Reproductive Physiology

Lecture 8

Hormones affecting female breast

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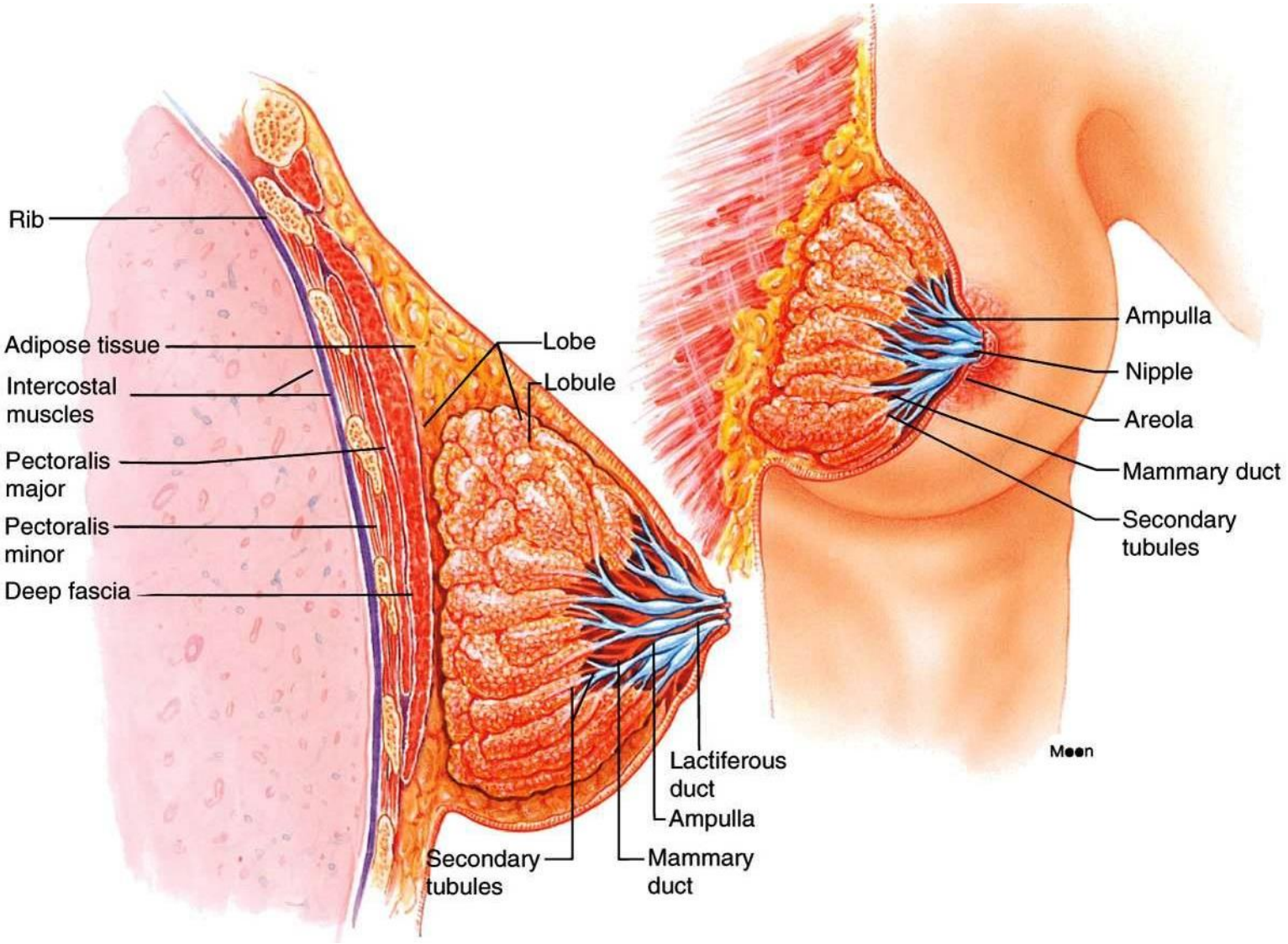
Objectives

By the end of this lecture, you should be able to:

- Know the physiologic anatomy of the breast.
- Describe the physiological changes that occur in the breast during mammogenesis, lactogenesis, and galactopoeisis and the hormones involved.
- Recognize the phases of lactogenesis.
- Describe the endocrine and autocrine control of lactation.
- Explain the physiological basis of suckling reflex and its role in lactation.

What is the structure of breast?

The structure of the **breast** and **mammary glands**



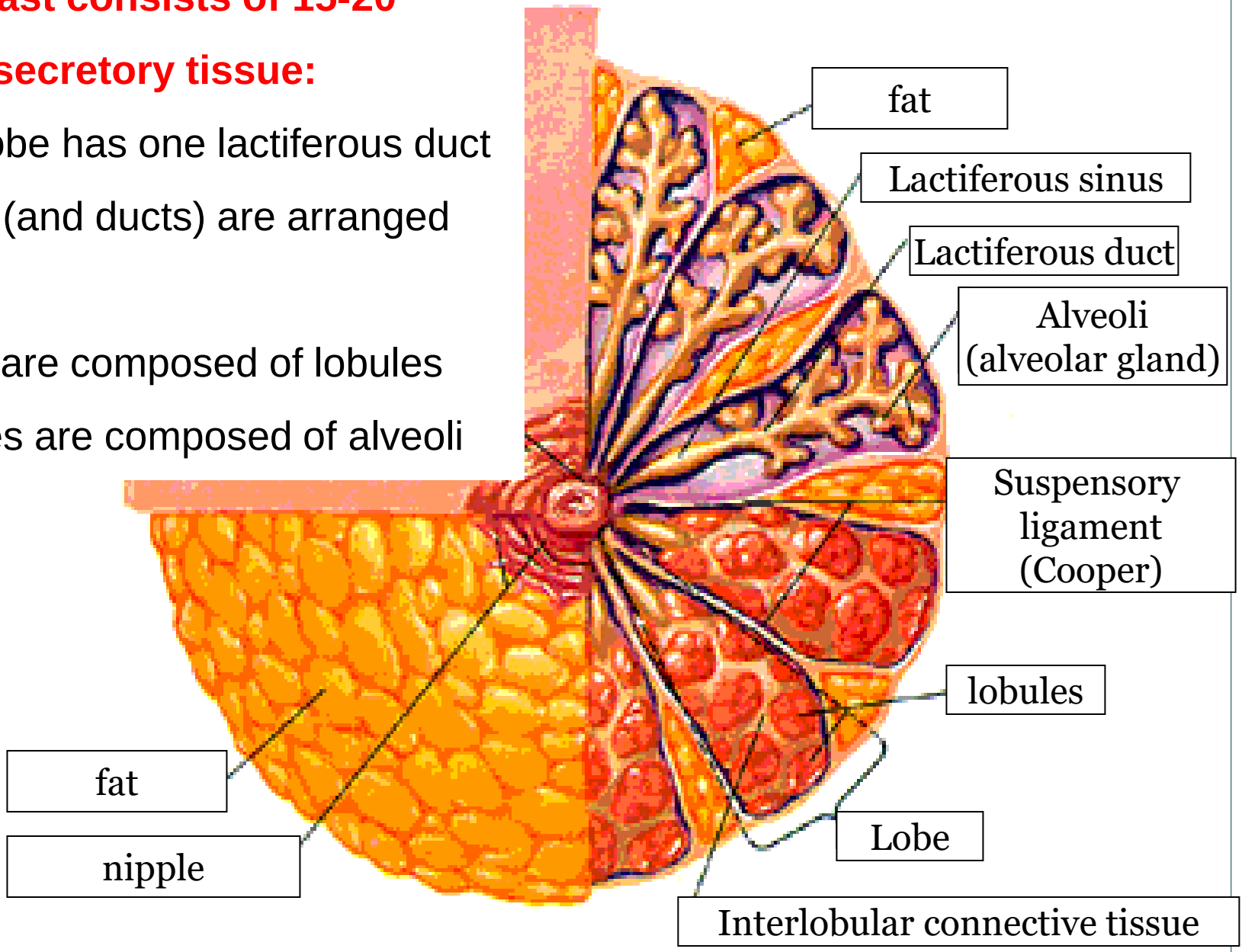
Each breast consists of 15-20 lobes of secretory tissue:

a. Each lobe has one lactiferous duct

b. Lobes (and ducts) are arranged radially

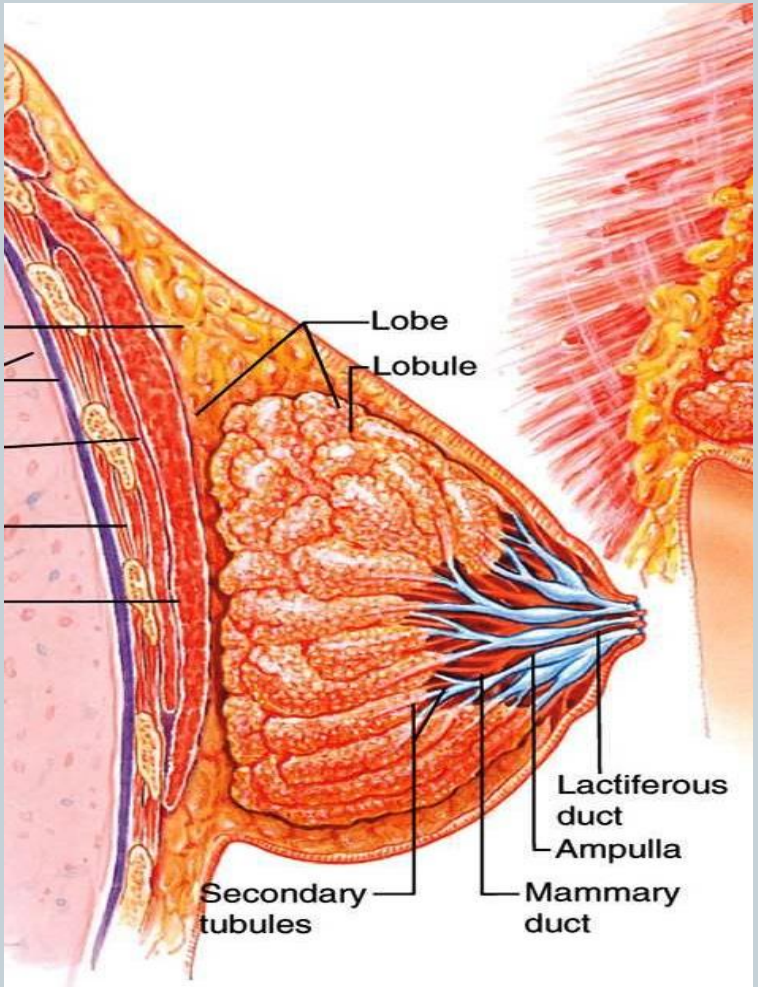
c. Lobes are composed of lobules

d. Lobules are composed of alveoli

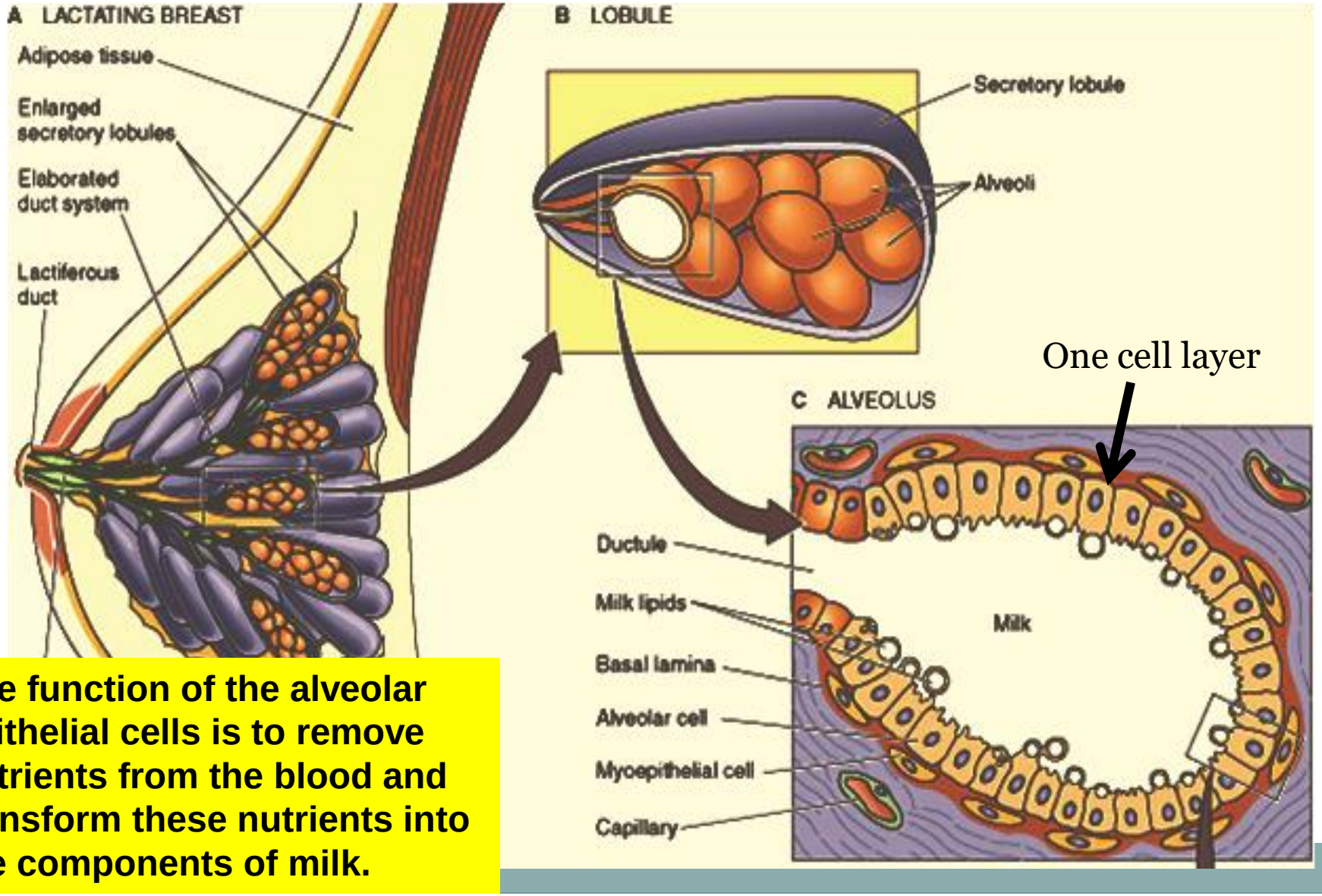


Ductal System

- **Alveolar tubule**
- **Secondary tubule**
- **Mammary duct**
- **Ampulla (lactiferous sinus)**
- **Lactiferous duct**



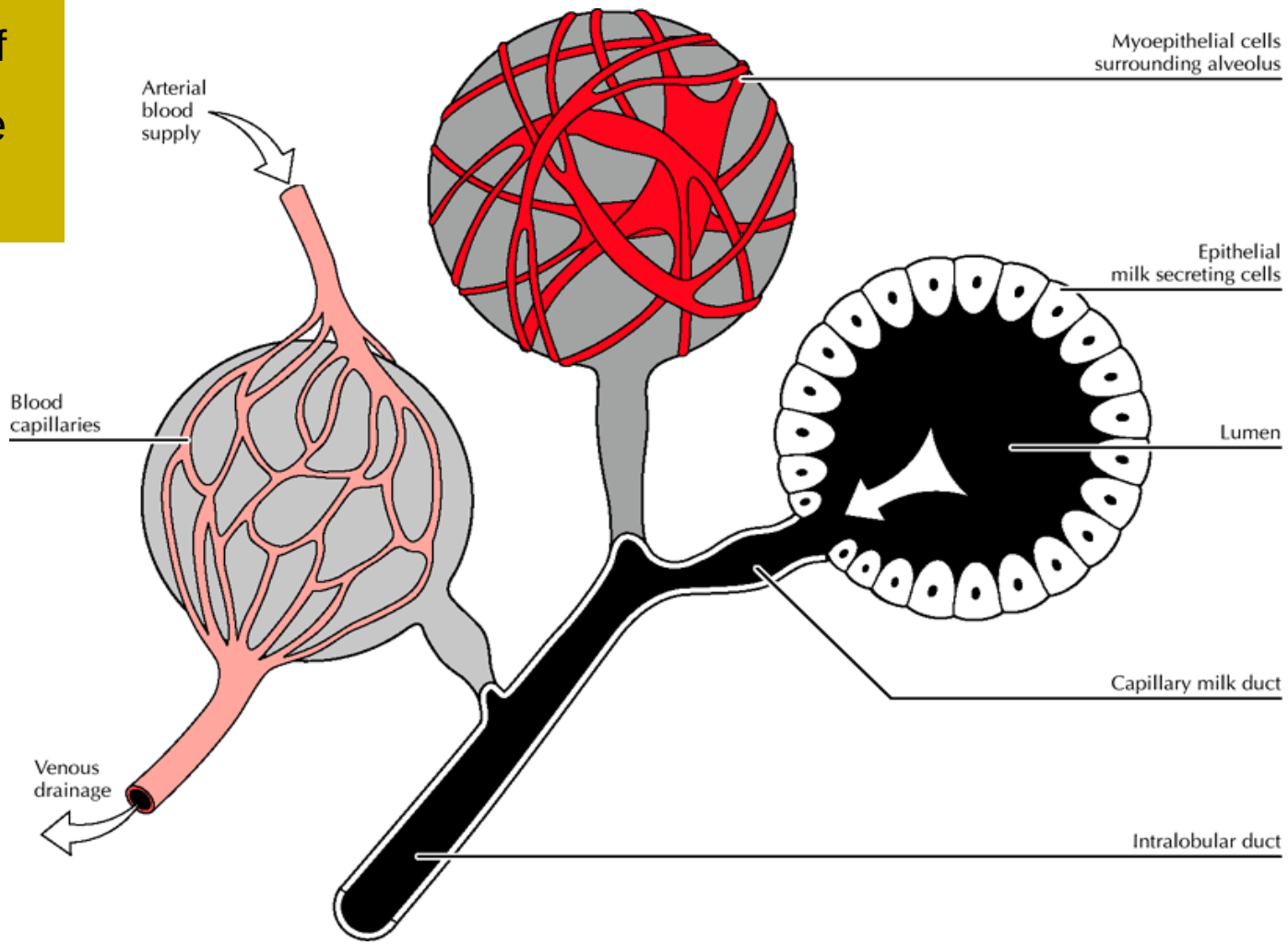
Lobule-Alveolar System



The function of the alveolar epithelial cells is to remove nutrients from the blood and transform these nutrients into the components of milk.

Where does milk come from?

The fundamental secretory unit of the breast is the **alveolus**



Stages of Mammary Gland Development

1) **Mammogenesis** *(growth and develpoment of mammary gland to a functional state).*

2) **Lactogenesis** *(initiation of milk secretion):*

   Phase 1
   Phase 2

3) **Galactopoiesis** *(maintenance of milk secretion* **in the postpartum period***)*

4) **Involution** *(cessation of milk production)*

Hormones affecting the female breast

- **Mammogenic hormones** (promoting the proliferation of alveolar and duct cells).
- **Lactogenic hormones** (promoting initiation of milk production by alveolar cells).
- **Galactokinetic hormones** (promoting contraction of myoepithelial cells, and thus milk ejection).
- **Galactopoietic hormones** (maintaining milk production after it has been established).

Mammogenic Hormones
(Hormones Involved in Mammary Growth)

Estrogens

Progesterone

} **During puberty** (ovarian hormones stimulate mammary growth)

Growth hormone

Cortisol

Insulin (IGF-1)

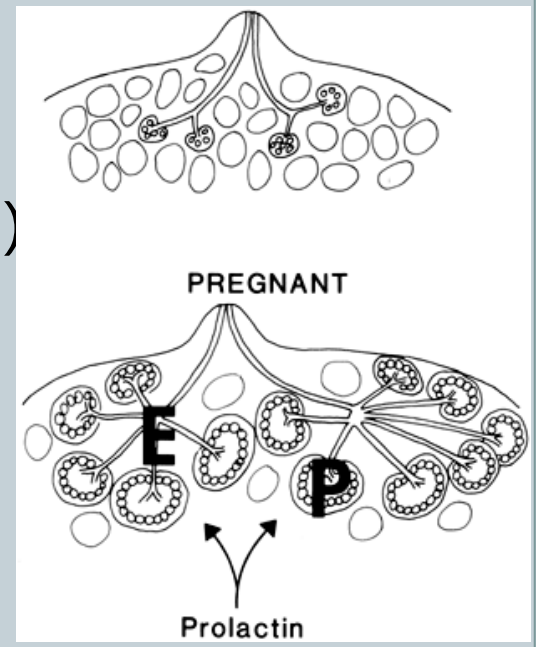
hPL also called *hCS*

Prolactin (PRL)

} **During pregnancy** (complete development of mammary glands)

Ovarian Hormones

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



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

Lactogenesis

- **Lactogenesis:** Cellular changes by which alveolar *epithelial cells* switch from a **non-secretory** to a **secretory tissues** (initiation of milk secretion).
- **Involves 2 Phases:**
  - **Lactogenesis 1**
  - **Lactogenesis 2**

Lactogenesis

- **Lactogenesis 1:** (*Histological* and *enzymatic* differentiations of alveolar epithelial cells).
  - Starts in mid-pregnancy and characterized by expression of many genes involved in the synthesis of milk components (increases in uptake transport systems for amino acids, glucose, and calcium required for milk synthesis).
  - Prolactin stimulates mammary secretory cells to produce milk.
  - Further differentiation is inhibited by high levels of progesterone from the placenta.

Lactogenesis

- **Lactogenesis 2:** (Copious secretion of all milk components), **starts 2-3 days postpartum**
  - At parturition, withdrawal of progesterone + high level of prolactin leads to:
    - Further increase in expression of milk protein genes
    - Glands absorb large quantities of metabolic substrates from the blood
    - Movement of cytoplasmic lipid droplets and casein into alveolar lumen
    - Transfer of immunoglobulins
    - Secretion of colostrum followed by milk
    - Suckling stimulates further increase in expression of genes involved in milk secretion with expansion of alveolar epithelium
    - Lactation is maintained by removal of milk
    - Switch from endocrine to autocrine control of milk production.

(Lactogenic Hormones)

Prolactin

hPL (hCS)

Growth hormone

Insulin (IGF-1)

Cortisol

Thyroid hormones

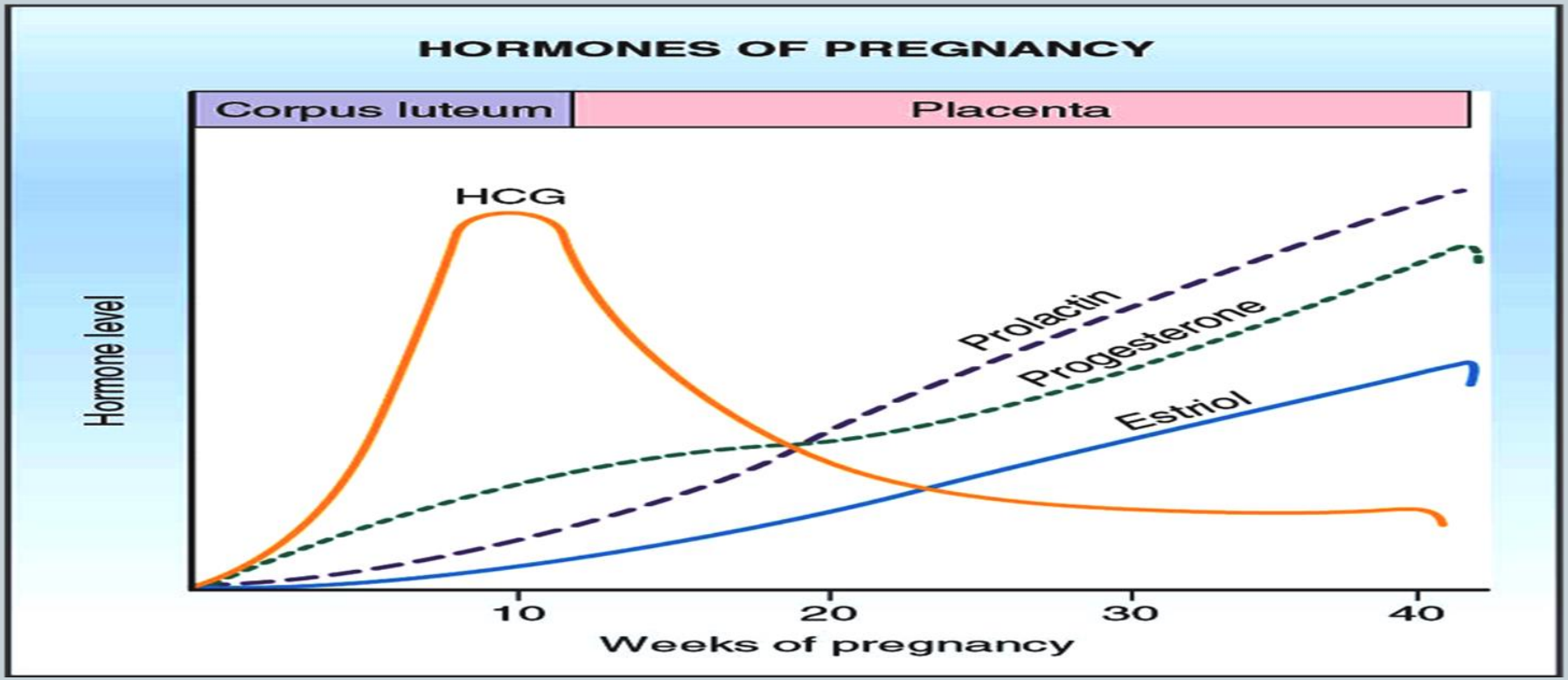
parathyroid hormones

Withdrawal of estrogens and progesterone

All are required to facilitate the mobilization of nutrients and minerals.

Prolactin (PRL)

- Secreted from the anterior pituitary gland (Lactotrophs).
- Its level rises **steadily** from the 5th week of pregnancy until birth (10-20 times the nonpregnant level) (enhanced by Estrogen)
- It has mammogenic, lactogenic and galactopoietic effects.
- It stimulates expression of genes that encode several milk components (casein/ lactalbumin, lactose and lipids)
  - Sudden drop in E & P after delivery allows milk production
  - It is inhibited mainly by hypothalamic hormone **(Dopamine)**
  - Thyrotropin-releasing hormone (TRH) can increase PRL

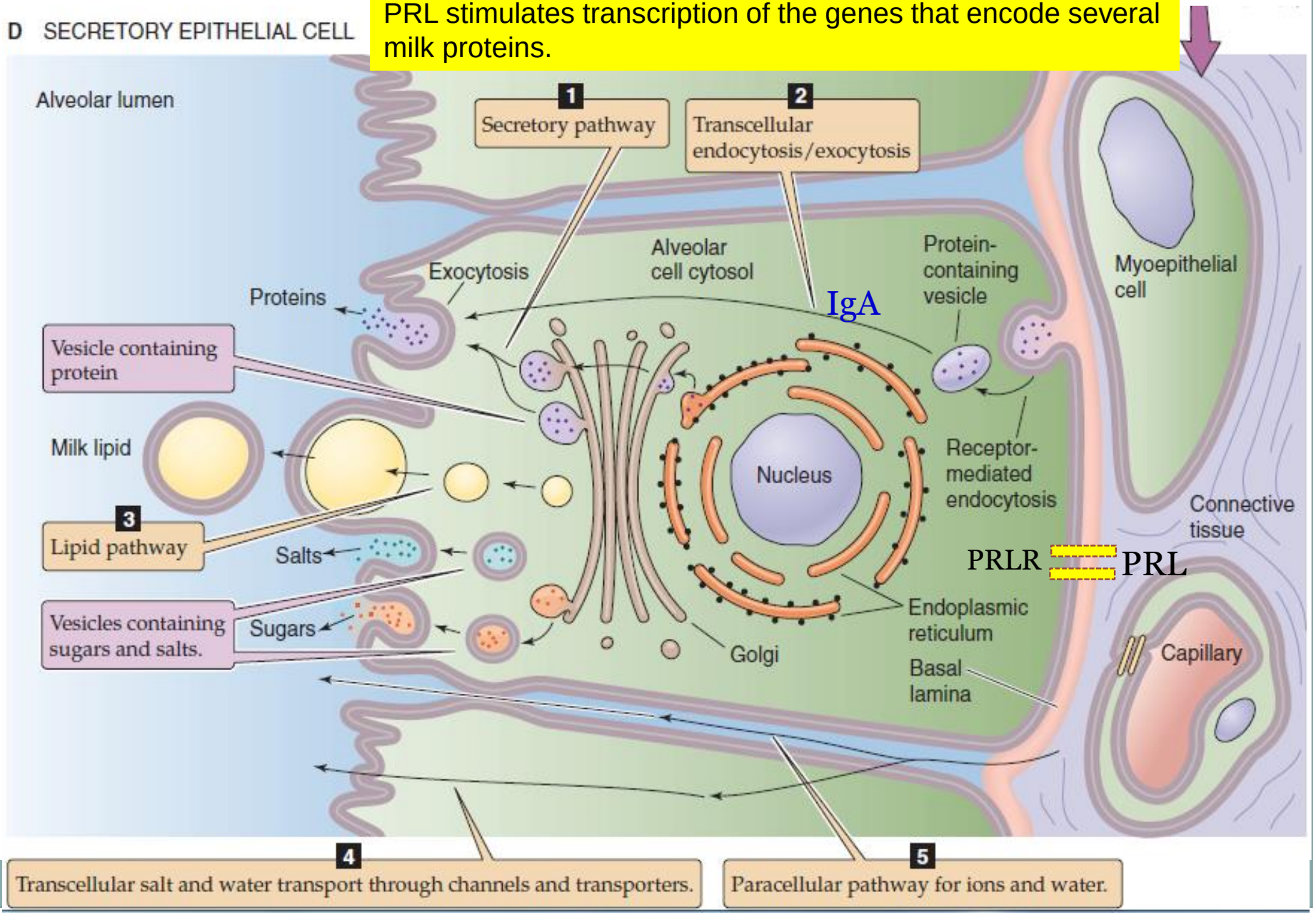

HORMONES OF PREGNANCY
Corpus luteum
Placenta
HCG
Prolactin
Progesterone
Estriol
Hormone level
10
20
30
40
Weeks of pregnancy

Human placental lactogen (human chorionic somatomammotropin, hCS**)**

- Secreted by the placenta at about the 5th week of pregnancy
- Its secretion increases progressively throughout the remainder of pregnancy in direct proportion to the weight of the placenta
- Causes at least partial development of the animal's breasts and in some instances causes lactation [facilitates growth of mammary glands, supports prolactin during pregnancy (lactogenic properties)]
- It has weak actions similar to those of growth hormone
- It decreases maternal insulin sensitivity, decreases utilization of glucose, and promotes the release of free fatty acids (Metabolic)

The alveolar cell secretes the components of milk through five pathways

PRL stimulates transcription of the genes that encode several milk proteins.



Galactopoeisis

- Galactopoeisis is defined as the maintenance of lactation once lactation has been established. **starts 9-15 days postpartum**

(Galactopoietic Hormones)

PRL (primary)
Cortisol and other metabolic hormones (permissive)

Oxytocin and psychic stimuli initiate milk ejection (“let-down”)

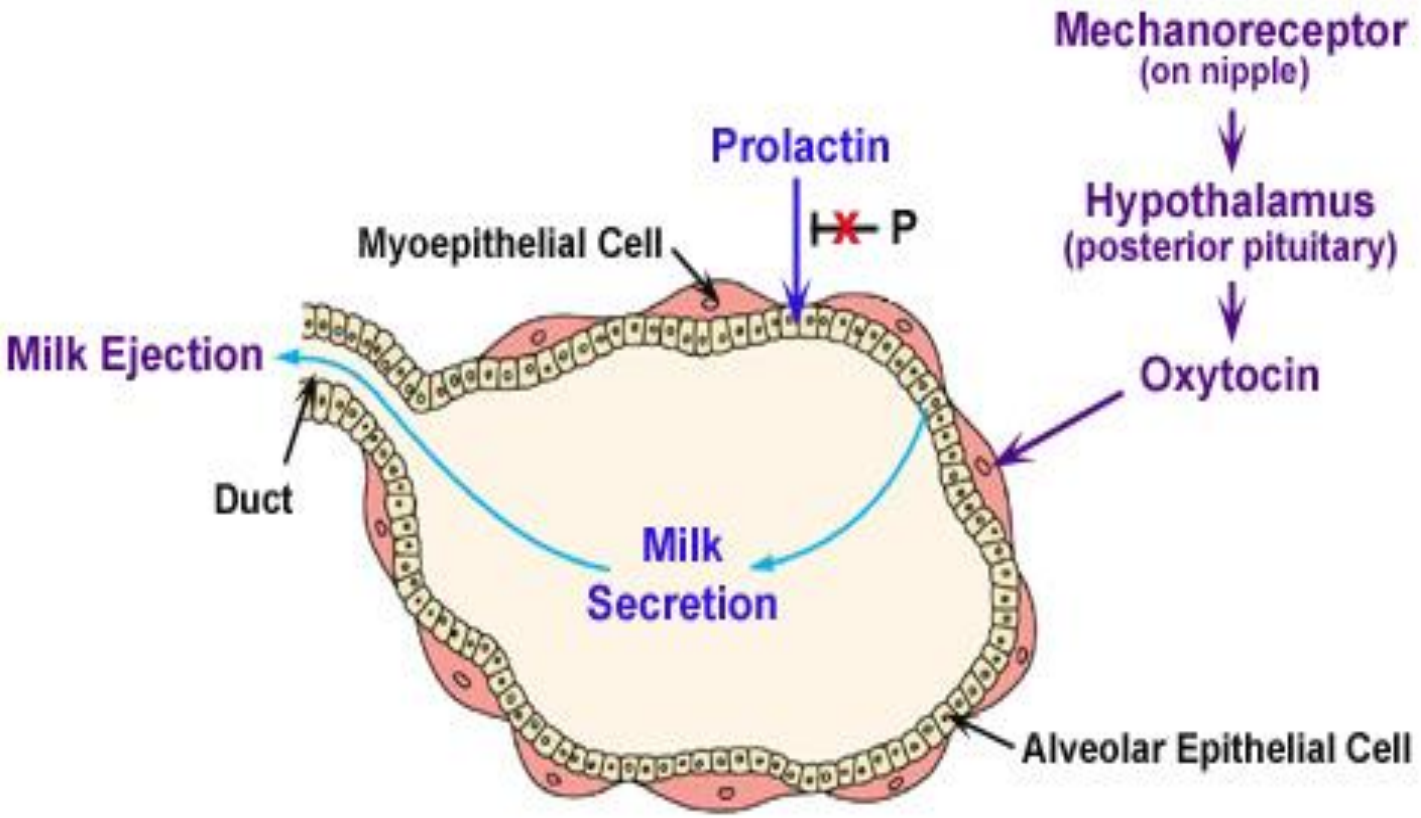
- **Milk Ejection Reflex:**

Oxytocin contracts the myoepithelial cells, forcing milk from the alveoli into the ducts and sinuses where it is removed by the infant **(galactokinetic effect).**

(Galactokinetic Hormones)

Oxytocin (OT)

Vasopressin



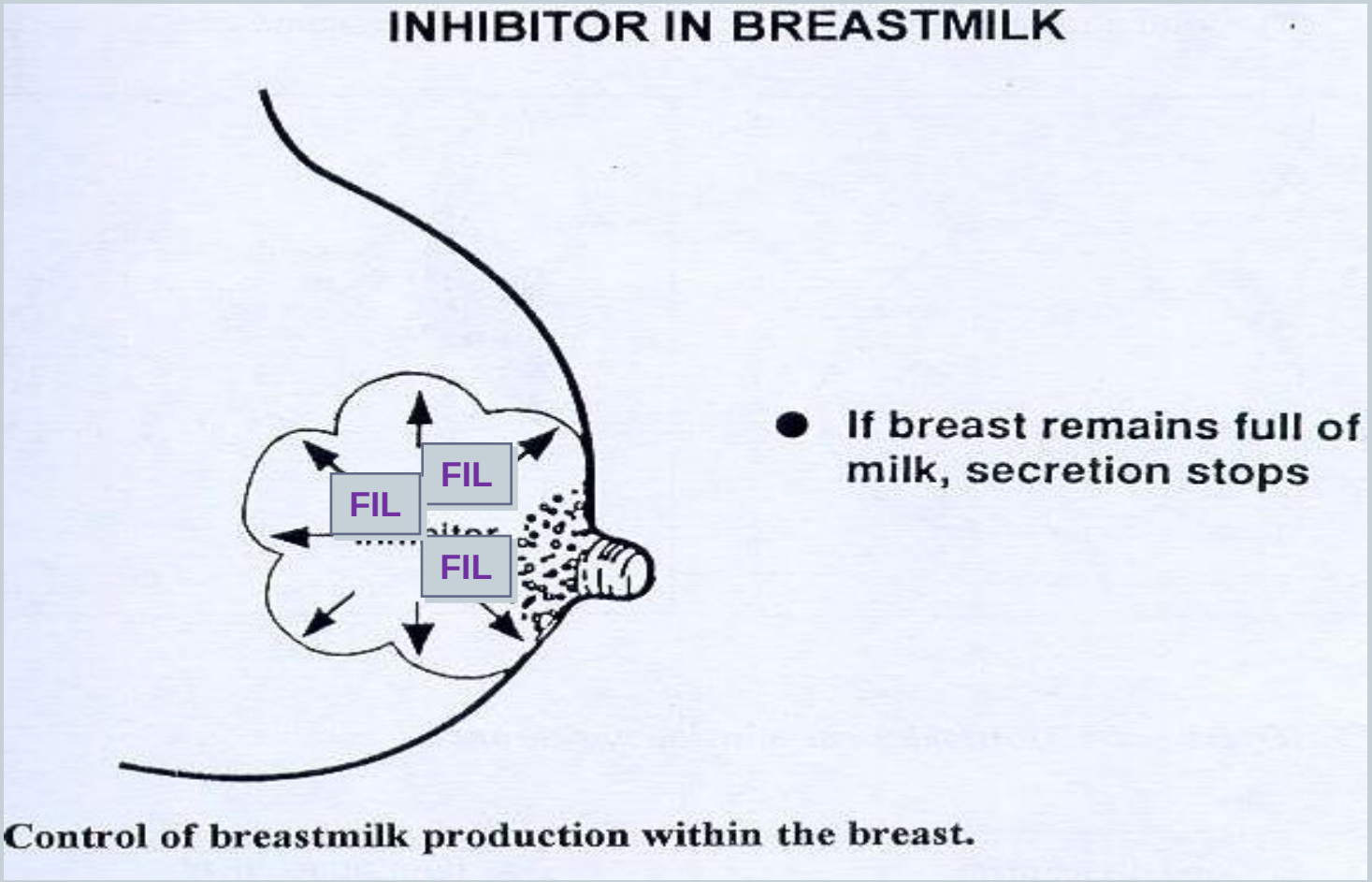
Alveolus of Mammary Gland

Autocrine Control of Lactation

Influence of Local Factors Acting on the Breasts

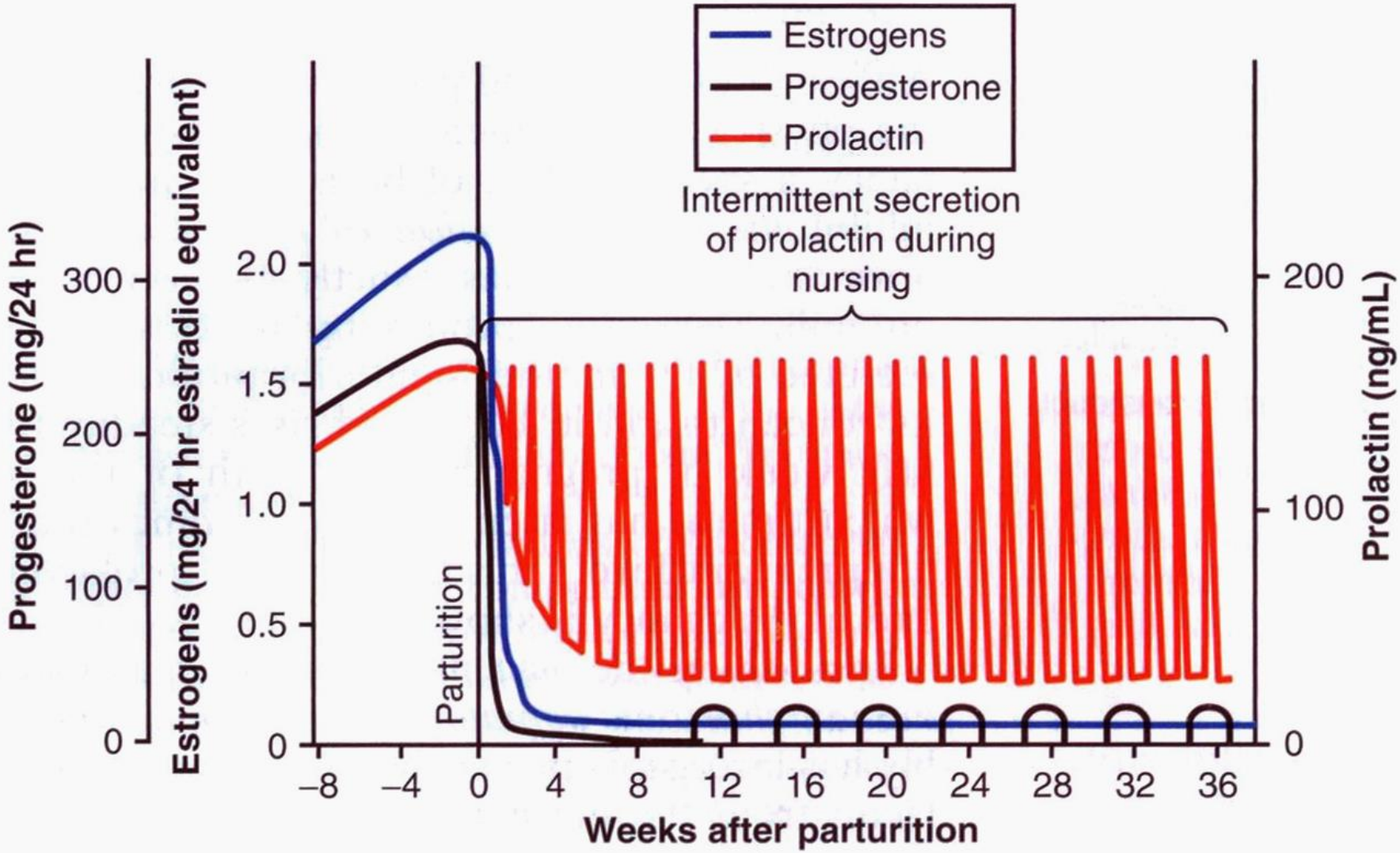
- It is not just the level of maternal hormones, but the efficiency of ***milk removal*** that governs the volume product in each breast
- A protein factor called ***feedback inhibitor of lactation (FIL)*** is secreted with other milk components into the alveolar lumen
- ***FIL***, insensitive to prolactin → ⬇ milk production

Autocrine Control of Lactation



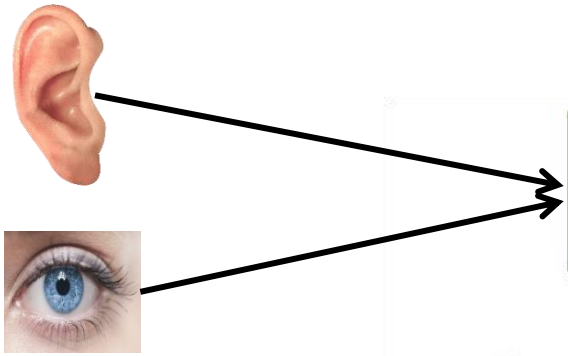
Suckling and Prolactin Secretion

Suckling is the most powerful physiological stimulus for PRL release

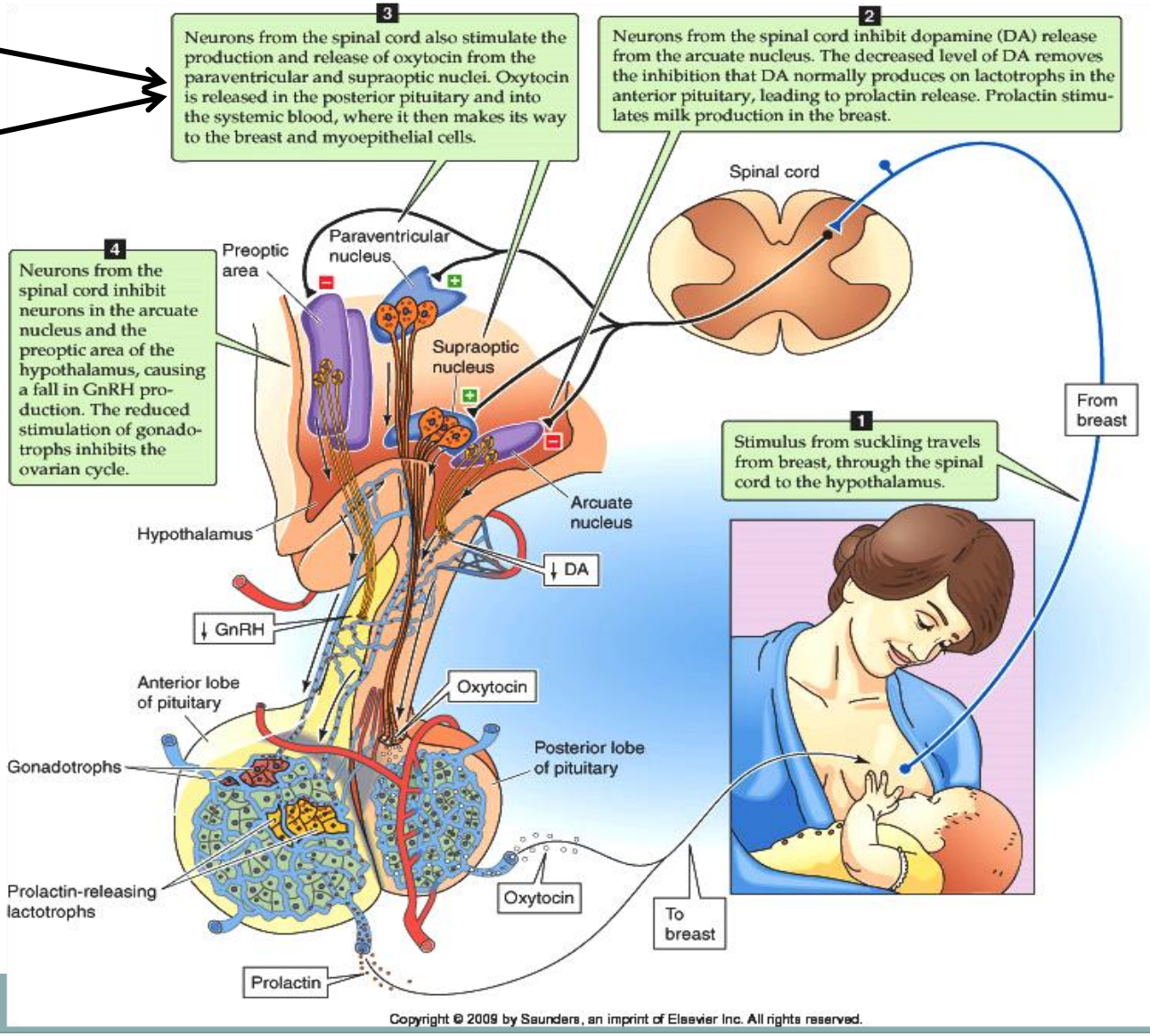


psychic stimuli

Suckling reflex



suckling stimulates the release of **TRH** from the hypothalamus



Milk production

- Milk production is a "use it or lose it" process.
  The more often and effectively the baby nurses, more milk will be produced.
- Milk production <100 ml/day in day 1 postpartum.
- Milk production by day 3 reaches 500 ml/day.
- **Involution:** when the breasts stop producing milk completely after weaning.

AAP Recommendations

- Exclusive breastfeeding for the first **six** months of life
- Continued breastfeeding for at least one year, ‘As long as is desired by mother and child’

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American Academy of Pediatrics (2005). "Breastfeeding and the Use of Human Milk." Pediatrics 115(2): 496-506.

The End

Thank You