

# Hormones affecting the breast

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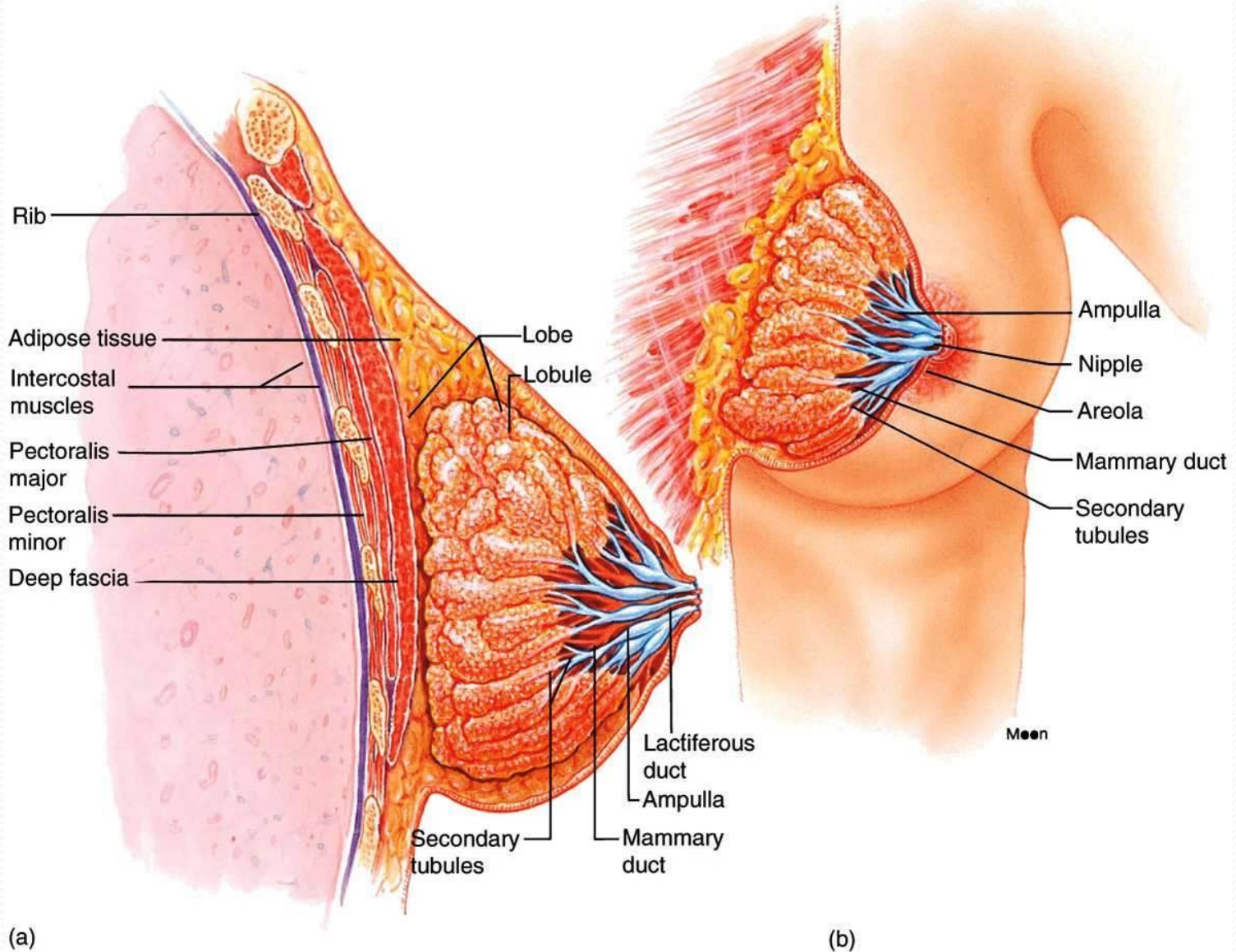
# Objectives

- Physiological anatomy of the breast
- Physiological changes during breast development (**Mamogenesis**)
- Physiological changes during lactation (**Lactogenesis**) and their physiological action
- Phases of lactogenesis.
- Physiological changes during **Galactopoeisis**.
- Endocrine and autocrine control.
- **Involution** (the termination of milk production).

# Small group activity

- What is the structure of human breast?





(a)

(b)



### A LACTATING BREAST

Adipose tissue

Enlarged  
secretory lobules

Elaborated  
duct system

Lactiferous  
duct

Ampulla

### B LOBULE

Secretory lobule

Alveoli

### C ALVEOLUS

Ductule

Milk lipids

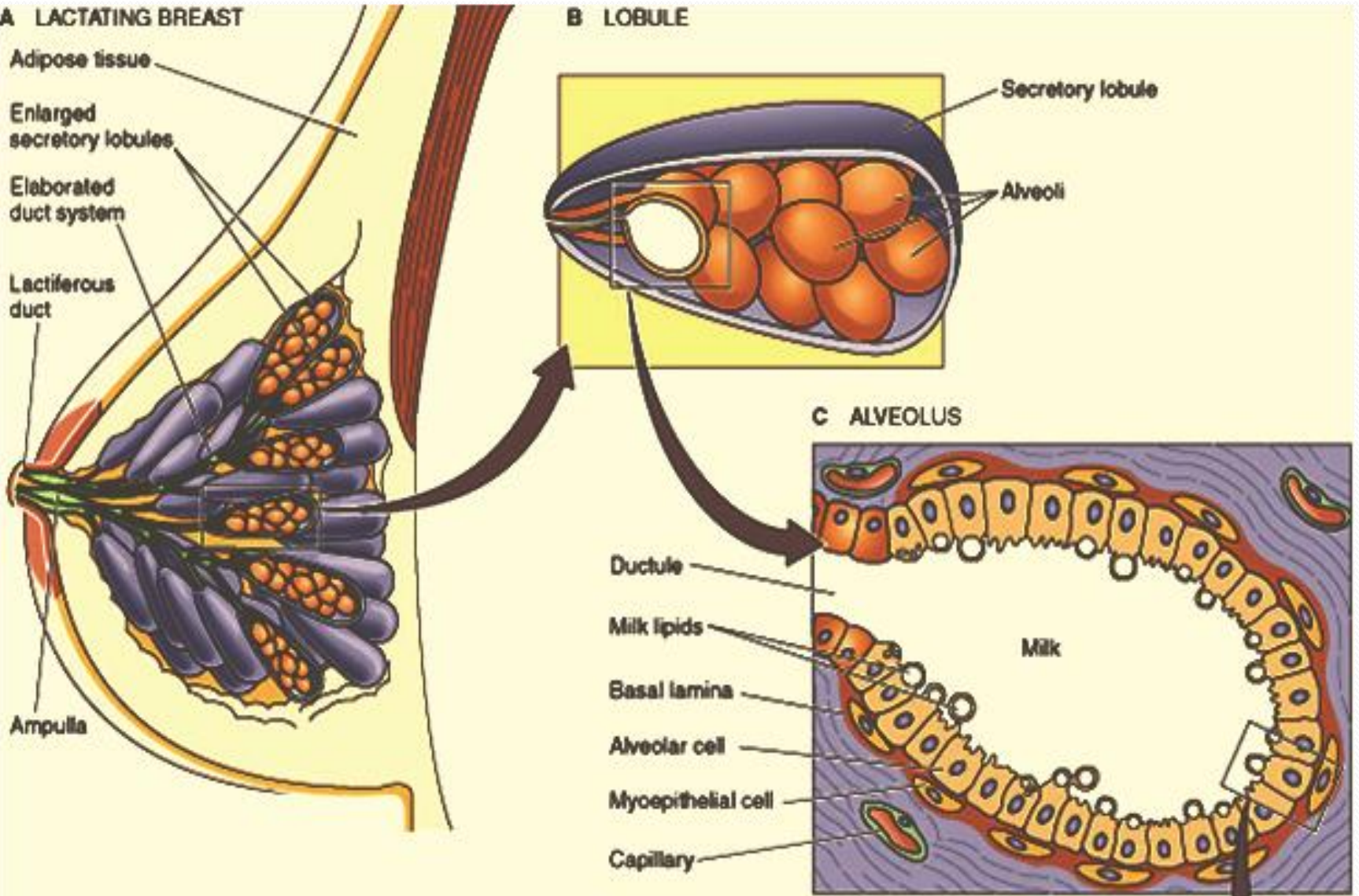
Basal lamina

Alveolar cell

Myoepithelial cell

Capillary

Milk



# Small group activity

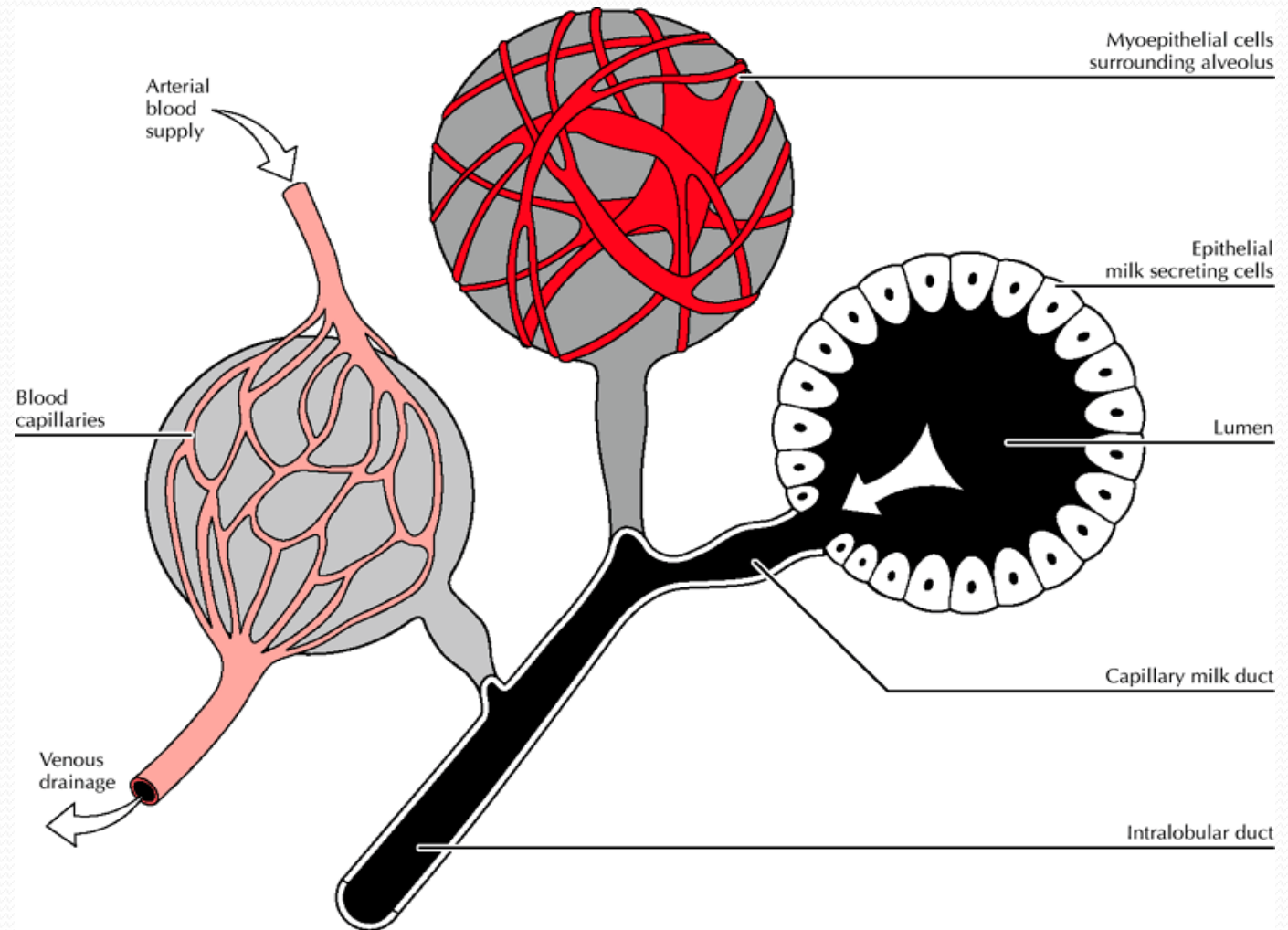
- Where does milk come from?



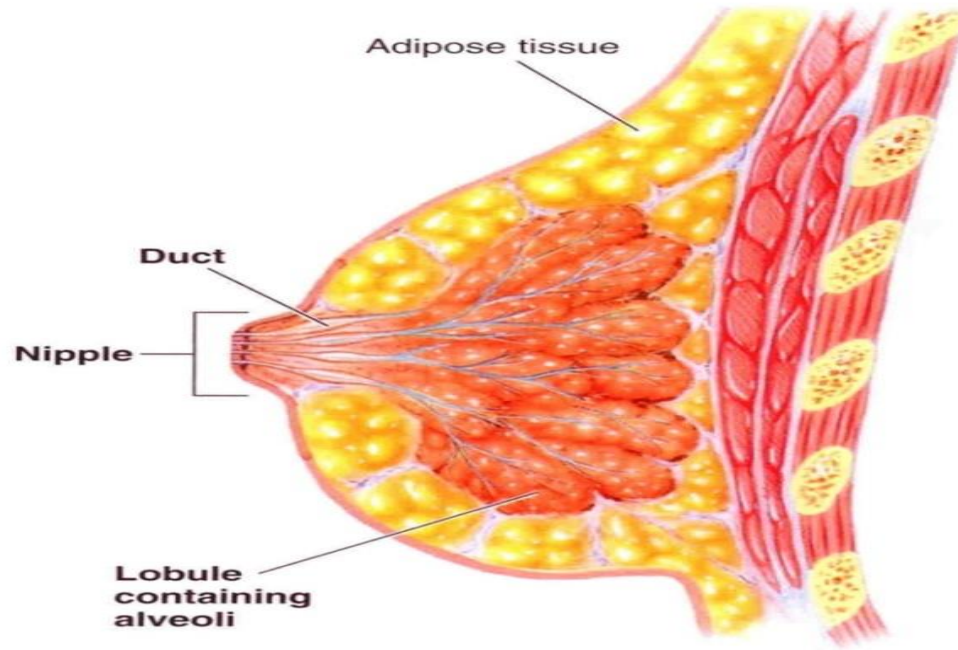
# Theories

- **Uterine milk theory:** Vessel connecting the uterus to the breast (diversion of menstrual blood to the breast)
- **Chyle theory:** Milk is derived directly from chyle (milky fluid of emulsified fat absorbed from the intestinal tract into lymphatic system).
- **Synthesis theory:** Milk is formed from substrates carried to the gland in the blood

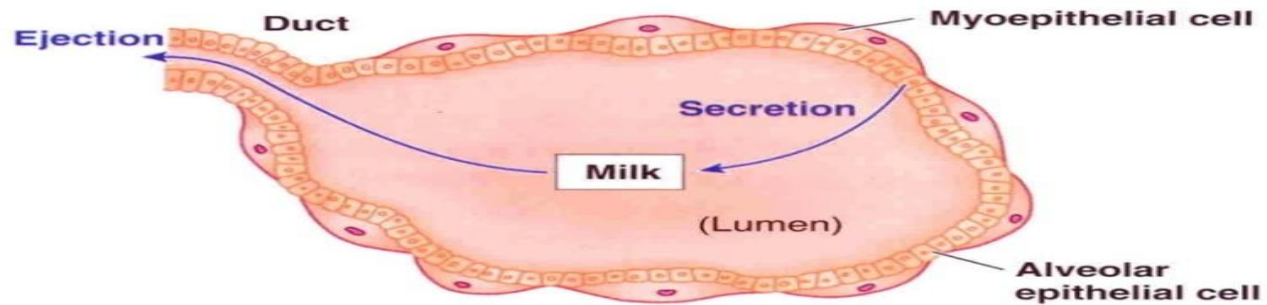
# Where does milk come from?







(a) Internal structure of mammary gland, lateral view



(b) Alveolus within mammary gland

- **FIGURE 20-34 Mammary gland anatomy.** The alveolar epithelial cells secrete milk into the lumen. Contraction of the surrounding myoepithelial cells ejects the secreted milk out through the duct.

# Mamogenesis

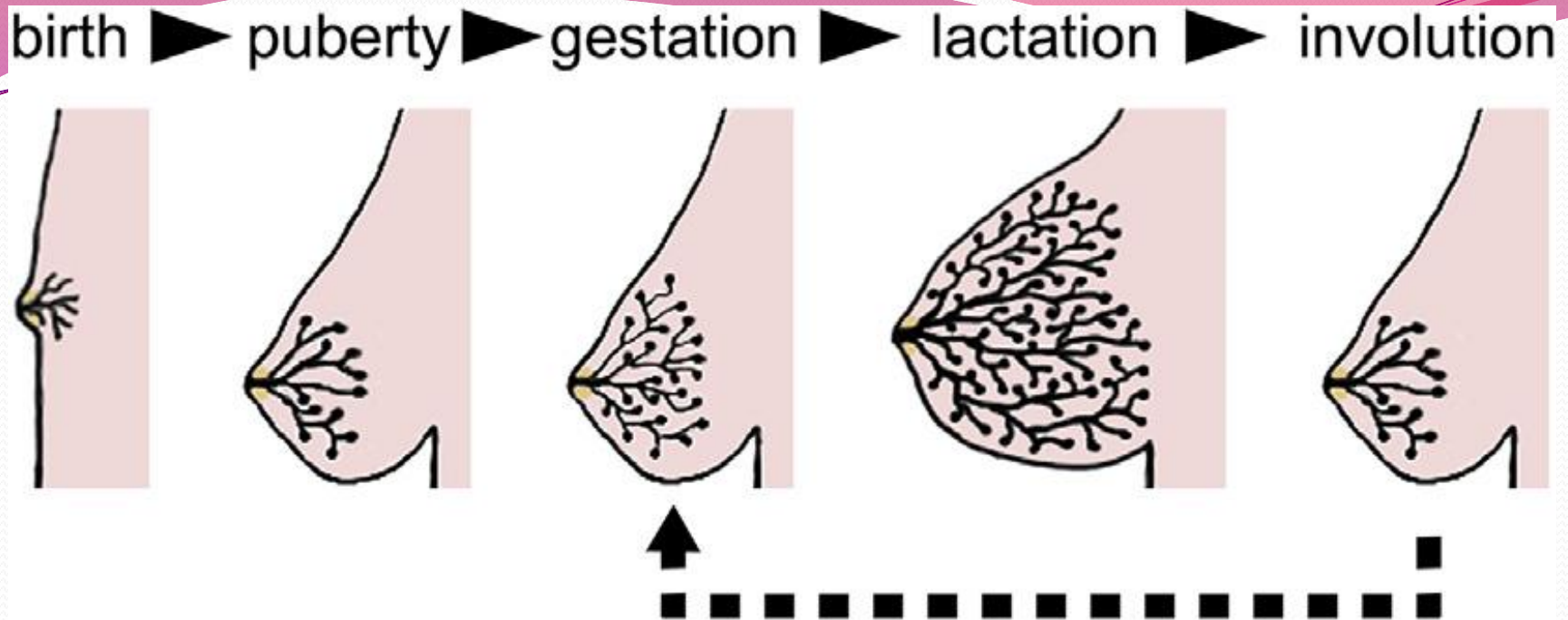
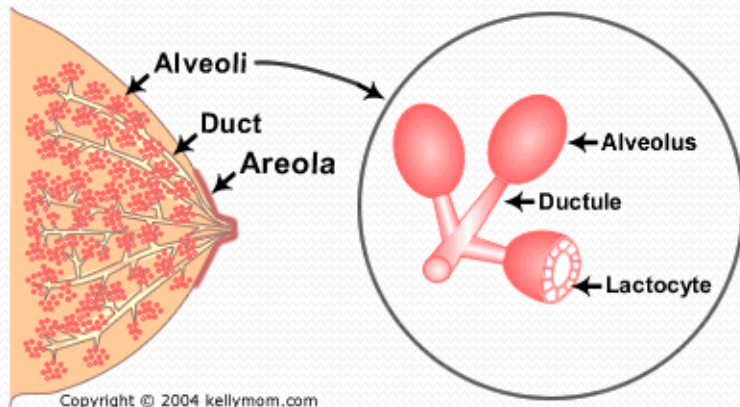


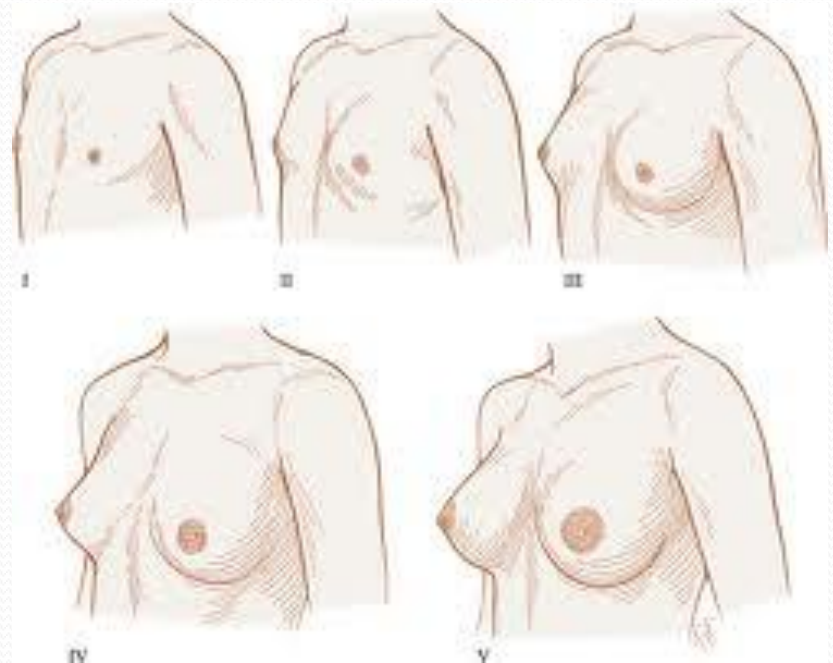
Fig. 1. Mammary gland development. The postnatal development of female mammary tissue occurs in several steps regulated by hormones. **At birth**, the mammary epithelium consists of limited ducts. **At puberty**, high levels of circulating hormones stimulate both the proliferation of the mammary epithelial cells (MECs) and the enlargement of the surrounding fat pad. At the onset of **pregnancy**, epithelial ducts elongate, branch and alveoli develop. During **lactation**, the mammary epithelium reach its maximal development containing numerous alveoli, which produce huge amounts of milk. Upon **weaning**, milk production ceases, the mammary alveoli regress (**involution**) and the mammary epithelium returns to a non-pregnant state.

# Breast development (mamogenesis)

- During puberty
  - Estrogen stimulate proliferation of ducts and deposition of fat
  - Progesterone stimulate development of lobules

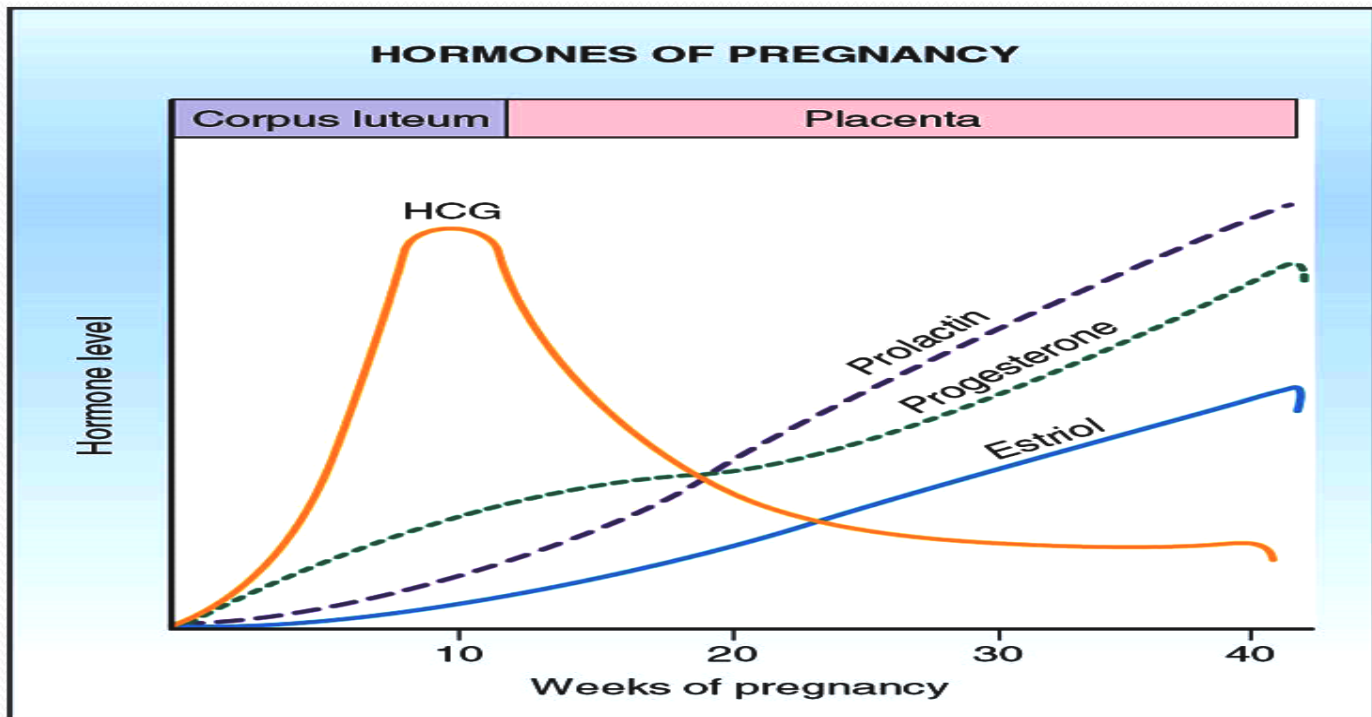


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# Breast development (mamogenesis)

- During pregnancy
  - Complete development of glandular tissue

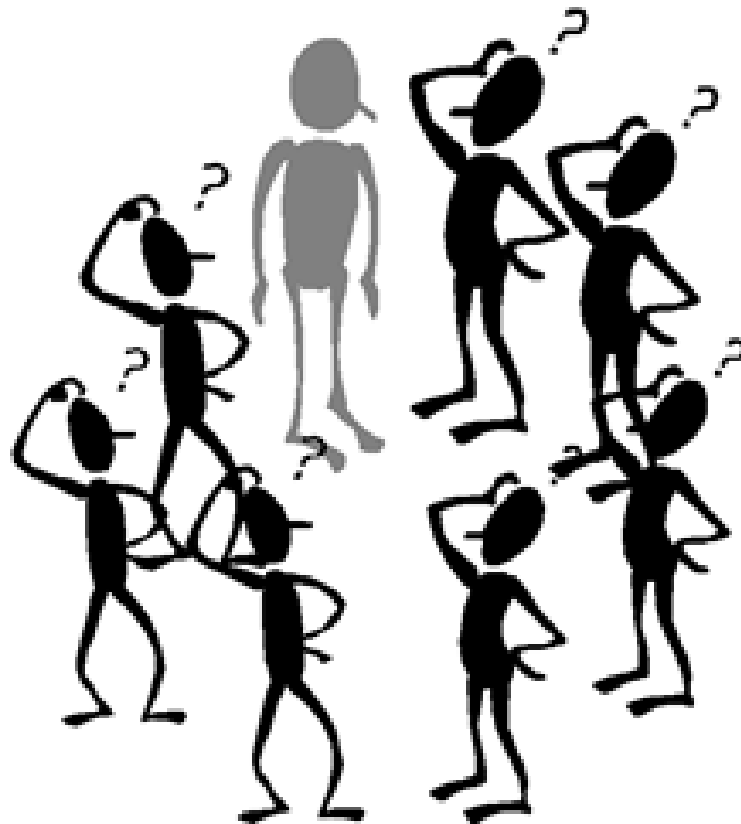




# Breast development (mamogenesis)

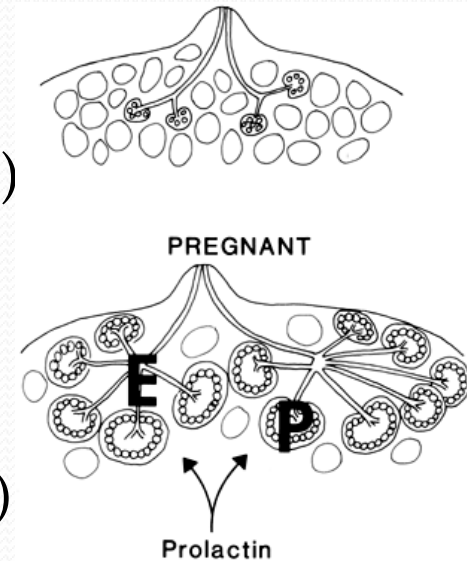
- Endocrine system plays a major role in synchronizing development (mamogenesis) and function (lactogenesis) of mammary gland with **reproduction**
- Three categories of hormones:
  - **Reproductive hormones** (endocrine)
    - Estrogen, progesterone, prolactin, oxytocin and hPL
  - **Metabolic hormones** (endocrine)
    - GH, corticosteroids, thyroxin, PTH and insulin
  - **Mammary hormones** (autocrine)
    - GH, prolactin, parathyroid hormone-related protein (PTHrP) and leptin

# Size of the breast & lactation



# Breast development (mammogenesis)

- **Reproductive hormones** (direct effect)
  - **Estrogen** (placenta)
    - Growth & branching of ductal system (with GH)
    - Fat deposition in the stroma
  - **Progesterone** (placenta)
    - Growth of lobule-alveolar system (budding of alveoli and secretory changes in epithelial cells )



Although **estrogen** and **progesterone** are essential for **physical development** of the breasts, they **inhibit** actual secretion of milk

# Breast development (mamogenesis)

- **Prolactin** (anterior pituitary)
  - Its level increases during pregnancy (10-20 times)
  - Its main function is milk production
  - Sudden drop in E & P after delivery allows milk production
  - It is controlled mainly by hypothalamic hormone
    - **PIH (Dopamine)**
- **Human placental lactogen** (placenta)
  - Facilitate mammogenesis
  - Delay milk production

# Lactogenesis



# Lactogenesis

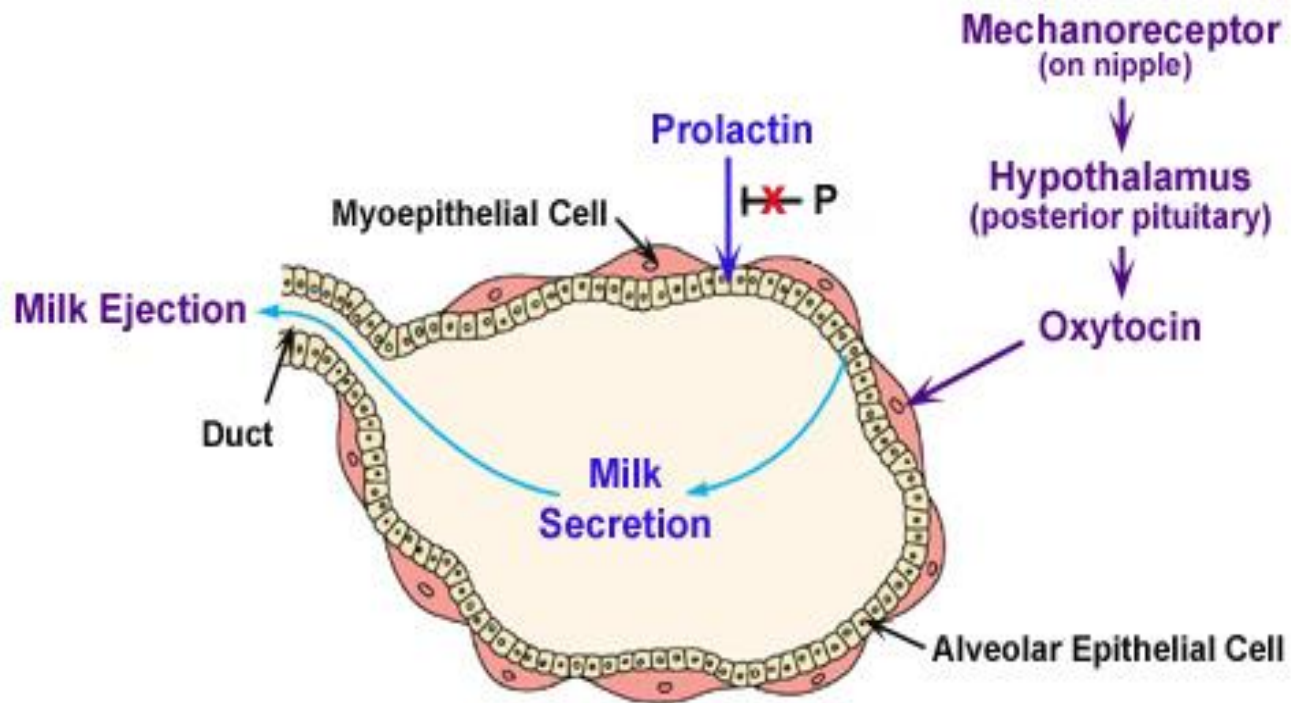
- Lactogenesis: cellular changes by which mammary epithelial cells are converted from a non secretory state to a secretory state: 2 stages
- **Lactogenesis 1**: (Cytologic and enzymatic differentiation of alveolar epithelial cells).
  - Starts in **mid pregnancy** and characterized by expression of many genes involved in synthesis of milk components (increase in the uptake transport systems for amino acids, glucose, and calcium required for milk synthesis).
  - Hormones involved:
    1. Progesterone (suppresses milk secretion)
    2. **Prolactin** and/or placental lactogen
    3. Growth hormone
    4. Glucocorticoids (**Cortisol**)

# Lactogenesis

- **Lactogenesis 2**: (Copious secretion of all milk components).
  - Around parturition withdrawal of **progesterone** + high level of **prolactin** leads to:
    - Further increase in expression of milk protein genes
    - Glands absorb increased quantities of metabolic substrates from the blood.
    - Movement of cytoplasmic lipid droplets and casein into alveolar Lumina
    - Transfer of immunoglobulins
    - Secretion of colostrum followed by milk

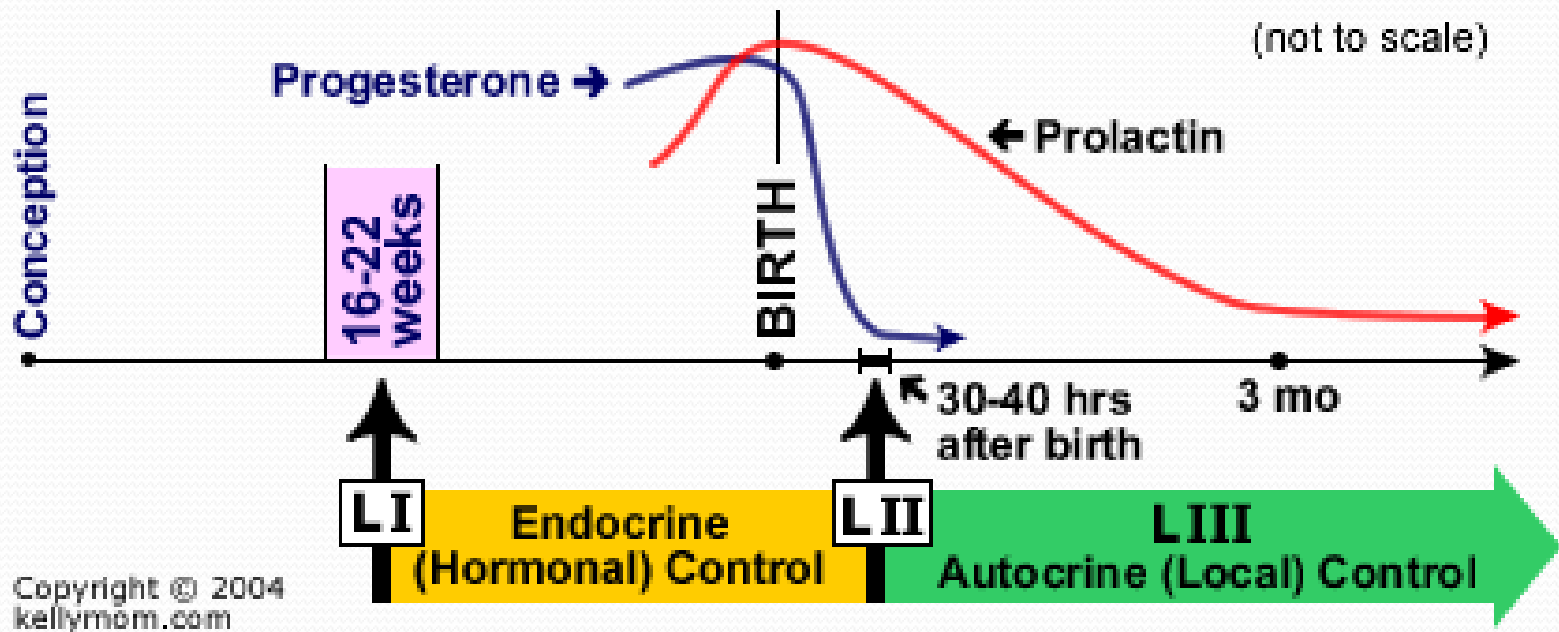
# Lactogenesis

- Lactogenesis 2:
  - Suckling stimulates further increase in expression of genes involved in milk secretion with expansion of alveolar epithelium
  - Lactation is maintained by removal of milk
  - 2 hormones involved
    - Prolactin (milk production)
    - Oxytocin (milk let-down)



**Alveolus of Mammary Gland**

# Stages of lactogenesis



Mamogenesis

Lactogenesis

Galctopoesis





# Hormonal regulation of lactogenesis

- Metabolic hormones (direct effect)
  - **GH**
    - Can be produced locally
    - Its secretion is stimulated by progesterone
    - Increases production of IGF-1 by the liver and locally.
    - Mediate cell survival and ductal growth
  - **Corticosteroids**
    - Increases during pregnancy (five fold)
    - Involved in breast development (permissive action on milk protein synthesis)

# Hormonal regulation of lactogenesis

- **Thyroxin**

- Essential for milk production
- Thyroxin & TSH level decreases during lactation
- TRH increases leading to stimulation of PRL (nasal administration to treat inadequate lactation )

- **Insulin**

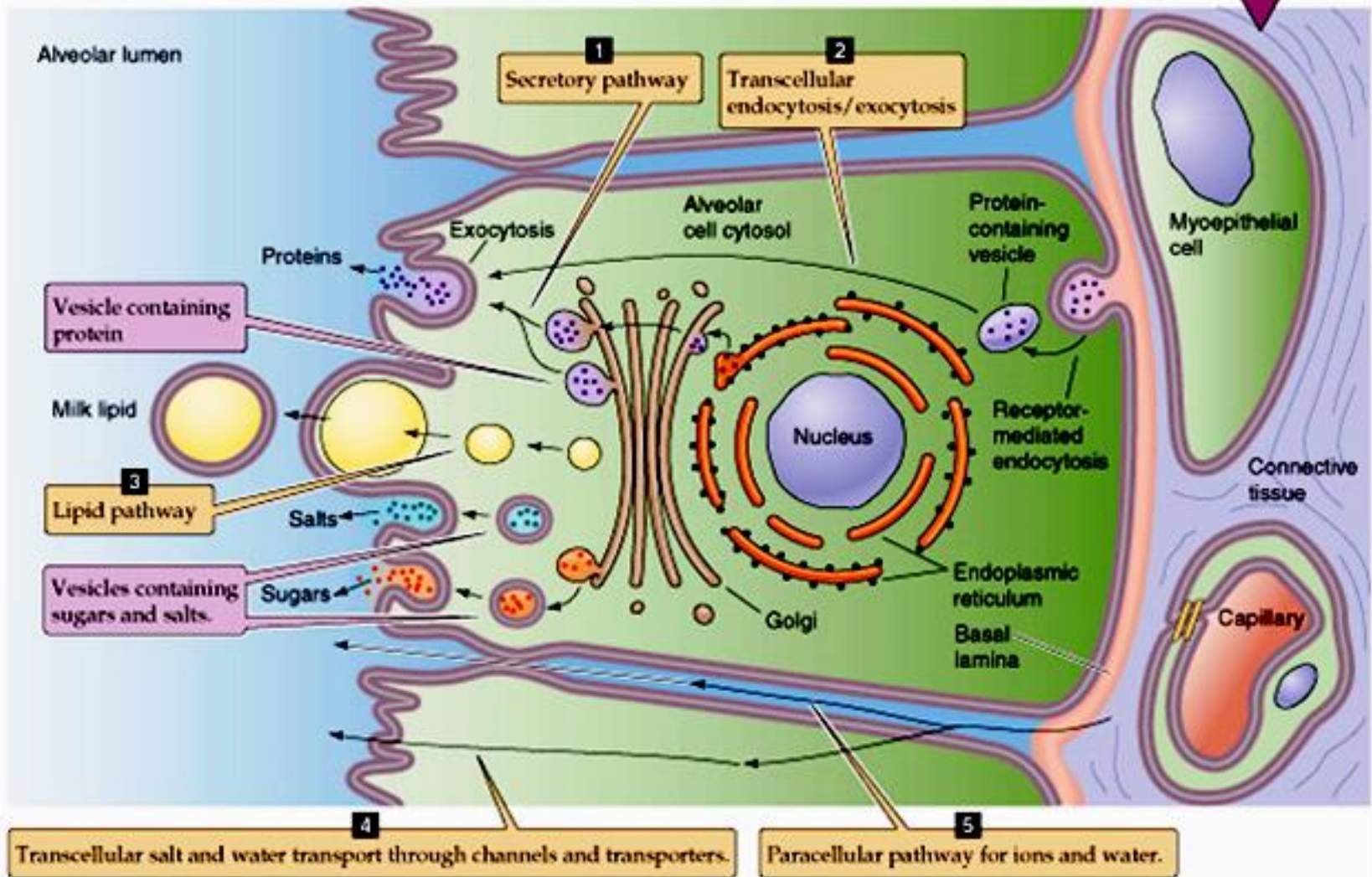
- Low during lactation
- Shunt of nutrients from storage depots to milk synthesis

# Hormonal regulation of lactogenesis

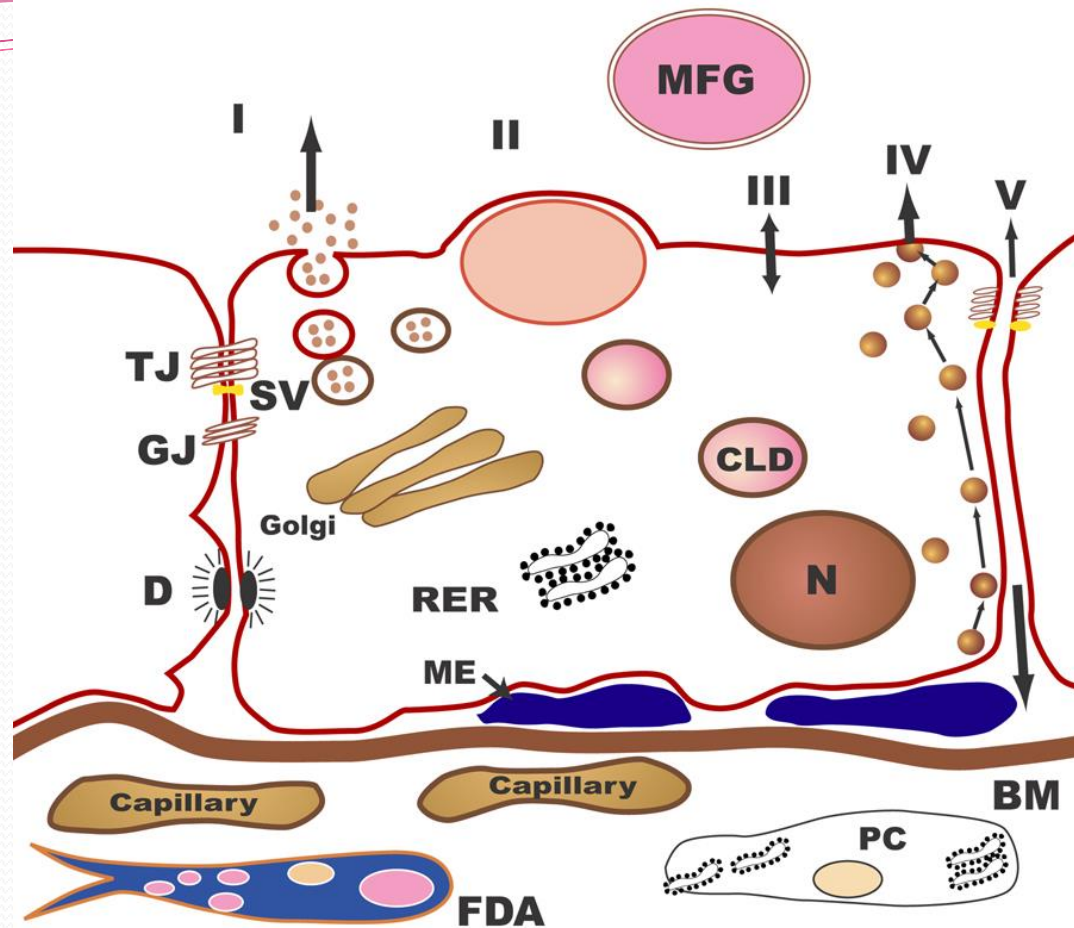
- Mammary hormones
  - **GH**
    - Progesterone stimulates its secretion
  - **Leptin**
    - Increases during pregnancy (increase adipose tissue)
    - Decreases with lactation
  - **PTHrP**
    - Increases during lactation
    - Mobilizes bone calcium
    - Increase in alkaline phosphatase



D SECRETORY EPITHELIAL CELL







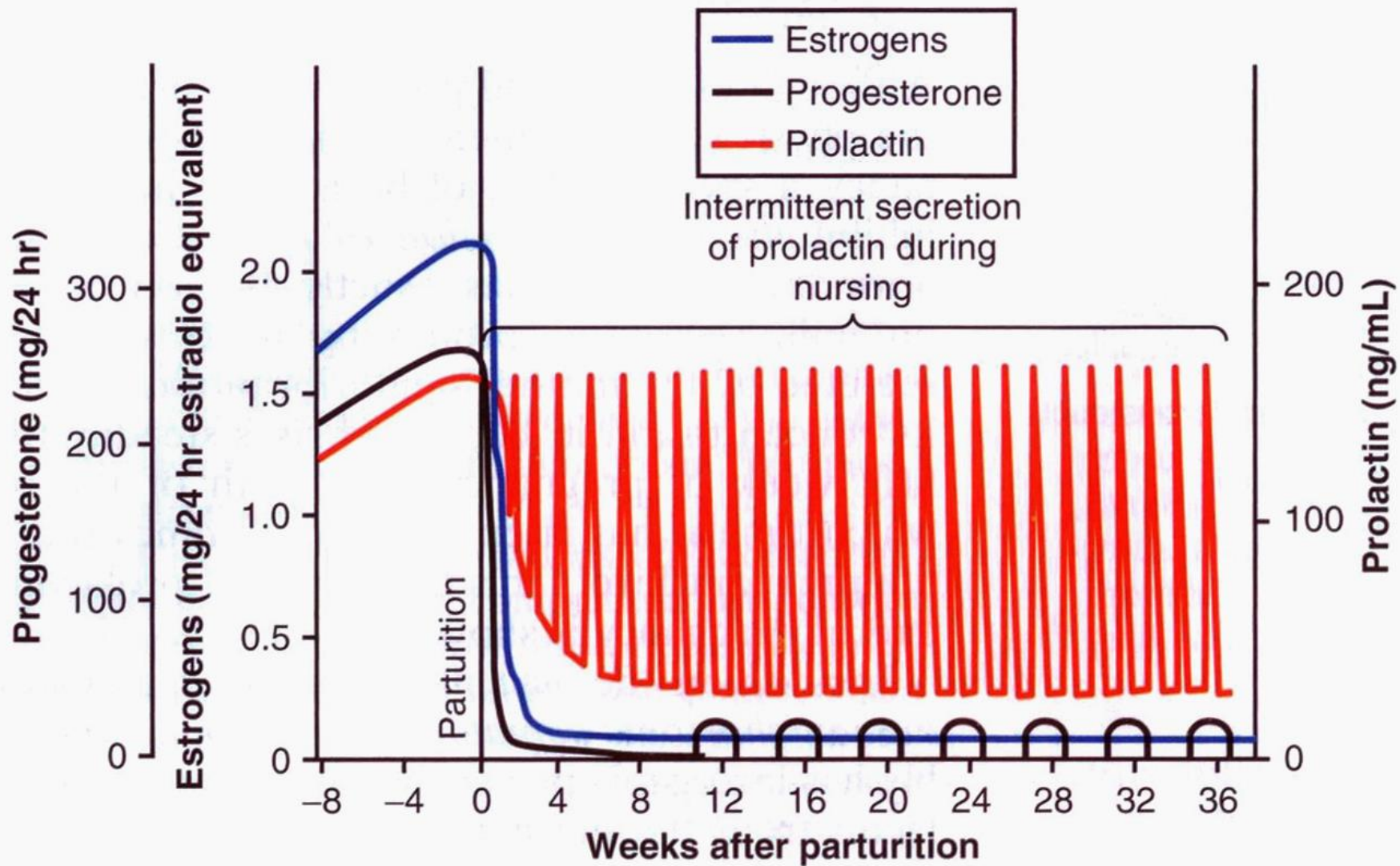
The pathways for milk secretion and synthesis by the mammary epithelial cell. I: Exocytosis of milk protein, lactose, and other components of the aqueous phase in Golgi-derived secretory vesicles. II: Milk fat secretion via the milk fat globule. III: Direct movement of mono valent ions, water, and glucose across the apical membrane of the cell. IV: Transcytosis of components of the interstitial space. V: The paracellular pathway for plasma components and leukocytes. Pathway V is open only during pregnancy, involution, and in inflammatory states such as mastitis. SV = Secretory vesicle; RER = Rough endoplasmic reticulum; BM = Basement membrane; MFG = Milk fat globule; CLD = Cytoplasmic lipid droplet; N = Nucleus; PC = Plasma cell; FDA = Fat-depleted adipocyte; TJ = Tight junction; GJ = Gap junction; D = Desmosome; ME = Myoepithelial cell.



# Galactopoeisis

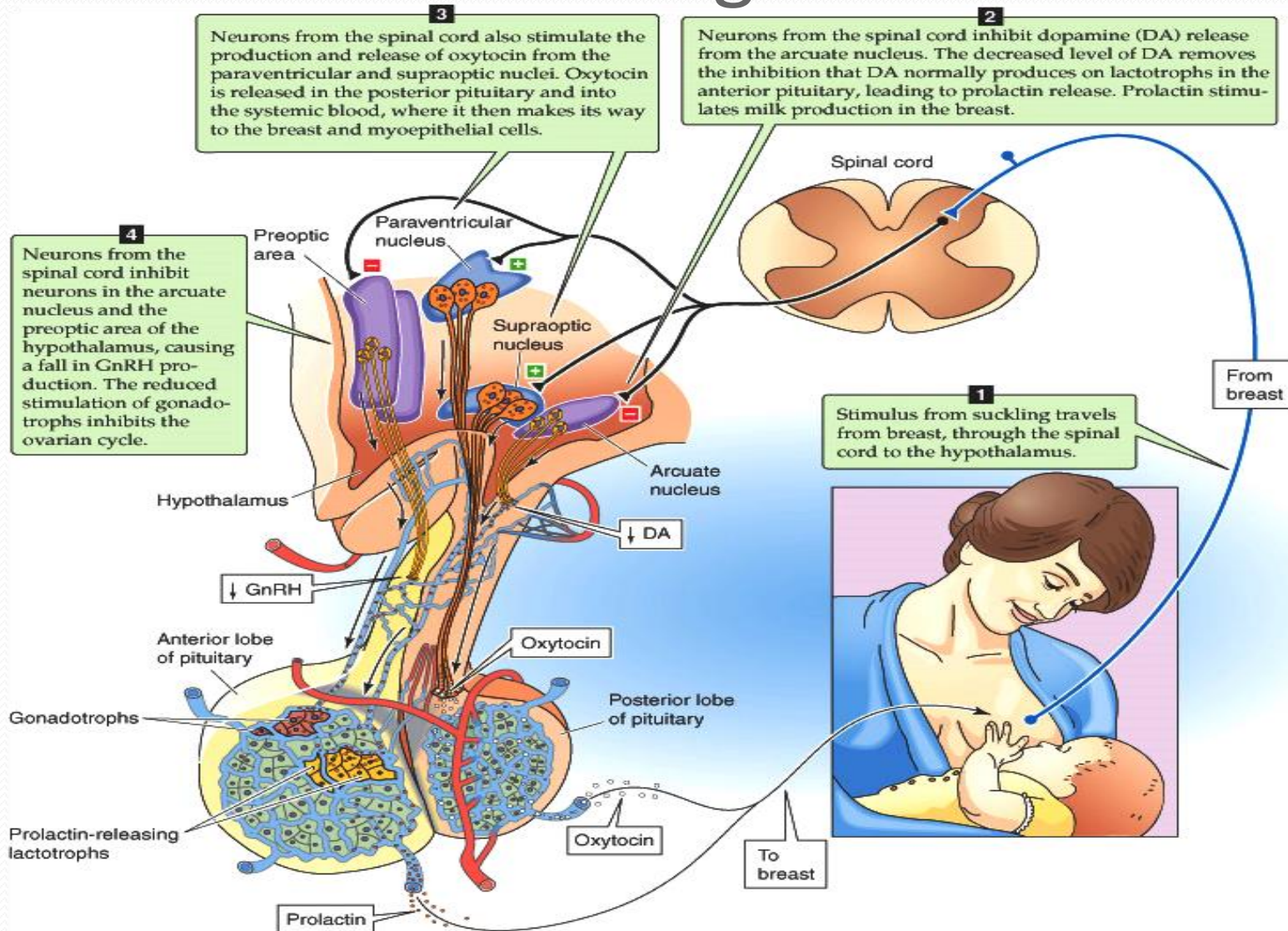
- **Definition:** Galactopoeisis is defined as the maintenance of lactation once lactation has been established.
- **Role of Hormones**
  - **Prolactin:** milking-induced surge is a direct link between the act of nursing (or milk removal) and the galactopoeitic hormones involved in maintaining lactation.
  - **Growth Hormone:** support increase in synthesis of lactose, protein, and fat in the mammary gland
  - **Glucocorticoids:** galactopoeitic in physiological doses

- **Thyroid Hormones:** galactopoeitic
- **Ovarian Hormones :**
  - **Estrogen** in very low doses is galactopoietic
  - **Progesterone** alone has no effect on galactopoeisis because there are no progesterone receptors in the mammary gland during lactation





# Suckling reflex



# Suckling reflex

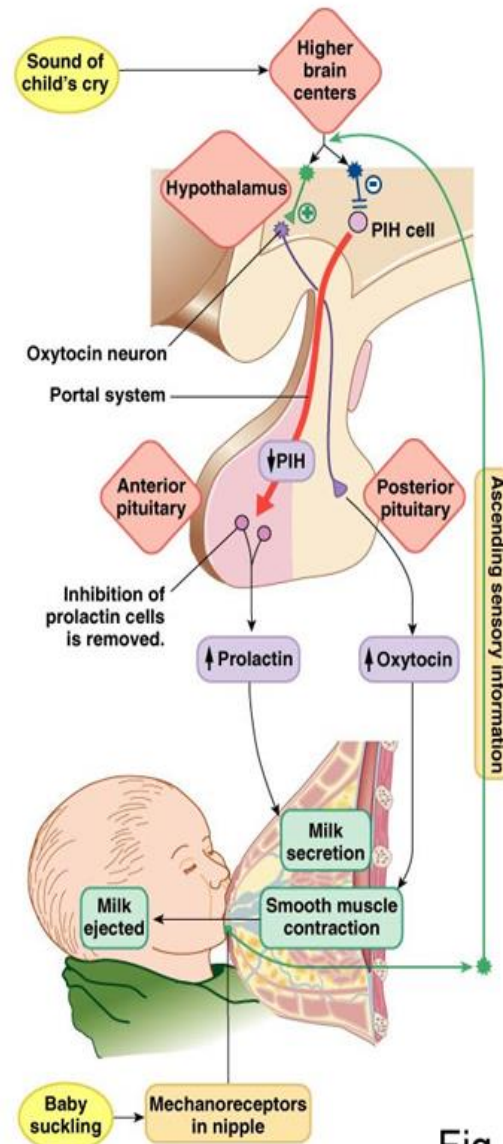


Fig. 26-23

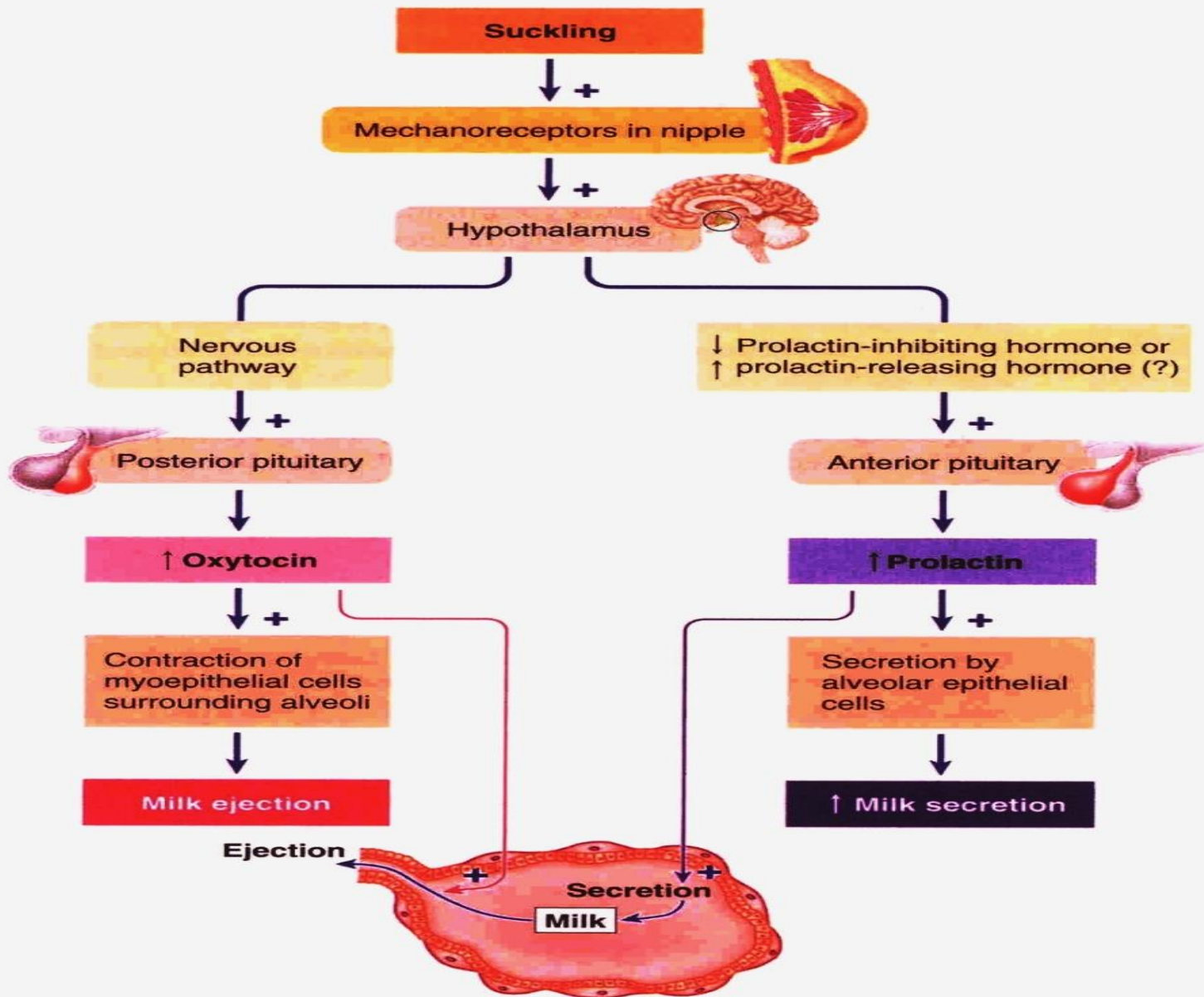


- Milk production is a

"use it or lose it" process.

The more often and effectively the baby nurses, the more milk will be produced

- Milk production <100 ml/day in day 1 postpartum
- Milk production by day 3 reaches 500 ml/day
- Milk composition changes dramatically( $\downarrow$ Na<sup>+</sup>& Cl<sup>-</sup>) due to closure of tight junctions that block paracellular pathway



● **FIGURE 20-35 Suckling reflexes.**

- يقول تعالى (والوالدات يرضعن أولادهن حولين كاملين لمن أراد أن يتم الرضاعة) [البقرة . 233]:
- وفي إشارة علمية دقيقة أخرى للقرآن الكريم نراه يحدد مدة الرضاعة بما يقرب من الحولين ، في الآية رقم (14) في سورة لقمان : (ووصينا الإنسان بوالديه حملته أمه وهنا على وهن وفصاله في عامين) ،
- والآية (15) في سورة الأحقاف : [حملته أمه كرهاً ووضعته كرهاً وحمله وفصاله ثلاثون شهراً]
- ويفهم من هذا أن إرضاع الحولين ليس حتماً ، بل هو التمام ، ويجوز الاقتصار على ما دونه ، كما أشارت الأحكام الإسلامية الخاصة بالرضاعة إلى ذلك ، اعتماداً على قوله تعالى (فإن أراداً فصلاً عن تراضٍ منهما وتشاورٍ فلا جناح عليهما) الآية 233 البقرة .

# AAP Recommendations

- Exclusive breast feeding for the first six months of life
- Continued breast feeding for at least one year, 'As long as is desired by mother and child'



# Failure of breast feeding



قَالَ إِنَّمَا أَشْكُو بَثِّي وَخُزْنِي إِلَى  
اللَّهِ وَأَعْلَمُ مِنَ اللَّهِ مَا لَا تَعْلَمُونَ

يوسف : ٨٦

