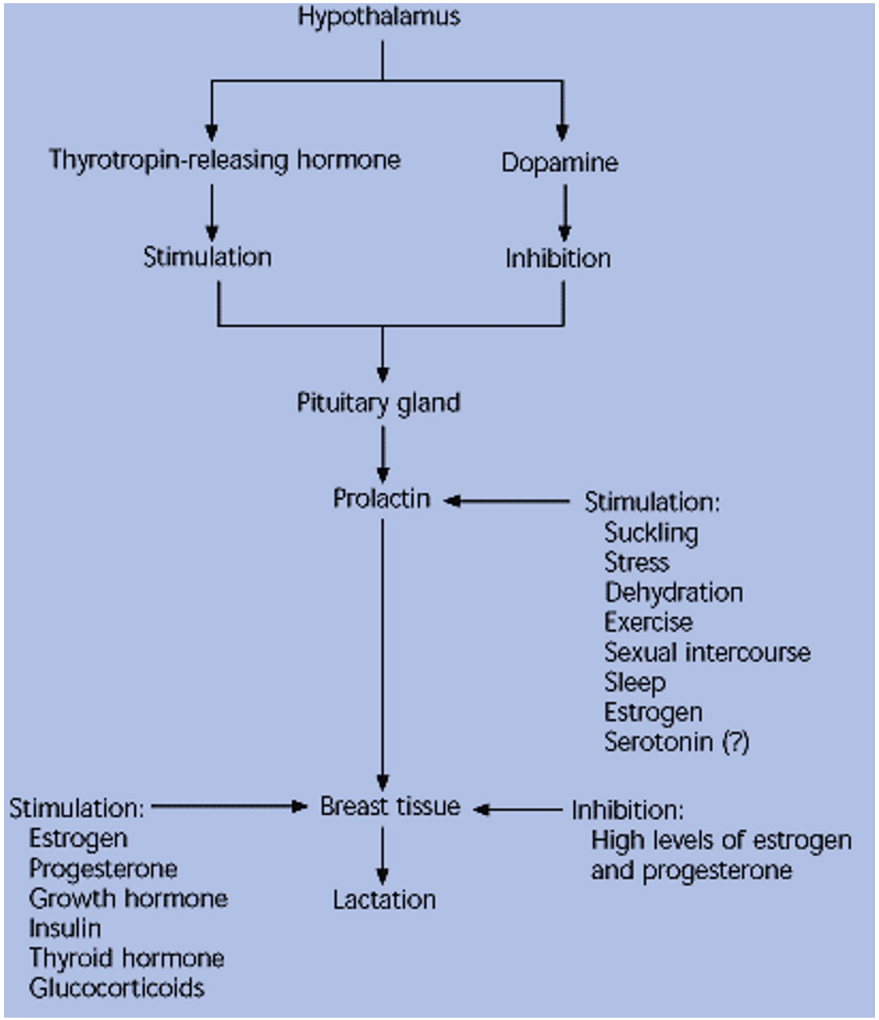
Anterior Pituitary hormones part2

1- Somatotropic Hormones

Prolactin (PRL)

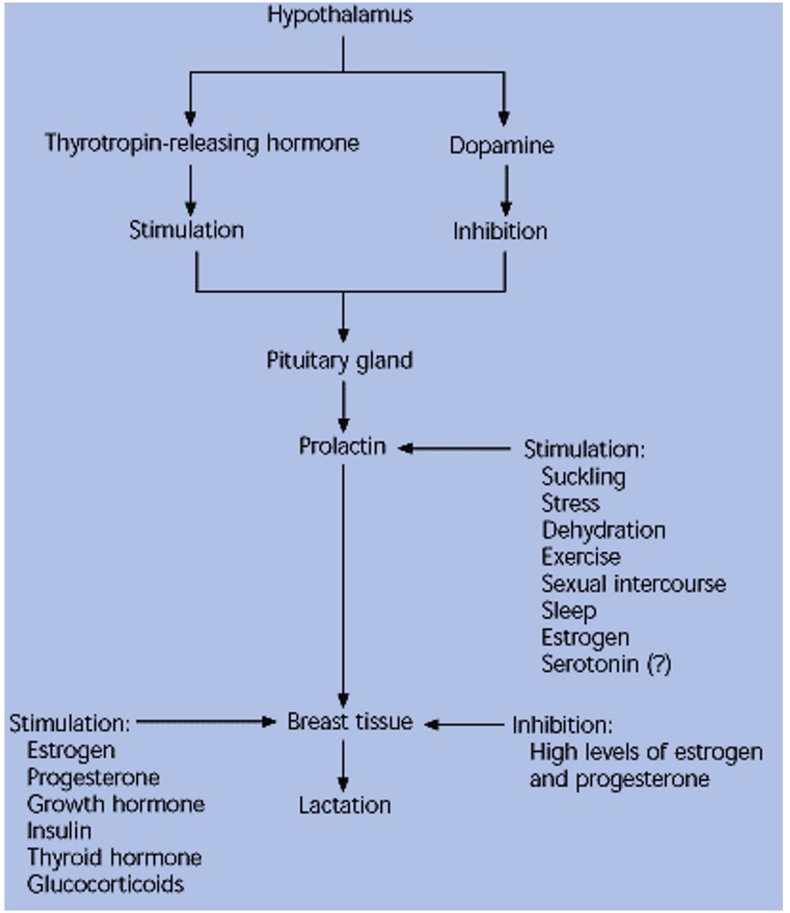
- Production stimulated by high estrogen levels in pregnancy & by suckling in post-partum period

- Prepares breast for lactation and milk production



Prolactin stimulation and inhibition pathway

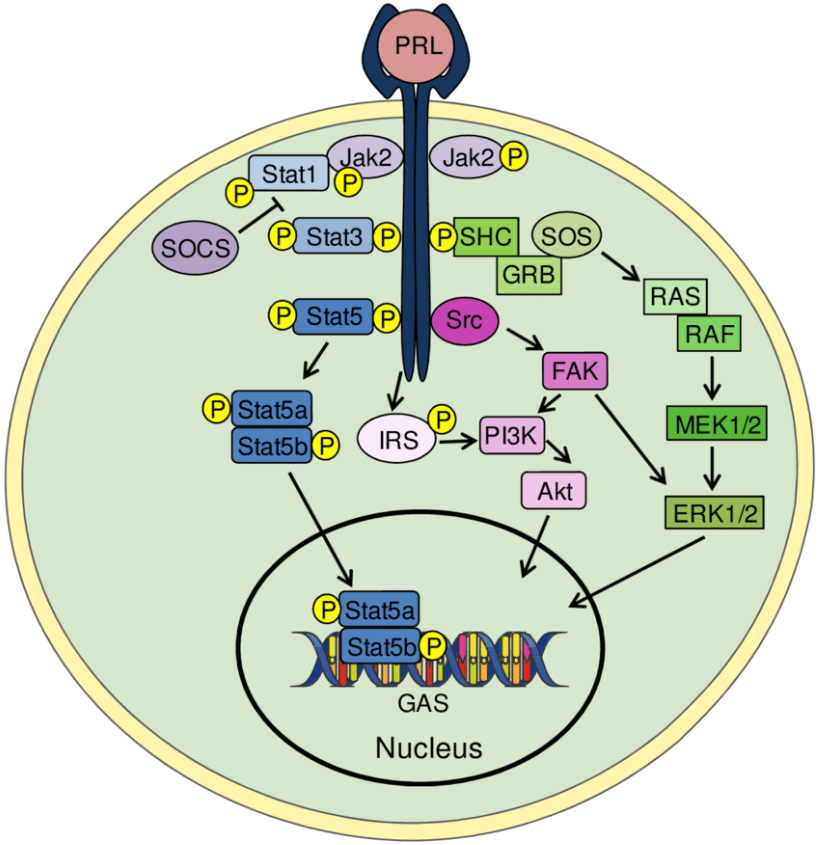
- Inhibition of dopamine results in a release of prolactin as is seen in non-secreting pituitary tumors or trauma that disrupts the pituitary stalk, thereby preventing dopamine from inhibiting prolactin release.
- Estrogen is a potent stimulator of lactotroph proliferation and raises the possibility that exogenous estrogen could increase the growth of prolactinomas,
- Thyrotropin-releasing hormone (TRH) and vasoactive intestinal peptide (VIP) also stimulates the release of prolactin, so when hypothyroidism increases TRH release from the hypothalamus, it causes hyperprolactinemia. In addition to hypothalamic control, prolactin secretion is induced by sleep, stress, chest wall stimulation, and pregnancy.
- During pregnancy, high levels of estrogen and progesterone inhibit lactation, and their postpartum decline permits lactation accompanied by the secretion of oxytocin in response to suckling.



Mechanism of action of Prolactin

- Prolactin binds to the prolactin receptor, which is a member of the type 1 cytokine receptor family.
- Janus kinase-2 is a protein kinase that is associated with the prolactin receptor and mediates prolactin's effect in the target cells
- The prolactin receptor is also the receptor for placental lactogens, which are hormones synthesized during pregnancy and which are also a result of prolactin or growth hormone gene duplication.
- Regulation of prolactin secretion by lactotrophs is primarily under the inhibition of dopamine, which acts through the D2-type receptors on lactotrophs.

The binding of PRL induces PRL receptor (PRLR) receptor dimerization and phosphorylation of Jak2. This results in the recruitment and phosphorylation of Stat5, Stat3, and Stat1. Activated Stat5a/b dimerizes and is translocated to the nucleus where it binds to gamma-activated sequence (GAS) consensus elements in the promoters of target genes. PRL can also activate the mitogen-activated protein kinase (MAPK) and phosphatidylinositol-3-kinase (PI3K)/Akt pathways.



Prolactin

Functions in relation to reproduction

- Breast growth during pregnancy
- Milk secretory activity (lactation) after birth Females: stimulates breast development and milk production.
- Males: involved in testicular function

- Direct effector hormone

Regulation:

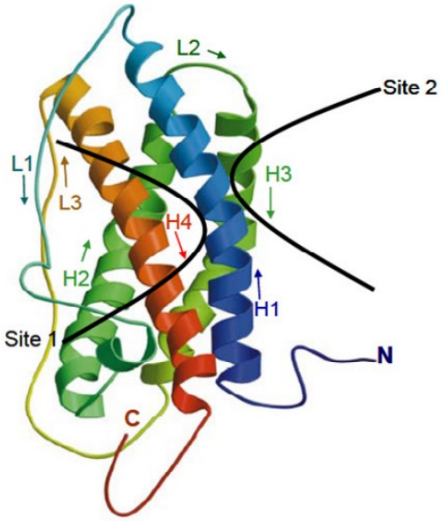
1. Inhibited by prolactin release-inhibiting hormone (Dopamine).
2. No hypothalamic stimulation except during lactation.
3. Stimulated by TRH but this is of pathological importance.

Prolactin (Prl)

Structure:

- Prolactin is a peptide hormone, which is encoded by the *PRL* gene on chromosome 6 in human.
- The human prolactin cDNA contains a 681-nucleotide open reading frame, thereby producing a precursor protein with 227 amino acids. After cleavage of the 28 amino acid signal peptide, the mature 23 kDa human prolactin is produced.
- A high-resolution NMR solution structure of human prolactin revealed that the core of the human prolactin structure is made up by four major α-helices
- prolactin circulates in the blood as monomers of 23–26 kDa

The Human PRL Protein



Secretion:

Lactotropes of the Anterior Pituitary.

The normal concentration for prolactin is less than 15 to 20 pg/mL in women and less than 10 to 15 pg/mL in men.

Level:

Starts early in the fetal stages.

Decline shortly after birth and remain low in males.

In female increase with pregnancy to reach a maximum level at term and remains high during lactation.

Prolactin imbalance:

Hyperprolactinemia:

- Hyperprolactinemia means abnormally high levels of prolactin (PRL) in the blood.
- Normal PRL levels (may vary according to the lab):
- < 23.5–25 ng/mL or µg/L for non-pregnant women
- 80–400 ng/mL or µg/L for pregnant women
- < 20–21.5 ng/mL or µg/L for men

Epidemiology

- Occurs in < 1% of the general population
- The most common form of pituitary hormone hypersecretion (hyperpituitarism) in both men and women

Causes:

Tumors in the lactotropes.

Dopamine antagonists.

Hypothyroidism associated with high level of TRH.

Hypothalamus or Anterior Pituitary disorders.

Sympotoms:

In females: Galactorrhea, Amenorrhea, Infertility.

In males: Galactorrhea, Impotence, Infertility.

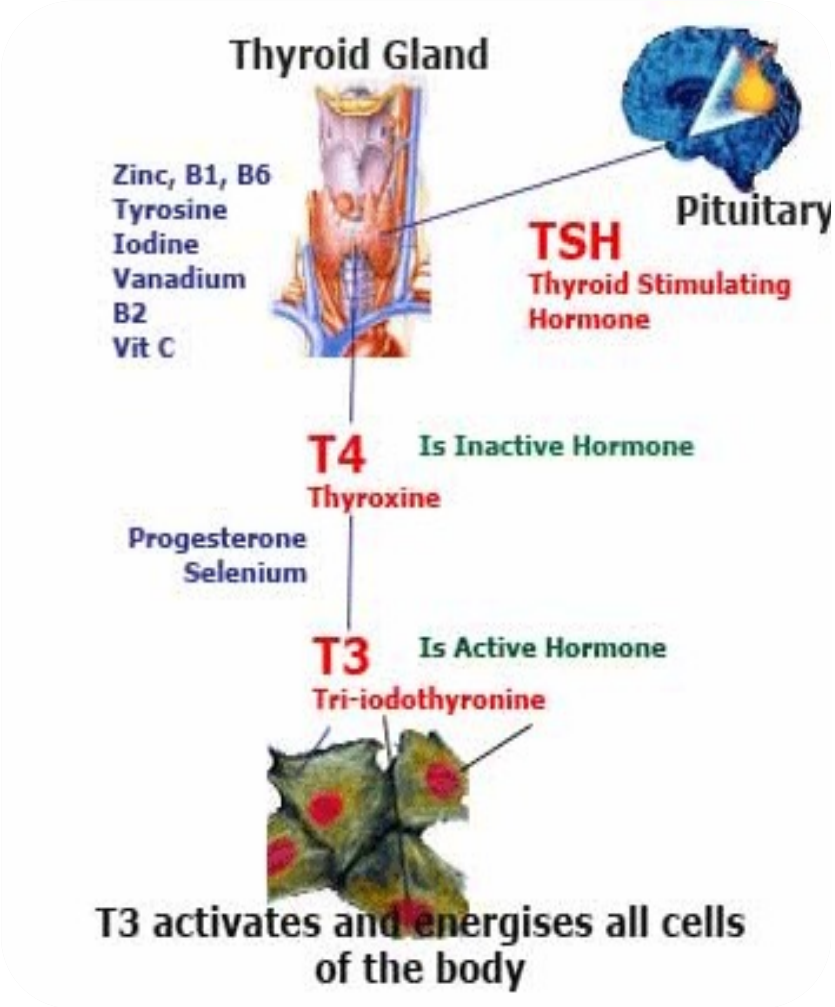
- Treatment:

Dopamine agonists: (Parlodel®)

2- Glycoprotein Hormones:

A. Thyroid-stimulating Hormone (TSH): stimulates the secretion of thyroid hormone & growth of thyroid gland

- Target gland is thyroid
- Leads to synthesis of T_3 & T_4
- T_3 & T_4 begins negative feedback inhibition of TRH & TSH production



B. Follicle-stimulating Hormone (FSH):

C. Luteinizing Hormone (LH):

- **Secretion:**
  - LH and FSH are secreted from the Gonadotropes of the Anterior Pituitary.
- **Regulation:**
  - **Stimulation:** Gonadotropin-Releasing Hormone from the hypothalamus (Gn RH).
  - **Inhibition:** Feed back mechanism by sex hormones.

Physiological effects:

- **In Males:**
  - **LH:** Stimulate production of androgens (Testosterone).
  - **FSH:** Enhance normal sperm production.
- **In Females:**
  - **LH:** Induce Ovulation and stimulate Progesterone production.
  - **FSH:** Enhance production of Estrogen and development of follicles (ovary).

- Uses:

  - Diagnostic uses:
    - **Reproductive system disorder in males and females.**

  - Therapeutic uses:
    - **Male infertility.**
    - **Female infertility.**

3- Pro-Opiomelanocortin (POMC) derived Hormones:

- The POMC family consists of peptides that act as hormones (ACTH, LPH, MSH) and others that may serve as neurotransmitters (endorphins) (see Figure).
- POMC is synthesized as a precursor molecule of 285 amino acids and is processed in the pituitary.
- The POMC gene is expressed in the anterior and intermediate lobes of the pituitary

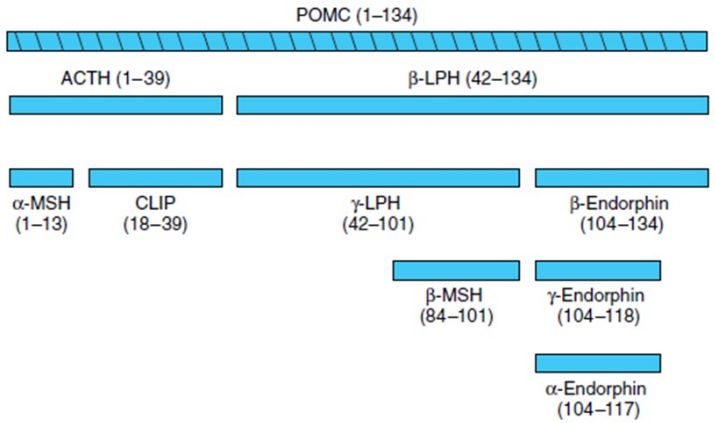


Figure 42–15. Products of pro-opiomelanocortin (POMC) cleavage. (MSH, melanocyte-stimulating hormone; CLIP, corticotropin-like intermediate lobe peptide; LPH, lipotropin.)

There are two basic peptide groups:

1. ACTH (1- 39) , which can give rise to α-MSH
2. β-lipotropin (β-LPH) (42- 134), which can yield γ-LPH, β-MSH, and β-endorphin (and thus α- and γ-endorphins);

Adrenocorticotropic Hormone (ACTH)

Structure:

Peptide hormone composed of 39 amino acid residues.

Function:

- Target cell= adrenal cortex
- Promote growth of adrenal cortical tissue otherwise atrophy of the gland takes place.
- Stimulate the production of adrenal steroids (cortisol).

Control:

- Feed-back inhibition by cortisol.
- Diurnal variation
- Highest levels between 6-8 am
- Lowest levels between 6-11 pm

Endorphins

play role in endogenous control of pain, they have higher analgesic potencies (18-30 times) than morphine

Anterior Pituitary Hormones

Hormone	Target Gland	Classification	Feedback Hormone	Function
Luteinizing hormone (LH)	Gonad	Tropic	Sex steroids	Directs testosterone production
Follicle stimulating hormone (FSH)	Gonad	Tropic	Inhibin	Ovarian recruitment
Thyroid stimulating hormone (TSH)	Thyroid	Tropic	Thyroid hormones (T4/T3)	Directs thyroid hormone production
Adrenocorticotropin hormone (ACTH)	Adrenal	Tropic	Cortisol	
Growth hormone (GH)	Multiple	Direct effector	Insulin-like growth factor	
Prolactin	Breast	Direct effector	Unknown	