Endocrine Pharmacology

Disclaimer

All the content material provided here is only for teaching purpose.

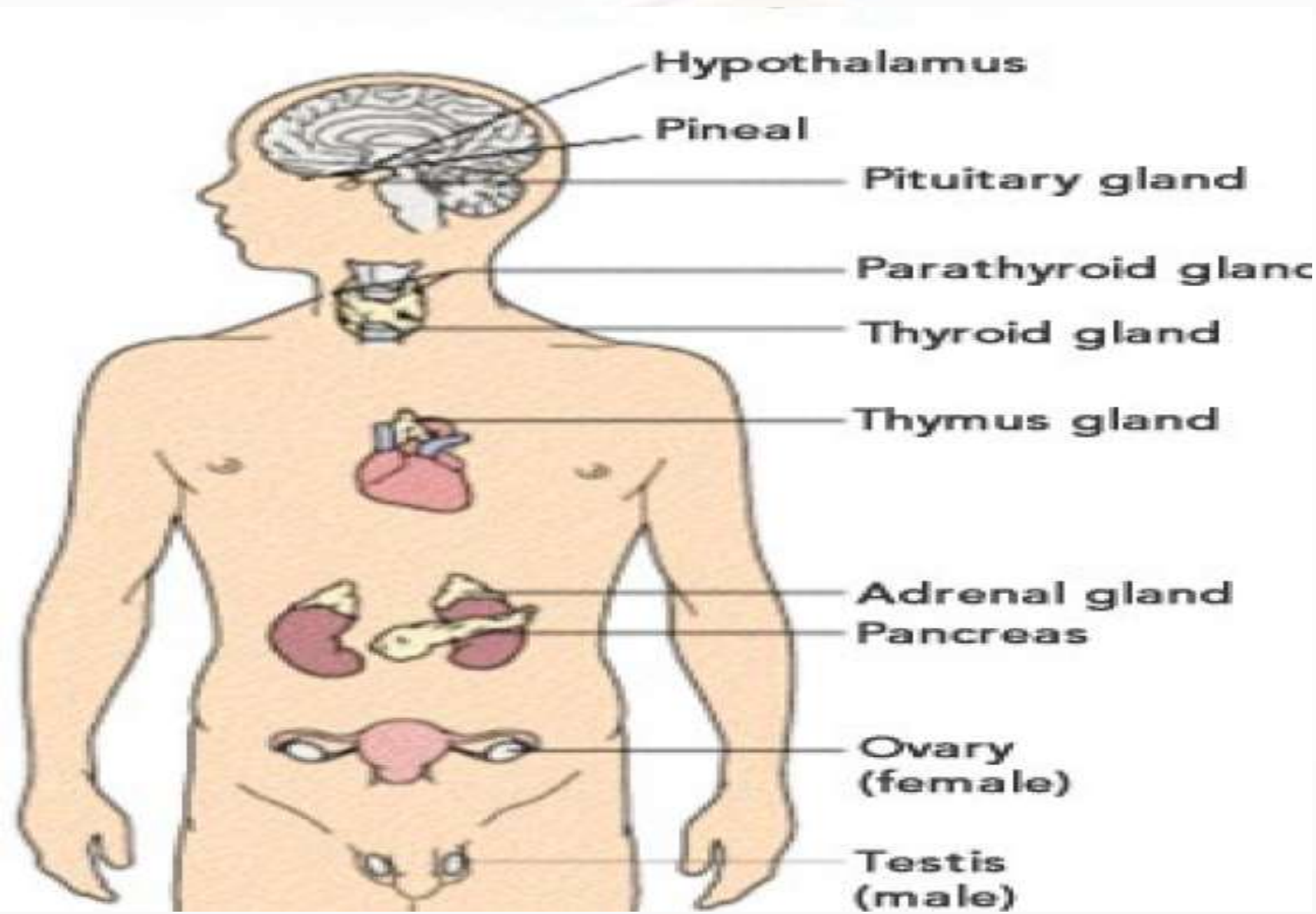
Endocrine Pharmacology

Hormone is a substance of intense biological activity that is produced by specific cells in the body and is transported through circulation to act on its target cells.

These substances are secreted by one cell (Secretary cell) and perform action on other cells (Target Cell).

The word endocrine means '**Ductless gland**' i.e.- this secretion directly goes to the blood from the secretary cell.

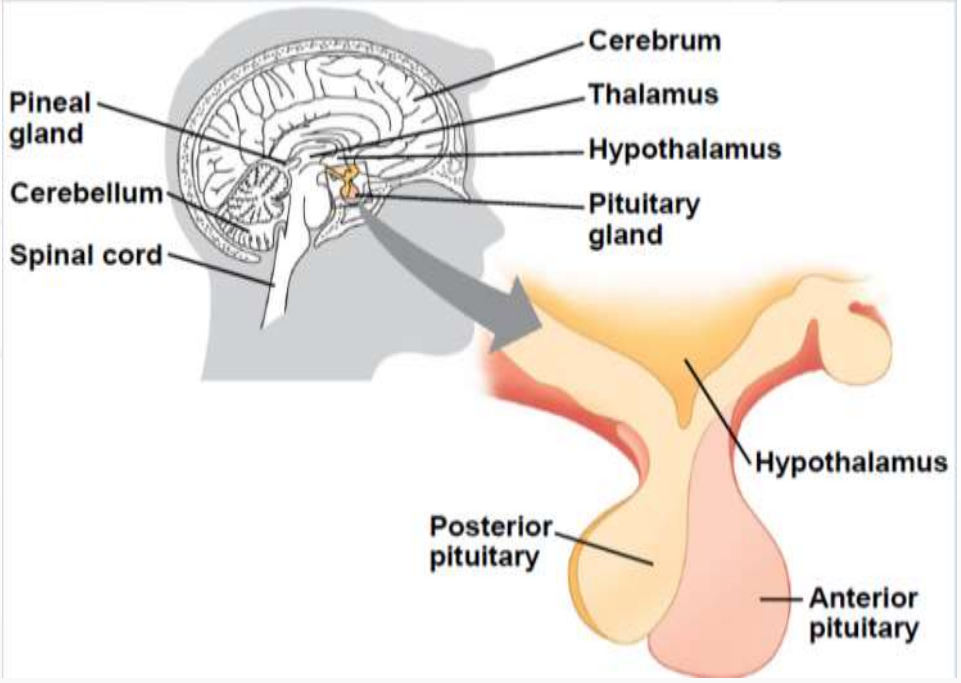
Endocrine glands:



Hypothalamic & Pituitary Hormones

The output of the hypothalamus-pituitary unit regulates the function of the thyroid, adrenal and reproductive glands and also controls somatic growth, lactation, milk secretion and water metabolism.

Hypothalamic Hs can have effect of stimulating or inhibiting the release of ant. Pit. Hs. Called RELEASING HORMONES “RH” or INHIBITING HORMONES “IH” respectively, reflecting their influence on ant. Pit. Hs.



The Pituitary Gland is divided into 2 areas, *with separate types* of hormone production.

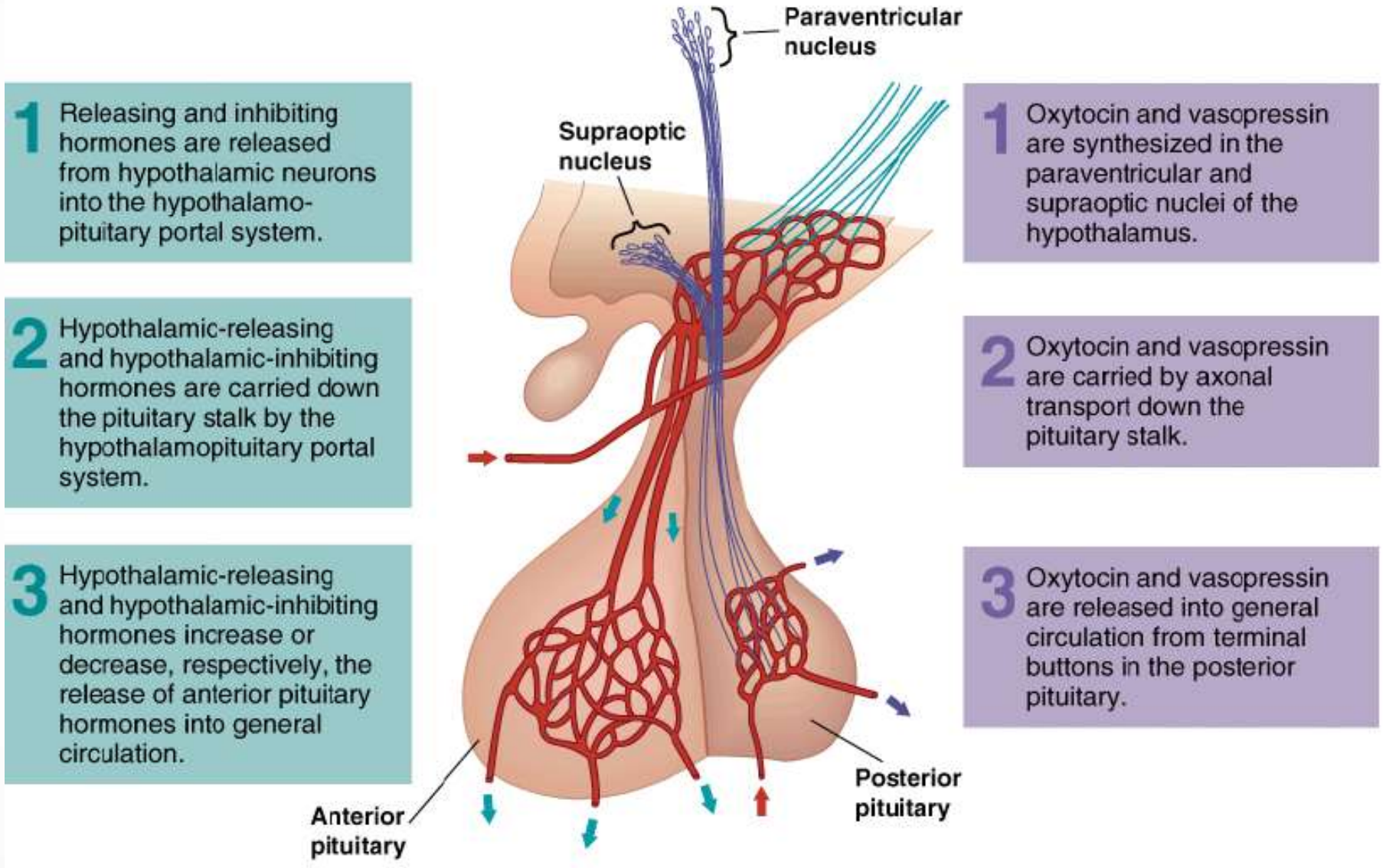
Anterior pituitary

- Growth Hormone (**GH)**
- Thyroid-stimulating Hormone (**TSH)**
- Adrenocorticotropin (**ACTH)**
- Follicle-stimulating Hormone (**FSH)),**
- Leutinizing Hormone (**LH),**
- Prolactin

Posterior pituitary

- Oxytocin and
- Antidiuretic hormone (**ADH)**

Control of Pituitary glands by Hypothalamus



Anterior Pituitary Hormone:

Growth Hormone

Derived from the somatotroph cells

Its secretion is controlled by GHRH and somatostatin

- GH secretion is high in newborn, deceasing at 4 yr to an intermediate level, which is then maintained until puberty, when there is further decline

- Insulin-like growth factor 1 (IGF-1) released from the liver inhibits GH secretion by stimulating somatostatin secretion from the hypothalamus

Growth Hormone Activity

- Increases plasma free fatty acids (source of energy for muscle tissue)
- Increases hepatic glucose output
- Decreases insulin sensitivity in muscle
- Is protein anabolic hormone

Growth Hormone Deficiency

- In childhood: short stature and adiposity, hypoglycemia.
- Adults : generalized obesity, reduced muscle mass.

Growth Hormone Excess

- In adults causes acromegaly
- If this occurred before the long bone epiphyses close, it leads to the rare condition, gigantism

Thyroid-stimulating Hormone (TSH)

- Also called thyrotrophin
- Stimulates secretion of thyroid hormone & growth of thyroid gland.

Adrenocorticotropin (ACTH)

- Stimulates cortisol secretion by the adrenal cortex & promotes growth of adrenal cortex

Follicle –*stimulating hormone (FSH)*

- Females: stimulates growth & development of ovarian follicles, promotes secretion of estrogen by ovaries.
- Males: required for sperm production

Leutinizing hormone (LH)

- Females: responsible for ovulation, formation of corpus luteum in the ovary, and regulation of ovarian secretion of female sex hormones.
- Males: stimulates cell in the testes to secrete testosterone

Prolactin

- Secreted by lactotroph cells of the ant. Pit., which increase in number during pregnancy.
- Its secretion is stimulated by estrogen
- Females: stimulates breast development and milk production.
- Males: involved in testicular function

Posterior pituitary Hormones

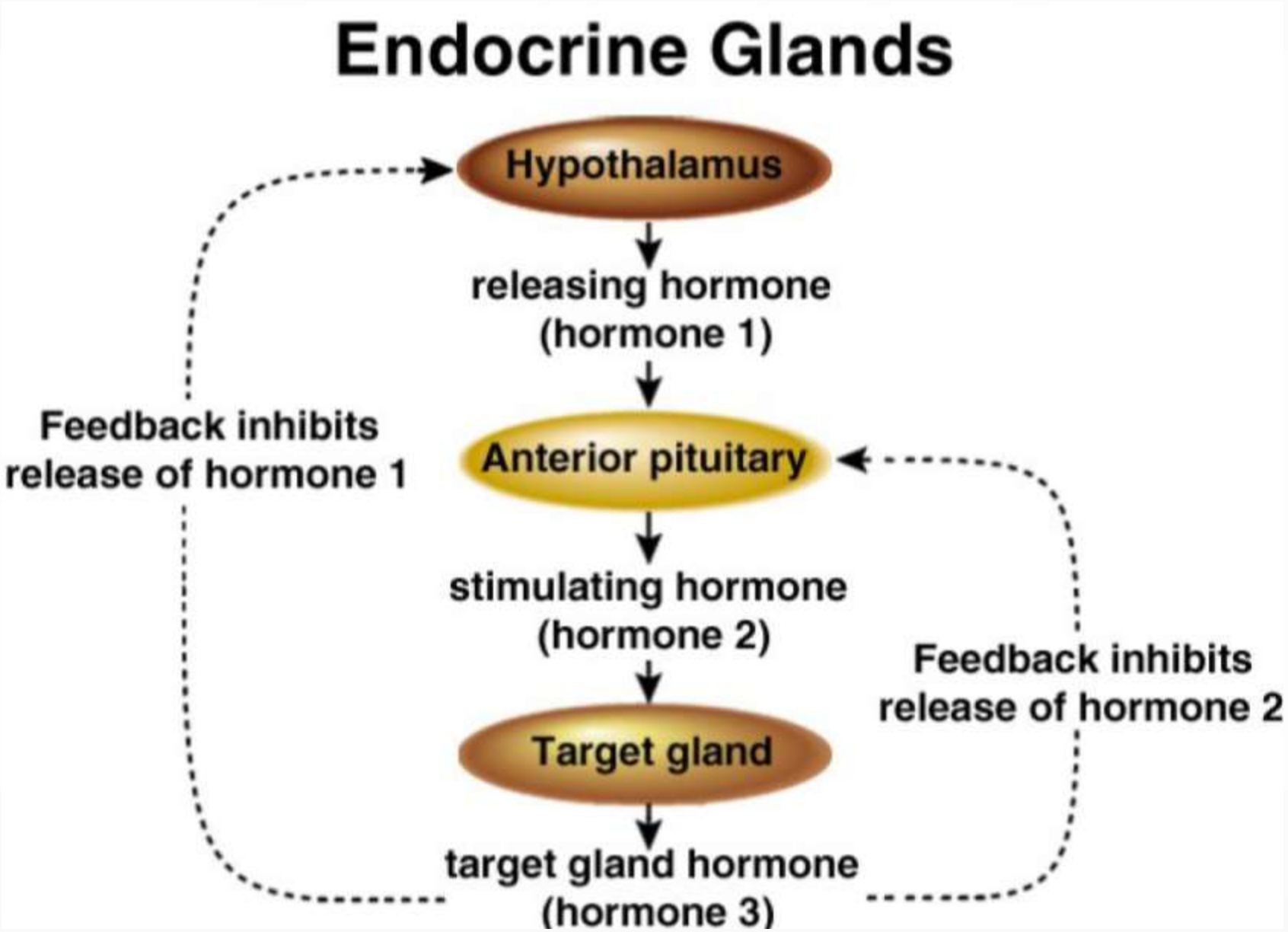
Oxytocin

- It is synthesized in the hypothalamus & transported to the post. Pit.
- It is an effective stimulant of uterine contractions & is used intravenously to induce or reinforce labor .
- Induces the release of milk
- Suckling sends a message to the hypothalamus via the nervous system to release oxytocin, which further stimulates the milk glands

Vasopressin (antidiuretic hormone ADH)

- The function of ADH is to increase water conservation by the kidney.
- ADH release increases if blood pressure falls or blood becomes too salty.
- ADH causes peripheral blood vessel constriction to help elevate blood pressure .

Regulation of Hormonal secretion by Hypothalamus and Pituitary Gland



Thyroid Hormones

Triiodothyroxine T3

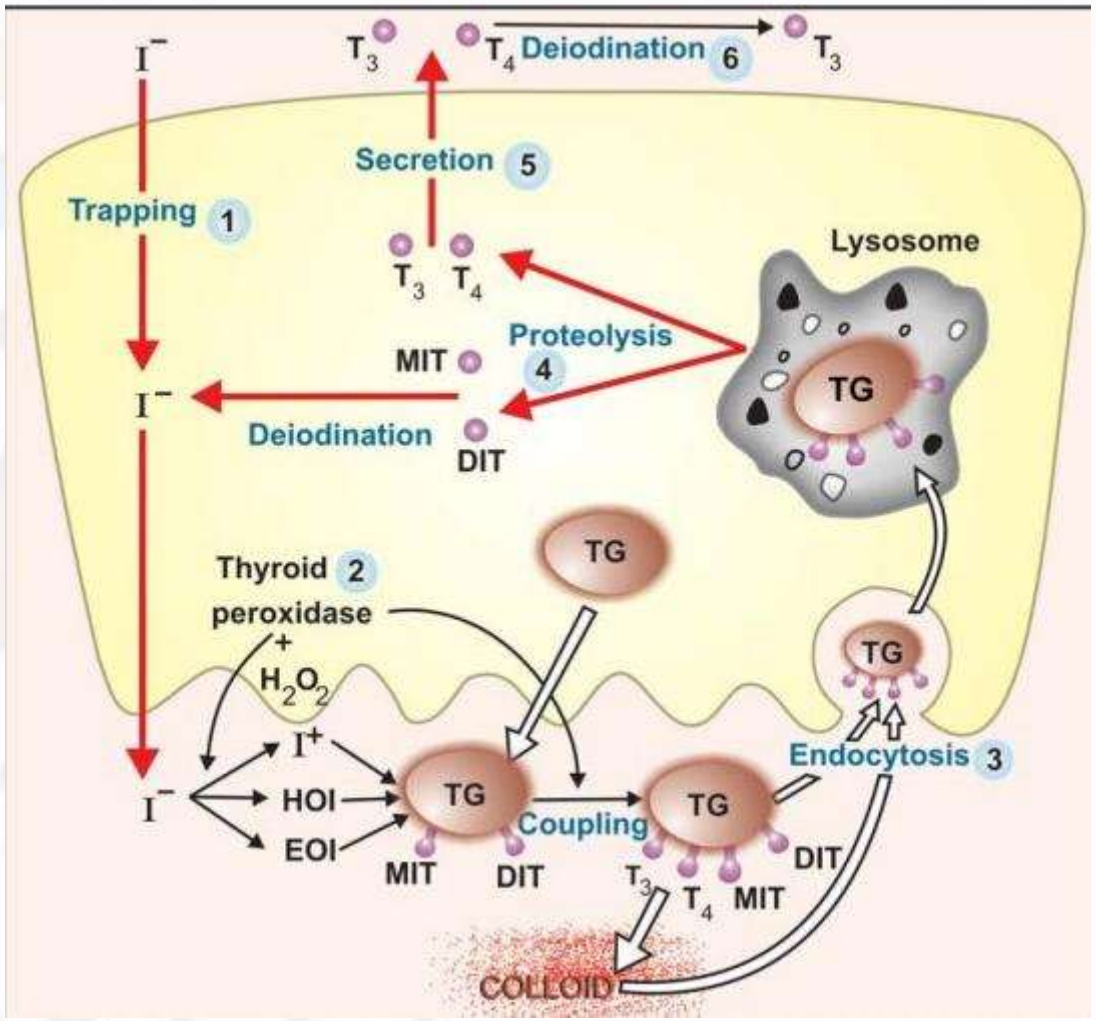
Tetraiodothyroxine T4

Calcitonin(Parathyroid)

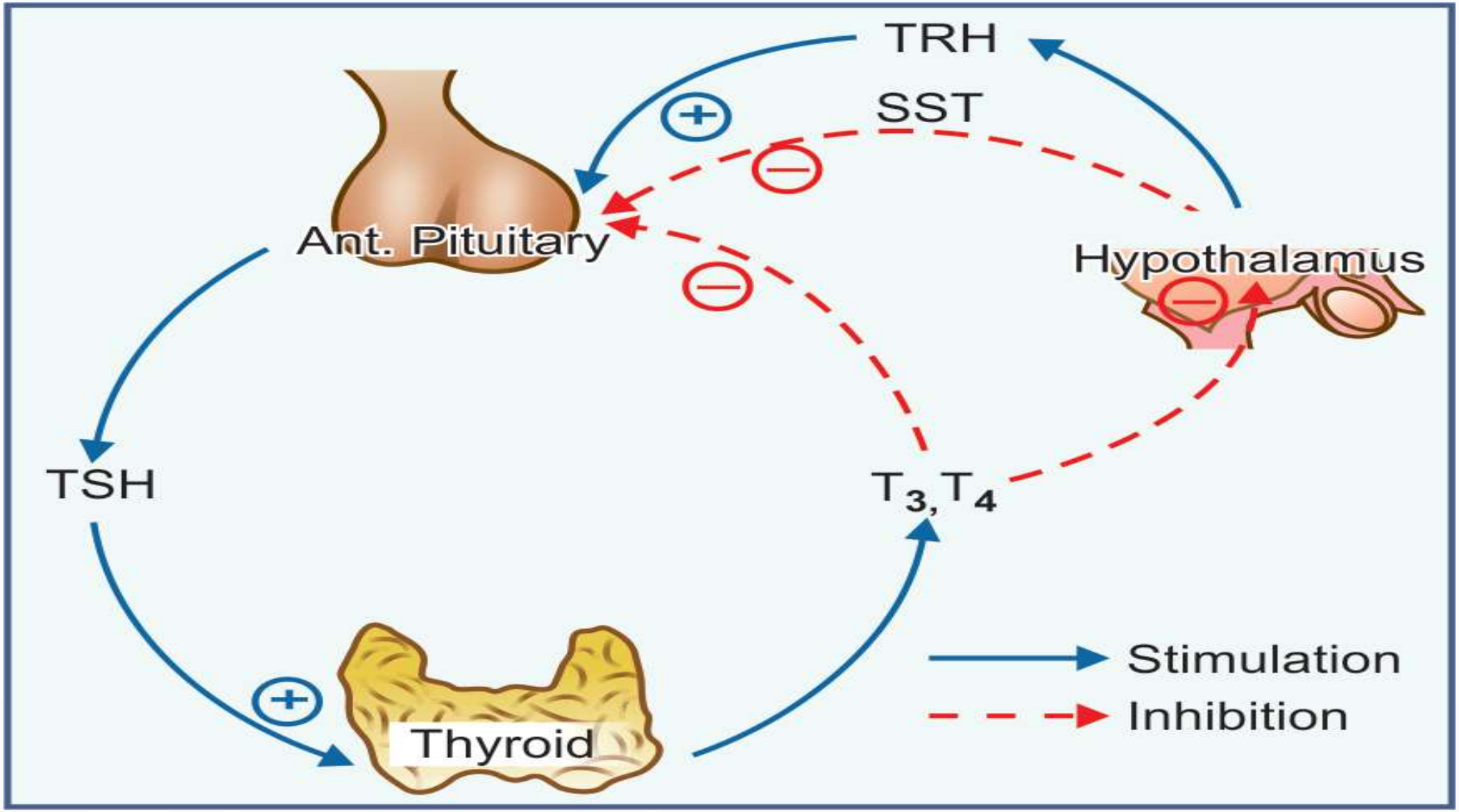
Synthesis of T3 and T4

It involves the following steps:

- Iodide Uptake
- Oxidation and Iodination
- Coupling
- Storage and release
- Peripheral conversion of T4 to T3



Regulation of T3 and T4



Physiological action

Metabolism

- Glucogenolysis and gluconeogenesis →increase blood glucose level. ↑ lipolysis.
- Increase BMR, induction of haemopooesis and increase peristalsis of GIT.

Hypothyroidism: Deficiency of thyroid hormones revealed the following effects:
In the Children: *Cretinism (mentally retarded*, dwarf).
In the adult: Myxoedema: myxomatous tissues get deposited on the face and lead to weight gain, decrease BMR, heart rate, body temperature.and in the females, additionally cause amenorrhoea.
Endemic goiter: Increase the size of thyroid gland**.**

Antithyroid Drugs

A. Inhibit hormone synthesis: Propyluracil, Methimazole, Carbimazole

B. Inhibit iodide trapping (ionic inhibitors): Thiocynates (–SCN), Perchlorate (CLO4–), Nitrates (NO3–)

C. Inhibit hormone release: Iodine, Iodide of Na and K, organic iodides

D. Destroyed thyroid tissue: Radioactive iodine (131I, 125I, 123I)

Thioamides

MOA: Bind to the thyroid peroxidase and prevent oxidation of iodide/ iodotyrosyl residues, thereby;

- (i) Inhibit iodination of tyrosine residues in thyroglobulin
- (ii) Inhibit coupling of iodotyrosine residues to form T3 and T4.

Pharmacokinetics:

- All antithyroid drugs are quickly absorbed orally
- widely distributed in the body, enter milk and cross placenta
- Metabolized in liver
- Excreted in urine primarily as metabolites

Adverse effects:

- Hypothyroidism and goiter

Parathyroid Hormones:

These hormones are secreted by Parathyroid gland situated just behind the Thyroid gland.

- Parathyroid Hormones is secreted by the chief cells of the parathyroid glands as polypeptide containing 84 amino acids .
- It acts to regulate the concentration of calcium (Ca2+) and Phosphate in the blood.
- Important in bone remodeling, which is an ongoing process in which bone tissue is alternately resorbed & rebuilt over time.

Function of Parathyroid Hormones (Pth)

- Increase the osteoclast cells activity → resorption of bone Ca2+ → increase blood Ca2+ level → hypercalcemia.
- Increase the intestinal absorption of Ca2+ → increase blood Ca2+ level
- Increase Po4–3 excretion.

Function of calcitonin: Opposite to Parathyroid hormone.

Hypoparthyroidism Low plasma level of Ca2+ and tetany, laryngospasm.

Hyperparathyroidism Hypercalcemia, decalcification of bones (osteoporosis) ostitis fibrosa cystic and renal stone.

Vitamin D

- **D2** Calciferol (ergocalciferol): Obtained from plant sources–food.
- **D3** Cholecalciferol: Synthesized in the skin under the influence of UV radiation.
- **D3** → Calcitriol (active form of D3 –1, 25 dihydroxy cholecalciferol) which is responsible for physiological function and which is similar to parathyroid hormone.

- **Uses of vitamin D**: In rickets, senile or postmenopausal osteoporosis, hypoparathyroidism, and Fanconi syndrome.

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