Reproductive Physiology

Hormones affecting female breast

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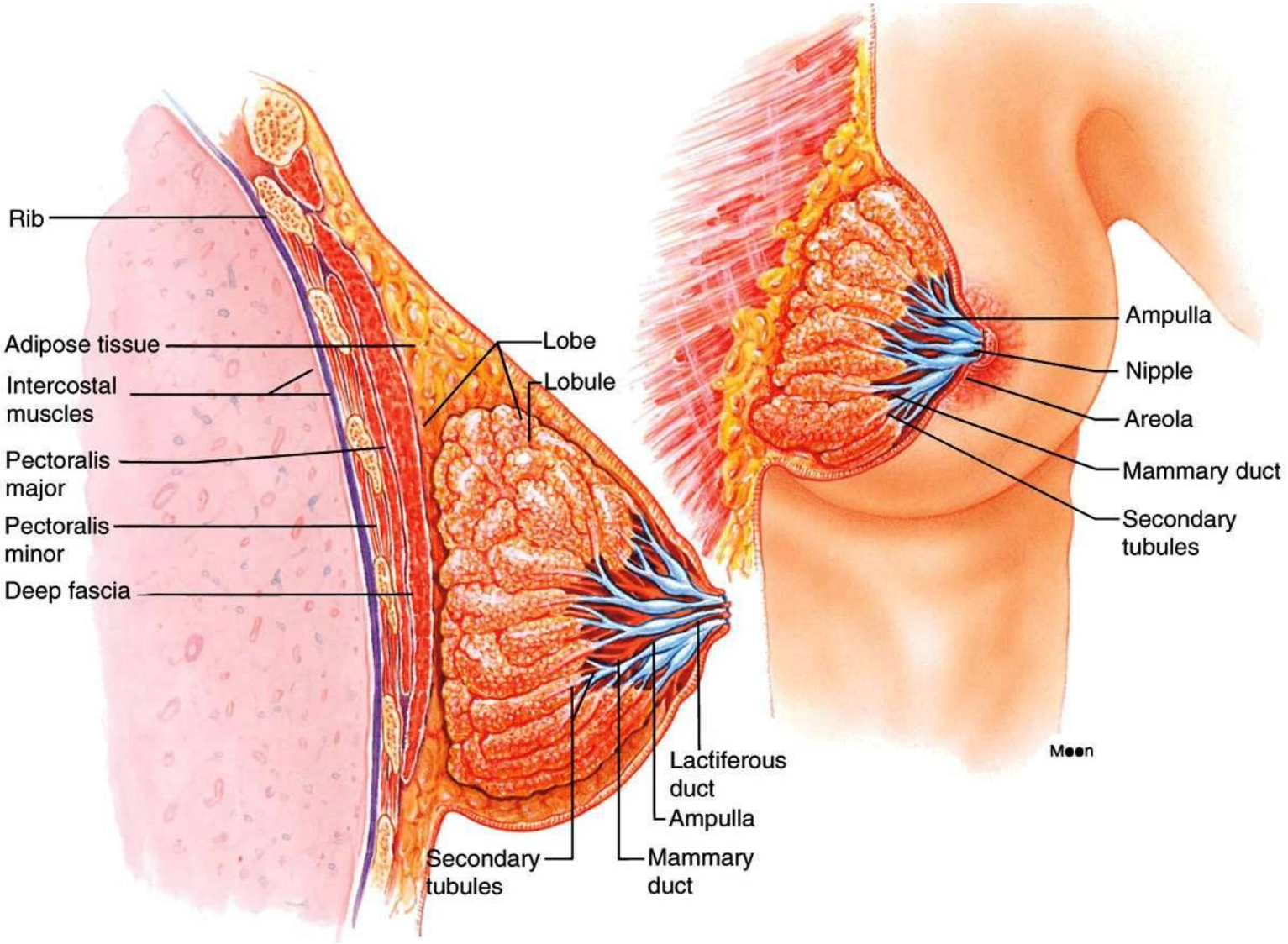
Objectives

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.

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



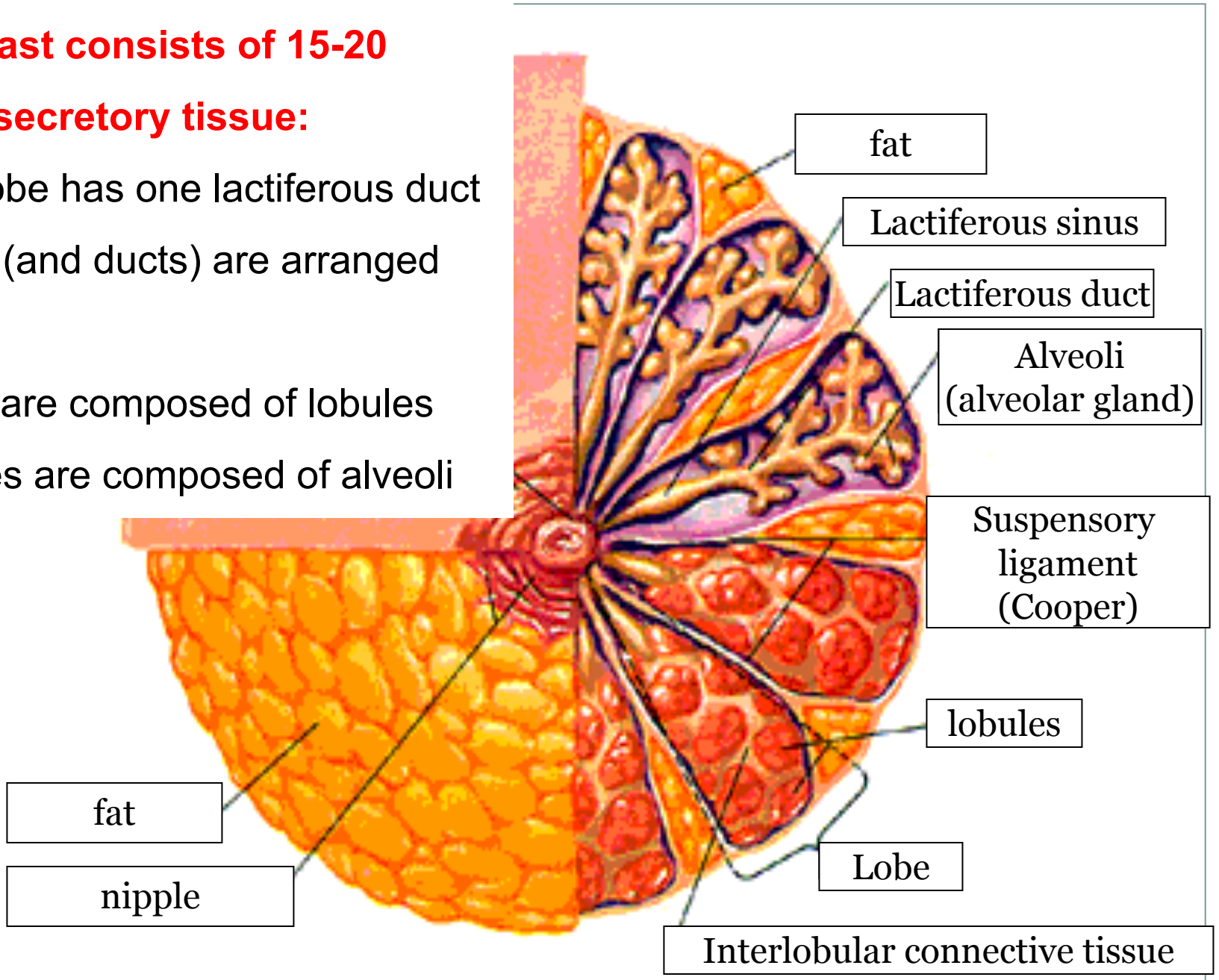
Each breast consists of 15-20 lobes of secretory tissue:

a. Each lobe has one lactiferous duct

b. Lobes (and ducts) are arranged radially

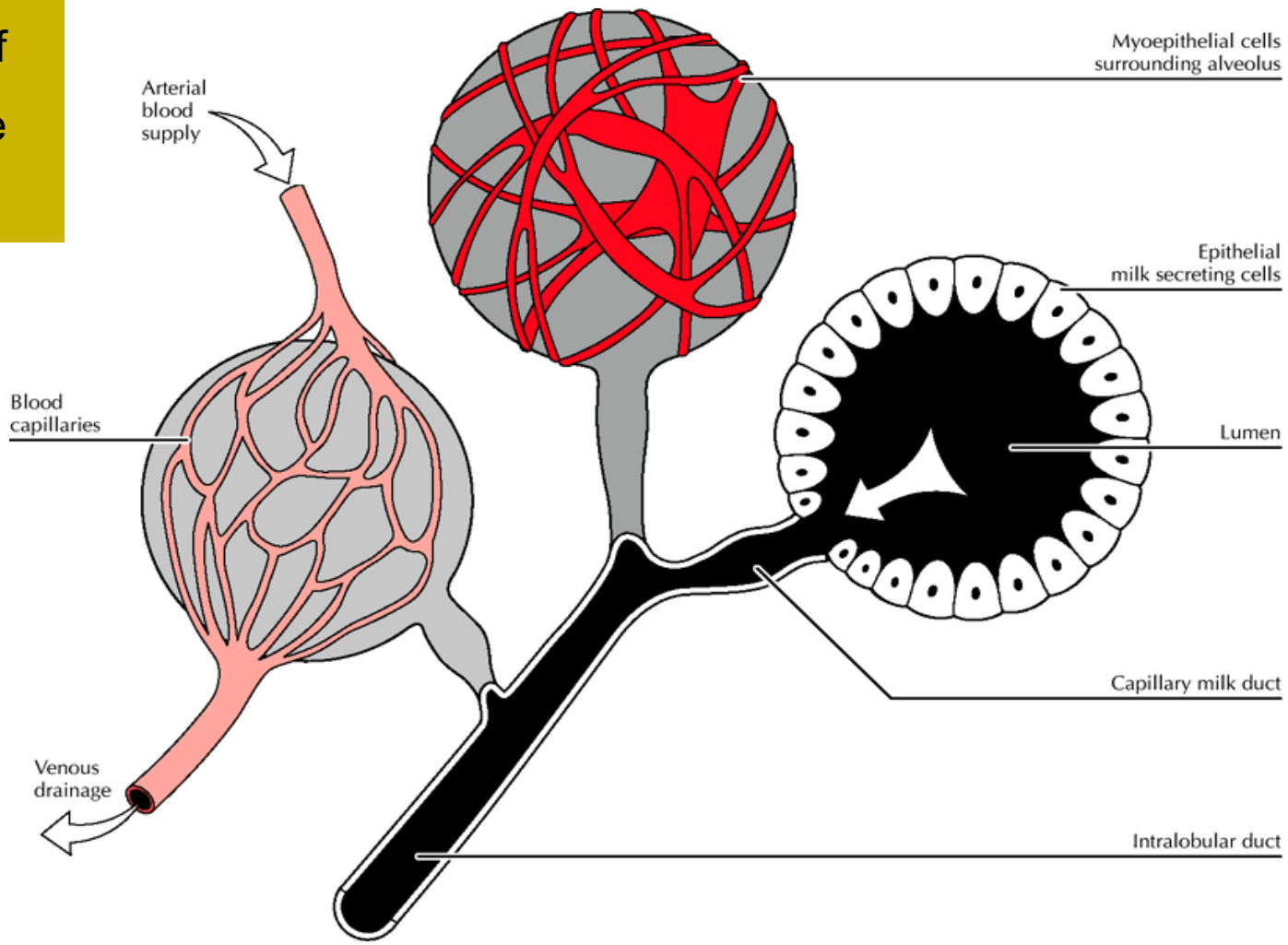
c. Lobes are composed of lobules

d. Lobules are composed of alveoli

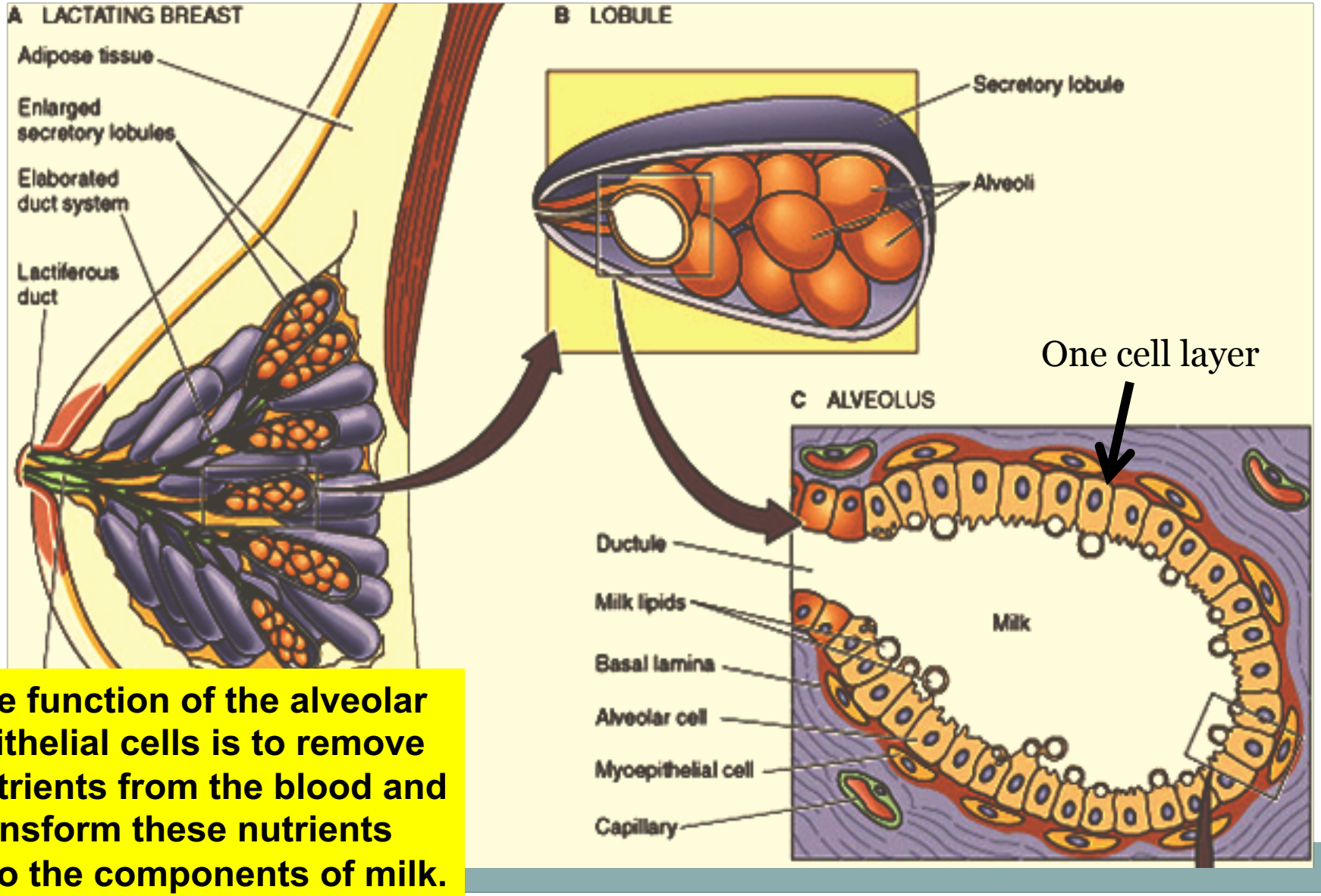


Where does milk come from?

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



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.

Stages of Mammary Gland Development

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

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

   Lactogenesis 1
   Lactogenesis 2

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

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

Hormones affecting female breast

Mammogenic Hormones (promoting the proliferation of ductal and alveolar cells) [ductal & alveolar morphogenesis]

Estrogens

Progesterone

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

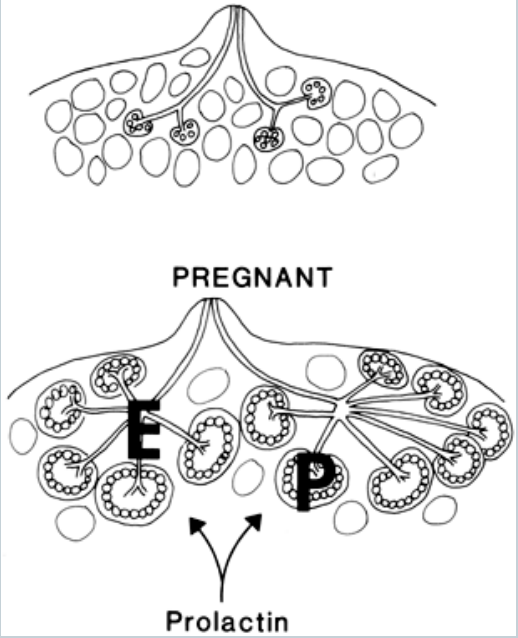
Prolactin (PRL)

Growth hormone

Glucocorticoid (Cortisol)

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).

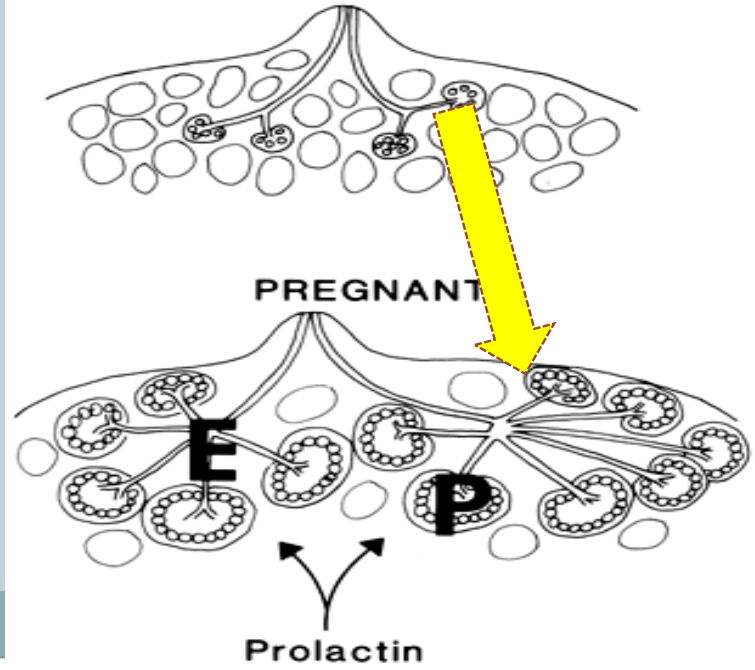


Although progesterone and estrogen are essential for physical development of the breasts, they inhibit the actual secretion of milk during pregnancy by interacting with prolactin receptors.

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**

❖**Lactogenic hormones** (promoting initiation /onset of milk production by alveolar cells)



Lactogenesis 1

(*Histological* and *enzymatic* differentiations of alveolar epithelial cells).

- Starts in mid-pregnancy and characterized by expression of many (but not all) of genes involved in the synthesis of milk components (increases in uptake transport systems for amino acids, glucose, and calcium required for milk synthesis).
- Hormones involved:
  - **Progesterone**
  - **Prolactin (PRL)**

  } **Alveologenesis**
  - **hPL (hCS)**
  - **Growth hormone**
  - **Glucocorticoid (Cortisol)**

Production and secretion of milk components in this stage are restricted to a limited number of alveolar epithelial cells with incompletely developed secretory mechanisms.

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 (IgA)
- Secretion of colostrum followed by milk
- Suckling stimulates further increase in expression of most of genes involved in milk secretion with expansion of alveolar epithelium
- Switch from endocrine to autocrine control of milk production

Hormones affecting female breast

Lactogenesis 2 hormones

Prolactin (PRL)

Growth hormone

Glucocorticoid (Cortisol)

Thyroxine

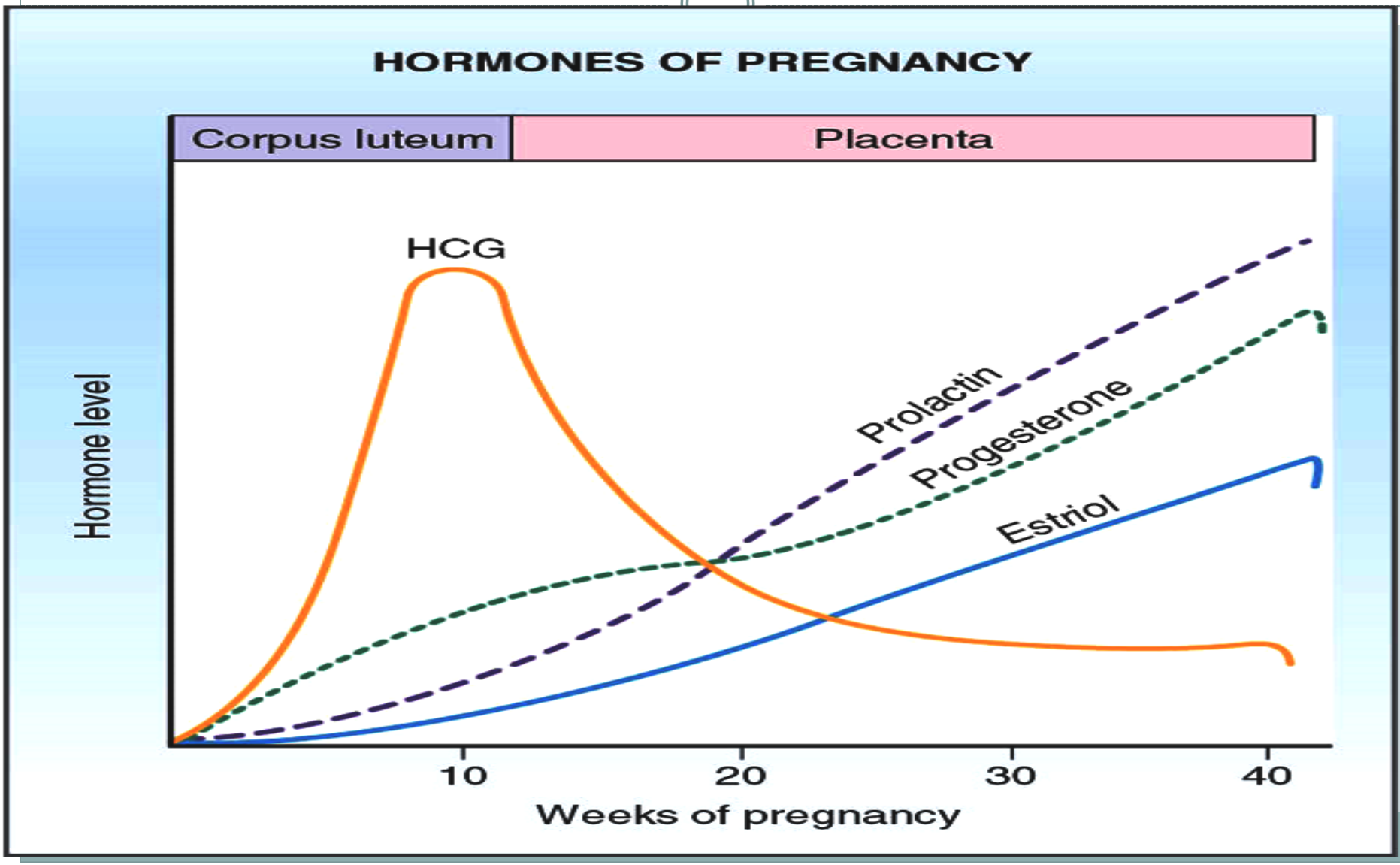
Insulin

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

Prolactin (PRL)



Galactopoeisis

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

Galactopoietic Hormones: maintaining milk production after it has been established

PRL (primary)

Cortisol, Insulin, Thyroid and Growth hormones (permissive)

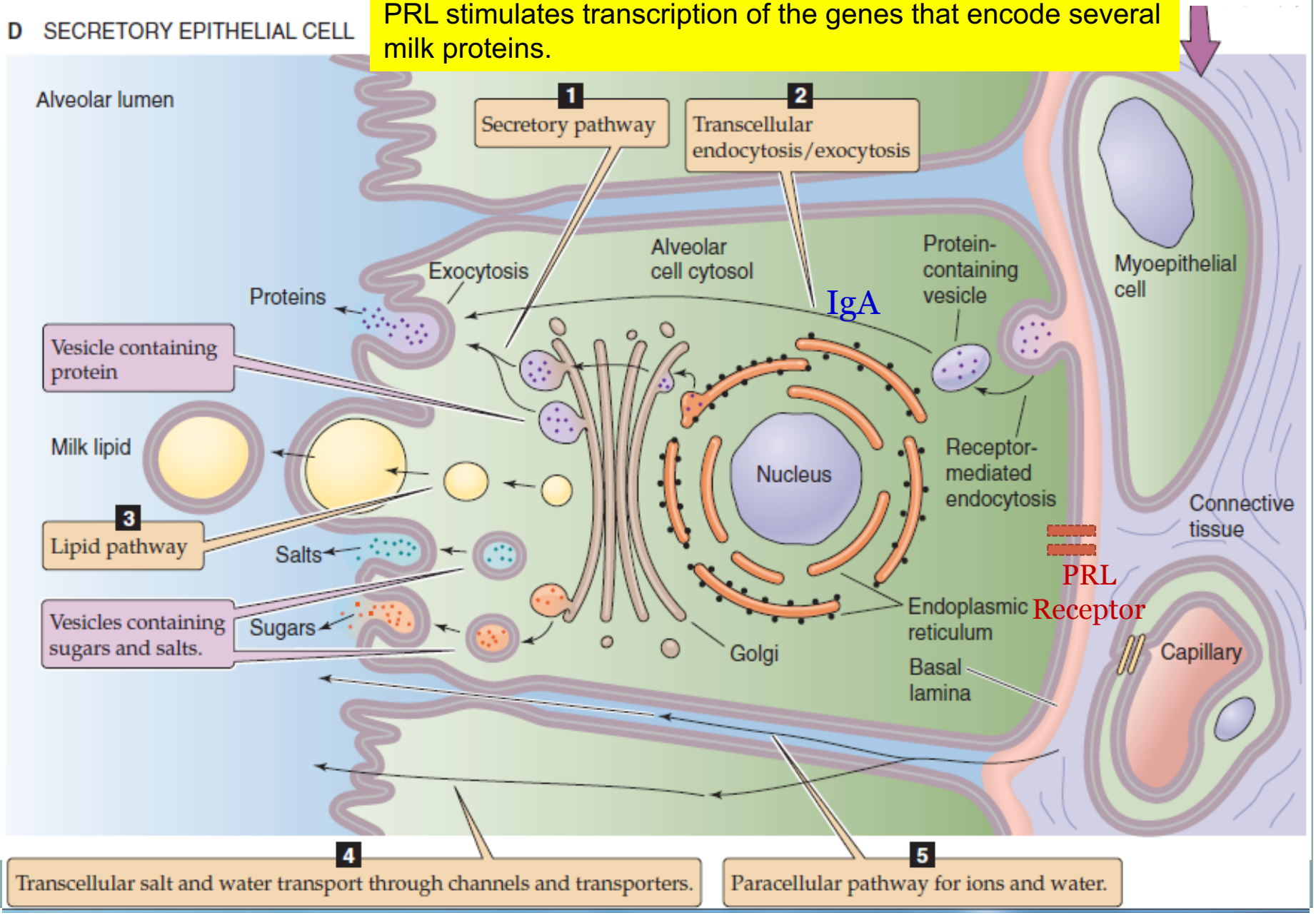
Oxytocin

Estrogen (very low dose is galactopoietic)

Progesterone (alone has no effect on galactopoeisis because it has no receptors in mammary glands at this stage)

The alveolar cell secretes the components of milk through five pathways

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



Oxytocin and psychogenic stimuli initiate milk ejection ("let-down")

Galactokinetic Hormones: (promoting contraction of myoepithelial cells, and thus milk ejection).

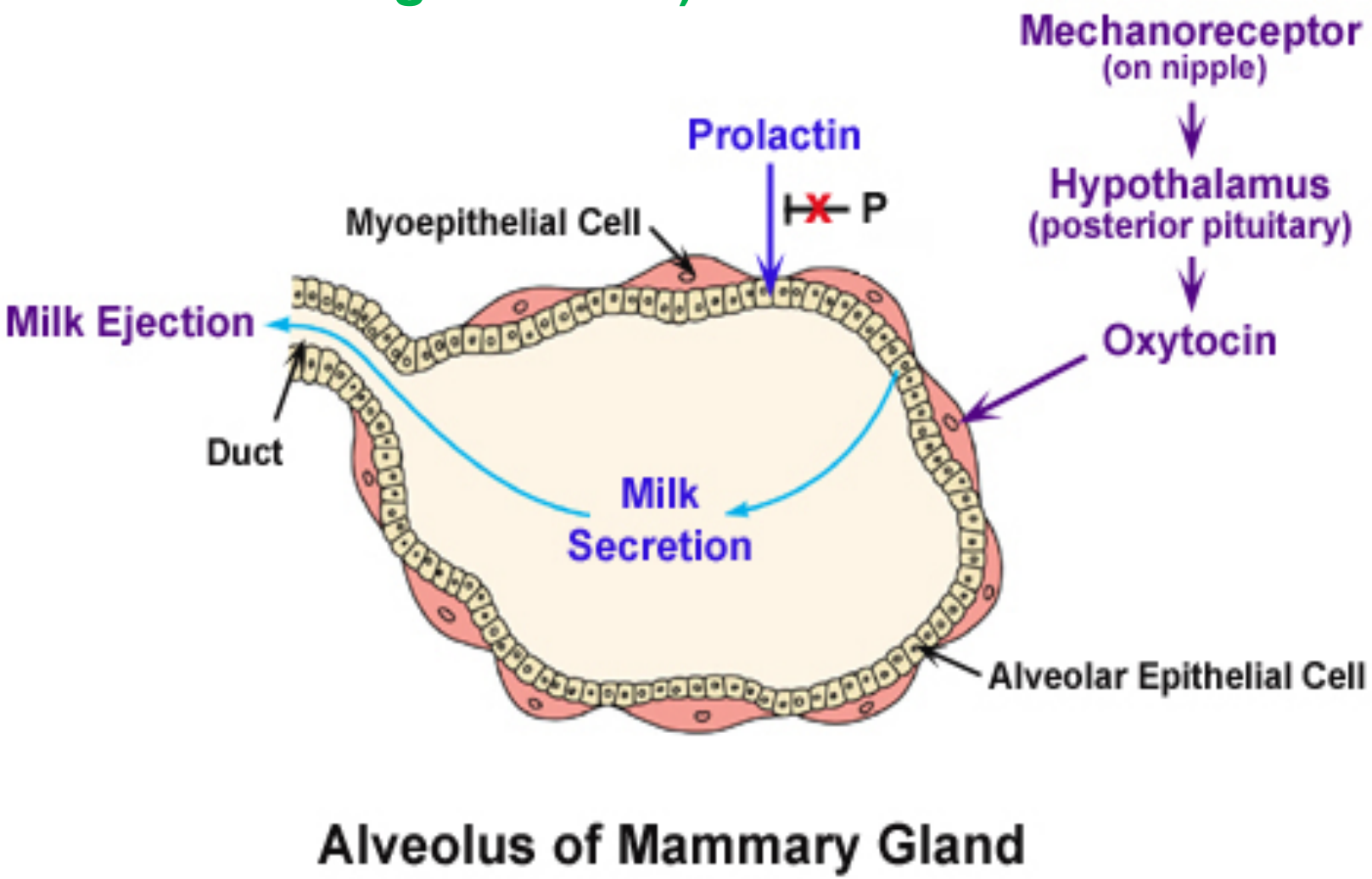
- Oxytocin (OT)

- **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).**

After delivery of placenta

(withdrawal of high P conc.)



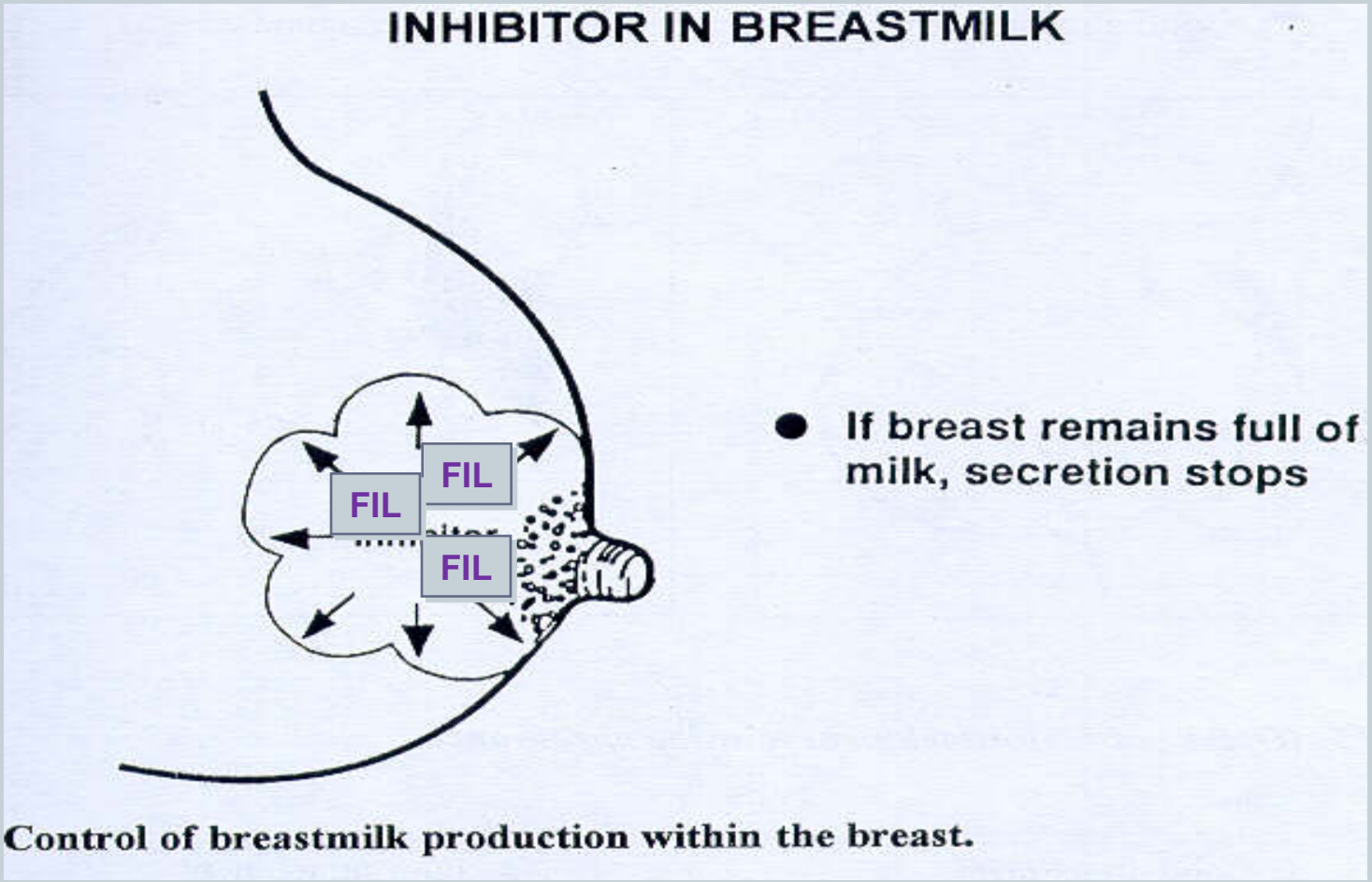
Alveolus of Mammary Gland

Autocrine Control of Lactation

Influence of Local Factors Acting on the Breasts

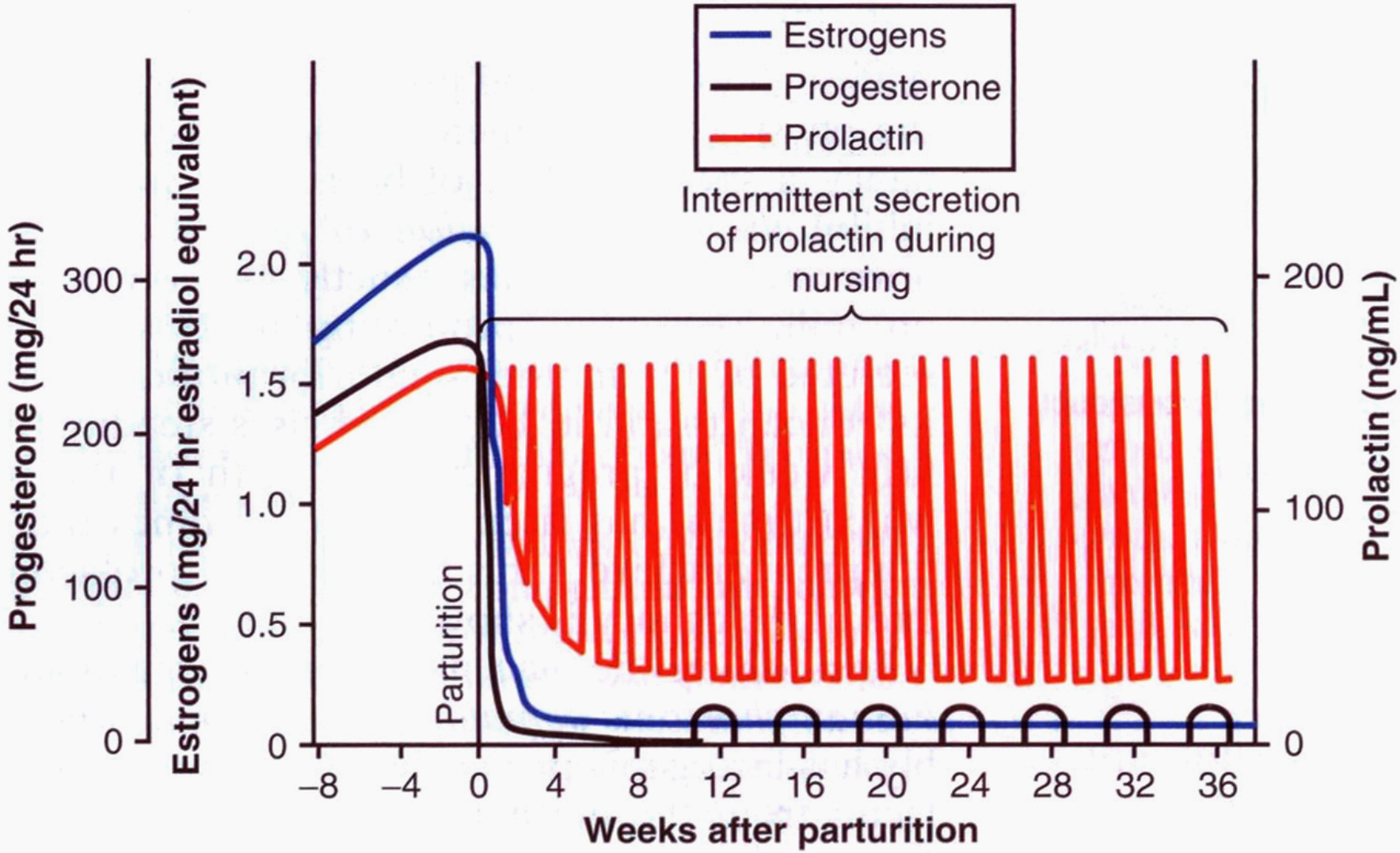
- It is not just the level of maternal hormones, but the efficiency of ***milk removal*** that governs the volume product in each breast
- A protein factor called ***feedback inhibitor of lactation (FIL)*** is secreted with other milk components into the alveolar lumen
- ***FIL***, insensitive to prolactin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

Autocrine Control of Lactation



Suckling and Prolactin Secretion

Suckling is the most powerful physiological stimulus for PRL release

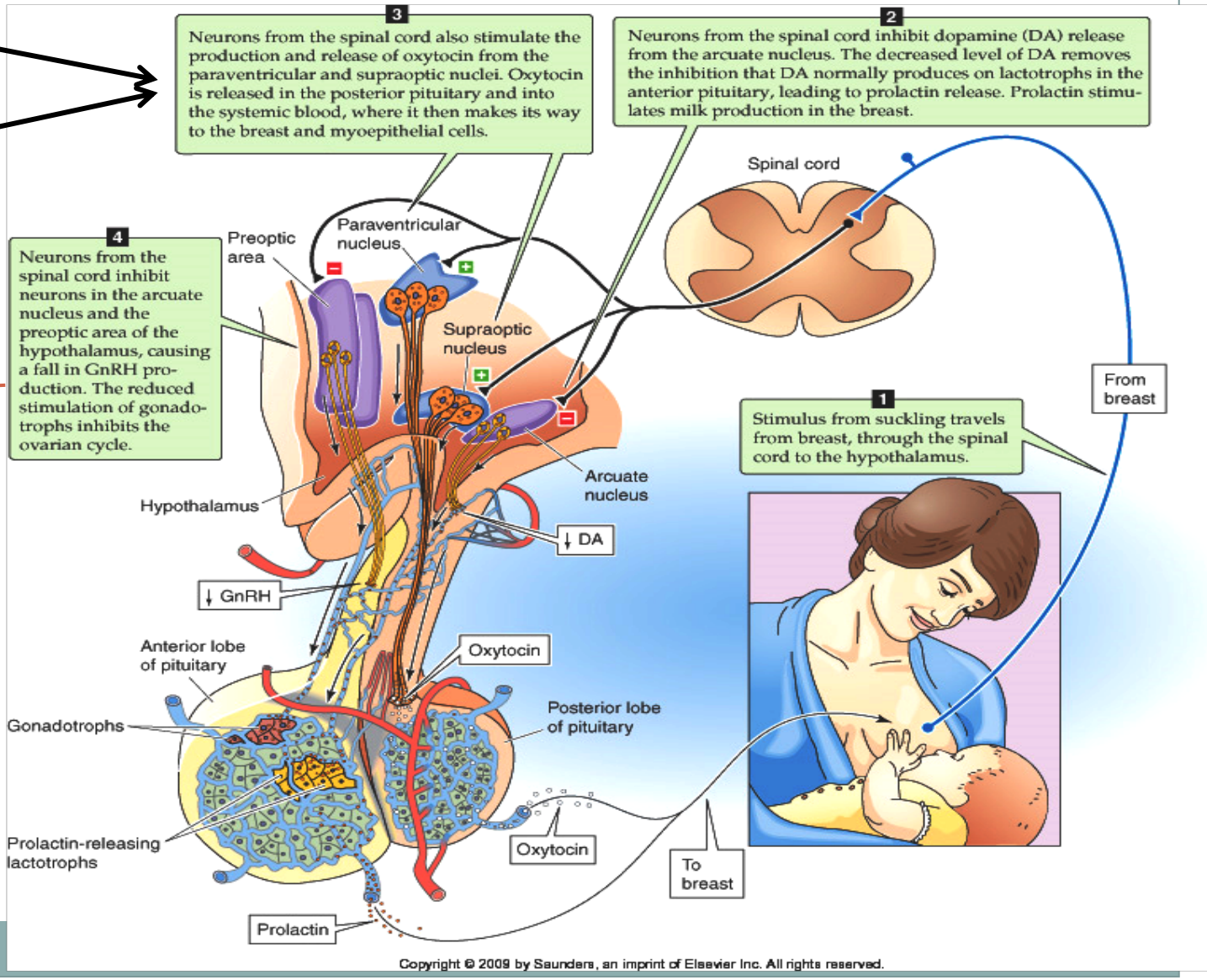


Psychogenic stimuli

Suckling reflex

Prolactin (−)

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.
- Lactation is maintained by continuous removal of milk.
- 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