

Reproduction

The mammary gland

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I. Introduction

Mammary gland is highly evolved skin gland of mammals, which is also a major characteristic of mammalian species. Mammary glands are bilateral accessory reproductive organs or glands located on the ventral surface with a compound, branched tubulo-alveolar structure that secretes milk as a source of nutrition of offspring and is essential for postnatal survival and for reproductive success in almost all mammals. **Breast** is a term for mammary gland most typically used to denote the human mammary gland, while **udder** is typically used to denote the complex of the mammary glands of ruminants and some other animals. The basic microscopic structure of the milk-secreting tissue is remarkably constant among species, but there are wide variations in the gross anatomy of the glands, the composition of milk, the patterns of suckling, and the length of lactation to meet the requirements of each species. In contrast, male mammals have rudimentary ducts and teats. Lactation is a most adaptable and efficient method of providing early nutrition for young mammals and has played an important part in the evolutionary success of mammals as a group. Domestication, selective breeding, and improved nutrition have extended the **period of** lactations and massively increased the milk yield potential of cows, sheeps and goats for the benefit of human nutrition.

II. Anatomy of mammary gland

Mammary glands may be found on the thorax (e.g. **human**, elephants, and bats), inguinally (e.g. cows and other ruminants), on the abdomen (whales), covering the ventral surface of the thorax and abdomen (mice, rats, rabbits, dogs, cats, and pigs), or even along the sides of the body as in the coypu. Part of the duct system may be adopted for storage, seen at its most developed in the large cavity or gland cistern in the udder of ruminants. In women, terminal duct leading to the nipple are dilated into storage sinuses. The number (from 2 to 18), size, and disposition of the mammary glands vary in different mammalian species. They are usually paired structures and in some species lack teats.

The two major tissue compartments constitute the mammary glands: the **glandular tissue**, which consists of extensive duct systems (lactiferous ducts) and milk producing lobules of alveoli (**Fig. 1**); and stroma consists of fat cells and connective tissue, which is collectively known as the **mammary fat pad**. In woman, the glandular tissue of the mammary gland is arranged in approximately 15-20 lobes. The lobes, lobules, and their ducts are surrounded and separated from each other by bundles of connective tissue or stroma. Each lobe consists of a branching structure made up of 20-40 lobules and finally terminates in clusters of acine (or alveoli). The alveoli are lined by a single layer of secretory epithelial cells, which are joined just below their luminal surface by tight junctional complexes and are surrounded by a diffuse layer of contractile basal-myoe epithelial cells involved in milk ejection. The alveolus is then surrounded by a basement membrane. Outside the basement membrane is found a rich vascularized connective-tissue stroma that contains lipid-depleted adipocytes and fibroblasts. There is a fat mass overlying the breast just under the breast skin. Except for the smooth muscle of the areola-nipple complex, there is no muscle in the breast itself. It consists of ducts, lobules, and alveoli of the gland tissue, a lot of fatty tissue, and connective tissue. The lumen of the alveoli connects to collecting interlobular ducts, which empty into the main 15 to 20 lobular collecting ducts. In turn, each lobe drains into the nipple. The breast of a non-pregnant woman contains just a few alveoli that have budded off from the ends of the ducts.

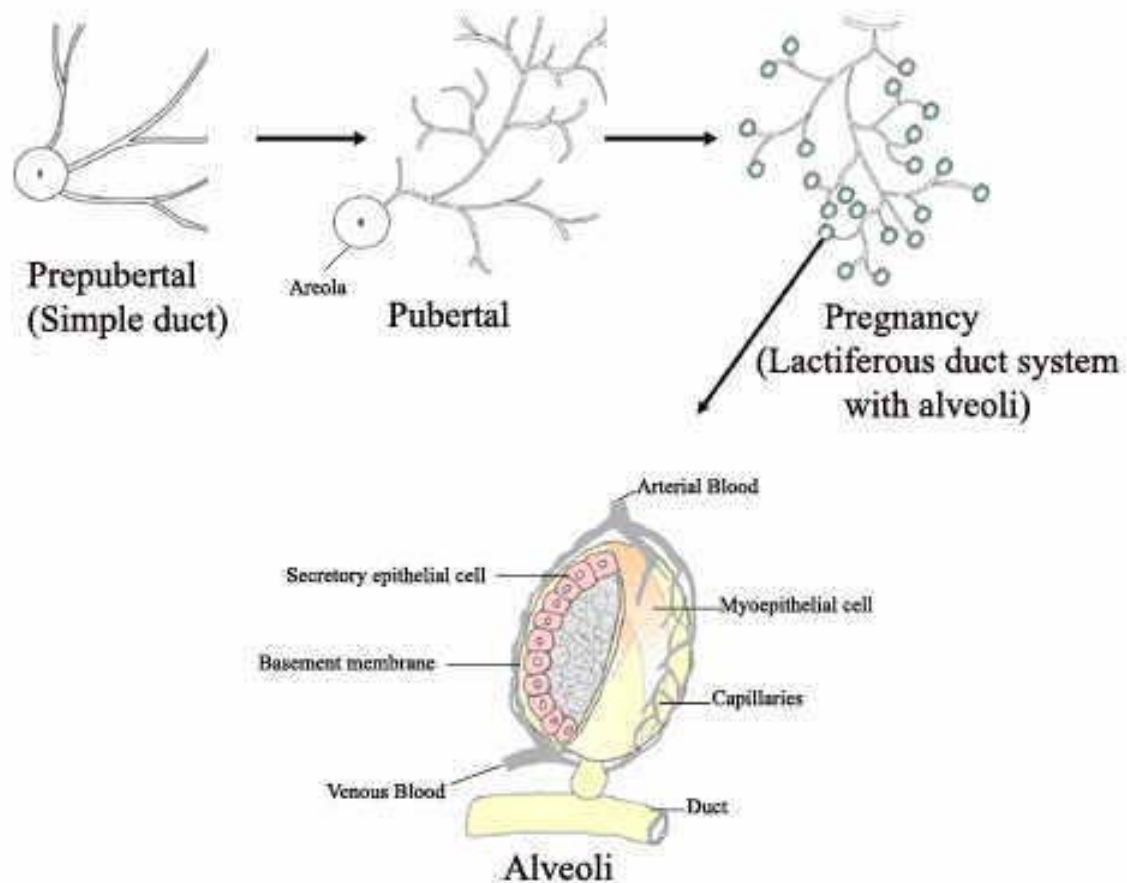


Fig. 1 Development of Mammary Gland

The lactiferous ducts enlarge slightly into a lactiferous sinus before emerging, and the nipple is then perforated by 15-20 tiny openings. An area of pigmented skin called areola surrounds the nipple, which serves as the termination point for the lactiferous ducts. The areola contains sebaceous glands named **Montgomery's follicles** and sweat glands, which increase in size and number during pregnancy and lactation and important in the lubrication of the nipple. The skin of the areolae and the nipple contain numerous longitudinally and circularly arranged smooth muscle fibers that are responsible for erection of the nipples when they are stimulated tactilely or by exposure to cold. The areola serves as the termination point for the fourth intercostal nerve, which carries the sensory information about suckling to the spinal cord and brain. By contrast, monotremes have mammary glands without a nipple or central lumen and the ducts open directly to a confined area known as the milk patch.

The lactating alveolar cells are highly active secretory cells and the cytoplasm of cells is filled with numerous mitochondria and an extensive rough endoplasmic reticulum network (**Fig. 2**). In addition, there is a well-developed Golgi apparatus, and secretory vesicles containing casein micelles are present in the apical region of the cell. Swelling of trans-most elements of the Golgi network results from the osmotic influx of water due to the high concentrations of lactose synthesized within this compartment. Lactating alveolar cells have well-developed synthetic capabilities for lipid and possess a unique mechanism for lipid secretion that results in the secretion of triglyceride droplets surrounded by a specialized milk fat droplet

membrane. Epithelial cells are connected to each other through an apical junctional complex composed of adherens and tight-junctional elements that function to inhibit direct paracellular exchange of substances between vascular and milk compartments during lactation. The basal side of alveolar epithelial cells contacts myoepithelial cells and the basement membrane, which separates the epithelial compartment from the stroma and the vascular system.

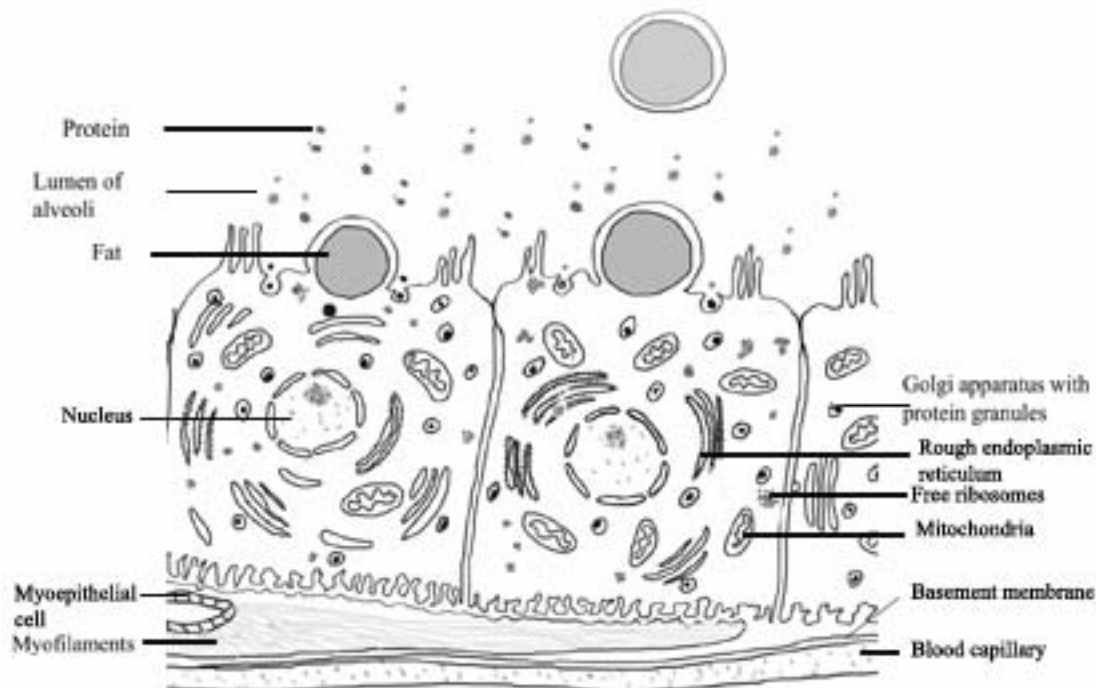


Fig 2 Structure of Secretory Epithelial Cell

The mammary parenchyma and capillary network develop in parallel at a comparatively slow rate until a woman / female become pregnant. The branching and ductal development of the breast / udder parenchyma then matures along with growth of mammary vessels. At parturition most of the blood flow to the foeto-placental unit is directed from the uterus to the mammary glands. An optional blood flow is essential for milk production in order to provide the precursors of all the necessary elements for milk synthesis. The major blood supply to the breasts is from a branch of subclavian artery called the internal mammary, with additional contributions from the thoracic branch of the axillary artery. The veins that drain the blood from the breast follow a pathway that quickly leads into that large vein, the superior vena cava that enters the right side of the heart.

In the breast / mammary gland, most of the lymph from the central part of the mammary gland, the skin, nipple and the areola drains laterally toward the axilla. From there the lymph passes to the central axillary nodes embedded in a fat pad in the center of armpit. The flow then proceeds to the upper part of the axilla to the lateral nodes along the axillary vein and then deep axillary or subclavicular nodes. From the back of the breast, the lymph is drained to several interpectoral (subscapular) nodes located between the pectoralis major and pectoralis minor muscles. The internal mammary nodes that lie along the sternum lie in the pathway of the lymph channels that drain from the inside or medial part of the breast. Thus the blood vessels, nerves and lymphatics run in the septae, which merge imperceptibly with the fascia at the anterior thoracic wall.

III. Development of mammary gland

The development of the mammary gland occurs in three major phases: in utero, at puberty, and during pregnancy (**Fig. 1**). This process has been best studied in the rodent. The development of the mammary gland begins in the skin of the fetus, by migration of cells to form paired mammary buds in positions corresponding with the mature mammary glands. These cells then begin to divide, leading to the formation of elongated cords of cells that penetrate from the skin into the underlying dermis. The number of these cords determines the number of primary ducts. The primary ducts ending in short ductules lined by one to two layers of epithelial cells and one layer of myoepithelial cells. The epithelial cells have an eosinophilic cytoplasm and fine cytoplasmic vacuolization, with typical apocrine secretion.

During childhood, development of mammary gland keeps pace with the general growth of the body. In the period that precedes puberty, the mammary gland of the female grows at a rate faster than general body growth (allometric growth). In species, such as mice, rats, and pig, this is a period of duct elongation to reach the limits of the mammary fat pad. The breast development in humans before puberty is largely stromal and duct elongation and increasing complexity of the parenchyma occur only after repeated menstrual cycles. In general during puberty, the mammary glands show growth activity both in the glandular tissue and in the surrounding stroma. Glandular increase is due to the growth and division of small bundles of primary and secondary ducts. They grow and divide partly dichotomously (repeated bifurcation) and partly sympodially (involving the formation of an apparent main axis from successive secondary axis), on a dichotomous basis. The duct grows, divide, and form club-shaped terminal end buds. Terminal end buds give origin to new branches, twigs, and small ductules or alveolar buds.

During pregnancy, the breast attains its maximum development; it occurs in two distinct phases. The early stage is characterized by growth consisting of proliferation of the distal elements of the ductal tree, resulting in the formation of lobules of alveoli (**Fig. 1**). The secretory alveoli formed during pregnancy is a terminal outgrowth that marks the end of glandular differentiation. The mammary changes that characterize the second half of pregnancy are chiefly accumulation of the secretory activity. The switch-on of the gene responsible for the synthesis of milk-specific products by the secretory cells starts from mid-pregnancy (Lactogenesis stage 1). During this period, a yellowish fluid containing a high concentration of protein is secreted into the mammary alveoli and may be expelled from nipple. There are no major changes of the mammary gland are observed during lactation. During post-lactation, the regression or cell autolysis take place with collapse of acinar structures and narrowing of the tubules, and appearance of round cell infiltration and phagocytes in and about the disintegrating lobules, and finally, regeneration of the peri-ductal and peri-lobular connective tissue with renewed budding and proliferation in the terminal tubules. The growth, differentiation and secretory activity of mammary gland during puberty, pregnancy, and lactation are strictly regulated by the coordinated action of various steroid and peptide hormones: such as prolactin, estrogen, progesterone, adrenal corticoids, insulin, growth hormone, thyroid hormone and other locally produced growth factors (**Fig. 3**). The allometric growth of mammary gland preceding puberty has been shown to be dependent on estrogen. The hormones controlling lobulo-alveolar growth are estrogen, progesterone, adrenal corticoids, somatotropin, prolactin, and, in some species, placental lactogen. Prolactin is critical to control mammary gland growth and development. It is important in all phases of the proliferation of alveolar epithelium, its differentiation and its survival. Estrogen acts on mammary gland tissue to promote ductal outgrowth or development and alveolar expansion

by regulating cell proliferation and cellular turnover. Insulin and IGF-I are necessary for prolactin and other hormones to exert their effects on the mammary gland tissues. It is essential for the most phases of mammary gland growth and secretion. Its cytoplasmic receptors are present in lactating mammary tissues. Thyroid hormone is essential in indirect way for development of mammary tissues probably contributing the normalcy of the process in intact animal. Glucocorticoids are essential for the most phases of mammary gland growth and secretion. Growth factors known to stimulate mammary gland development include insulin-like growth factors I and II, members of the epidermal and fibroblast growth factor families. Inhibitory growth factors are also implicated, notably transforming growth factor-beta.

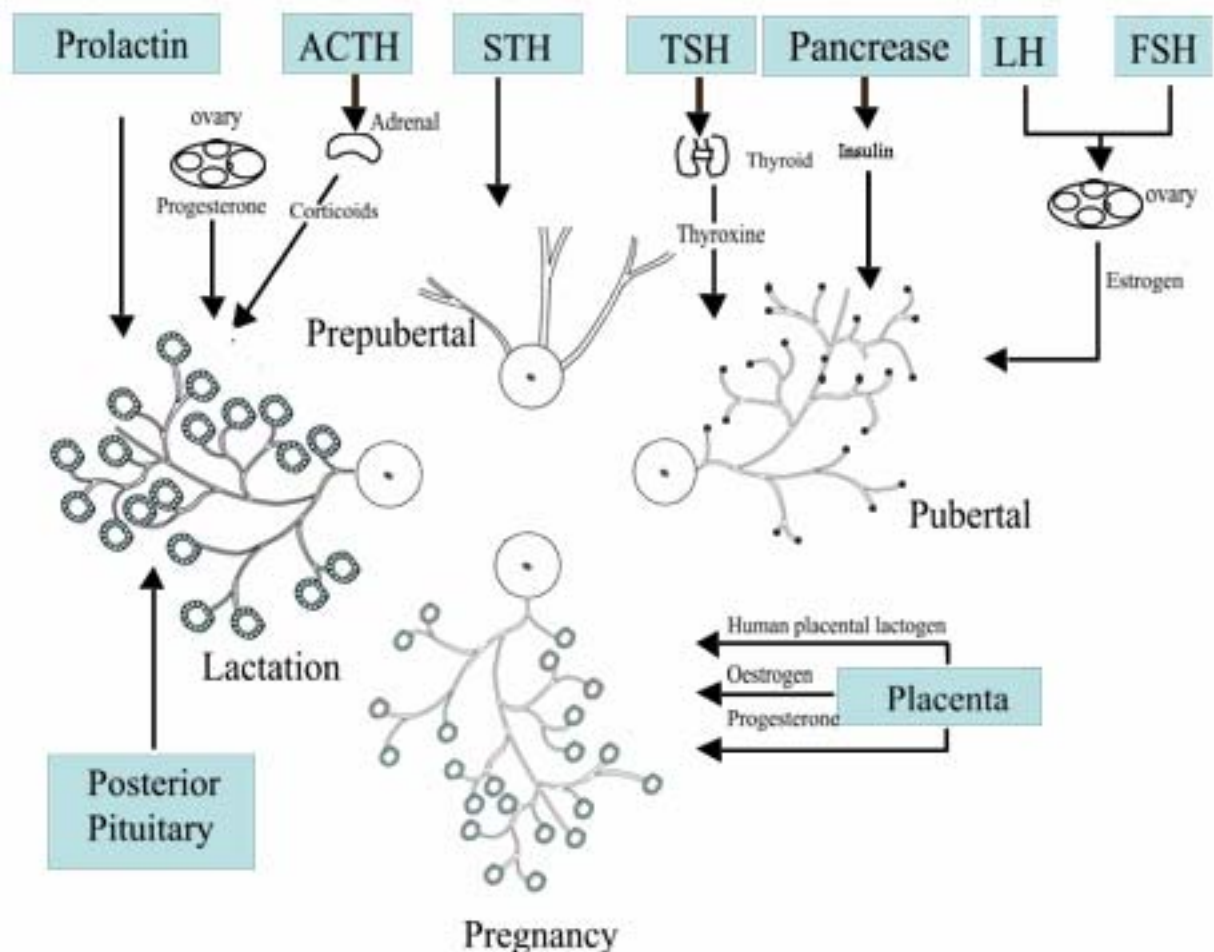


Fig. 3 Hormonal Regulation of Growth and Differentiation of Mammary Gland

IV. Synthesis and Secretion of Milk

To provide milk to their neonates, at the end of pregnancy, around the time when the young is born, the mammary glands undergo a process that initiates milk secretion, called **Lactogenesis**. Lactogenesis is the synthesis of milk by the mammary epithelial cells and passage of milk from the epithelial cell to the alveolar lumen. Milk provides an almost complete nutrition for young mammals from birth to weaning. There are large variations between species in the composition of Milk (**Table 1**). The major constituents are milk fat, carbohydrates, proteins, ions, and water. In each of these major categories are a large number of individual constituents, which vary between species, between stages of lactation, and even between individuals. Milk also contains other quantitatively minor, but biologically significant components, such as vitamins, hormones, and growth factors. All the components are either synthesized by secretory epithelial cells, or transported from blood or stroma through a complex process of transcellular and paracellular routes.

Table 1

Average concentrations of major constituents of Milk

<i>Species</i>	Total Solids (g/100 ml)	Fat (g/100 ml)	Casein (g/100 ml)	Lactose (g/100 ml)
Cow	12.7	3.7	2.8	4.8
Goat	13.2	4.5	2.5	4.1
Sheep	19.3	7.4	4.6	4.8
Horse	11.2	1.9	1.3	6.2
Man	12.4	3.8	0.6	7.0
Rat	21.0	10.3	6.4	2.6
Rabbit	32.8	18.3	10.4	2.1
Polar bear	47.6	33.1	7.1	0.3
Blue whale	57.1	42.3	7.2	1.3

Lactogenesis has two main phases. The initiation phase (**lactogenesis I**) is characterized by increased expression of some milk protein genes and biosynthetic enzymes, and accumulation of neutral lipid droplets. Alveolar cells become capable of limited secretion of some milk components during initiation phase, which in human is detected by measurement of increased concentrations of lactose and alpha-lactalbumin in plasma or urine. Thus the secretion of lactogenesis is restricted to a limited number of alveolar cells with incompletely developed secretory mechanisms. Copious milk secretion is induced during the secretory activation phase of differentiation (**lactogenesis II or Galactopoiesis**) that occurs at the end of pregnancy in rodents and ruminants, and shortly after parturition in human. This phase is characterized by homogeneous expression of milk protein genes by alveolar cells, induction of additional milk protein gene and biosynthetic enzyme expression, polarization of organelles, expansion of mitochondria and RER, maturation of golgi apparatus, and closure of tight-junctional complex. These changes in the cellular and gene expression properties of alveolar cells are reflected in dramatic modifications of the solute composition of milk and increased secretory volume and indicate coordinated maturation of secretory mechanisms and alterations in transport pathways.

The major carbohydrate in most milk is the disaccharide, **lactose**. It is synthesized from UDP-galactose and glucose within the Golgi complex. The enzyme, lactose synthetase, catalyzes

the final step in lactose synthesis. This enzyme is consisting of two proteins, the enzyme galactosyl transferase, which occurs in several tissues, and α -lactalbumin, a protein unique to the mammary gland. α -Lactalbumin has no enzyme activity but functions to increase the affinity of galactosyl transferase for glucose, allowing the synthesis of lactose. The high concentrations of lactose present in the golgi during lactation leads to the osmotic influx of water that contributes to the fluidity of milk.

The mammary gland synthesizes a variety of proteins from amino acids. The most important quantitatively and nutritionally are the caseins, a group of phosphoproteins specific to milk. In milk, the casein is present as spherical bodies known as micelles. Calcium originates from the plasma, entering the alveolar cytoplasm located at the basal membrane. It is transported from the cytoplasm into secretory vesicles by an ATP-dependent Ca^{2+} pump that is found on golgi and secretory membrane. Within the vesicles calcium forms large micellar structures with casein and also complexes with phosphate and citrate to effectively reduce Ca^{2+} levels. The phosphates in secretory vesicles are partly derived from the hydrolysis of UDP-galactose during the synthesis of lactose. Citrate is generated endogeneously within the cytoplasm of the alveolar cell and transported into the golgi lumen. Micelles thus contain calcium and inorganic phosphate, plus small amounts of citrate and magnesium, thereby supplying components essential for skeletal development.

Immunoglobulins (Igs) form another important protein component of milk and are at particularly high concentrations in the first milk, colostrums. They are selectively transferred from blood or synthesized locally by cells of the immune system. Until their own immune systems become mature, young mammals depend on the passive transfer of antibodies from their mothers to protect them from infection. The transfer of **immunoglobulins** may also occur in utero across the placenta. In addition to antibodies, milk contains other components that can provide protection against pathogens, such as lactoferrin, lysozyme, and the lactoperoxidase system.

Lipids are among the most variable components of milk, differing between species but also with factors such as diet, stage of lactation, and breed. Mammary epithelial cells of most species have well developed lipid synthetic, storage and secretions capabilities. A process unique to mammary epithelial cells secretes lipids and lipid-associated proteins. Milk lipids, primarily triglycerides and phospholipids are synthesized in the smooth endoplasmic reticulum in the basal region of the cell from precursor fatty acids and glycerol. Newly synthesized lipid molecules form into small protein coated storage structures called lipid bodies or cytoplasmic lipid droplets that coalesce and are transported to the apical plasma membrane where they are secreted by a unique budding process, as membrane enveloped structures called milk fat globules (MFGs). The MFG is a major neonatal energy source in mammalian species. The milk fat globule membrane is known to contain numerous enzymes, including oxidases, reductases, hydrolases and purine oxidizing enzyme xanthine oxidoreductase (XOR).

Many substances in the milk are transported through the secretory epithelial cells. It includes a wide range of macromolecular substances derived from serum and stromal or alveolar cells, including serum proteins (Igs, albumins, transferring), low density lipoprotein (LDL), hormones (insulin, prolactin, estradiol) and stromal derived agents such as IgA, cytokines and lipoprotein lipase. Transcellular transfer of these molecules or substances such as monovalent (sodium, potassium, chloride, iodide) and polyvalent (calcium, phosphate) ions and small molecules (glucose, amino acids) from blood to milk requires the presence of specific transporter at the basal and apical plasma membranes, or at the basal plasma membrane and golgi or secretory membranes.

Changes in the solute composition of milk are an index of the relative activities of solute synthesis / transport pathways. Three temporally distinct changes in milk composition take place at the onset of lactation. The earliest is a fall in sodium and chloride and an increase in the lactose concentrations of milk. These modifications occur immediately after delivery and are largely complete by 72 h postpartum. They precede increases in the milk volume by at least 24 h, and can be explained by closure of the tight junctions that block the paracellular pathway. Blocking this pathway prevents lactose made by epithelial cells, from passing from the lumen of the alveolus to the plasma, and sodium and chloride from directly entering the lumen from the interstitial space. These changes result in decreased concentrations of sodium and chloride, and increased concentration of lactose in the mammary secretion.

Second, there are transient increases in the rates of secretion of IgA and lactoferrin in the milk of women shortly after delivery. The concentrations of these two protective proteins remain high, comprising as much as 10% of milk for the first 48 hrs after birth then fall rapidly after day 2, both from dilution as milk volume secretion increase and from actual decreases in their rates of secretion, particularly of immunoglobulin. Although both these proteins are found at high concentrations in colostrums; they are likely to be secreted by different mechanisms. In addition, the peak secretion rate of lactoferrin occurs at the same time as that of lactose and the major milk proteins, while IgA secretion peaks 1 day earlier.

The third phase occur about 36h postpartum and is associated with massive and concerted increases in milk volume and the rates of synthesis and / or secretion of almost all the components of mature milk including, but not limited to, lactose, protein (mainly casein), lipid, calcium, glucose and free phosphate. The secretions of these substances are tightly synchronized by the common activation switch and mechanisms for coordinating their activities.

Milk is synthesized and released into the mammary acini and ductal-system, although it can be stored for up 48h before the rate of milk synthesis and secretion begins to decrease. As long as milk is removed regularly from the mammary gland, the alveolar cells continue to secrete milk. The accumulation of milk in the ductoacinar lumina and within the cytoplasm of the lactogenic epithelial cells that occurs after weaning has an inhibitory effect on further milk synthesis. Once lactation is established by the process of **lactogenesis**, it must be maintained. The maintenance of lactation or the enhancement of established lactation is called **galactopoiesis**.

Hormonal regulation of lactation, secretory activation and transport processes of milk: Lactation begins when the maternal mammary gland, primed by long exposure to high levels of prolactin, estrogen, and progesterone, is subjected to sudden withdrawal of the latter two placental hormones. Thereafter, lactation proceeds in an environment of relatively high (although declining) prolactin and low estrogen and progesterone. A low level of estrogen in the circulation stimulates the pituitary to increase its output of prolactin. The fall in progesterone at parturition is required for the onset of milk secretion, and activation of milk protein gene expression and biosynthetic processes. In human it is known to **the** removal of the placenta, the source of progesterone is necessary for the initiation of milk secretion, and retention of placental fragments with the potential to secrete progesterone delays lactation.

Although estrogen prepares the breast for eventual milk formations but inhibit lactations. Like estrogen, progesterone inhibits lactation and antagonizes inductive action of glucocorticoids, and/or prolactin, on tight junction formation. Thus, estrogen together with progesterone affects survival of alveolar cells by paracellular transport and the maintenance of lactation. Prolactin along with adrenal corticoids play important role in lactogenesis. Prolactin perhaps being necessary for the expression of the synthetic activities of the alveolar

cells and adrenal corticoids probably influencing through the supply of milk precursors. Prolactin also activates exocytosis and lipid secretion, amino acid transport, glucose transport and monovalent ion transport along with other hormones. Prolactin also controls many steps of milk secretion, including the synthesis of the milk proteins casein and α -lactalbumin.

V. Milk ejection

Milk ejection refers to the active process by which milk stored within the mammary gland is actively ejected and delivered to the sucking infant. This process is also referred to as “milk letdown” or “the draft”. The newly secreted milk is stored within the mammary alveoli or in specially modified parts of the duct system. Milk within the alveoli cannot be removed by sucking due to surface tension, but has to be actively ejected by the action of special contractile cells called myoepithelial cells. The process of milk ejection (**Galactokinesis**) is therefore different from the process of milk secretion (**Galactopoiesis**). Milk ejection is a **neuroendocrine reflex** processes referred to as “the milk-ejection reflex” (**Fig. 4**). The afferent component of the reflex arc is neuronal, whereas the efferent limb is hormonal. When the receptors in the teats are stimulated, signals (milking / suckling stimulus) are carried to the brain terminating in the supraoptic and paraventricular nuclei of the hypothalamus. In these nuclei oxytocin is synthesized and then transported to the neurohypophysis from which it is released into the circulation. Oxytocin circulates to the mammary gland where it causes contraction of the myoepithelial cells and ejection of the milk.

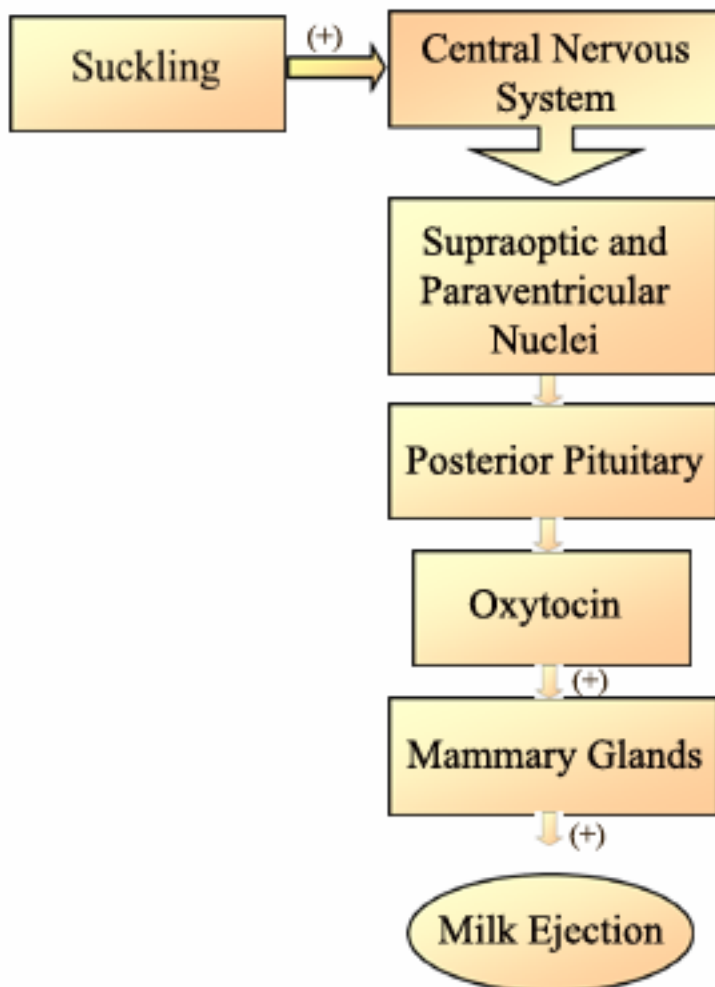


Fig. 4 The Milk-Ejection Reflex

Besides oxytocin, prolactin and vasopressin are also released by suckling or milking that is transmitted via dorsal nerve roots to the hypothalamus. Release of oxytocin and prolactin is independent, and one may be liberated without the other. Vasopressin is important for milk ejection in dehydrated ruminants living in desert conditions. Beside these hormones, cortisol is released during milk ejection. The cortisol has a general effect on metabolisms in lactating animal and required to maintain the secretory activity of the epithelial cells.

VI. Milk composition

Milk is the product secreted by the mammary gland during lactation and is a white liquid, containing proteins, sugar, lipids, water, lactose, fat, minerals, and vitamins. Milk composition varies among species, strains or breeds within a species, stage of lactation, even during a milking. **Colostrum** is the term used for the first secretion from the mammary gland after parturition. Colostrum is a hyaline, eosinophilic, proteinaceous, low fat secretion. It is composed of 87% water, 1.3% fat, 3.2% lactose, 7.9% protein (principally alpha lactalbumin,

lactoferrin, and immunoglobulin A), and 0.6% mineral containing ash. In woman 2-3 days after parturition with the decline in estrogen and progesterone levels in maternal plasma, the fat content of the mammary secretion increases. Human milk is isotonic with plasma. It has the following composition: 87% water, 4.5% fat, 6.8% lactose, 0.9% casein, 0.4% lactalbumin and other proteins, and 0.2% mineral-containing ash. Colostrum generally has higher concentrations of immunoglobulins (antibodies) than mature milk. The exact composition of milk widely varies among the mammalian species (**Table 1**). The composition of cow milk is 87% water, 3.7% fat, 5% lactose, 3% casein, 1% lactalbumin and other proteins, and high percentage of mineral-containing ashes.

The characterization of the caseins of cow milk recognized four major casein components: αS_1 -, αS_2 -, β -, and κ -casein. Caseins, studied by protein and gene sequencing have been found to be homologous in all species examined to date. The αS_1 -, αS_2 -, and β -casein are precipitated by calcium at the concentrations found in most milk. However, κ -casein is not only soluble in Ca^{2+} but also interacts with and stabilizes the other calcium caseinates to initiate formation of the stable colloidal state. The casein micelle is composed of spherical aggregates of the individual caseins (submicelles) that are held together by calcium phosphate linkages. The major differences between the ruminant milk and human milk arise from changes in the protein and lactose contents. Human milk has lower casein but higher lactose content. The lower casein content is also reflected in the lower ash content. The total caloric value of the ruminant and human milks are approximately equivalent.

Protective factors in milk include such antimicrobial proteins as **lactoferrin** (binds iron required for bacterial growth; also binds directly to microorganisms), **lysozyme** (glycosidase enzyme that hydrolyzes bacterial cell walls), **lactoperoxidase** (in the presence of hydrogen peroxide generated by bacterial action, it will oxidize bacterial components), and **secretory immunoglobulin** (specifically **IgA** and **IgM**; secreted in many exocrine glands). These types of mucosal secretory factors are extremely effective in protecting tissues exposed to the external environment (skin, eyes, mouth, etc), especially when they are present together and their activities synergize. In fact, milk contains many of these protective components. The specific set of antimicrobial components and how effective they are is dependent on the species. For example: Cow milk normally has low lactoferrin, low lysozyme activity, and low IgA, although lactoperoxidase activity is high. In contrast, human milk is normally high in lactoferrin, high in lysozyme activity and high in IgA and has a higher antimicrobial activity overall compared with cow milk, although human milk is low in lactoperoxidase activity.

Importance of milk: Milk is of paramount importance to survival, proper development, and vigorous growth of the neonate. At birth, the neonate is suddenly exposed to a potentially cold and dry environment. It is exposed to many potentially harmful organisms, ranging from disease-causing microorganisms to large carnivorous predators in the wild. The process of being born also involves a dramatic switch from fetal metabolism and growth to neonate metabolism and growth. The neonate undergoes rapid changes in metabolism during the initial days after birth. Thus milk is the only supply of the water, organic nutrients, and minerals except air to which the neonate has access. It has a high caloric value and generally is balanced for the nutrient needs of the rapidly developing young of that species. For an infant, about one litre of human milk (about daily yield of mother) supplied a good balance of protein, calcium and calories. Both cow and goat milks are superabundant in nutritional content for infants. About one litre of cow milk would supply much of an adult person's protein and calcium requirements. Colostrum (the first milk taken from the mammary gland after parturition) and mature milk also contain nonnutrient substances (such as antibodies and bioactive factors) that may be important for growth, development, and survival of the

neonate. Thus milk provides a balanced nutrient source for the young, as well as a range of protective factors and bioactive factors.

VII. Lactation and Fertility

Besides providing nutrition and immunological protection for young mammals, the other most important function of lactation is spacing births. The stimulus of suckling leads to a period of lactational **amenorrhea**, and acts as a natural contraceptive. **Depending on the species, suckling suppresses the implantation of a fertilized egg or ovulation.** The mechanism involved in lactational **control of fertility** are still not clearly known, but it is suggested that suckling disrupts the normal pattern of pulsatile release of gonadotropin-releasing hormone in the hypothalamus, resulting in a reduction in the secretion of luteinizing hormone, the hormone responsible for ovulation. With the result, young are not born until after the weaning of the previous dependent offspring. The effectiveness of lactational amenorrhea as a method in human family planning has been much disputed, but recent studies confirm that women who are fully breast-feeding and do not have menses are at less than 2% risk of becoming pregnant within the 6 months after the birth of a child. Breast-feeding prevents more pregnancies worldwide than any other contraceptive methods.

Conclusions

Lactation and reproductive processes are intimately intertwined in mammals. Reproduction and lactation are part of the same overall process. The ultimate objective of reproduction is to produce the next generation of reproductively viable offspring prior to birth. The fetus is in the sterile, protected, moist, and warm environment of the uterus. The fetus is provided with all necessary nutrients, oxygen, and developmental factors that it needs to grow and develop. All of its metabolic, digestive, and sensory functions are geared toward this *in utero* environment. The mammalian species have relatively large and complex brains and complex body systems. Therefore, development of the offspring takes a fairly long period of time. Part of this development occurs intrauterine during gestation. However, in mammals much of this development continues after birth and is extra-uterine development. The female mammal (mother) makes a large metabolic investment in the early development of the offspring. A newborn mammal is not sufficiently developed digestively to get dietary value from exogenous food, etc. In that sense, the newborn mammal is still very much dependent on the mother for provision of a nutrient supply that matches its digestive capabilities. This nutrient supply is **maintained through milk**. This investment continues until the offspring is metabolically independent from the mother. Lactation is a continuation of the metabolic investment of the mother and is the most energetically demanding part of reproduction. During pregnancy, the interrelationships between mother and offspring occur in uterus. After birth, the metabolic interrelationships occur outside of the uterus via production of milk by the mammary gland. During lactation, the mother undergoes substantial changes in metabolism to account for the increased demands of milk synthesis. From this perspective, the mammary gland is continuing the function of the placental-uterine unit in providing nutrient and protective factors for the offspring. Thus it is critical for the newborn mammal to be able to obtain milk from the mother soon after birth. The dynamic processes of parturition and initiation of lactation are closely coordinated in the mother.

In the absence of successful lactation (or in the absence of human intervention) the neonate will not survive after birth even with optimal success of all the complex processes involved in estrous cycles, conception, pregnancy, fetal development, and parturition. **It will only lead to a failure of the reproductive process.**