Endocrine Physiology Fall 2020

Lecture 3
Anterior Pituitary Hormones: Prolactin Hormone

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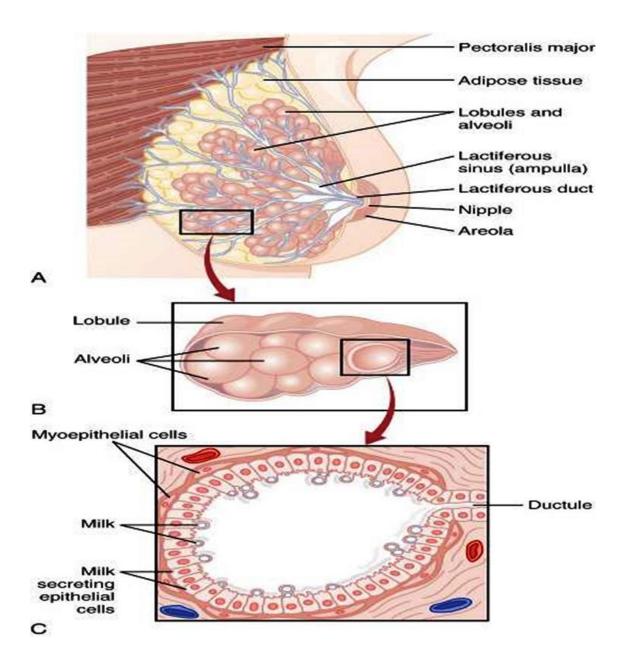Professor of Physiology

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Prolactin

- A polypeptide hormone synthesized and secreted by lactotrophs in the anterior pituitary gland

- The lactotrophs account for approximately 15–20% of the cell population of the anterior pituitary gland,

- This increases dramatically in response to elevated estrogen levels, particularly during pregnancy.

- Prolactin levels are higher in females than in males, and the role of prolactin in male physiology is not completely understood.

- Plasma concentrations of prolactin are highest during sleep and lowest during the waking hours

The mammary gland.

Actions of prolactin

- Stimulates breast development of breast including growth and development of the mammary gland tissue and ductal proliferation

- These actions are enhanced by estrogen during pregnancy.

- Stimulates milk production in the breast by
  - stimulates glucose and amino acid uptake by mammary gland cells
  - synthesis of the milk proteins β-casein and α-lactalbumin, the milk sugar lactose, and milk fats by the mammary epithelial cells
  - Inhabits gonadotropin-releasing hormone (GnRH) during pregnancy leading to amenorrhea

- Inhibits spermatogenesis (by decreasing GnRH) when secreted in large amounts (Pituitary adenoma)

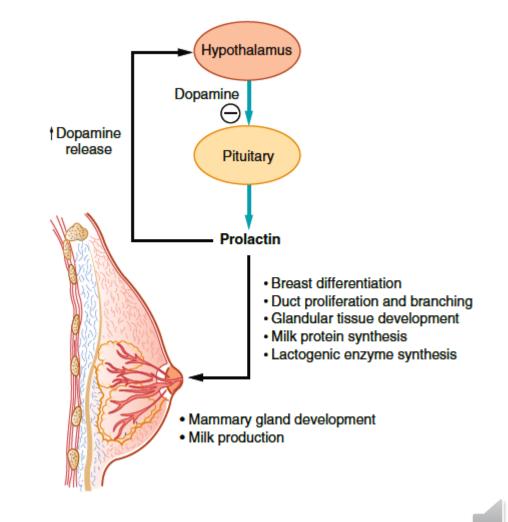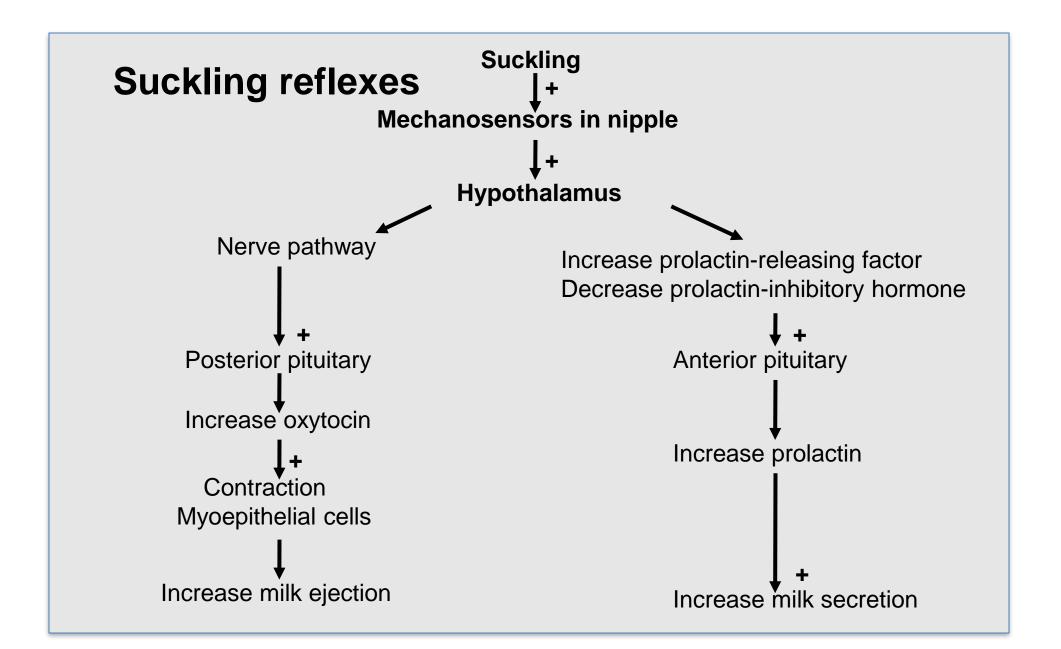- modulates reproductive and parental behavior

Physiologic effects of prolactin and its regulation b y dopamine

Prolactin release is predominantly under negative feedback control by hypothalamic dopamine.

Suckling stimulates the release of prolactin by releasing the tonic inhibition of dopamine.

Prolactin inhibits its own release by stimulating dopamine(feed back regulation)

The release of prolactin in response to suckling is neuroendocrine reflex

Suckling reflexes

Suckling
↓ +
Mechanosensors in nipple
↓ +
Hypothalamus

Nerve pathway
↓ +
Posterior pituitary
↓
Increase oxytocin
↓ +
Contraction
Myoepithelial cells
↓
Increase milk ejection

Increase prolactin-releasing factor
Decrease prolactin-inhibitory hormone
↓ +
Anterior pituitary
↓
Increase prolactin
↓ +
Increase milk secretion

Control of prolactin secretion

- Prolactin release is predominantly under tonic inhibition by dopamine derived from dopaminergic (D2) neurons of the hypothalamus.

- D2 inhibition of lactotroph release of prolactin is mediated by D2 Gαi protein–coupled receptors.

- Prolactin release is affected by :
    - suckling of breast during lactation increase prolactin secretin
    - increased levels of ovarian steroid hormones, primarily estrogen.

- This surge in prolactin release in response to a suckling stimulus is mediated by a decrease in the amount of dopamine released at the median eminence, relieving the lactotroph from tonic inhibition.

- Estrogen stimulates growth of the lactotrophs during pregnancy as well as prolactin gene expression and release.

- TRH has identified as potential prolactin-releasing factors

Regulation of Prolactin Secretion

Factors that Increase Prolactin Secretion

- Estrogen (pregnancy)
- Breast-feeding
- Sleep
- Stress
- TRH

Factors that Decrease Prolactin Secretion

- Dopamine
- Bromocriptine (dopamine agonist)
- Somatostatin
- Prolactin by negative feedback
- Placental progesterone during pregnancy

Mechanism of prolactin on breast and mammary glands

- The effects of prolactin on the breast and mammary gland are mediated by a cytokine cell membrane receptor

- Hormone receptor biding that stimulates the *Janus kinase* (*JAK*) and signal transducer and activator of transcription (STAT) pathway

- Commonly known as the *JAK*/STAT signaling pathway

- Progesterone produce by the placenta during pregnancy interferes with prolactin binding to the receptors on the alveolar cells within the breast, thereby directly suppressing milk production during pregnancy

- High levels of prolactin during lactation and as lactation continues, suppresses **ovulation** because prolactin inhibits GnRH secretion by the hypothalamus and FSH and LH secretion by the anterior pituitary.

- Although not 100% effective, breastfeeding is method of contraception and family spacing in some regions of the world.

Disorders of prolactin secretion

- Hyposecretion (*Prolactin deficiency*)
  - Infarction of pituitary (Sheehan's syndrome)
  - Drugs Dopamine agonist
- Hypersecretion : Caused by
- Hypothalamic damage (due to loss of the tonic "inhibitory" control by dopamine)
- a hormone-producing pituitary adenoma
  - Prolactinomas are the most common tumors of pituitary gland
  - Usually benign neoplasm.
- Patients with a prolactinoma present with
  - elevated levels of prolactin (hyperprolactinemia)
  - excessive secretion of milk (galactorrhea)
  - reproductive dysfunction including loss of libido , amenorrhea
  - In males, prolactinomas may cause infertility by producing hypogonadism due to inhibition of GnRH. can be treated with bromocriptine, which reduces prolactin secretion by acting as a dopamine agonist.

CLINICAL CORRELATION CASE A

- A mother of two school-age children still in her reproductive years consults her physician because she has had no menstrual periods for the past 6 months. A pregnancy test is negative, and she is not taking any medications. She also complains of problems with her peripheral (temporal) vision and has also noted milky discharge from her nipples. A magnetic resonance image (MRI) scan of the brain reveals a pituitary mass.

- On physical examination, she is afebrile and has a normal blood pressure. Laboratory values are within normal ranges for serum glucose, Na+ and K+. Increased levels of prolactin are measured, with normal levels of all other pituitary hormones. She is diagnosed as having a prolactinoma.

- Prolactinomas account for 50% of functioning pituitary tumors and are more frequent in females than in males.

- Tumor size is correlated with prolactin levels.

- Women present with amenorrhea (lack of menses), galactorrhea (milk discharge from nipples), and infertility.

- Large tumors extending caudal to the pituitary are associated with visual defects due to compression of the optic chiasm.

- In males, presentation is impotence, loss of libido, and infertility as well as headaches

- Administration of dopamine agonists to reduce prolactin production

- Tumors that do not shrink in size with medical treatment may require focused radiation therapy and/or surgical removal.