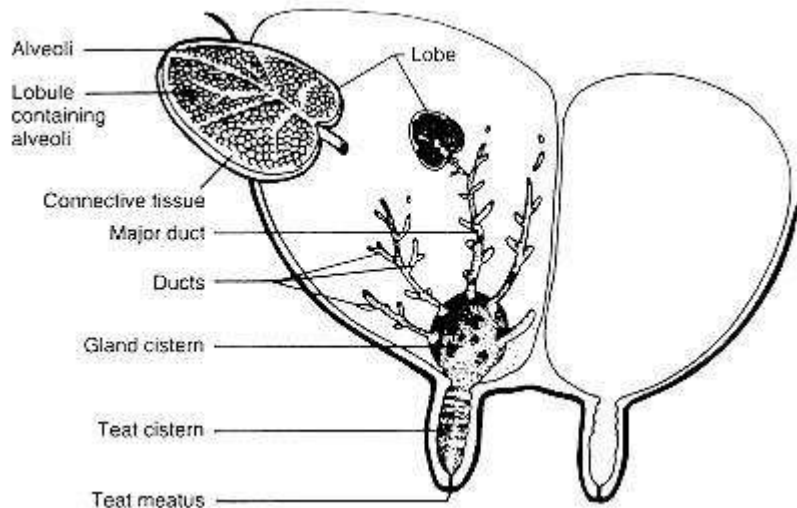


Figure 2 - Diagram of the duct system in one quarter of the mammary gland of the cow with a single lobe illustrated. Four quarters are fused into a single gland complex.

About 50% of all cows have supernumerary teats (extra teats). Some of these extra teats open into a "normal" gland, but many do not. Generally they are removed before one year old. A pseudo-teat has no streak canal, and therefore, no connection to the internal structures of the gland.

The only orifice of the gland between internal milk secretory system and the external environment is called streak canal or teat meatus. The teat meatus is made up of three to five convex epithelial projections that lie close together to make a star-shaped slit. The projections are held closed by involuntary sphincter muscles around the orifice. The teat meatus prevents the escape of milk between two milkings and is the main physical protection against bacteria and foreign material, preventing intramammary infection. When a cow is milked, the sphincter muscles relax allowing the orifice to open. The teat meatus remains open for an hour or more after milking. This provides ready access of bacteria to the inside of the mammary gland. Post-milking germicidal teat dips are designed to help minimize the chance of bacteria gaining access to the mammary gland after milking. Keeping cows standing for a time after milking, such as providing access to fresh feed, also helps minimize teat end contamination before the teat meatus closes again. The rate of milking of a cow is partially dependent on the size of the teat meatus. Faster-milking cows usually have a teat meatus of larger diameter.

During the dry period (nonlactating period), the epidermal tissue lining the teat meatus forms a keratin plug that has antibacterial properties, this is an effective seal off the orifice.

1.2. Secreting tissue and connective tissue

The mammary gland consists of secreting tissue and connective tissue. The amount of secreting tissue, or the number of secreting cells, is the limiting factor for the milk producing capacity of the udder. It is a common belief that a big udder is related to a high milk production capacity. This is, however, not true in general, since a big udder might include a lot of connective and adipose tissue. The milk is synthesized in the secretory cells, which are arranged as a single layer on a basal membrane in a spherical structure called alveolus (Figure 2). An alveolus is the discrete milk producing unit and the diameter of each alveolus is about 50-250 μm . The lumen of the alveolus is lined by a single layer of secretory epithelial cells. Several alveoli together form a lobule and each lobule contains 150-220 microscopic alveoli. Groups of lobules are surrounded by a connective tissue sheath and form a structure called lobe. The anatomy of this area is very similar to the anatomy of the lung. The milk which is continuously synthesized in the alveolar area, is stored in the alveoli, milk ducts, udder and teat cistern between two milkings. The most part of the milk (60-80%) is stored in the alveoli and small milk ducts, while the cistern contains 20-40%. However, there are relatively big differences between dairy cows when it comes to the cistern capacity.

A large proportion of ducts that are the tubing are presents in the mammary gland. These ducts allow the milk moves from the alveoli to the teat for milk removal. In addition, between the teat and the large ducts are open areas called teat cisterns. A teat cistern is a cavity where milk can collect between two milkings.

The gland cisterns or sinus lactiferous, also called the udder cistern, opens directly into the teat cistern.

The gland cistern and teat cistern are separated by the annular fold. The gland cistern function for milk storage (holds 100-400 ml). The gland cistern varies greatly in size and shape. There are often pockets formed in the cistern at the end of the larger ducts.

2. Neural system of the mammary gland

Milk ejection is important during milking or suckling to obtain the alveolar milk fraction, which can represent more than 80% of the milk stored in the udder of dairy cows. In response to tactile teat stimulation, either manually or by the milking machine, milk ejection is induced by the release of oxytocin, release from the pituitary gland, resulting myoepithelial contraction. The time from the start of a tactile stimulation until the occurrence of milk ejection spans between 40 s to >2 min and increases with decreasing degree of udder filling. Milk ejection is disturbed under several conditions such as during milking in unfamiliar surroundings or for several weeks immediately after parturition in primiparous cows. Disturbed milk ejection is due to a reduction of or absence of oxytocin.

The milk ejection reflex (let-down) actually is a neuroendocrine reflex (Figure 3). The reflex has an afferent pathway (neural) and an efferent pathway (hormonal, blood-borne). Few nerves go to the interior of the udder. That means that performing a biopsy of the gland to collect tissue can be done with only local anesthetic administered to the skin.

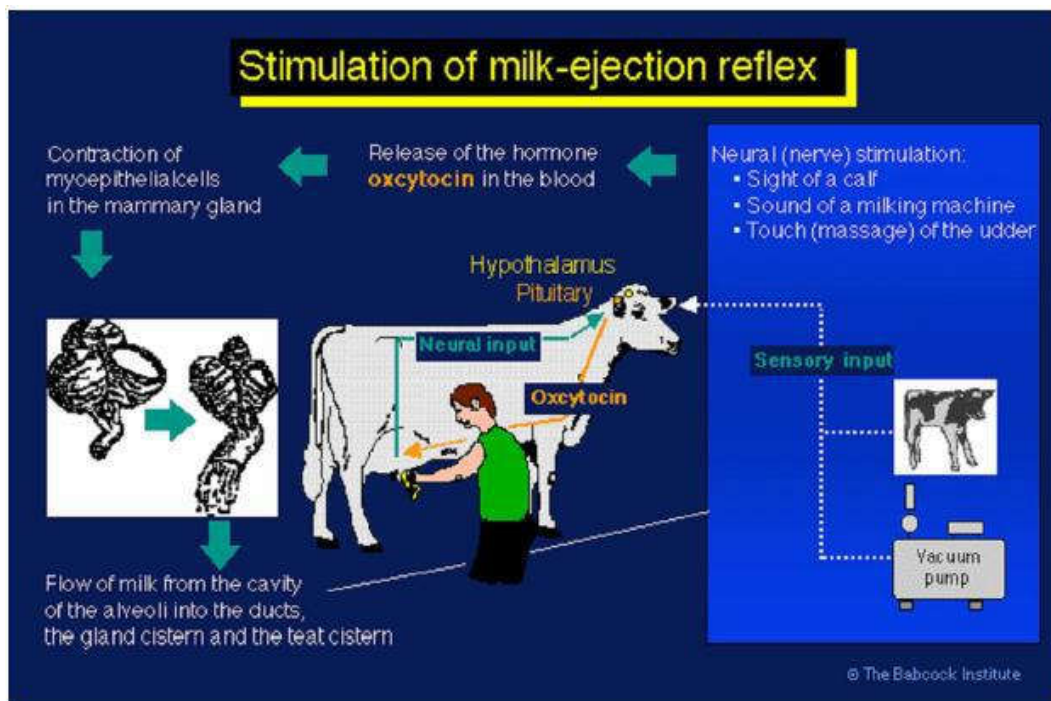


Figure 3 - The milk ejection reflex (The Babcock Institute, University of Wisconsin-Madison).

Afferent Pathway

The greatest amount of innervation in the mammary gland is in the teats, where there are pressure sensitive receptors in the dermis. Mechanical stimulation of the teats activates pressure sensitive receptors in the dermis where the pressure is transformed into nerve impulses that travel via the spinothalamic nerve tract to the brain. These nerves synapse in the paraventricular nucleus and in the supraoptic nucleus in the hypothalamus. When the cell bodies of the oxytocin-containing neurons are stimulated by these impulses originating in the teat, an action potential moves down the oxytocin-containing neurons from the cell body in the hypothalamus down the axon to the neuron ending in the posterior pituitary. This causes release of oxytocin into the blood. The efferent pathway starts at this point.

Efferent pathway

The efferent pathway begins with the release of oxytocin into the blood (Figure 3). The oxytocin then travels to the mammary gland via the blood, binds to oxytocin receptors on the myoepithelial cells,

causing the myoepithelial cells to contract, and resulting in increased intra-luminal (intramammary) pressure and ejection of milk from the alveolar lumen. Oxytocin receptors are associated with the myoepithelial cells, not the smooth muscle of the mammary gland.

Other mechanisms of milk ejection:

- Myoepithelial cells will also contract in response to vasopressin (ADH or antidiuretic hormone). Vasopressin has about 20% the oxytocic activity of oxytocin;
- Visual or auditory stimuli can cause milk ejection. Milk ejection is a condition response;
- Stimulation of the genital tract such as vaginal distention causes release of large amounts of oxytocin;
- The mechanical tap stimulus does not involve oxytocin. It will occur under anesthesia or denervation of the udder. It is not inhibited by epinephrine. Kneading or butting of the udder by the young may elicit this response. This may involve distortion of the alveolar structure or the myoepithelial cell structure, resulting in milk ejection.

Inhibition of milk ejection

Various stressful stimuli that inhibit milk ejection are associated with increased activity of the sympathetic nervous system. Oxytocin action can be blocked by the hormones catecholamines, which are made by the adrenal glands localized above the kidneys. The main catecholamines are dopamine, norepinephrine and epinephrine (which used to be called adrenalin). These hormones are released in response to stressful situations and increase the tone of the smooth muscles of the mammary ducts and blood vessels. This results in the reduction of oxytocin reaching the myoepithelial cells and partial occlusion of the mammary ducts (Figure 4). Moreover, epinephrine directly blocks oxytocin from binding to myoepithelial cells. This is termed peripheral inhibition of milk ejection. Therefore, in animals exhibiting peripheral inhibition a dose of exogenous oxytocin will not cause milk ejection

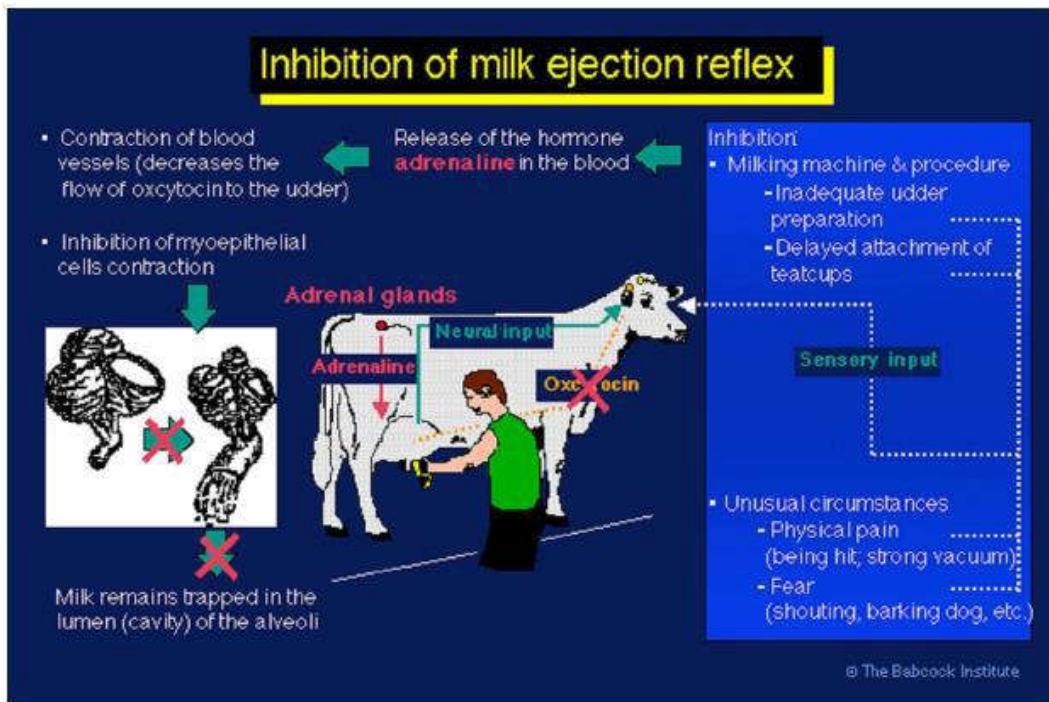


Figure 4 - The inhibition of milk ejection reflex (The Babcock Institute, University of Wisconsin-Madison).

A common cause of failure to milk ejection is associated with stress of milking in the early postpartum period especially for primiparous cows. The stress inhibits the release of oxytocin from the posterior pituitary gland. This is termed central inhibition of milk ejection. Exogenous oxytocin is usually administered in these cases causing milk ejection. Based on the above discussion about peripheral and central inhibition of milk ejection, it can be stated that milk ejection occurs as a result of oxytocin release, which is normally couples with inhibition of the central and peripheral inhibitory controls.

3. Blood supply

The blood supply to the mammary gland is extremely important for mammary function. All of the milk precursors come from blood. To produce 1 liter of milk 500 liters of blood have to pass through the udder. When a cow produces 60 liters of milk per day, 30,000 liters of blood are circulation through the mammary gland. This represents a blood flow of 1250 liters per hour.

There is a 2-6 fold increase in blood flow in the mammary gland starting 2-3 days prepartum. The decrease in production with advancing lactation is not due to decreased blood flow, rather it is due to the loss of secretory epithelial cells through a process programmed cell death, this process is called apoptosis.

3.1. Arterial system

Blood leaves the heart and flows towards the rear of the cow by the abdominal aorta (Figure 5). Two major arteries carry the blood to the udder, one for each half of the udder. These arteries, pudental arteries, enter the udder through the inguinal canal. The inguinal canal is the orifice in the body cavity in the inguinal region where blood vessels, lymph vessels and nerves enter and leave the body cavity to supply the skin in the posterior part of the animal. The pudental arteries are branches of the external iliac arteries, which are branches of the abdominal aorta. The external iliac artery becomes the femoral artery (supplies leg muscles). The external pudental arteries become the mammary arteries as mentioned above pass through the inguinal canal. The mammary arteries divide into caudal and cranial branches, which rebranch many times and end in small capillaries surrounding each alveolus. The pudental arteries make S-shaped curves (sigmoid flexures) as they emerge from the inguinal canal. This allows for downward distension of the udder as it fills with milk, without stressing the blood vessels. Perineal arteries supply blood to a small portion of the posterior dorsal part of the udder.

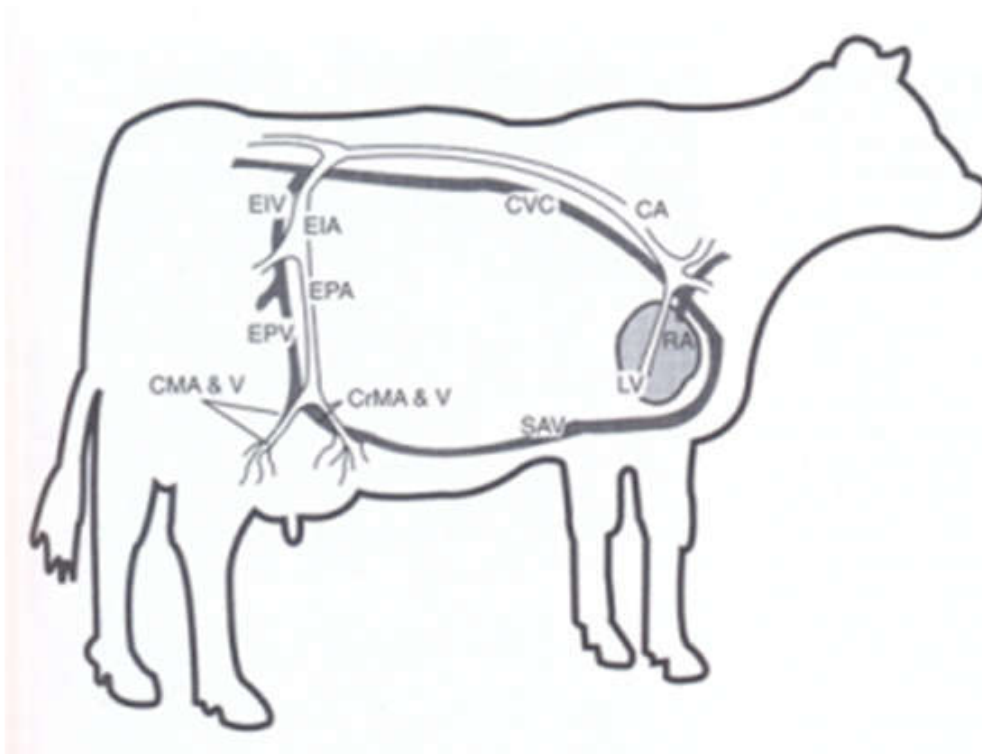


Figure 5 - Blood circulation to and from the udder.

RA= right atrium	LV= left ventricle	CA= caudal aorta	CVC= caudal vena cava
EIV= external iliac vein	EIA= external iliac artery	EPA= external pudendal artery	EPV= external pudendal vein
CMA&V= caudal mammary artery and vein	CrMA&V= cranial mammary artery and vein	SAV= subcutaneous abdominal vein	

3.2. Venous system

Veins leave the mammary gland anti-parallel to the arteries. There are three veins on each side that carry blood away from the gland:

1. **External pudendal** vein leaves the udder parallel to the external pudendal arteries;
2. **Subcutaneous abdominal vein (milk vein)** exits the gland at the anterior end of the front quarters and passes along abdominal wall. This is the large vein that is visible under the skin on the belly of the cow. It enters the body cavity at the xiphoid process via "milk wells", and eventually empties into vena cava.
3. Perineal vein leaves the rear of the gland parallel to the perineal artery and carries less than 10% of blood leaving udder.

3.3. Venous circle

Venous circle is formed by anastomoses between anterior and posterior mammary veins. It prevents pinching off of areas of venous outflow when the cow is lying down.

3.4. Lymphatic system

The lymphatic system carries lymph from the tissues toward the heart. Because many molecules of all sizes leave the capillaries but not all return to the venous blood drainage at the tissue level. Especially the larger molecules like proteins. These, along with cellular metabolites and some secretory products are in the interstitial (extracellular) spaces. If they stayed there, they would disrupt with the normal balance of osmotic pressure in the tissue, upsetting trans-capillary fluid exchange. Excess fluid (called extracellular fluid) would accumulate in the interstitial spaces. The lymph is drained toward the upper posterior part of the udder, where they converge on the convex surface of the supramammary lymph node.

3.5. Functions of lymphatic system:

- The extracellular fluids are drained from the tissue and conducted back to the circulatory system via the lymphatic network;
- Also, the lymphatics contain concentrated areas of leukocytes (particularly lymphocytes and macrophages) in lymph nodes; these leukocytes can mount an immune response to bacteria and foreign material;
- The lymphatic network serves to transport some elements in the body (vitamin K, lipids absorbed in the intestine).

3.6. Lymphatic network

Lymphatic network originates in tissue spaces as very thin, closed endothelial tubes (lymphatic capillaries). These are analogous to blood capillaries, but are much more permeable, with little resistance to passage. They have no basement membrane. Lymph capillaries converge to form larger vessels. Lymph flow is unidirectional from the tissues through lymphatic vessels, eventually dumping lymph into the vena cava.

Lymph is a clear, colorless liquid with a composition similar to blood plasma. Changes in plasma composition will change lymph composition. Protein concentration of lymph is lower than in plasma, 1.5% vs. 6%, respectively. Specific proteins differ, for example albumin is a smaller molecular size than

globulins and leaves the capillaries more readily than globulins, so the albumin: globulin ratio is 1.8 in plasma, 2.5 in lymph. Protein concentration in lymph varies inversely with rate of formation.

Lymph flow rate is usually low. It is influenced primarily by the rate of lymph formation. For example, if blood capillary pressure is increased by arterial vasodilation or venous constriction, the flow rate of lymph increases. Also, the flow rate is affected by compression of lymphatics by contraction of neighboring musculature and by negative intrathoracic pressure (breathing). Valves in the lymph vessels prevent retrograde flow similar to those in veins.

3.7. Udder edema

Edema is swelling of the udder. Although it occurs to some degree in most cows at calving time, heifers calving for the first time are especially prone to having udder edema. Fluid accumulates between skin and glandular tissue, as well as in the gland. Severe edema can strain supportive structures of udder. Udder edema is often caused by an imbalance of hydrostatic and osmotic pressures, increasing fluid flow out of the capillaries into the interstitial spaces. This may occur because of damage to the capillary walls or obstruction of the lymphatic system.

4. Galactopoiesis

Galactopoiesis is the maintenance of lactation once lactation has been established. Two key interrelated components contribute to the maintenance of lactation, galactopoietic hormones and removal of accumulated milk. Because of the importance of galactopoietic hormones in milk production, sometimes the word galactopoiesis also is used to indicate enhancement of lactation, especially in dairy animals. Inhibition of secretion of key galactopoietic hormones will depress milk production to varying degrees depending on the species, stage of lactation, and the particular hormone being suppressed. The role of galactopoietic hormones such as prolactin in maintenance of lactation is well established. Prolactin is released at the time of milk removal in ruminants and nonruminants, and it remains a key systemic modulator of milk secretion during lactation. Conversely, growth hormone is generally considered to be the predominant galactopoietic hormone in ruminants. Inhibition of prolactin secretion or administration of prolactin to lactating cows has little effect on milk yields.

Regardless of the hormones involved, all attempts to evaluate milk secretion must account for continued removal of milk. This is a reminder of the critical role of local mammary factors in maintenance of milk secretion. One such factor that plays a major role in regulating milk secretion in many species is a feedback inhibitor of lactation (FIL) found in milk. FIL is thought to be produced by the mammary cells as they synthesize and secrete milk. Accumulation of FIL in the milk-producing alveoli results in feedback inhibition of milk synthesis and secretion.

Frequent removal of milk from the gland minimizes local inhibitory effects of FIL and increases milk secretion. Milk removal involves several mechanisms that impact milk production, including removal of local inhibitory components, regulation of local blood flow, and even physical factors in the alveolus. The effects of frequency of milk removal are tied closely with the local regulation of milk secretion.

5. Lactation curve

The cow reaches her peak milk production approximately 3 to 6 weeks after parturition, and then a gradual decline in the yield takes place. A lactation period of 305 days is recommended to take advantage of 60 days of dry period and yearly calving interval. The body condition at calving of the cow is determines peak milk yield. Good body condition at calving and adequate feeding program after calving tend to increase peak milk production. There is a high correlation between global lactation and peak milk production.

The rate of decline in yield after calving is called persistency. Cows that have a sharp decline in milk yield after the peak have a low persistency. Cows must have high persistency as well as high production

for high-lactation milk yields. The rate of decline is accentuated by pregnancy, particularly starting at the twenty-second week of pregnancy, which occurs during the seventh to eighth months of the normal lactation period if the cow is bred back 60 days after calving.

There is a general inverse relationship between milk yield and milk protein and milk fat contents. As yield increase, the percentage composition of these two elements decrease. The protein and milk-fat percentages are at a low point during the peak of lactation and then gradually increase toward the end of lactation. Lactose content shows a very slight decline toward the end of lactation and ash content shows a very slight increase with advancing lactation.

6. Dry Period

The mammary gland of the dairy cow requires a nonlactating (dry) period prior to an impending parturition to optimize milk production in the subsequent lactation. This period is called the dry period, and it includes the time between halting of milk removal (milk stasis) and the subsequent calving. This period allows regenerating secretory tissue of mammary gland. In a 5-points notation scale for body condition score in dairy cows, the goal for ideal body condition score for the dry cow is 3.5. To achieve satisfactory health and performance early in the subsequent lactation condition score must fall between a minimum of 3 and a maximum of 4. Cows having a thin body condition at the end of lactation require a dry period to replenish their body supplies. Body fat can be utilized for milk production: 1 kg of body fat supplies energy to produce approximately 7 kg of milk. However, overconditioning may be detrimental, especially for heifers entering the dairy. A cow that is overconditioned at calving is also more susceptible to metabolic diseases, particularly ketosis.

The normal procedure to dry off a cow is to withdraw all grain and reduce the water supply several days before the start of the dry period. This drastically reduces the milk production during that time. Then milking is halted about 45 to 50 days before expected date of parturition. Infusion of the udder with antibiotics can help prevent infections that may occur in early involution. After milking is stopped intramammary pressure increases, milk products accumulate in the gland, and further milk secretion is inhibited. Sometimes if the udder becomes extremely congested, it may need to be re-milked. However, this practice stimulates further milk synthesis because intramammary pressure is reduced and pituitary hormones (oxytocin and prolactin) are released.

Pay attention during the dry period

- There is an optimum length of dry period;
- A dry period shorter than 40 days will decrease subsequent production (also long dry periods over 70 or 80 days will result in lowered production in the next lactation);
- Changes occur in the mammary gland during the dry period which influence mammary cell proliferation and mammary function in the subsequent lactation.

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A healthy mammary gland is one the basis to product commercialisable dairy products, in terms of quality and quantity. The knowledge from this distance learning course is essential to understand the functions of mammary gland and its anatomy.

Resource credits

Figure 5 - Blood circulation to and from the udder. p. 8

Reece et al., 2004