

PHYSIOLOGY

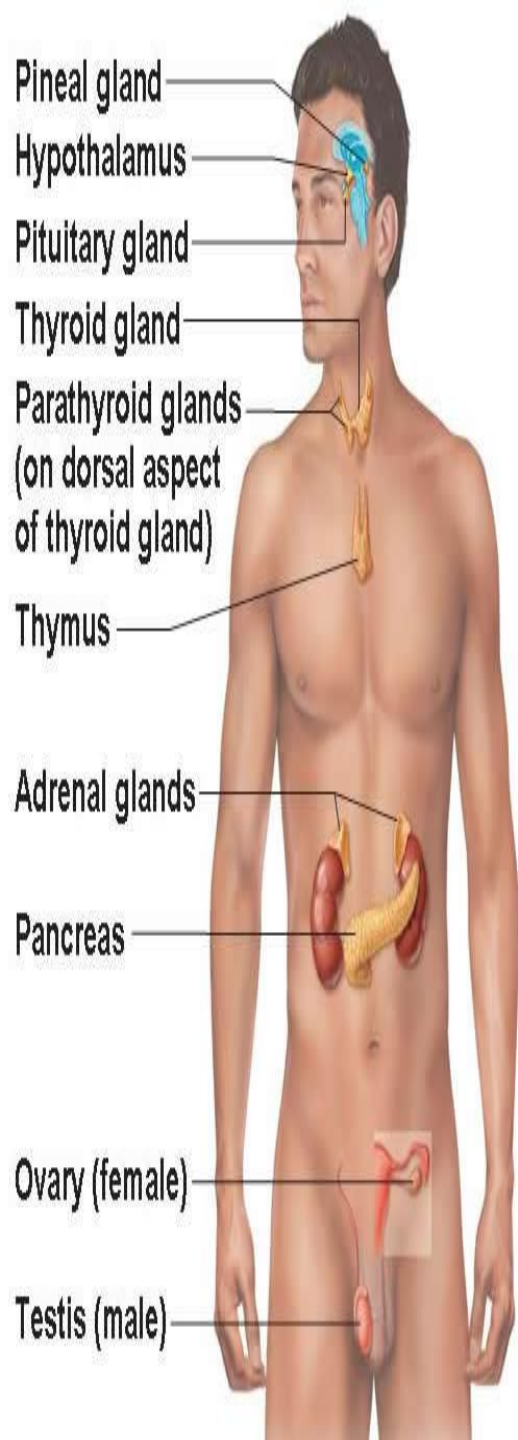
INTRO + AP 1&2

Endocrine Block

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baaah.

INTRO



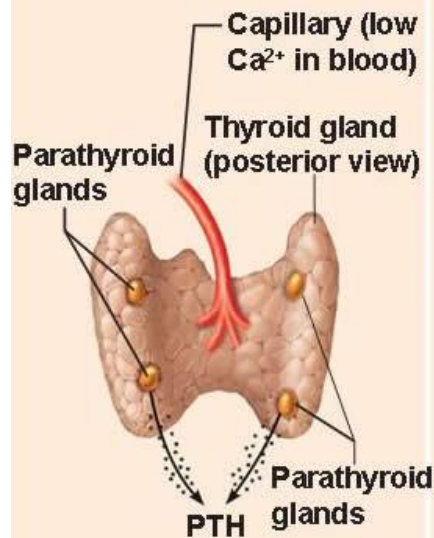
- ⊙ Exocrine glands: secrete its hormones in specific ducts, e.g. salivary gland.
- ⊙ Endocrine glands: secrete its hormones directly in blood.
 - ⊙ Pituitary, thyroid, parathyroid, adrenal, pineal, and thymus.
- ⊙ Some have more than an endocrine effect like:
 - ⊙ Pancreas, gonads, hypothalamus.

INTRO

- ⊙ What are hormones?
 - ⊙ Chemical signals secreted by cells for regulation of metabolism.
 - ⊙ Can be either: 1- Peptide, 2- Steroid, 3- Amine
 - ⊙ Solubility?
 - Lipophilic or lipophobic? (all amine-based are lipophobic except T4/T3 → lipophilic)
- ⊙ Stimulus?
 - ⊙ Humoral, neural, or hormonal
- ⊙ Effect? On their target tissue (receptor-specific)

(a) Humoral Stimulus

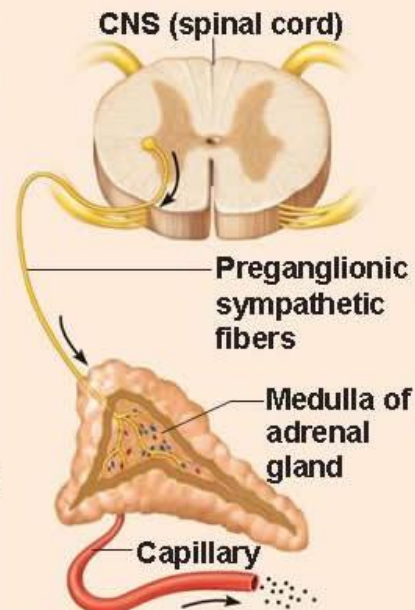
- ① Capillary blood contains low concentration of Ca^{2+} , which stimulates...



- ② ...secretion of parathyroid hormone (PTH) by parathyroid glands*

(b) Neural Stimulus

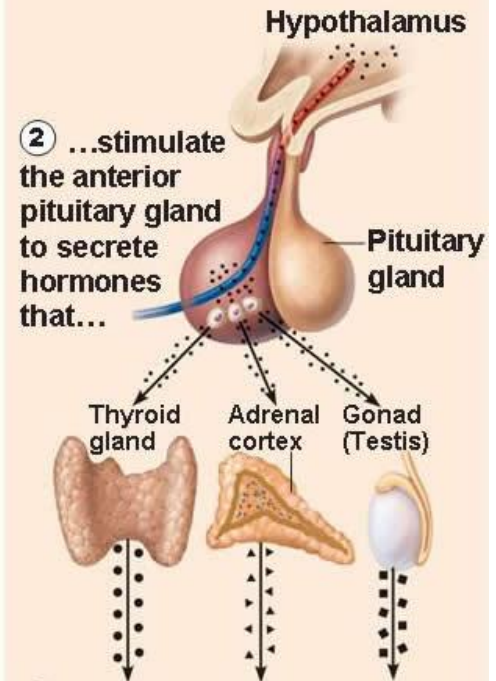
- ① Preganglionic sympathetic fibers stimulate adrenal medulla cells...



- ② ...to secrete catecholamines (epinephrine and norepinephrine)

(c) Hormonal Stimulus

- ① The hypothalamus secretes hormones that...



- ② ...stimulate the anterior pituitary gland to secrete hormones that...
- ③ ...stimulate other endocrine glands to secrete hormones



- ⊙ MoA?

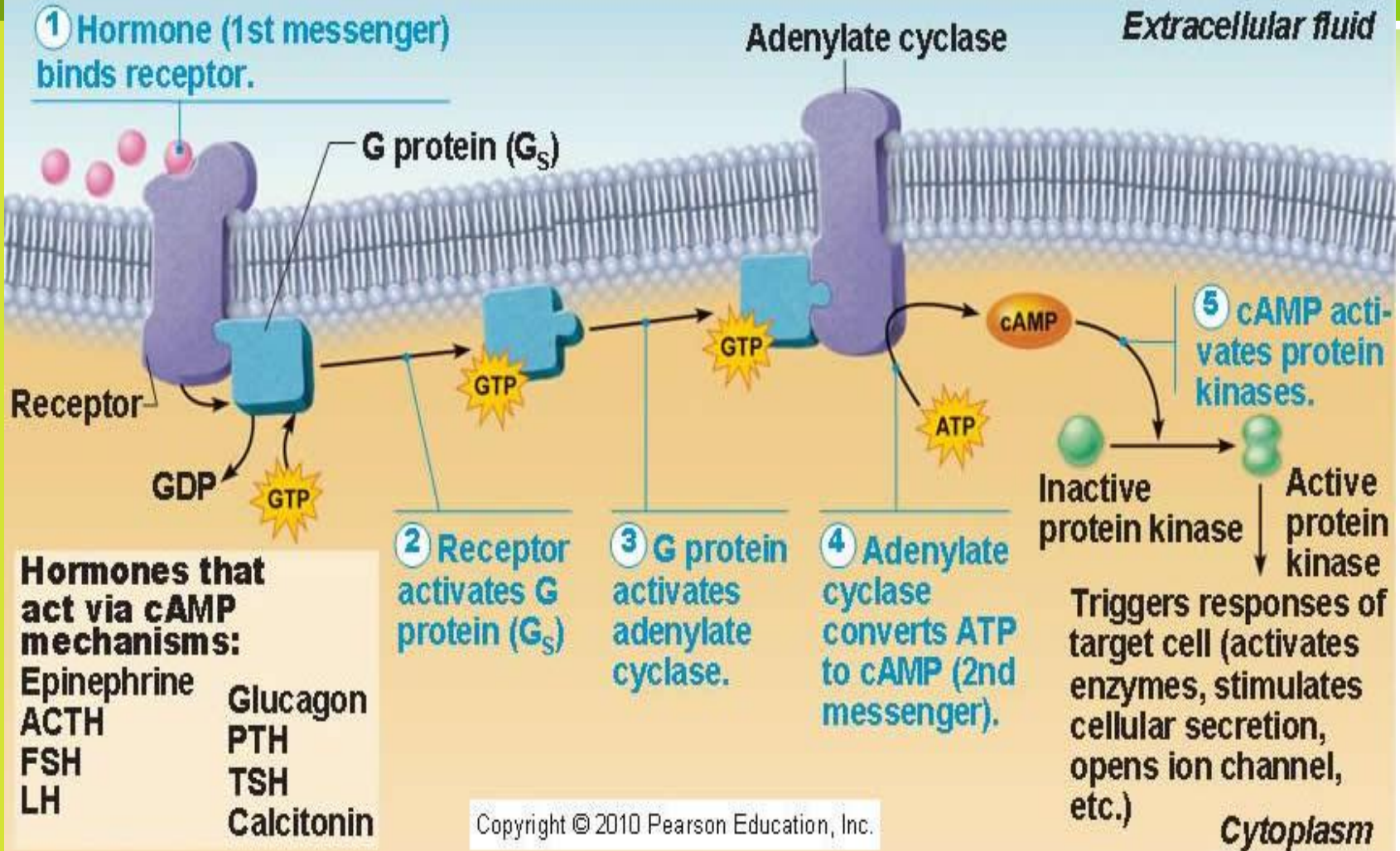
- ⊙ Change the permeability/potential
- ⊙ Activate/deactivate enzymes.
- ⊙ Induce secretion
- ⊙ Stimulate synthesis of proteins/regulatory mech.
- ⊙ Stimulate mitosis

- ⊙ We have 5 major mechanisms:

- ⊙ Act on cell membrane?
 - ⊙ cAMP , Phospholipase C, cGMP and tyrosine kinase mechanisms
- ⊙ Act intracellularly?
 - ⊙ Steroid, and thyroid mechanisms.

- ⊙ The mechanisms:
 - ⊙ Adenylyl-cyclase -----> 2nd messenger is cAMP
 - ⊙ Guanylyl –cyclase-----> 2nd messenger is cGMP
 - ⊙ Phospholipase C -----> 2nd messenger is Ca⁺⁺ /PIP
 - ⊙ Tyrosine Kinase -----> tyrosine chain
 - ⊙ And by intracellular receptor---> steroid and thyroid superfamily

1 Hormone (1st messenger) binds receptor.



Hormones that act via cAMP mechanisms:

- | | |
|-------------|------------|
| Epinephrine | Glucagon |
| ACTH | PTH |
| FSH | TSH |
| LH | Calcitonin |

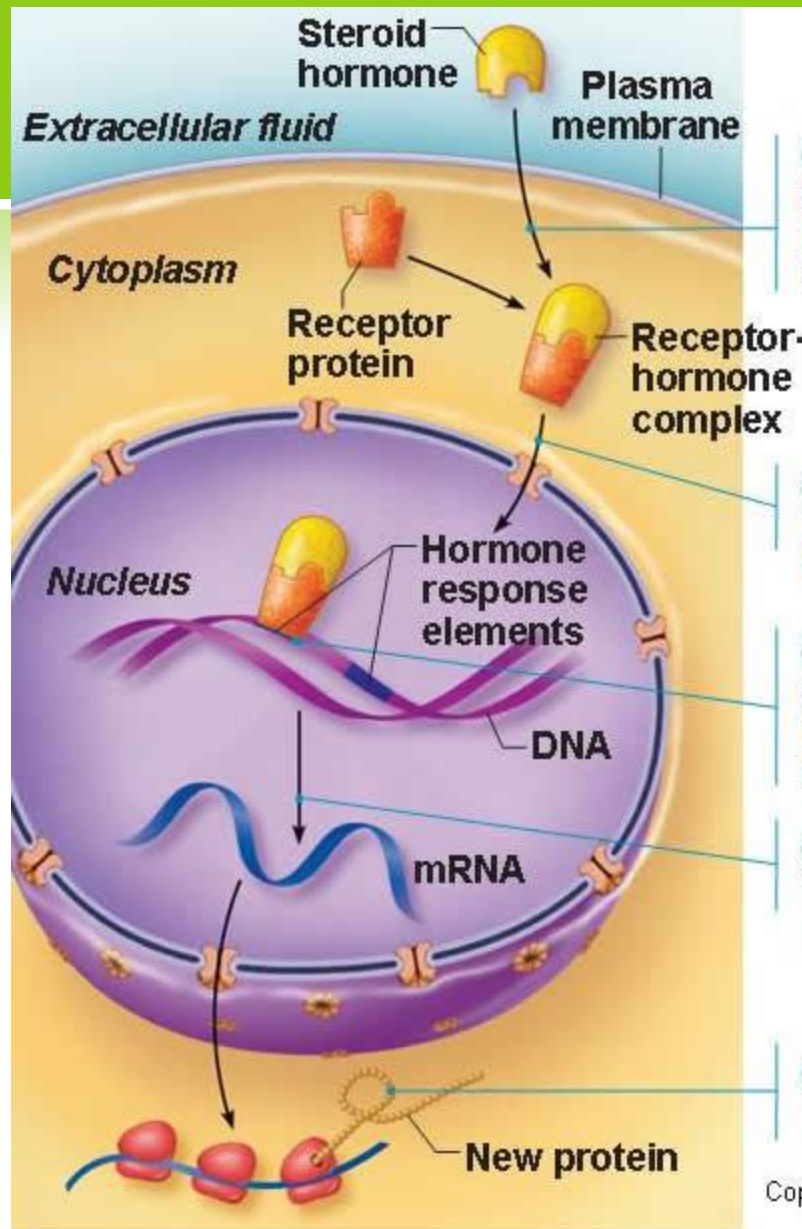
2 Receptor activates G protein (G_s)

3 G protein activates adenylyl cyclase.

4 Adenylyl cyclase converts ATP to cAMP (2nd messenger).

5 cAMP activates protein kinases.

Inactive protein kinase → Active protein kinase
Triggers responses of target cell (activates enzymes, stimulates cellular secretion, opens ion channel, etc.)
Cytoplasm



① The steroid hormone diffuses through the plasma membrane and binds an intracellular receptor.

② The receptor-hormone complex enters the nucleus.

③ The receptor-hormone complex binds a hormone response element (a specific DNA sequence).

④ Binding initiates transcription of the gene to mRNA.

⑤ The mRNA directs protein synthesis.

CONTINUED

- ⊙ The action of the hormone depend on either:
 - ⊙ The hormone
 - ⊙ The receptors
 - ⊙ The affinity between those two love-birds 😊
- ⊙ So %, sensitivity, elimination rate, binding, and its half-life?
 - ⊙ Half-life of water-soluble hormones is the shortest because of ease of elimination.

CONT

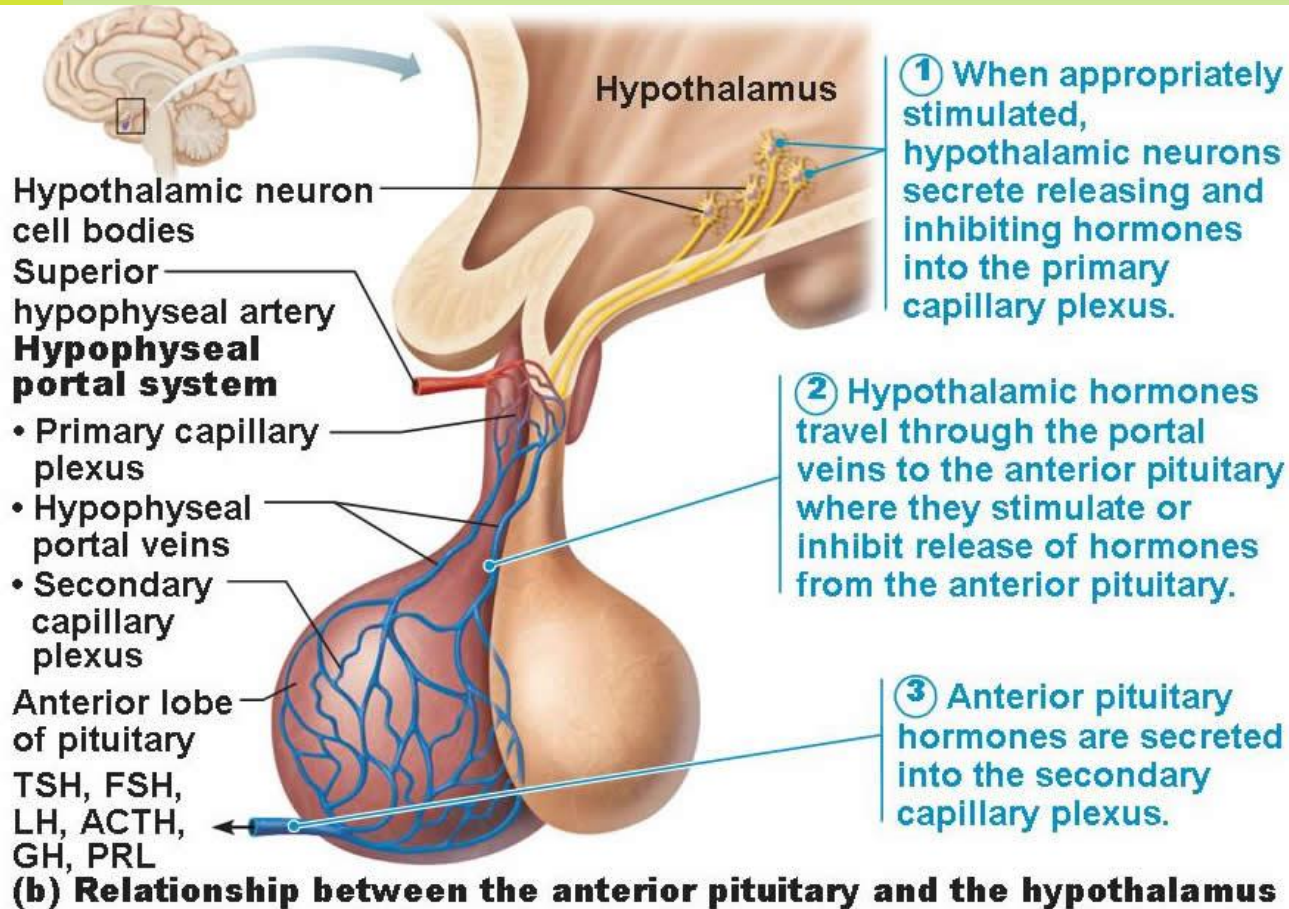
- ① The receptors can undergo either up, or down-regulation. Depends on the need.
- ① Negative feed-back mechanisms are called self-limiting
- ① Positive feed-back mechanisms are called self-augmenting
- ① Can anyone tell me an example of each?

CONTINUED

- ⊙ Interaction of hormones?
 - ⊙ Permissiveness
 - T4 and sex hormones also GH and prolactin.
 - ⊙ Synergism
 - Glucagon and NE -----> ex: in stimulation of glucose release from liver
 - ⊙ Antagonism
 - Glucagon and Insulin

HYPOTHALAMUS HORMONES

- ⊙ GHRH
- ⊙ Somatostatin
- ⊙ CRH
- ⊙ GNRH
- ⊙ TRH
- ⊙ PIH



ANT-PIT

- ⊙ Six hormones: (each from a troph-specific cell-line)
 - ⊙ GH, ACTH, FSH, LH, TSH, and Prolactin
 - ⊙ GH and Prolactin are related
 - ⊙ FSH, LH, and TSH are also cousins (alpha subunit is same)
 - ⊙ They are regulated by hypothalamic hormones that travel through the portal system (1st and 2nd capillary networks)



GH:

Regulated
by:

Negative
feedback

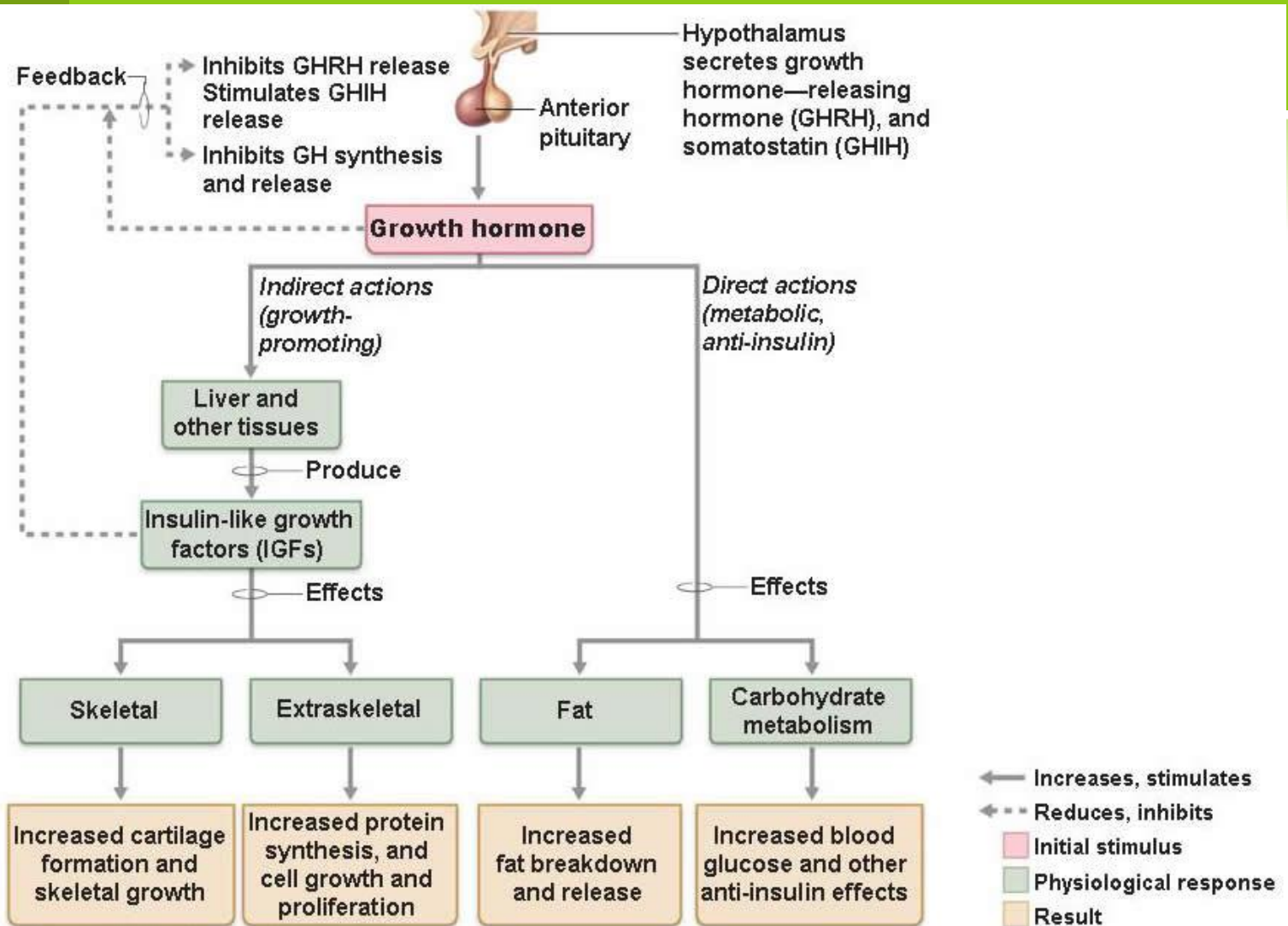
Of IGF and GH

- ⊙ GH: 191 polypeptide, from somatotrophs.
- ⊙ It stimulates the body to:
 - 1- increase in size 2- divide
 - Work on most tissues
 - Action by GH or IGF (from the liver)
 - Stimulated by GHRH(G+) and inhibited by Somatostatin (G-)
 - Excess cause
 - ⊙ gigantism in children, and acromegaly in adults
 - Deficiency cause:
 - ⊙ Dwarfism in children

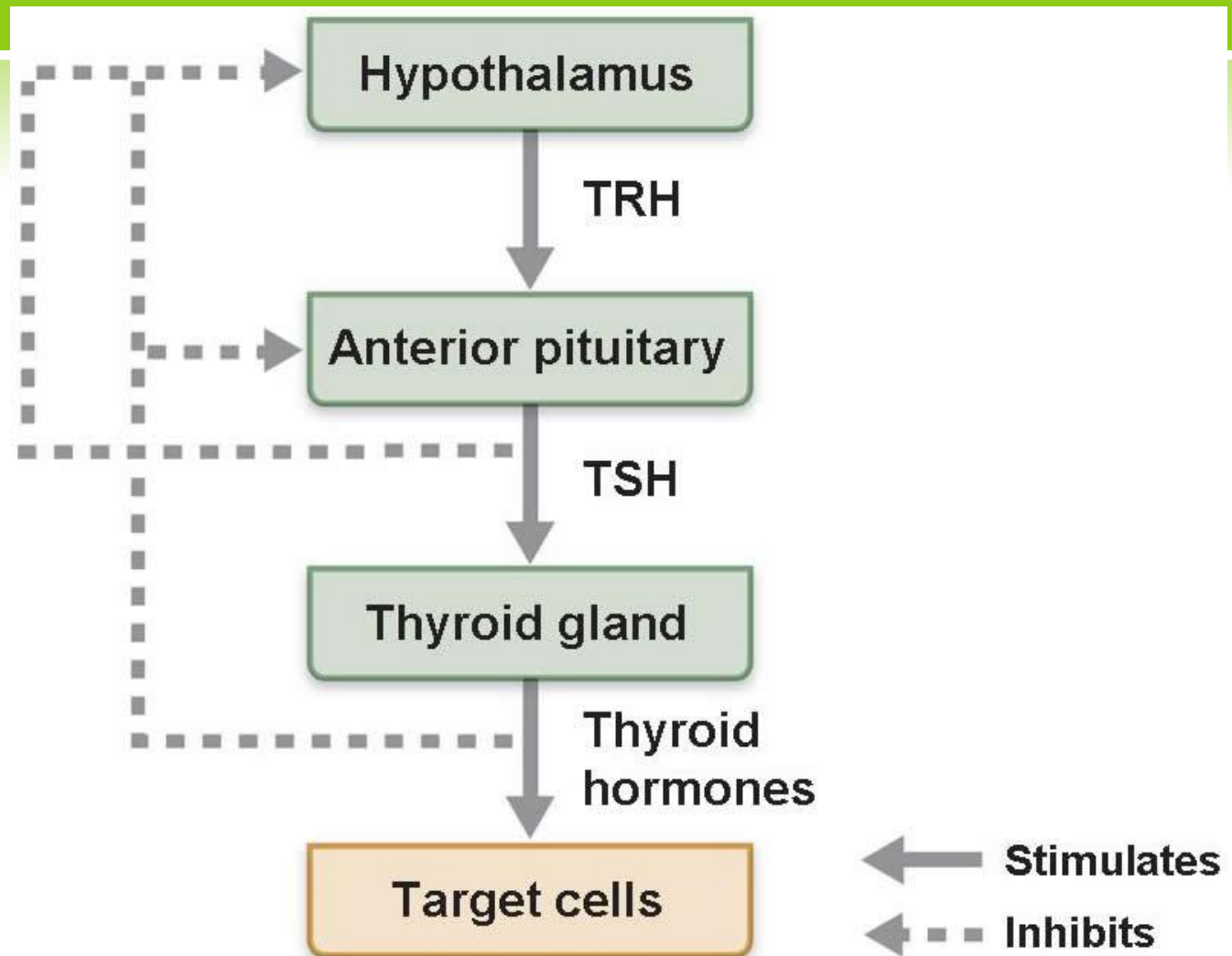


⊙ GH:

- ⊙ Cause diabetogenic effect: increase Glucose in blood:
 - By gluconeogenesis, glycogenolysis, and decreased utilization by tissue.
- ⊙ Cause lipolysis and anabolism of proteins
- ⊙ Retention of water and minerals
- ⊙ Don't forget that it is pulsatile!!! Every 2 hours
- ⊙ Time-line of secretion:
 - Increases from birth to childhood---> increasing slowly
 - rapid increase in puberty
 - Steady state in adult until old age when it falls.



- ⊙ TSH:
 - ⊙ Glycoprotein from thyrotroph cells
 - ⊙ stimulates the thyroid gland
 - Secretion and synthesis
 - Trophic effect



REMEMBER THE REGULATION?

- ⊙ We have three main negative feedback loops
 - ⊙ Long (from the end-result to the initiator)
 - ⊙ Short (shorter, AP---> hypothalamus)
 - ⊙ Ultrashort (autocrine, secreted and acted at the same site)



- ⊙ Prolactin:

- ⊙ secreted from lactotrophs.(15%)

- ⊙ 198 Amino acids in single chain of polypeptide

- ⊙ Related to GH

- Actions:

- ⊙ The major function of prolactin is milk production [lactose, casein & lipid synthesis]

- ⊙ Other functions are 1- Breast development and 2- Inhibition of ovulation by inhibiting GnRH

- ⊙ Prolactin is inhibited by PIH (dopamine)
- ⊙ Three sources of dopamine:
 - Dopaminergic neurons in hypothalamus and P.Pit.
 - Third is non-lactotroph cells in anterior pituitary
- ⊙ It is also stimulated by TRH but PIH's inhibition is more so net is decrease in secretion.
- ⊙ If lactating, prolactin increasing

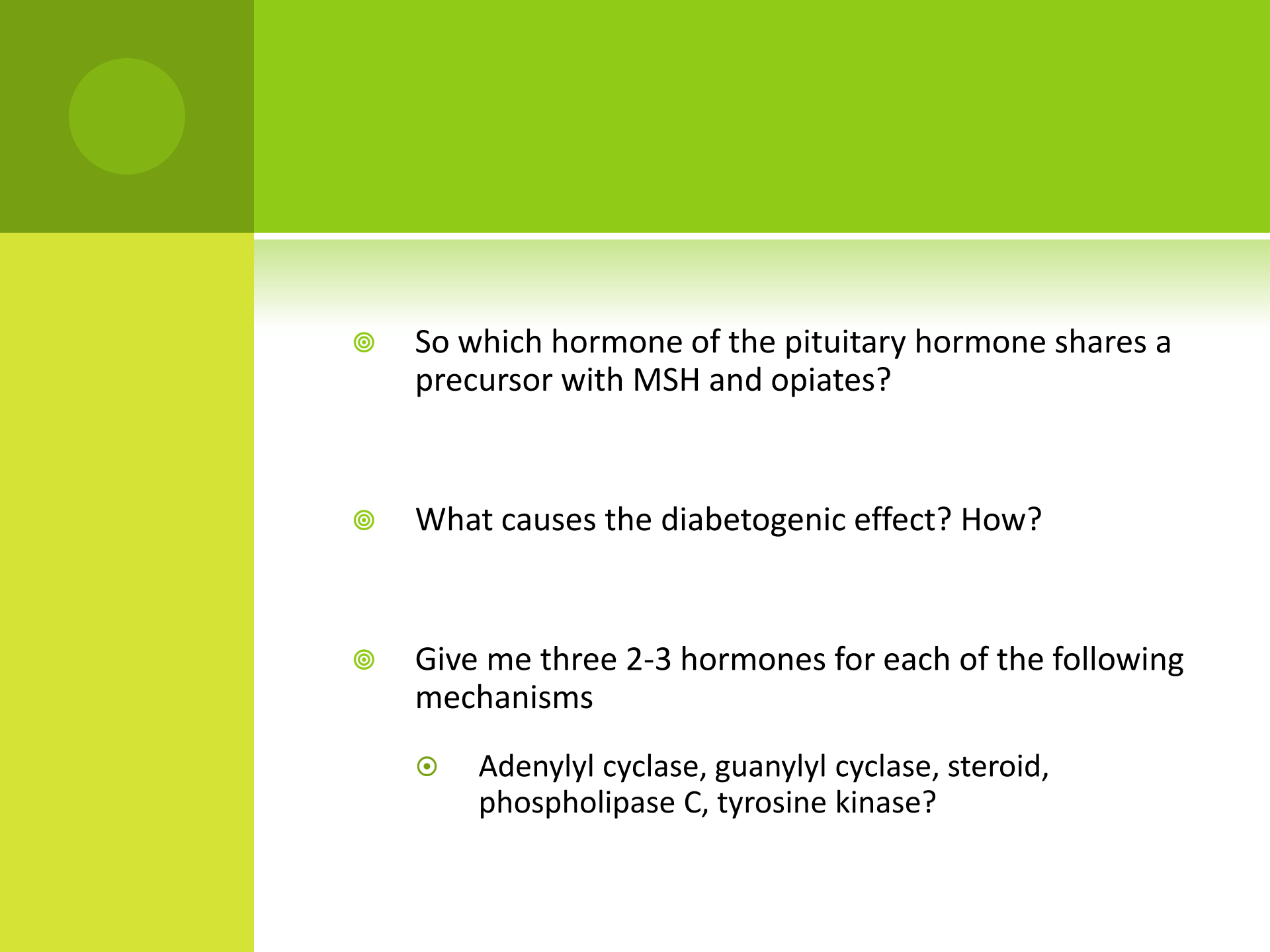
- ⊙ ACTH:
 - ⊙ Secreted from Corticotrophs.(15%)
 - ⊙ Melanocyte stimulating hormone [MSH] and β -endorphin are secreted with ACTH
 - ⊙ ACTH is first synthesized as Preproopiomelanocortin (POMC) then cleaved and secreted
 - Preproopiomelanocortin gives MSH/ ACTH and two opiates
 - ⊙ In Addison's disease, (low cortisol), POMC will increase giving MSH and ACTH ---> pigmentation on skin occurs as a positive symptom



◎ ACTH?

◎ Action?

- ◎ By stimulation of the adrenal gland
- ◎ Increase in steroid synthesis of the three layers
- ◎ Increase in cortisol, aldosterone, and adrenal sex hormones
- ◎ They have specific effects which we will talk about later!

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- ③ So which hormone of the pituitary hormone shares a precursor with MSH and opiates?

 - ③ What causes the diabetogenic effect? How?

 - ③ Give me three 2-3 hormones for each of the following mechanisms
 - ③ Adenylyl cyclase, guanylyl cyclase, steroid, phospholipase C, tyrosine kinase?