Hormones

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Thyroid stimulating hormone (TSH)

Source: Thyrotropes

Actions: Stimulates iodine uptake and production of thyroid hormones (T4 and T3) of thyroid gland;

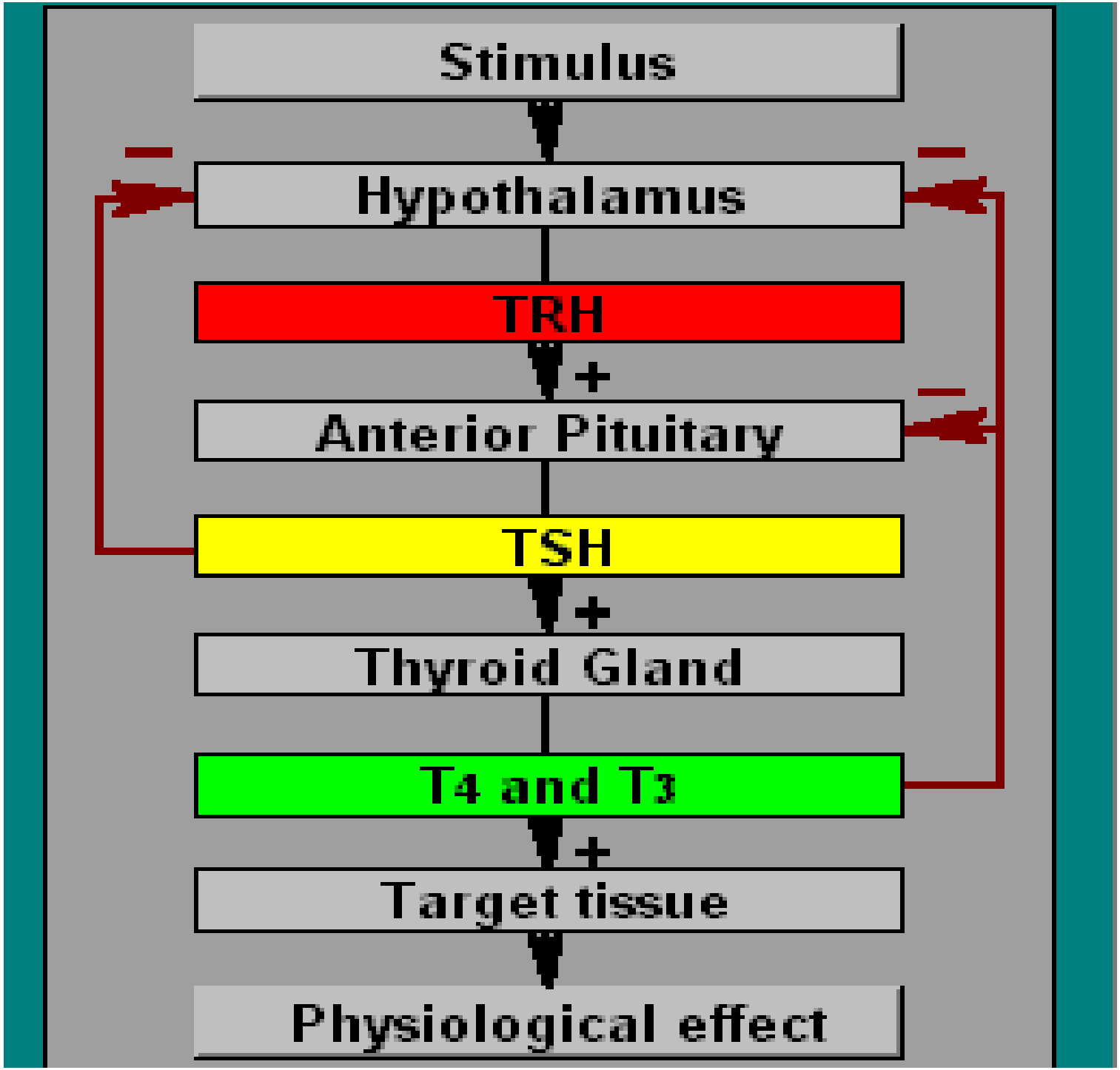
- T3 &T4 for energy production and maintains metabolic rate; body growth and organ differentiation.

Control:

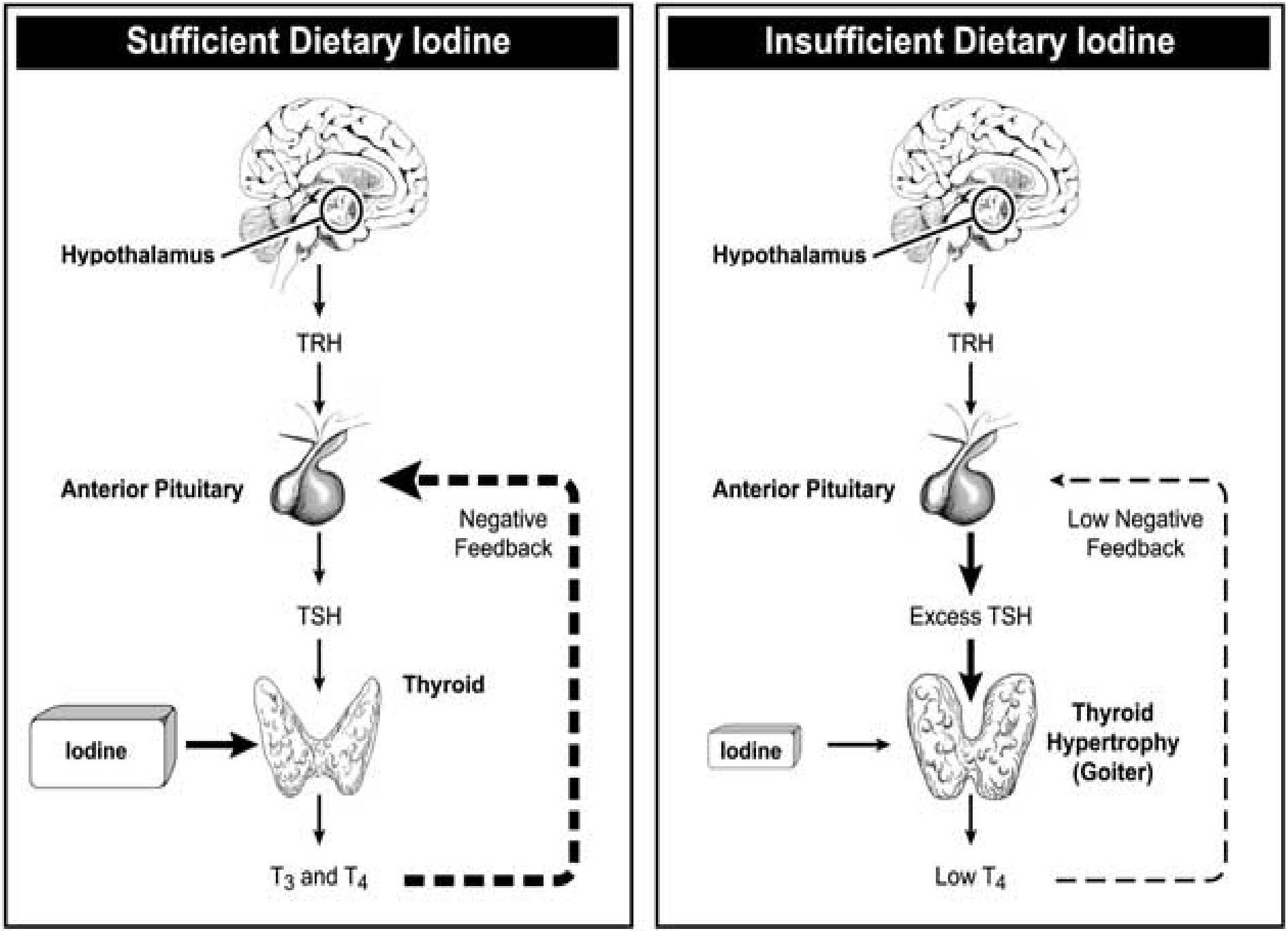
- Stimulated by hypothalamic TRH;
- Negatively feedback by T3 and T4

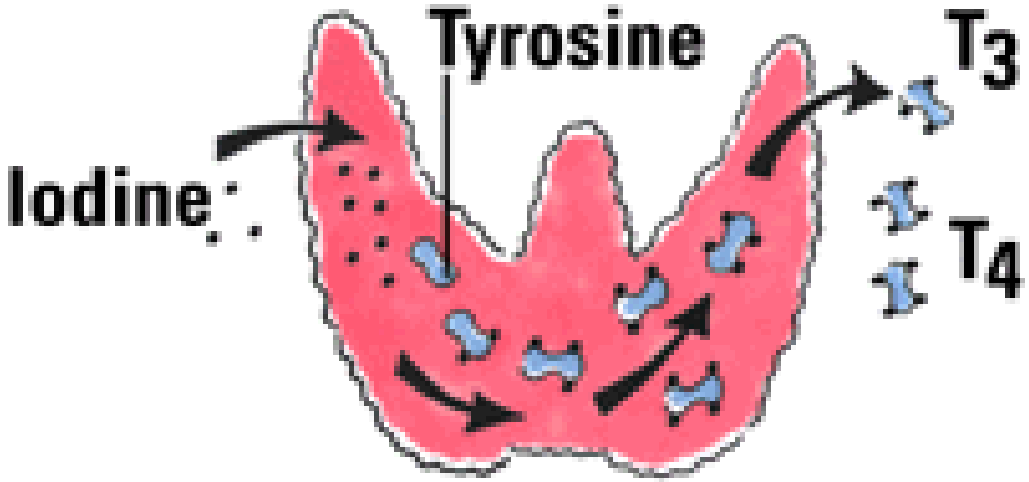
Excess: Hyperthyroidism:

- Graves Disease--autoimmune disorder characterized Thyroid stimulating immunoglobulins (TSI) which stimulate T3/T4 production (*reason*?)
- Symptoms: weight loss, heat intolerance, high BMR, heart failure & myopathy (muscle weakness due to excess protein breakdown).
- Treatment: Inhibitors of T3/T4 production (e.g., thiocarbamides)


Stimulus
Hypothalamus
TRH
+
Anterior Pituitary
TSH
+
Thyroid Gland
T4 and T3
+
Target tissue
Physiological effect
−
−
−

In the case of hyperthyroidism, or Graves' disease, the thyroid gland is enlarged and overactive, causing a groitier. The patient usually becomes hyperactive, nervous, and irritable, and suffers from insomnia. Hyperthyroidism can also be caused by thyroid tumor, wich is usually detected as a lump during physical examination. The treatment for hyperthyroidism is surgery in combination with administration of radioactive iodine. The prognosis for msot patients is excellent


Sufficient Dietary Iodine
Hypothalamus
TRH
Anterior Pituitary
Negative Feedback
TSH
Thyroid
Iodine
T_3 and T_4
Insufficient Dietary Iodine
Hypothalamus
TRH
Anterior Pituitary
Low Negative Feedback
Excess TSH
Thyroid Hypertrophy (Goiter)
Iodine
Low T_4

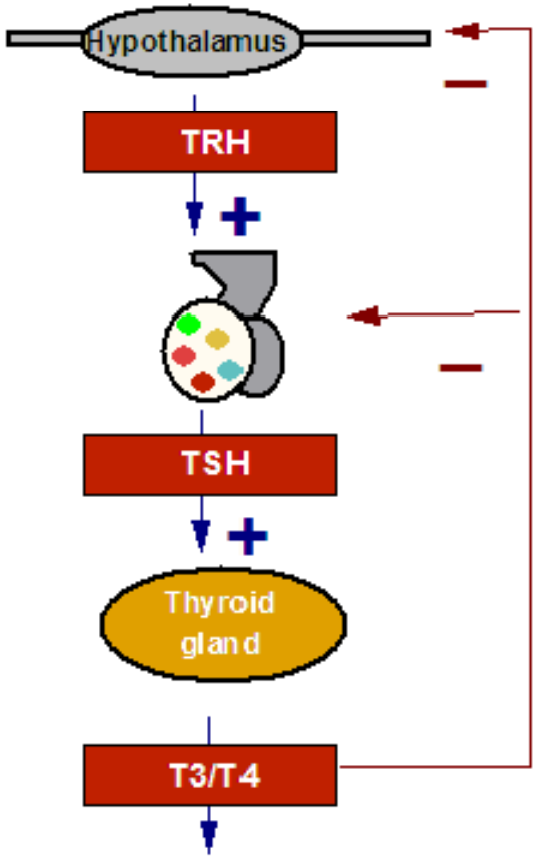

Tyrosine
T3
Iodine
T4

Thyroid stimulating hormone (TSH)--cont'd

Deficiency: Hypothyroidism:

- Congenital abnormality of hypothalamus-pituitary axis (TRH/TSH deficiency);
- autoimmune thyroiditis (Hashimoto's Disease)
- Iodine (dietary) deficiency:
  - Insufficient T3/T4 and decrease negative feedback leads to elevated TSH;
  - Thyroid hypertrophy (goiter)
- Symptoms:
  - Myxedema in adults--low BMR, sparse hair, dry & yellow skin, cold intolerance, husky & low voice, poor memory, mental instability (myxedema madness), abnormality in menstrual function;
  - Cretinism in children--dwarf, potbellied & mental retardation.
- Treatment: T3/T4 replacement; dietary iodine

Thyroid-Pituitary feedback regulation



- Increase metabolic rate and heat production;
- Enhancement of body growth, differentiation, development and cell functions.

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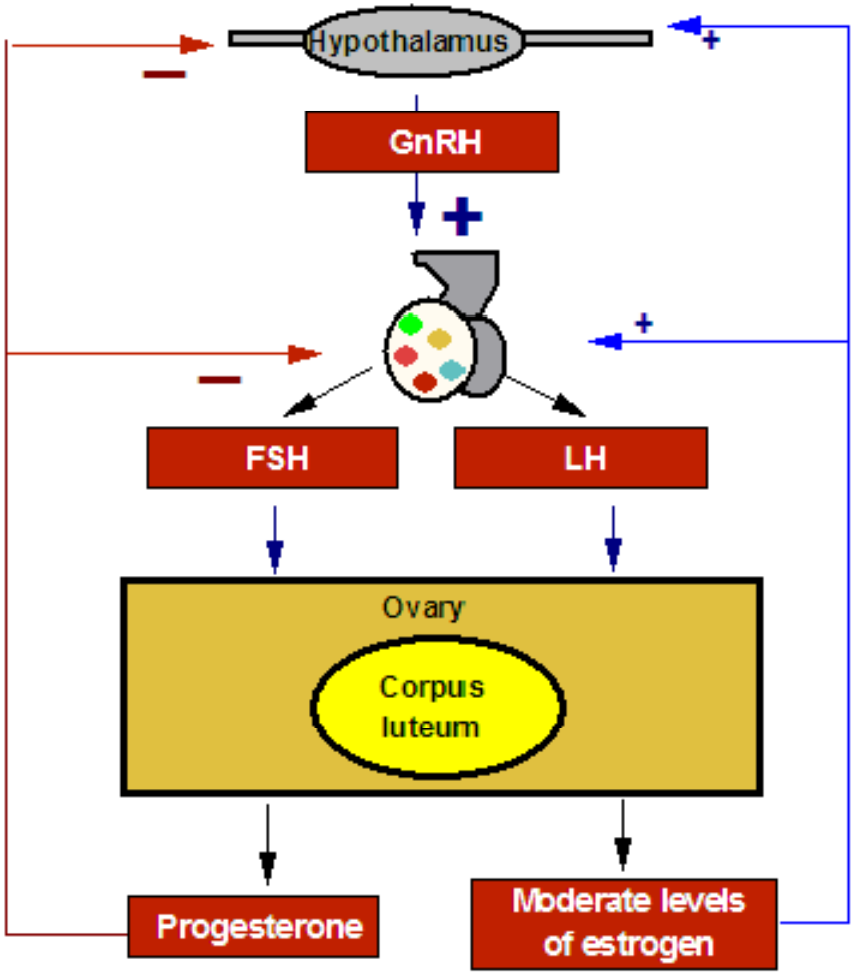
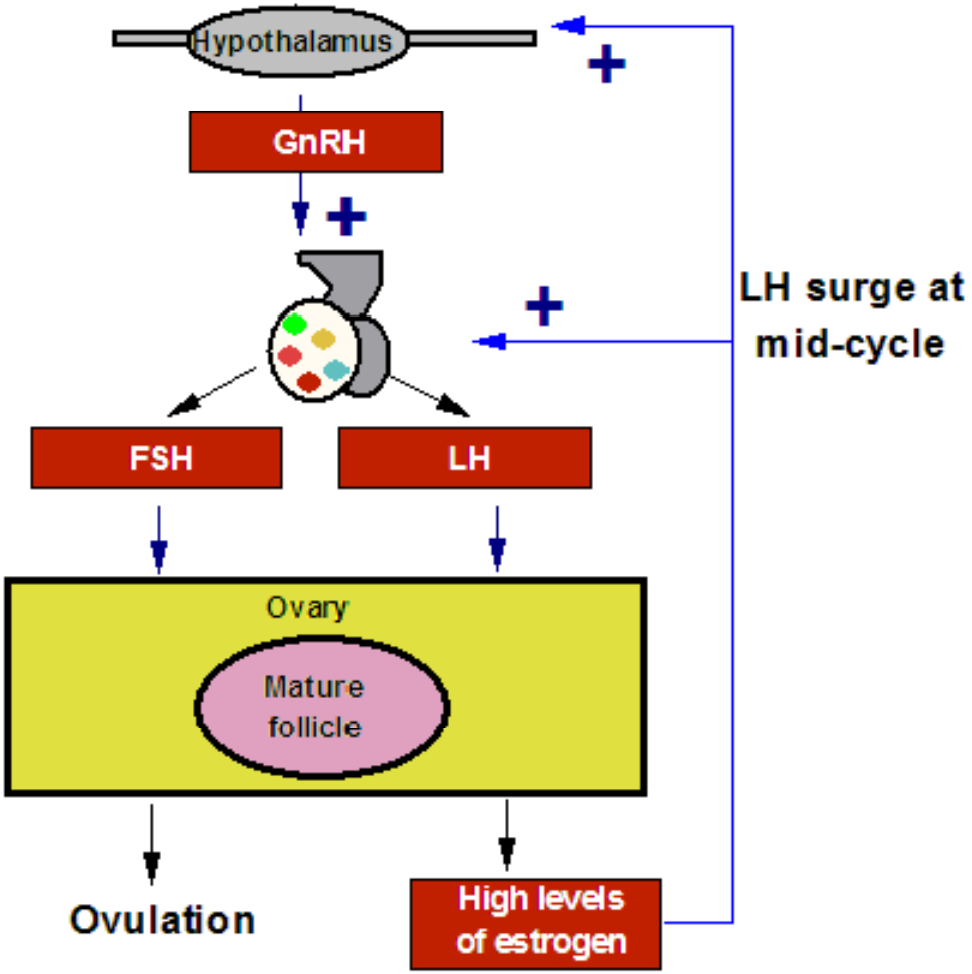
Measurement of Serum Thyroid Hormones: T4 by RIA. T4 by RIA (radioimmunoassay) is the most used thyroid test of all. It is frequently referred to as a T7 which means that a resin T3 uptake (RT3u) has been done to correct for certain medications such as birth control pills, other hormones, seizure medication, cardiac drugs, or even aspirin that may alter the routine T4 test. The T4 **reflects the amount of thyroxine in the blood.** If the patient does not take any type of thyroid medication, this **test is usually a good measure of thyroid function.**

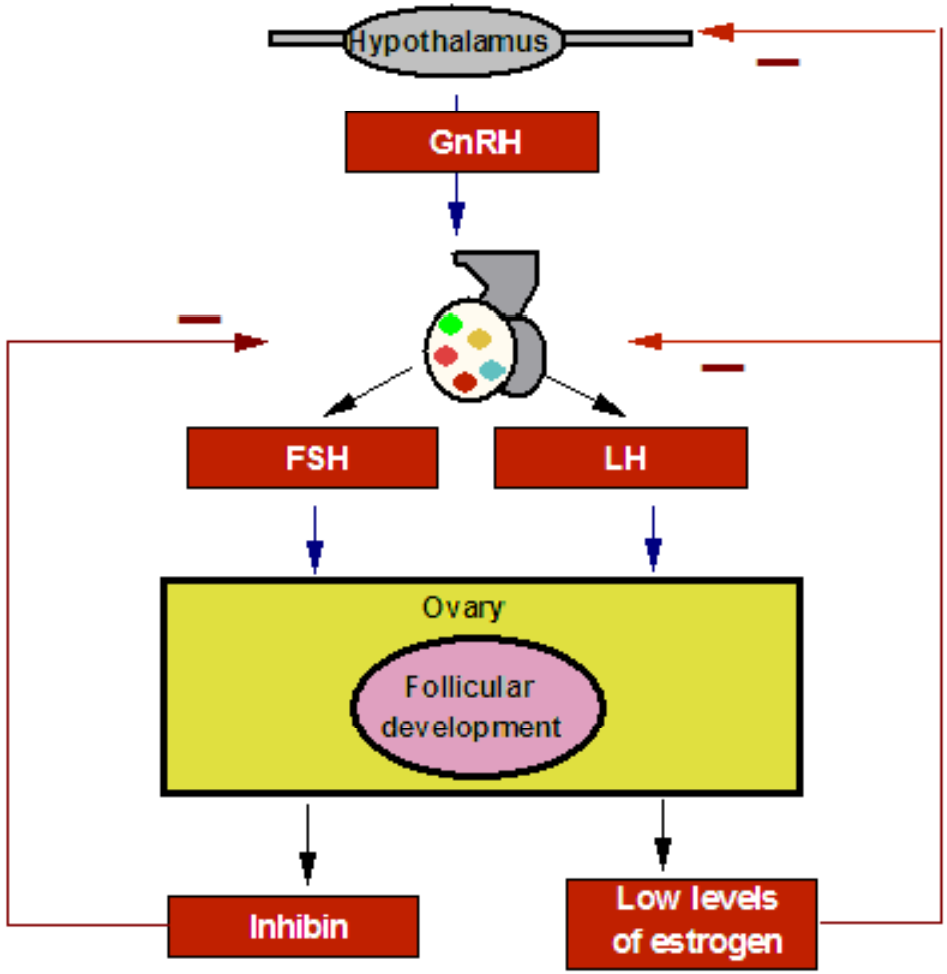
Gonadotropins feedback--Female (Luteal phase)



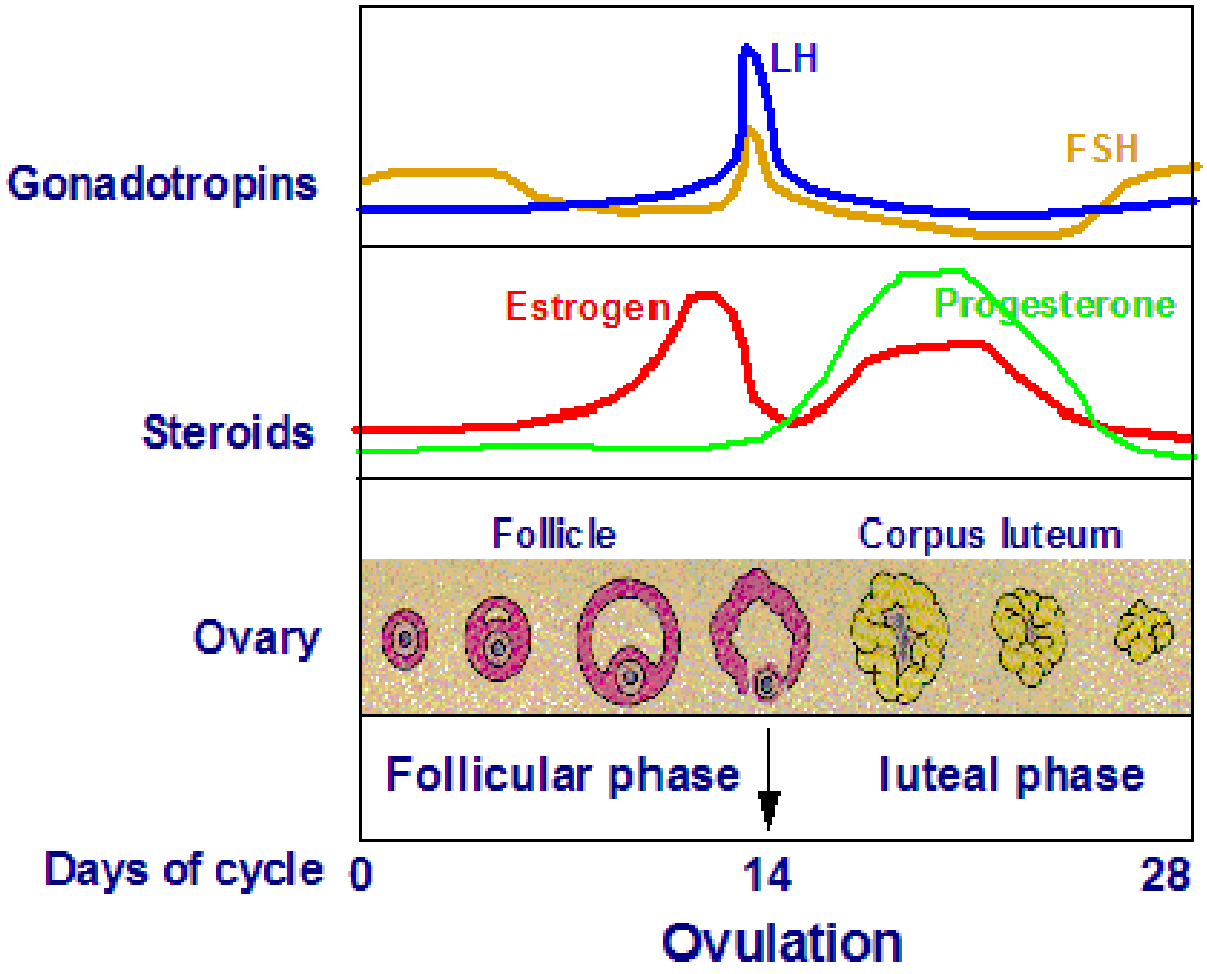
Gonadotropins feedback--Female (Mid-cycle)



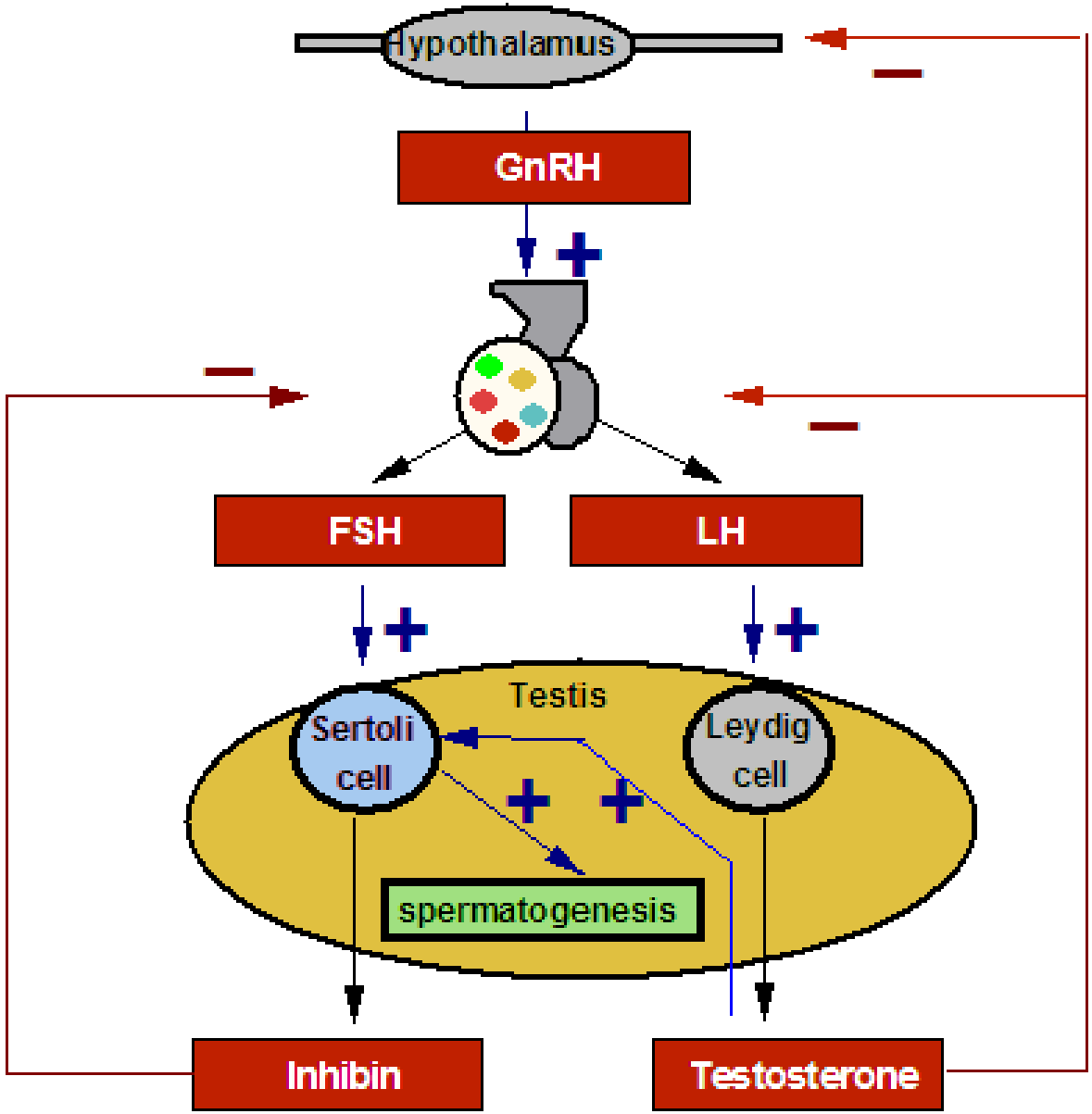
Gonadotropins feedback--Female (follicular phase)



Hormonal profiles of the ovarian (menstrual) cycle



Gonadotropin actions and feedback--Male



Gonadotropins--Luteinizing hormone & Follicle stimulating hormones (LH & FSH)

Source: Gonadotropes

Actions: Reproductive hormones acting on the gonads (See next 3 charts)

- LH stimulates sex steroidogenesis: estrogen, progesterone & testosterone;
- FSH stimulates growth of ovarian follicles and sperms

Control:

- Stimulated by hypothalamic GnRH; estrogen (high level);
- Inhibited by inhibin (from gonads), estrogen (low level); progesterone and testosterone.

Excess:

- Hypersecretion of GnRH & gonadotropins --true precocious puberty; treatment with supra-agonist of GnRH (mechanism?)
- Gonadotrope tumors are rare

Deficiency:

- GnRH deficiency (Kallmann's syndrome); hypopituitarism
- Reproductive failure due to insufficiency of sex steroids: abnormal development of genitalia and accessory sex organs, abnormal menstrual cycle, amenorrhea, infertility, delayed puberty;
- Treatments: GnRH and steroid replacement

Prolactin

Source: Lactotropes & somatomammotropes of anterior pituitary

Actions:
- Promotes growth & function of mammary gland--milk production;
- Increased maternal behaviour;
- Antagonizes gonadotropin action in gonads--↓ steroidogenesis.

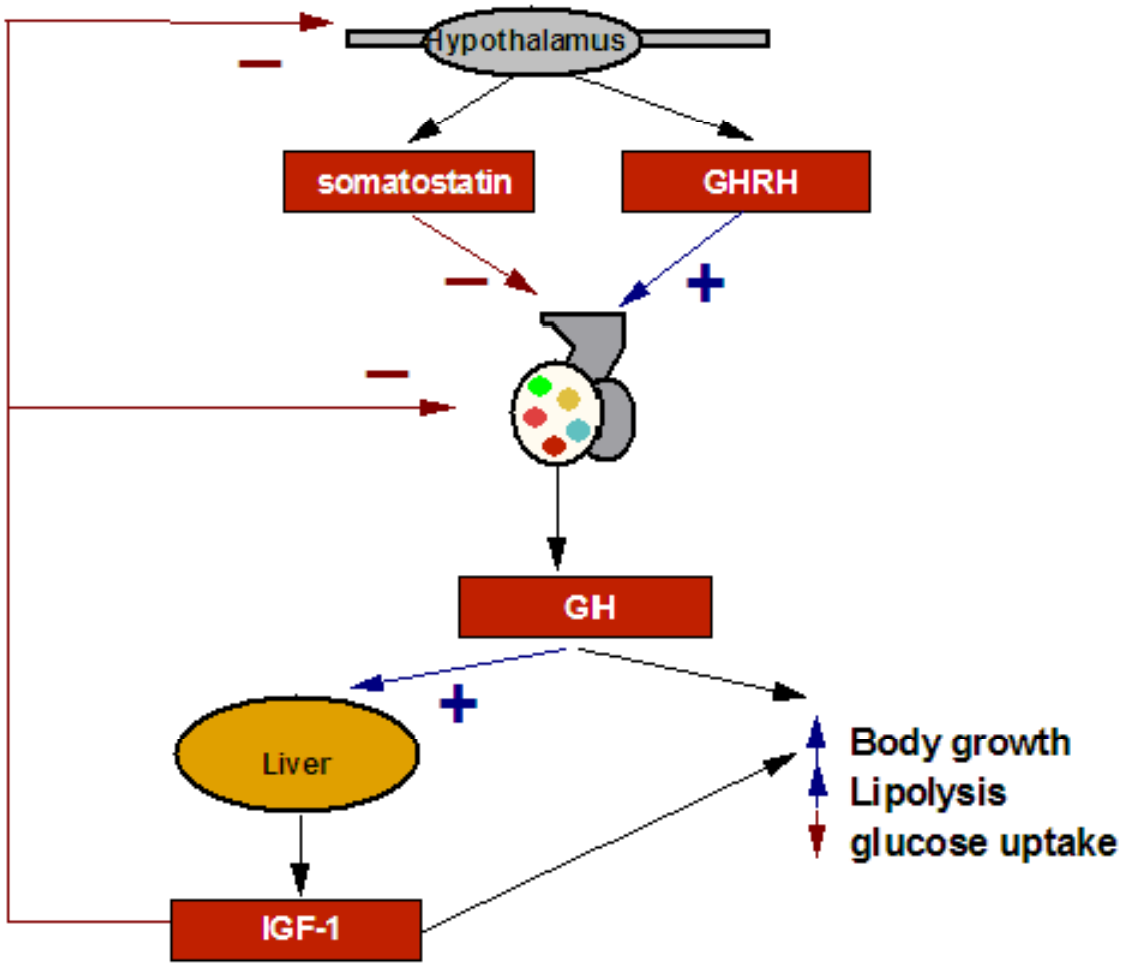
Control:
- Predominantly inhibited by hypothalamic Dopamine;
- Stimulated by oxytocin, TRH, VIP & estrogen.

Excess:
- Hyperprolactinemia : most common form of pituitary hyperfunction caused by microadenomas of lactotropes (majority of cases of pituitary tumors);
- Dopamine receptor blockers (some psychiatric medications);
- Stress; Vigorous exercises.
- Female: secondary amenorrhea (cessation of menstrual cycle); infertility, galactorrhea (inappropriate milk production);
- Male: impotence, decrease sperm count; infertility

Treatment: dopamine agonist (Bromocryptine/CB154/Parlodel) suppresses prolactin secretion & shrinks prolactinomas!

Deficiency: Rare

Feedbacks of GH secretion



Growth Hormone (Normal) GH-N (cont'd)

Excess: Somatotrope tumor:

- gigantism if GH excess occurs early in life (rare);
- acromegaly (excess soft tissue hyperplasia) if GH excess occurs after body growth stopped;

Treatment: tumor removal, SS analogs

Deficiency: Hypothalamic (GHRH deficiency) & pituitary lesions (tumor, injury, infection, congenital & genetic defects) leading to primary GH deficiency:

- dwarfism if occurs early in life;
- adult hypopituitarism: weakness, fine wrinkling & pale skin; loss of sex drive, genital atrophy, menstrual cycle cessation.

Other reasons for retarded growth (i.e., GH is good):

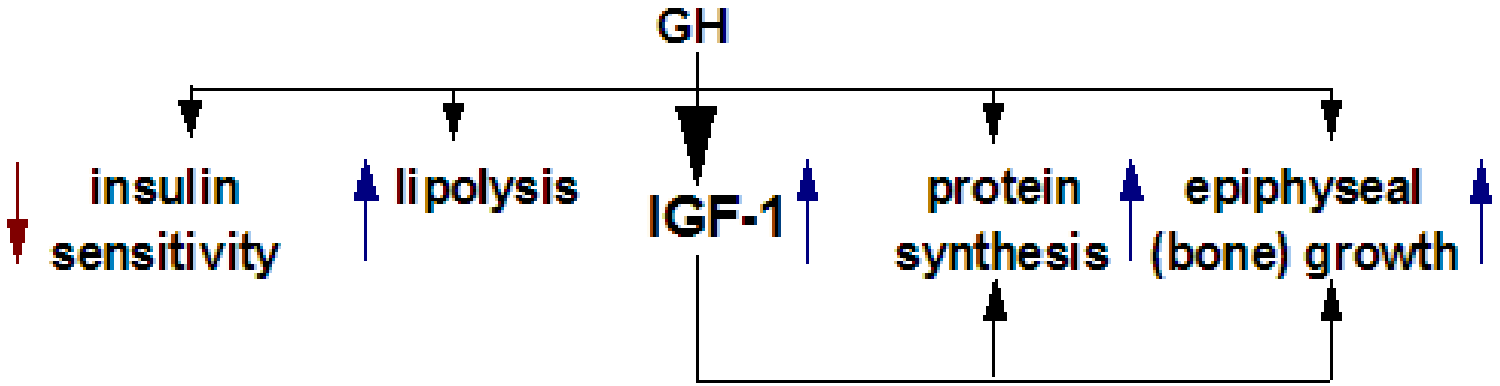
- GH receptor defect in target tissues (Laron Dwarfs);
- IGF-1 deficiency (African pygmies)

Treatment: GH and IGF-1 replacement

Growth Hormone (Normal) GH-N

Source: Somatotropes & somatomammotropes of anterior pitutiary

Actions:



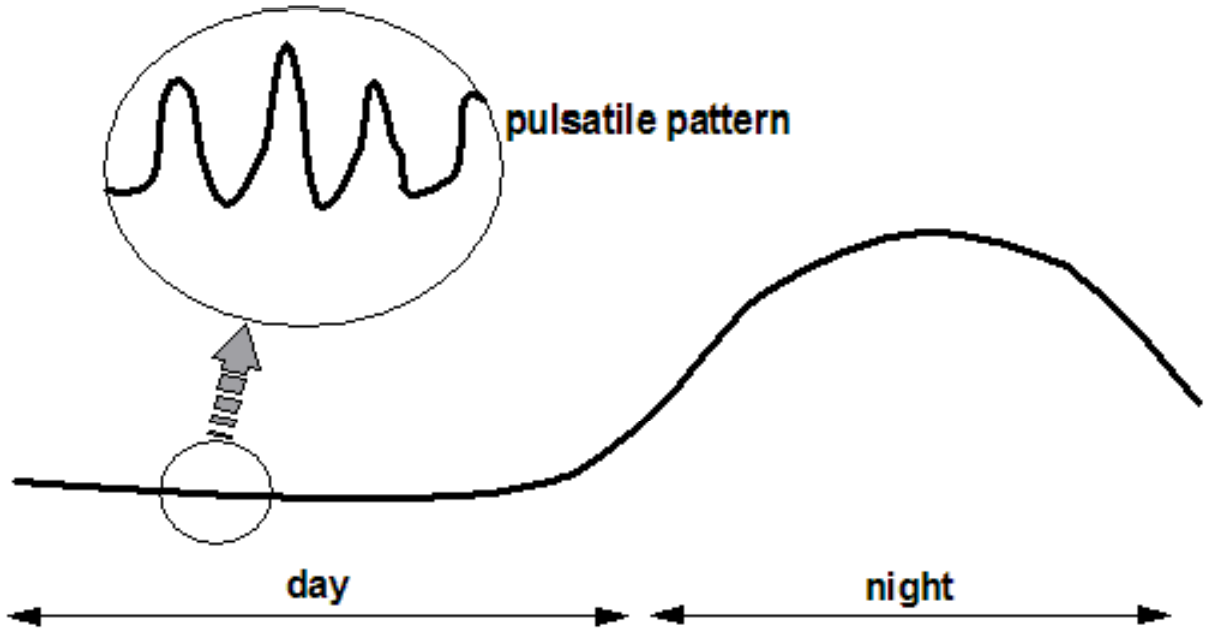
Control:

- Stimulated by GHRH, hypoglycemia, exercise, certain amino acids, sleep.
- Inhibited by somatostatin, IGF-1 (-ve feedback), hyperglycemia

Pulsatile hormone secretion by anterior pituitary

- fluctuation of neuronal activity
- rhythmic release of hypophysiotropic hormones

Diurnal (24-hour) growth hormone secretion:



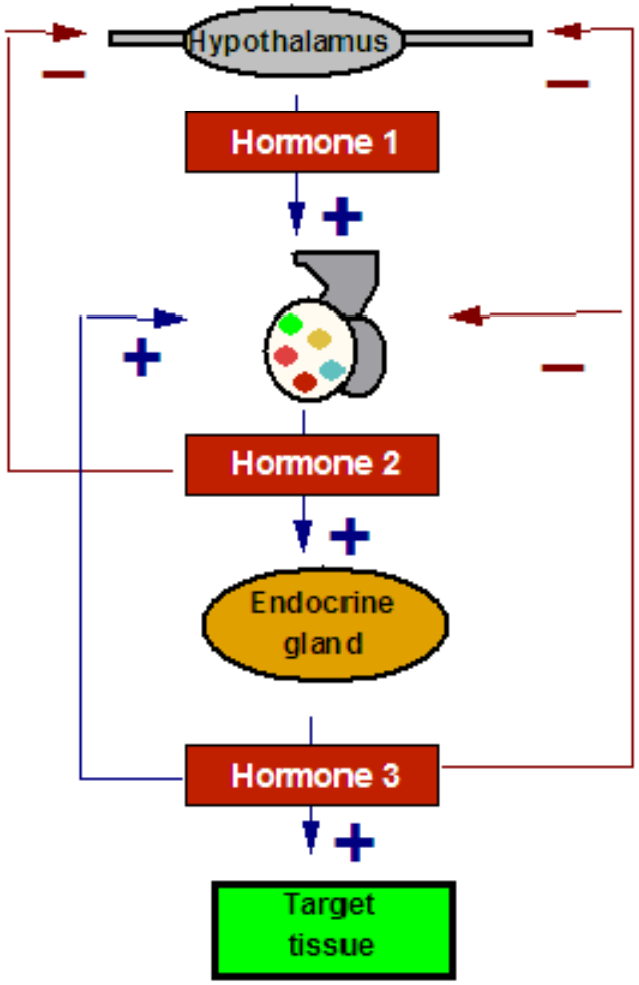
What do hypophysiotropic hormones look like?

TRH	Glu-His-Pro (3 amino acids)
LHRH	Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys (14 amino acids)
Dopamine	Hydroxylated & decarboxylate Tyrosine (one amino acid)

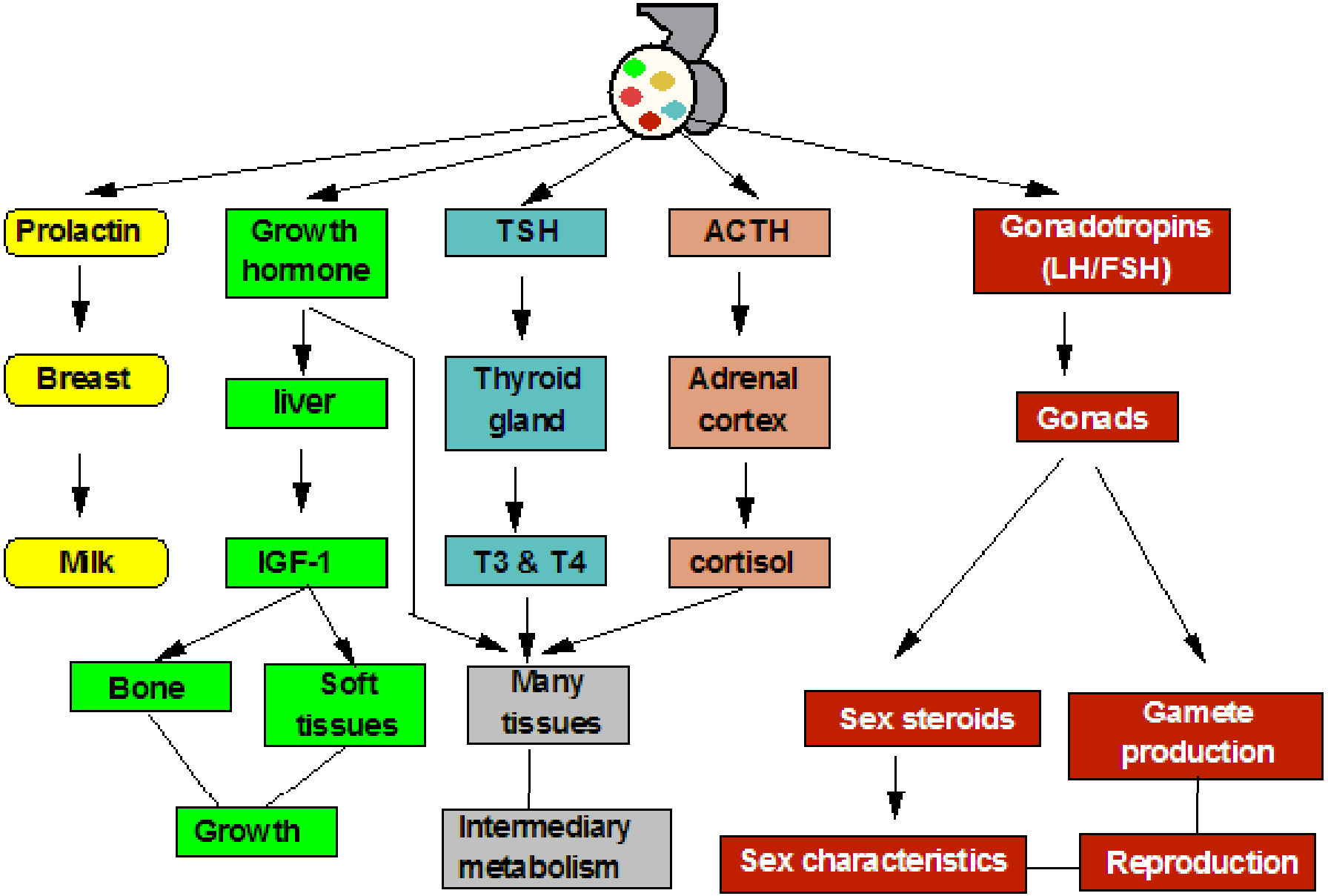
Major hypophysiotropic hormones

	Effects on anterior pituitary	
Corticotropin-releasing hormone (CRH)	↑	ACTH
Thyrotropin-releasing hormone (TRH)	↑	TSH Prolactin
Gonadotropin-releasing hormone (GnRH)	↑	LH/FSH
Growth hormone-releasing hormone (GHRH)	↑	GH
Somatostatin	↓	GH
Dopamine	↓	Prolactin

Feedback regulation of anterior pituitary hormones



Overview of anterior pituitary hormone functions



Adrenocorticotropic hormone (ACTH)

Source:

- Corticotrope;
- Cleavage product (by prohormone convertases PC1 & PC2) of larger precursor--Pro-opiomelanocortin (POMC) gives rise to ACTH, MSH, beta-endorphin, lipotropin

Actions:

- ACTH: stimulates adrenal cortex to produce glucocorticoids, mineralocorticoid and sex steroids;
- MSH: stimulates melanin of melanocytes (skin color);
- Beta-endorphin: morphine-like analgesic neurotransmitter (pain)

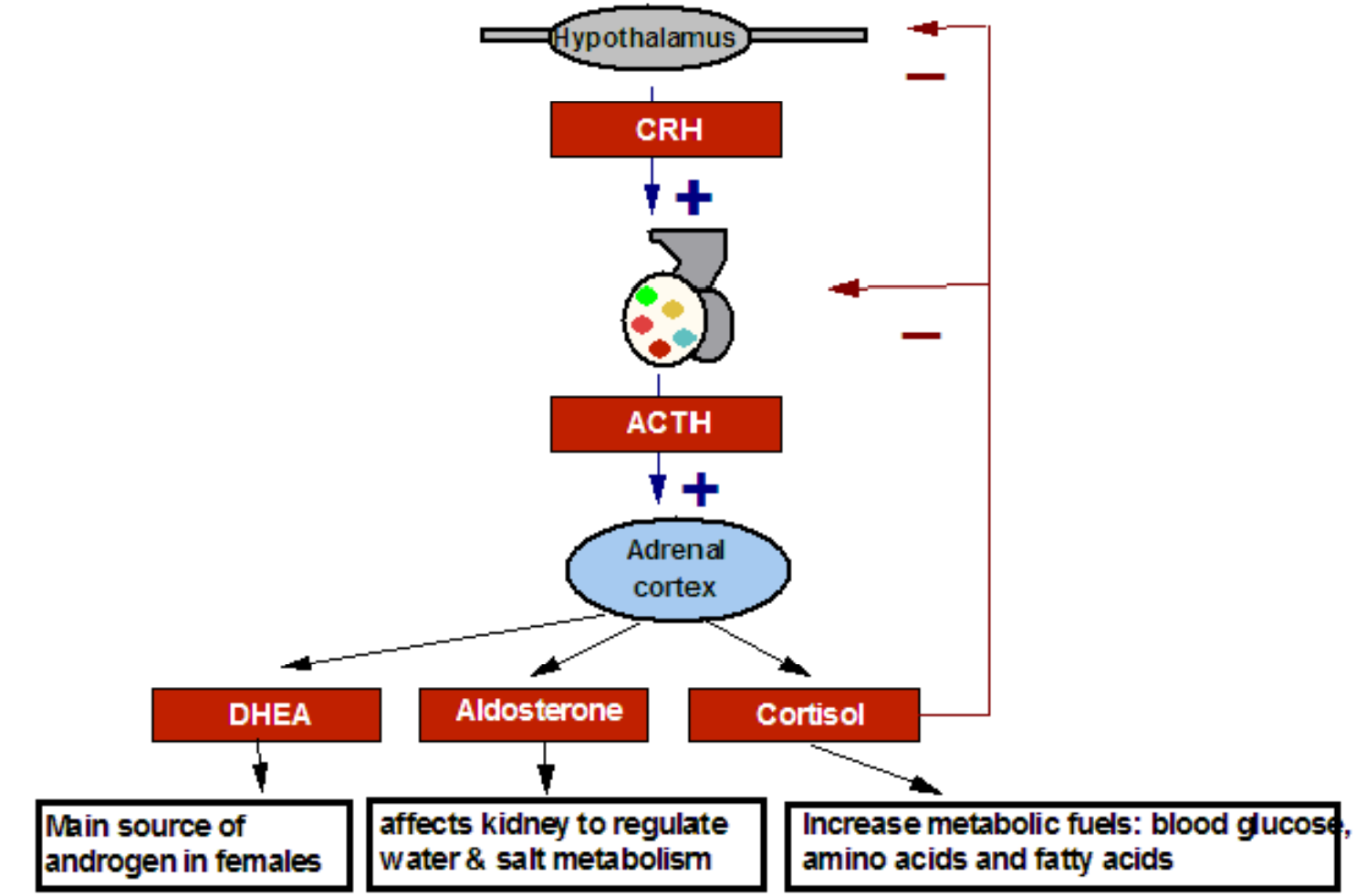
Control:

- Stimulated by hypothalamic CRF;
- Negatively feedback *only* by glucocorticoids

Excess:

- Primary adrenal hyperfunction--30%-- due to adrenal tumor
- Secondary Adrenal hyperfunction--70%(e.g., Cushing's syndrome)
  - ACTH-secreting microadenomas;
  - Hypersecretion of hypothalamic CRF;
  - Ectopic production of ACTH by non-pituitary tumors.
- Treatment:suppression or removal of tumors

Adrenal-Pituitary feedback regulation



Adrenocorticotropic hormone (ACTH)--cont'd

Excess:

- Elevated glucocorticoids (cortisol) result in:
  - excess protein catabolism, thin subcutaneous tissues, poor muscle development; loss of bone mass
  - characteristic body fat re- distribution in abdomin and upper back--"buffalo hump";
  - hyperglycemia leading to type II diabetes.
- Excess mineralocorticoid (aldosterone) leads to:
  - K+ depletion, excess Na+ & water retention, hypertension.
- Excess androgen (DHEA):
  - in boys causes precocious development of secondary sex characteristics without testicular growth (precocious pseudopuberty);
  - in girls, pseudohermaphroditism.

Deficiency:

- Primary adrenal insufficiency caused by adrenal failure (e.g., Addison's disease;
- Secondary adrenal insufficiency caused by decrease CRF and/or ACTH at the hypothalamus-pituitary axis.
- Excess Na+ loss, hypotension, abnormal metabolism of protein, carbohydrate and fat; fatal shock following minor stress.
- Treatment: cortisol, aldosterone replacement.