

Endocrine Part 1

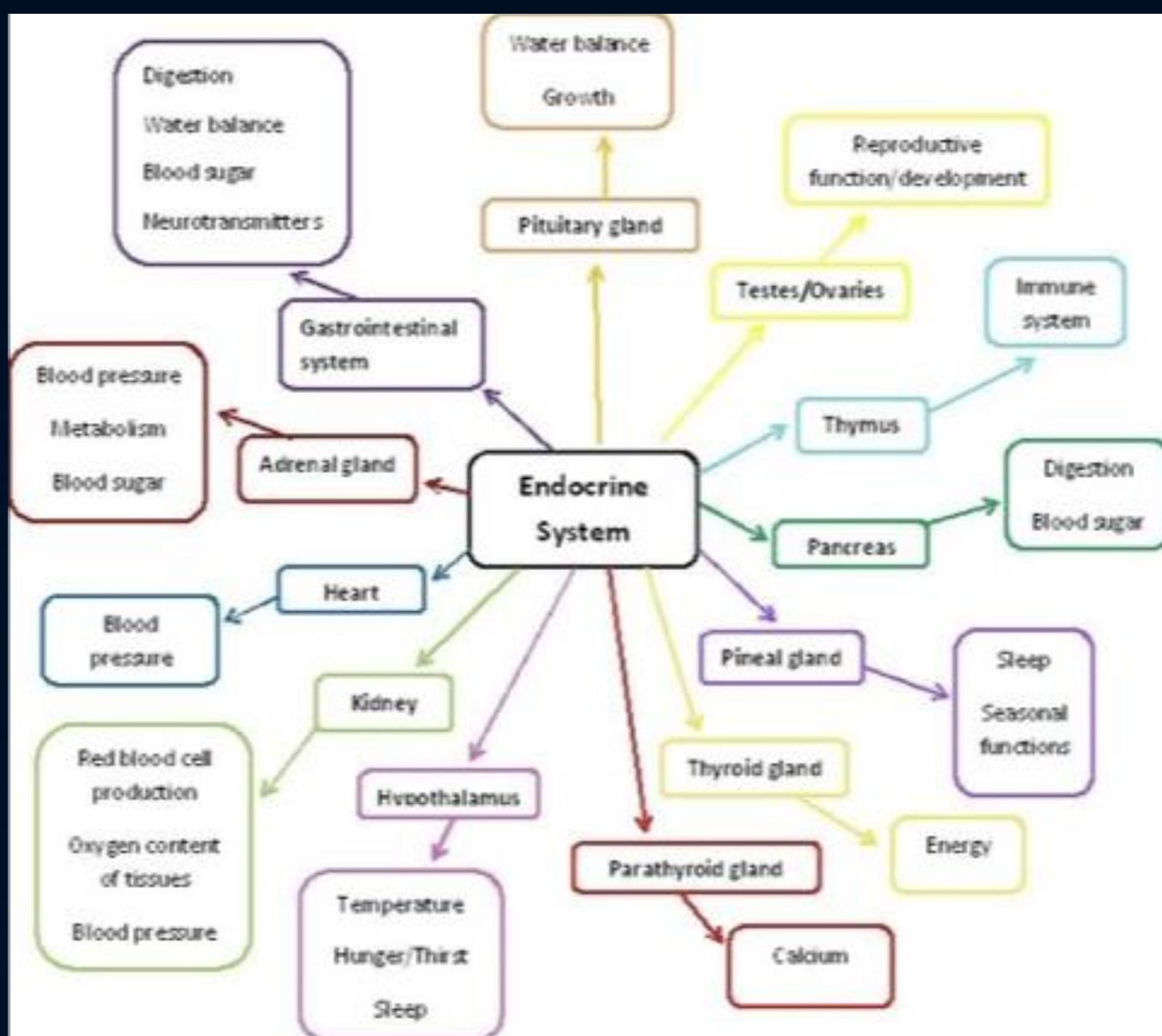
INTRO TO THE ENDOCRINE SYSTEM

Relevancies:

Regulate Body Vitals

Much of the medicine we use works via the endocrine system

Many of the issues we encounter are caused by errors in the endocrine system



This is a graphic representation of the complicated Endocrine System, demonstrating the varied effects that pesticides can have on the body.

Endocrine System - Overview

- **Endocrine system**
 - Hormones secreted directly into blood stream.
 - Exocrine system on the other hand has drugs, and excretes elsewhere, such as salivary glands, sweat glands, etc.
- Composed of ductless glands that synthesize and secrete **hormones**
 - Hormones are released into the blood and transported throughout the body
- **Target cells** have the specific receptors for a hormone
 - They bind hormone and respond
- Hormone transport to target cells:
 - Hormones released into interstitial fluid and then enter blood
 - Transported within blood
 - Randomly leave blood and enter interstitial fluid
 - Hormone binds to target cells' receptors

Pancreas has a dual role, exocrine (bile), and endocrine (insulin)

Involved organs:
Thyroid
Adrenal Gland
Pancreas
Testes/Ovaries

All of the above gets instructions from pituitary gland, which is directed by hypothalamus

Effector organs:
Kidneys
Heart

Endocrine System - Overview

- Transmits hormones through the blood
- Targets any cells in the body with correct receptors
 - Can be very widespread
- Exhibits longer reaction times-slower and longer than nervous system
- Has longer-lasting effects (minutes to days and weeks)

Hormone's will affect the entire body, wherever they can find receptors. That causes side effects

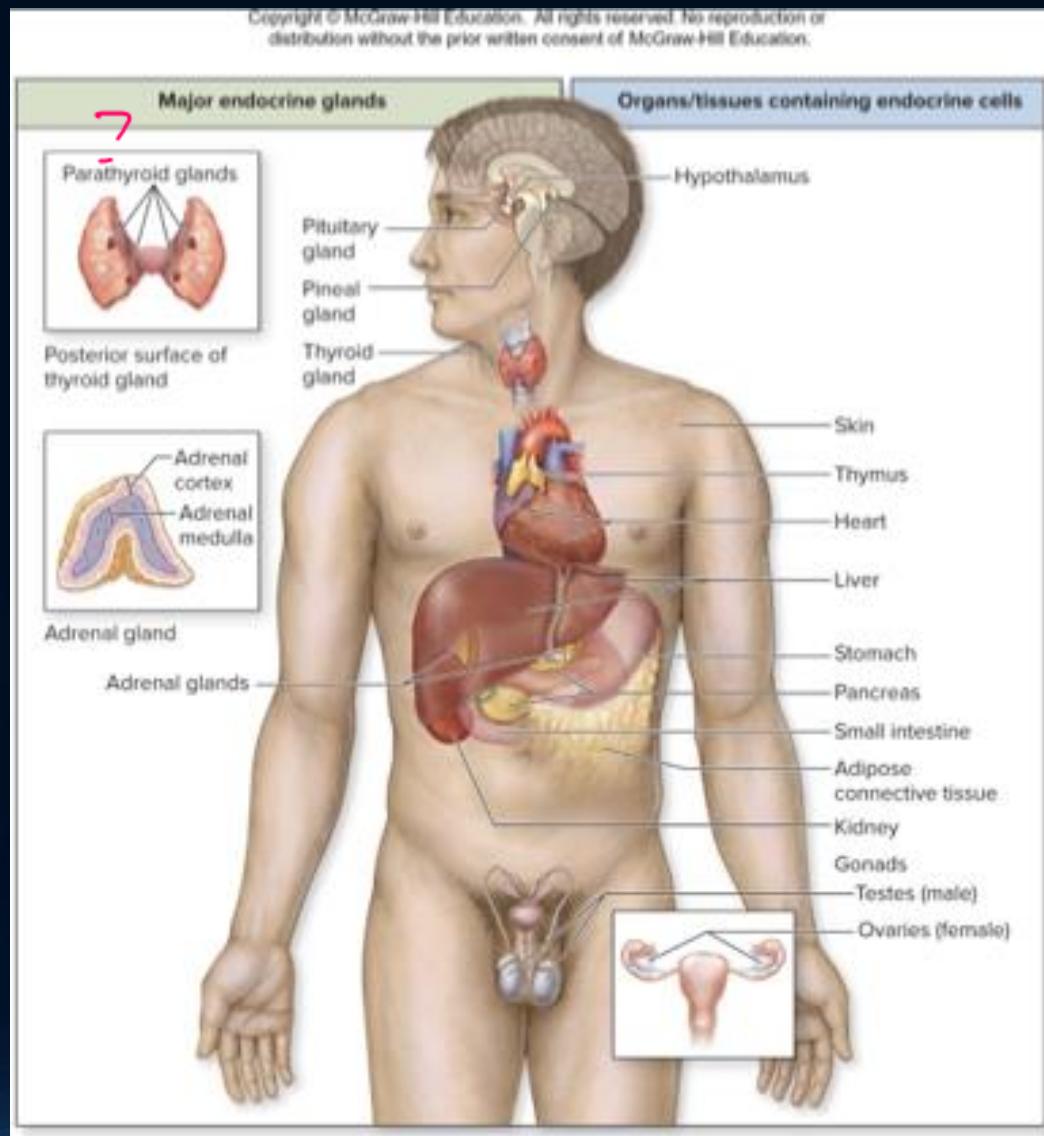
Endocrine System – General Function

- **Regulating development, growth, and metabolism**
 - Hormones help regulate embryonic cell division and differentiation
 - Hormones regulate metabolism (carbohydrates, protein, fat)
- **Maintaining homeostasis of blood composition and volume**
 - Hormones regulate blood solute concentrations (e.g., glucose, ions)
 - Hormones regulate blood volume, cellular concentration, and platelet number
- **Controlling digestive processes**
 - Hormones influence secretory processes and movement of materials in digestive tract
- **Controlling reproductive activities**
 - Hormones affect development and function of reproductive systems and the expression of sexual behaviors

Location of Major Endocrine Glands

- **Endocrine glands** contain epithelial tissue that make and secrete chemical substances (hormones) within a connective tissue framework
- **Endocrine organs** Include: pituitary, pineal, thyroid, parathyroid, and adrenal glands
- Some endocrine cells are found in clusters in organs with another function
 - Examples: hypothalamus, skin, thymus, heart, liver, stomach, pancreas, small intestine, adipose connective tissue, kidneys, and gonads
- Endocrine glands are ductless, secrete directly into bloodstream

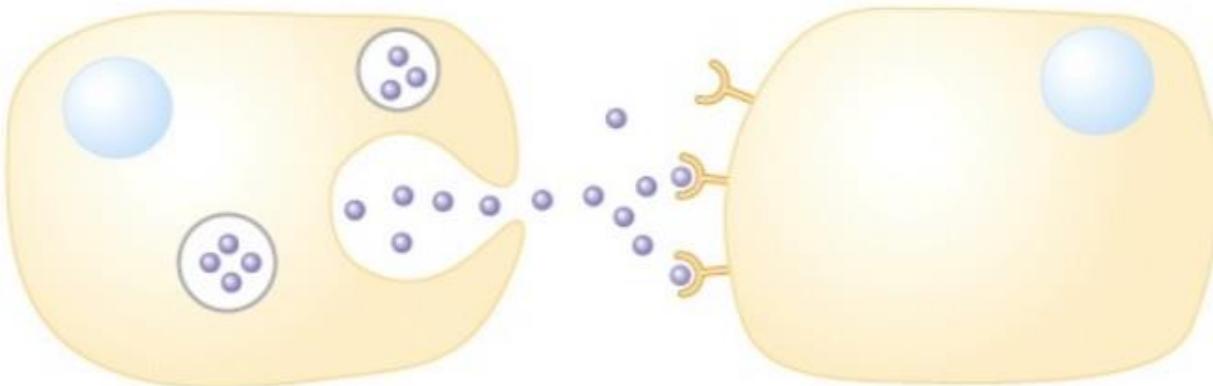
Location of Major Endocrine Glands, Organs, and Tissues Containing Endocrine Cells



3 Types of Signalling

1. Endocrine – somewhere else in body via bloodstream
2. Autocrine – self signalling
3. Paracrine – neighbouring cells

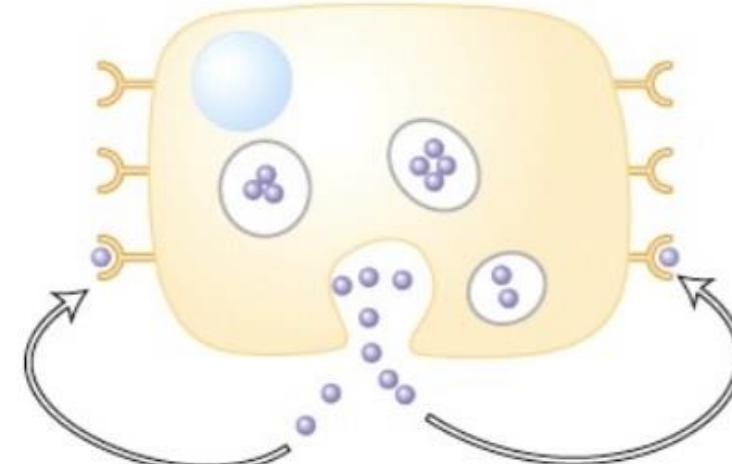
(b) Paracrine signaling



Secretory cell

Adjacent target cell

(c) Autocrine signaling

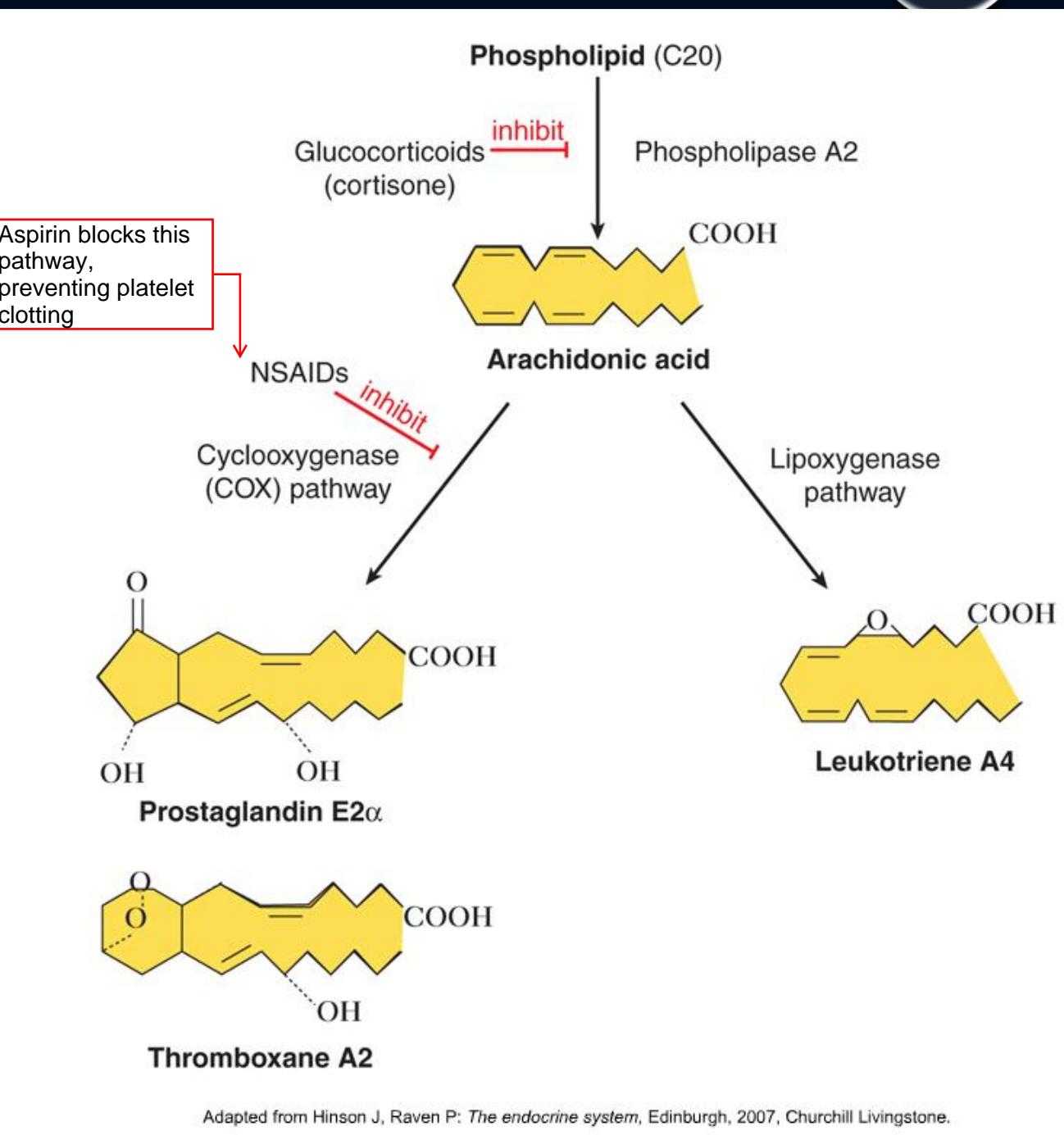


Target sites on same cell

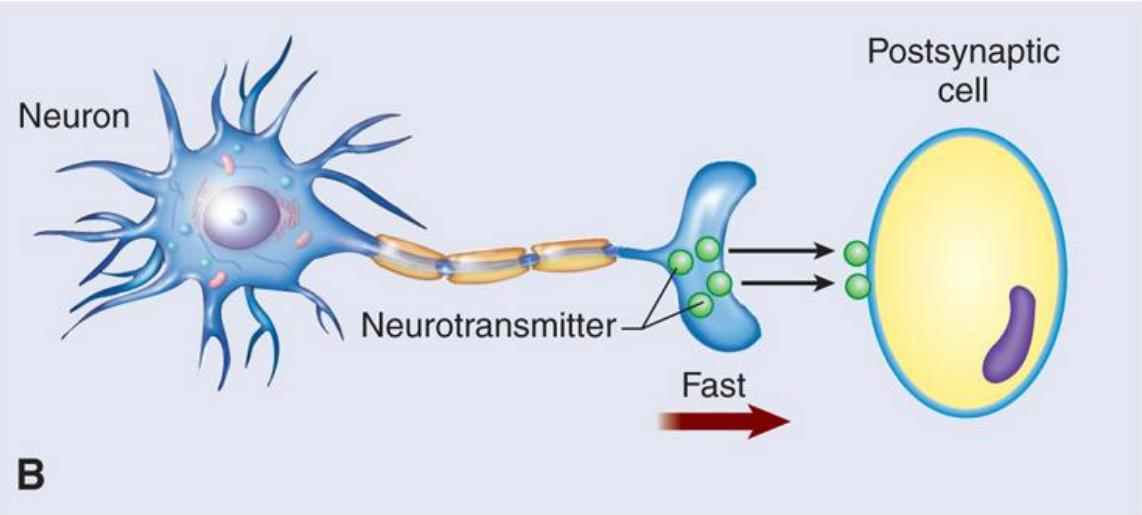
Key:

- Extracellular signal
- Receptor
- Membrane-attached signal

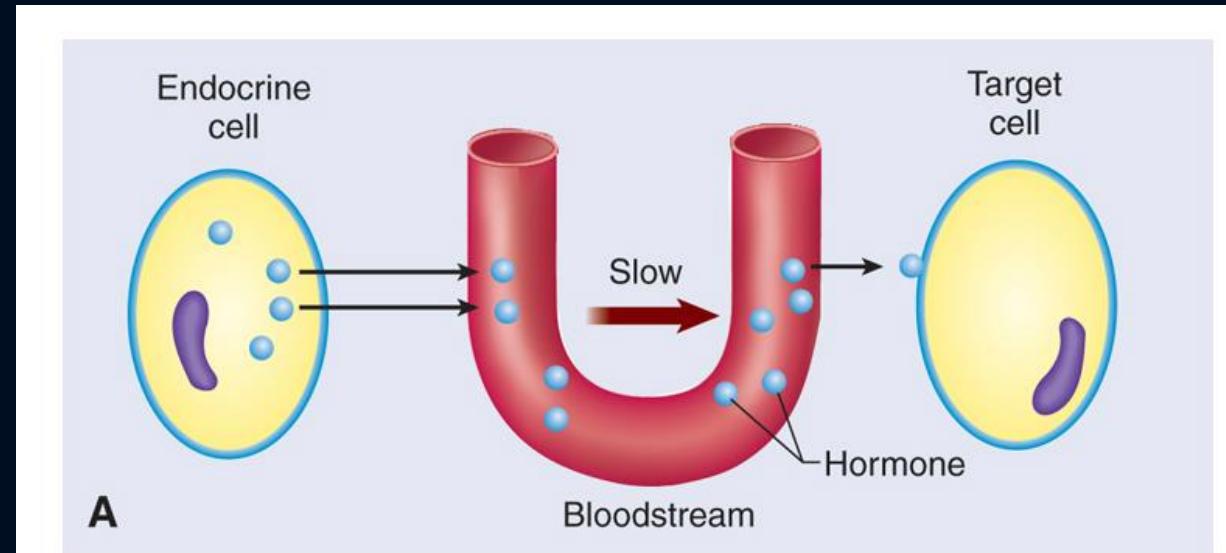
Local regulators – eicosanoids



Nervous vs Endocrine Communication

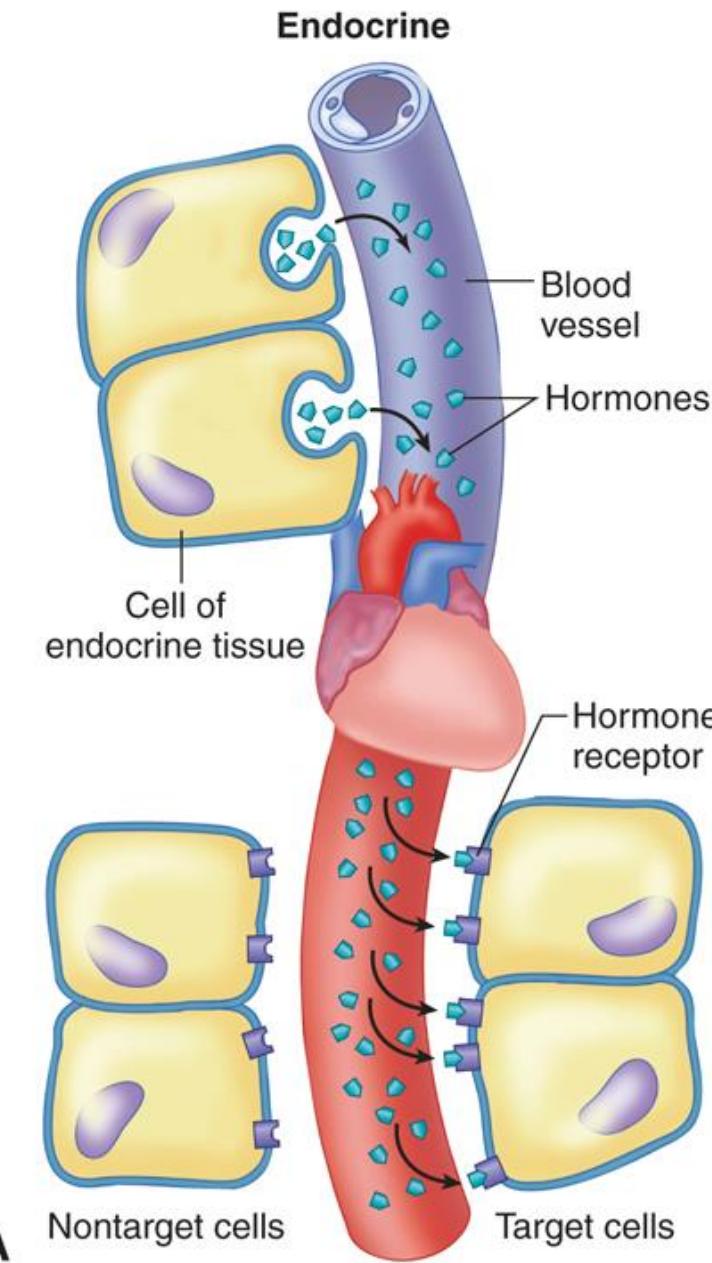


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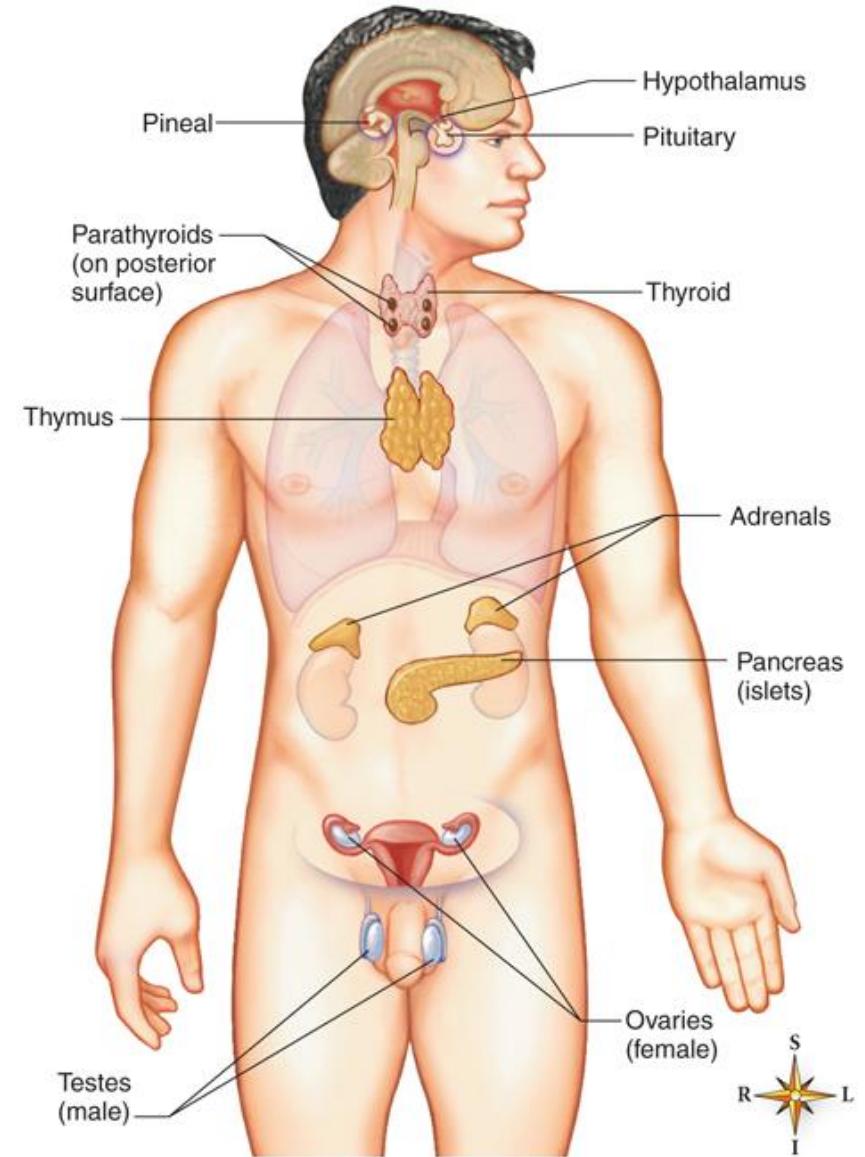


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Secretion to Action

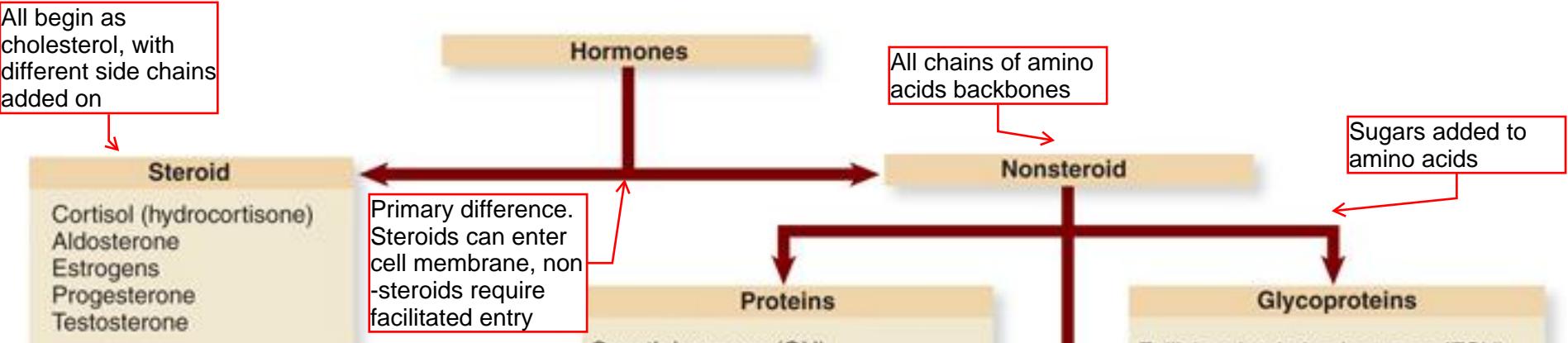


Primary Endocrine Glands



Endocrine Part 1

HORMONE CLASSIFICATION & SIGNALING MECHANISMS



Structural classifications of hormones

Peptides

- Antidiuretic hormone (ADH)
- Oxytocin (OT)
- Melanocyte-stimulating hormone (MSH)
- Somatostatin (SS)
- Thyrotropin-releasing hormone (TRH)
- Gonadotropin-releasing hormone (GnRH)
- Atrial natriuretic hormone (ANH)

Amino acid derivatives

Amines

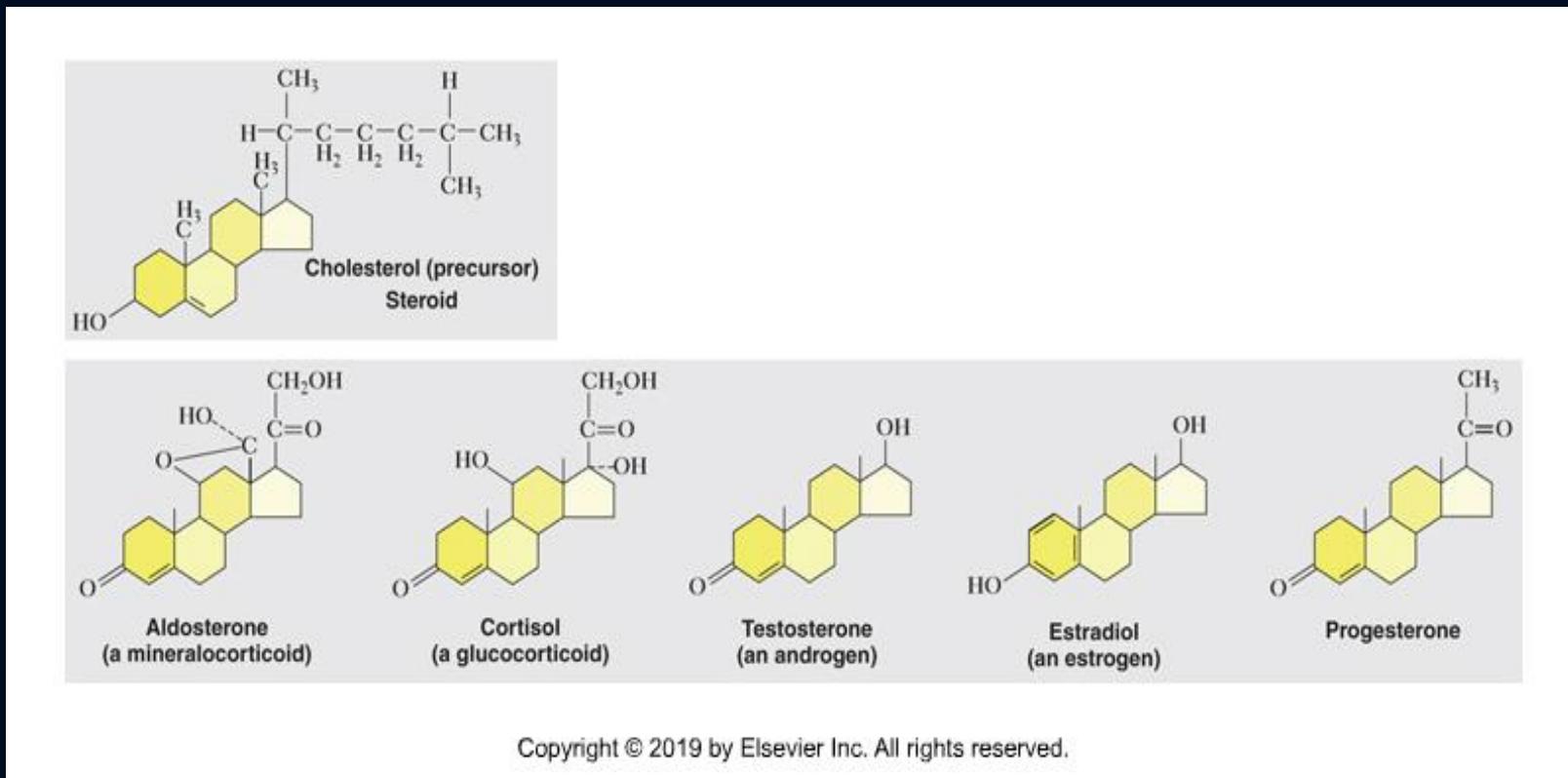
- Norepinephrine (NE)
- Epinephrine (Epi)
- Melatonin

Iodinated amino acids

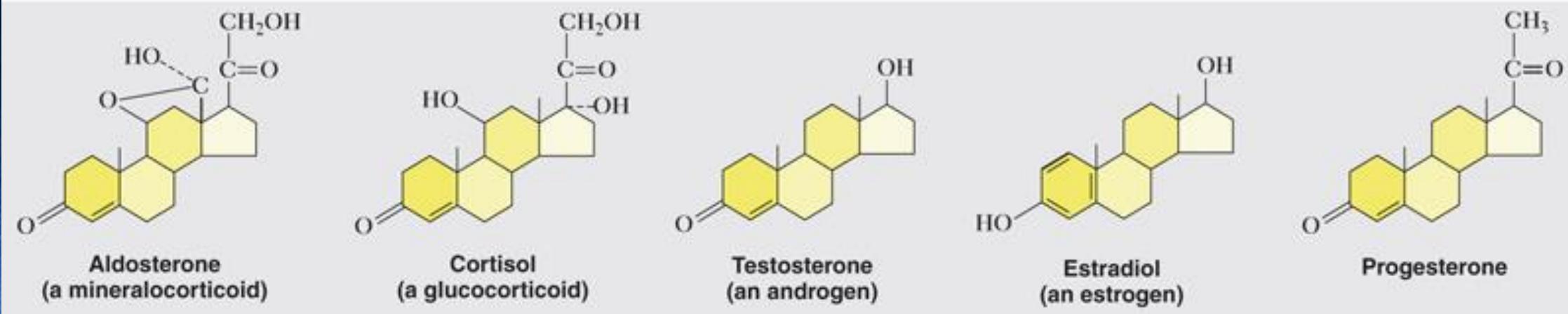
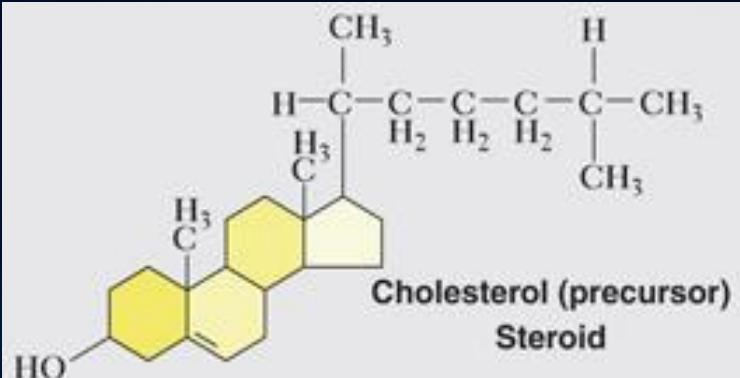
- Thyroxine (T_4)
- Triiodothyronine (T_3)

Steroid hormones

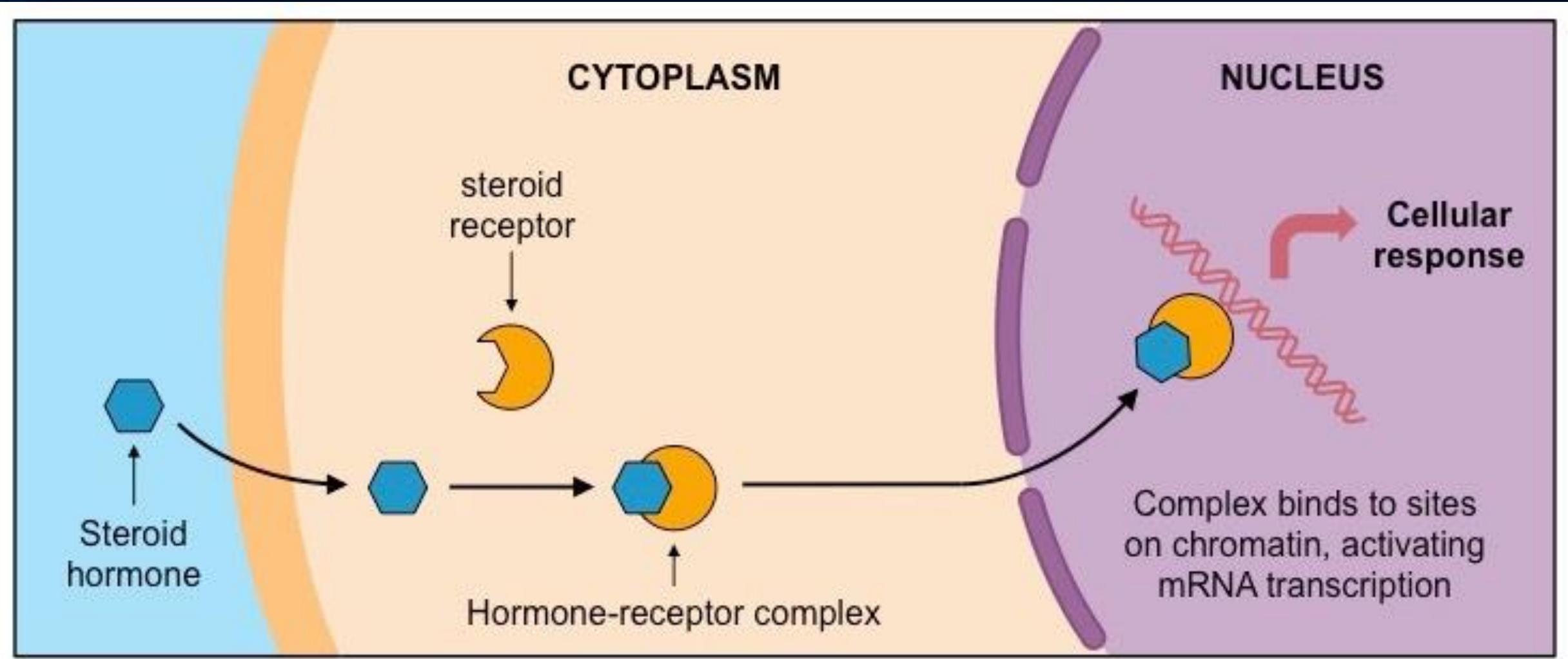
- Lipid-soluble molecules synthesized from cholesterol
- Includes gonadal steroids (e.g., estrogen)
- Includes steroid synthesized by adrenal cortex (e.g., cortisol)
- Calcitriol sometimes classified in this group, but more accurately called a *sterol*



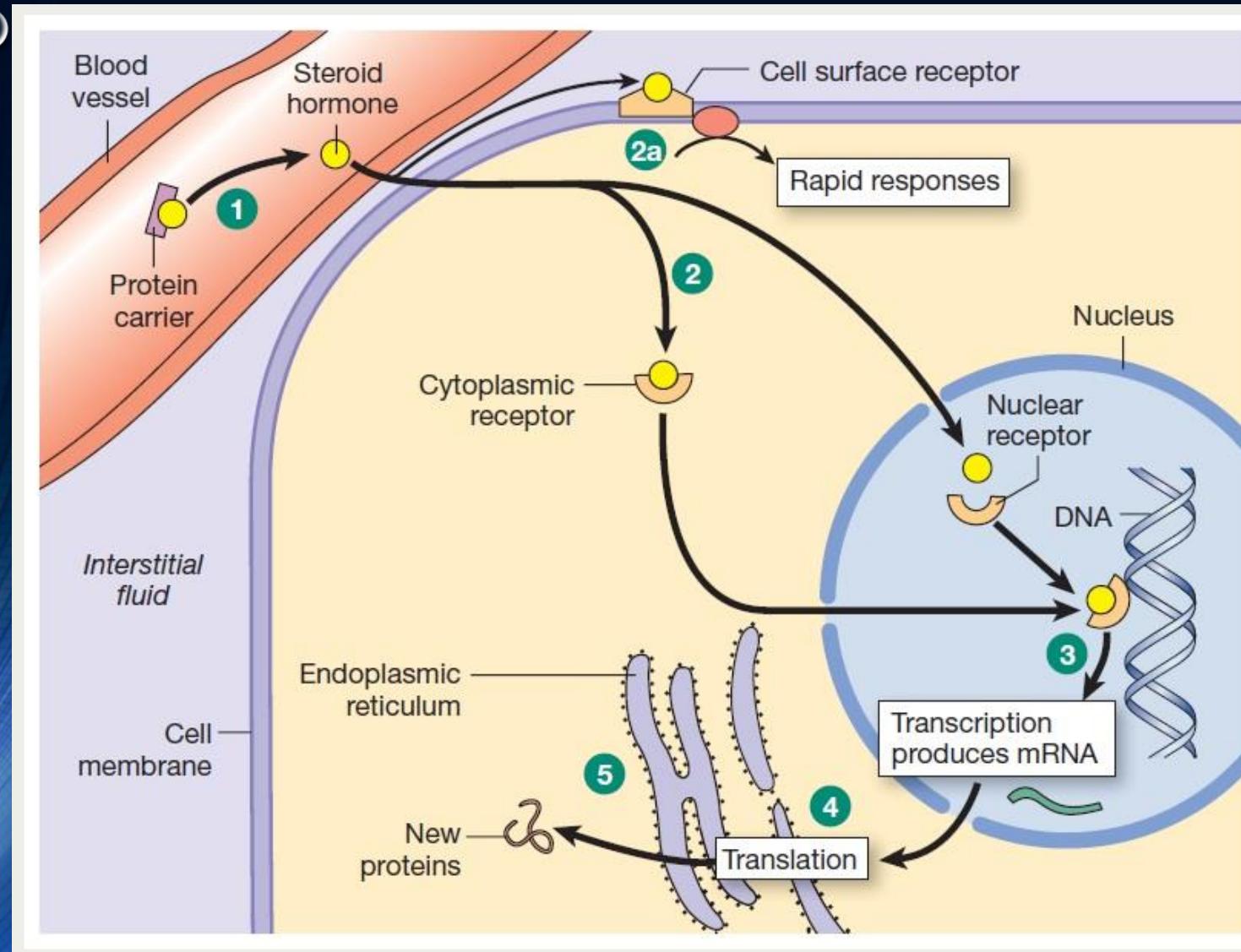
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Steroid Hormone Receptors

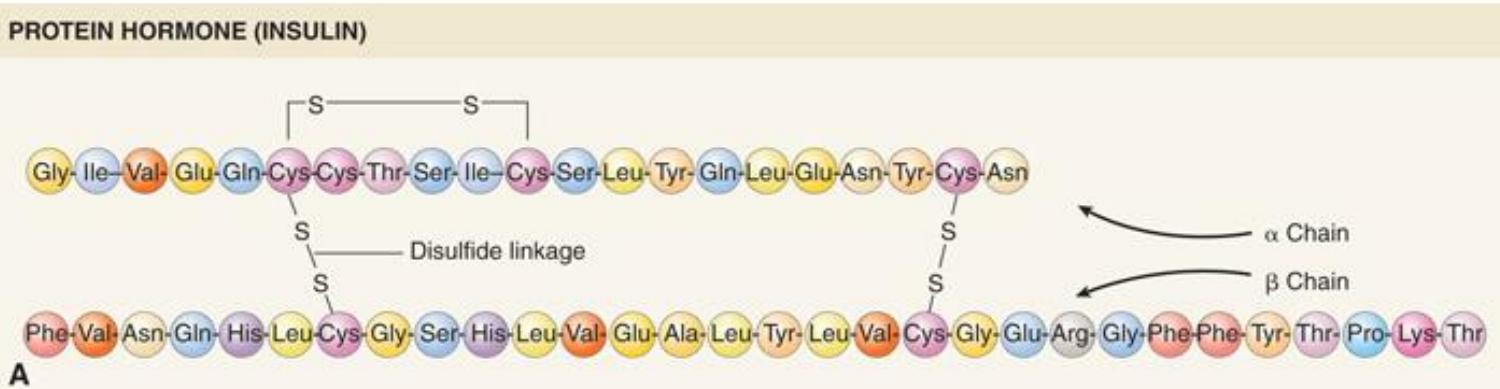


Steroid Hormone Signaling



- 1 Most hydrophobic steroids are bound to plasma protein carriers. Only unbound hormones can diffuse into the target cell.
- 2 Steroid hormone receptors are in the cytoplasm or nucleus.
- 2a Some steroid hormones also bind to membrane receptors that use second messenger systems to create rapid cellular responses.
- 3 The receptor-hormone complex binds to DNA and activates or represses one or more genes.
- 4 Activated genes create new mRNA that moves back to the cytoplasm.
- 5 Translation produces new proteins for cell processes.

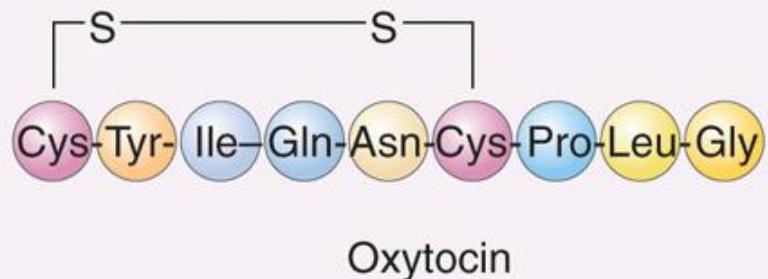
Protein & Peptide Hormones (Non-Steroid)



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- Most hormones are in this category
- Water-soluble chains of amino acids

PEPTIDE HORMONE (OXYTOCIN [OT])

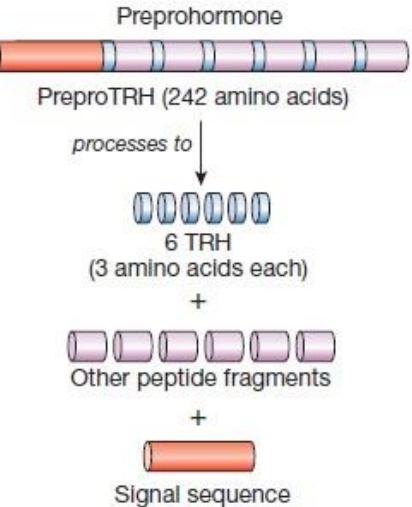


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Protein & Peptide Hormone Synthesis

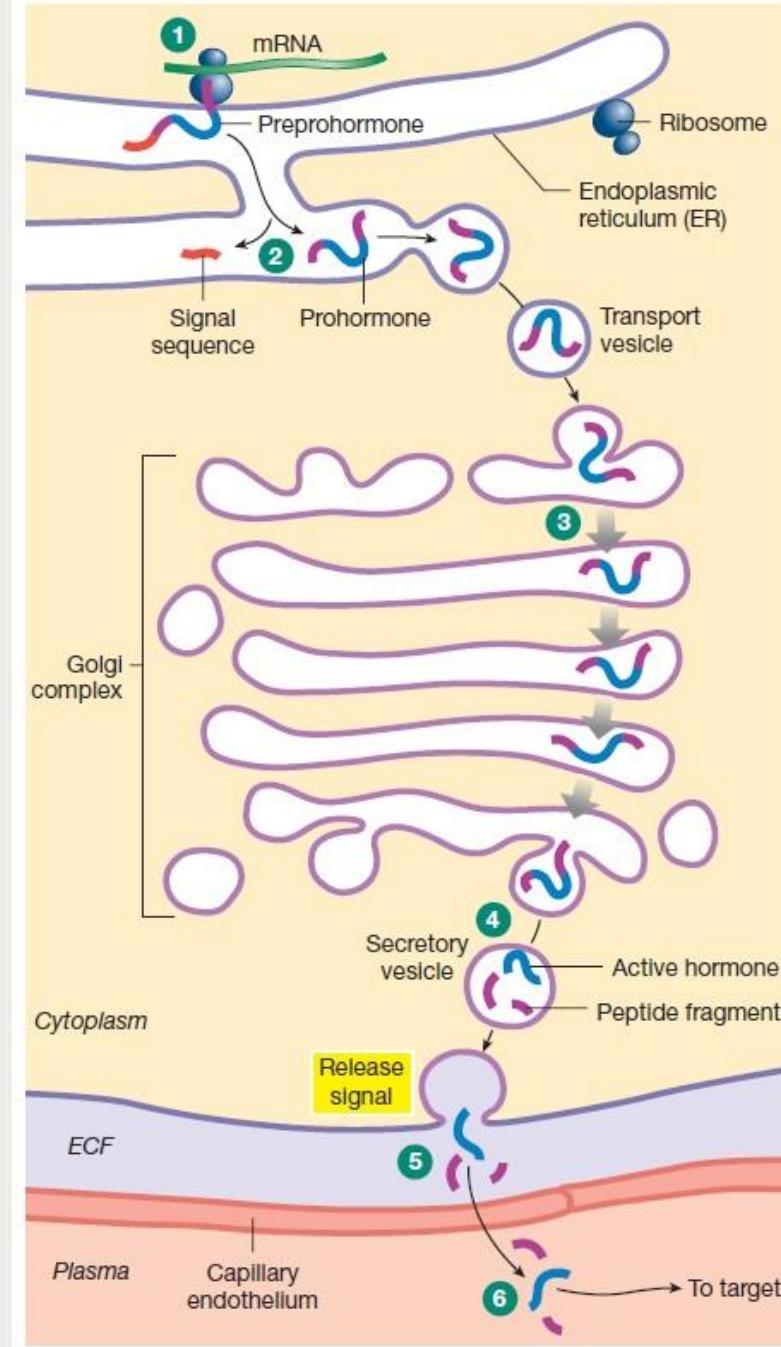
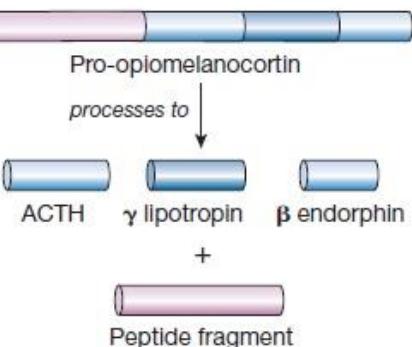
(a) Preprohormones

PreproTRH (thyrotropin-releasing hormone) has six copies of the 3-amino acid hormone TRH.



(b) Prohormones

Prohormones, such as pro-opiomelanocortin, the prohormone for ACTH, may contain several peptide sequences with biological activity.



1 Messenger RNA on the ribosomes binds amino acids into a peptide chain called a **preprohormone**. The chain is directed into the ER lumen by a **signal sequence** of amino acids.

2 Enzymes in the ER chop off the signal sequence, creating an inactive **prohormone**.

3 The prohormone passes from the ER through the **Golgi complex**.

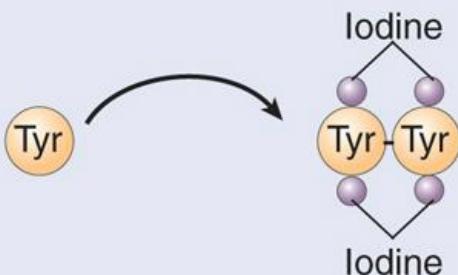
4 Secretory vesicles containing enzymes and prohormone bud off the Golgi. The enzymes chop the prohormone into one or more active peptides plus additional peptide fragments.

5 The secretory vesicle releases its contents by exocytosis into the extracellular space.

6 The hormone moves into the circulation for transport to its target.

Amino Acid Derivative & Glycoprotein Hormones

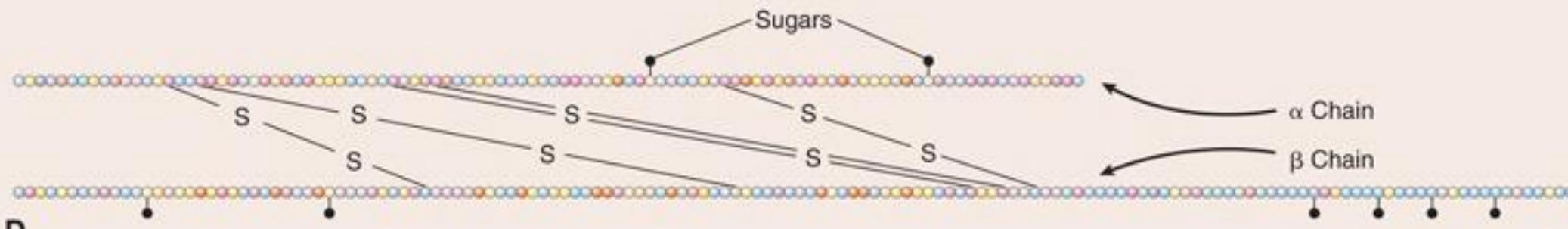
AMINO ACID DERIVATIVE (THYROXINE [T₄])



C

Made up of one type of amino acid, whereas peptide hormones are chains of multiple different acids.

GLYCOPROTEIN HORMONE (HUMAN CHORIONIC GONADOTROPIN [hCG])



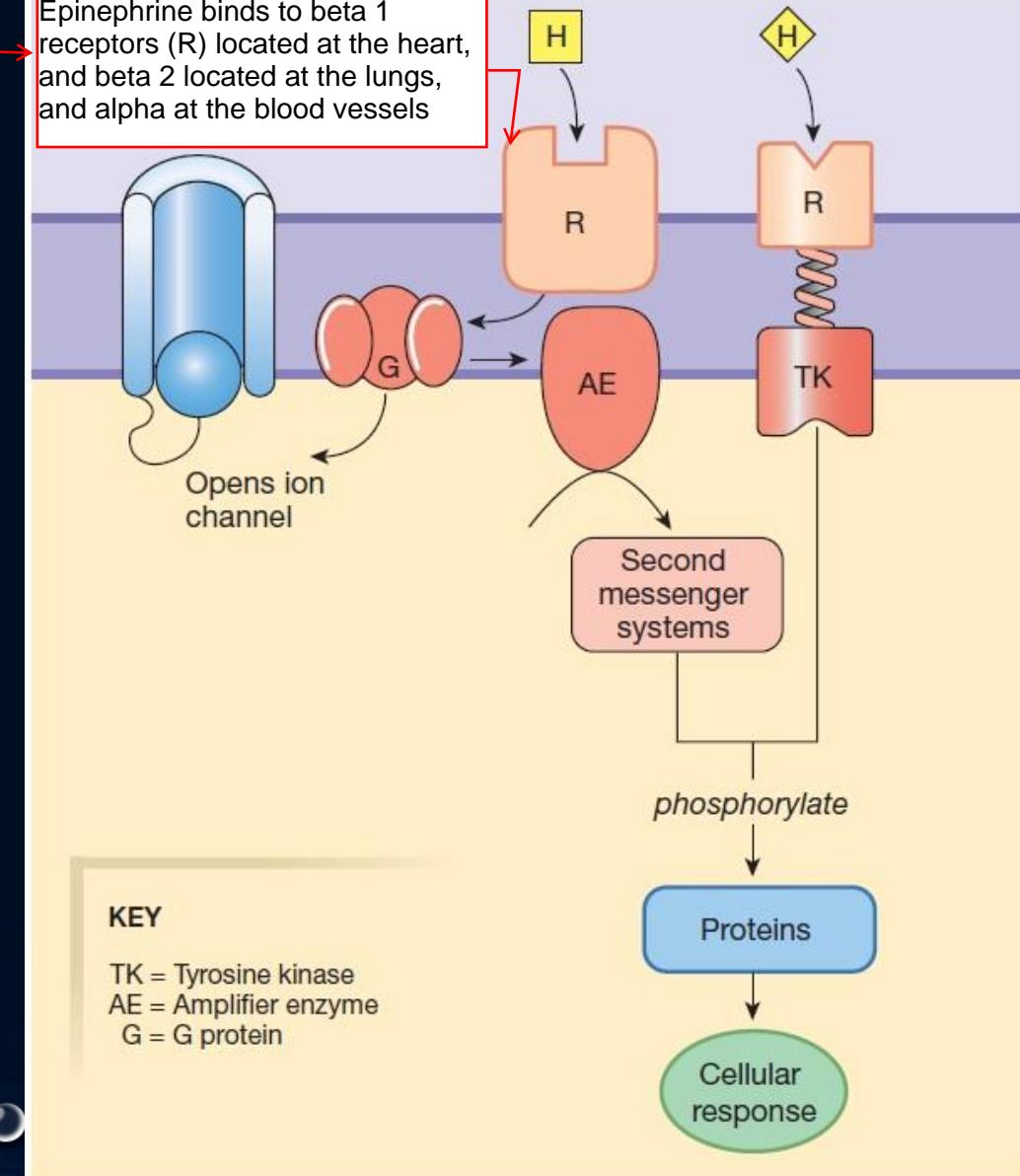
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Non-steroid Hormone Signaling

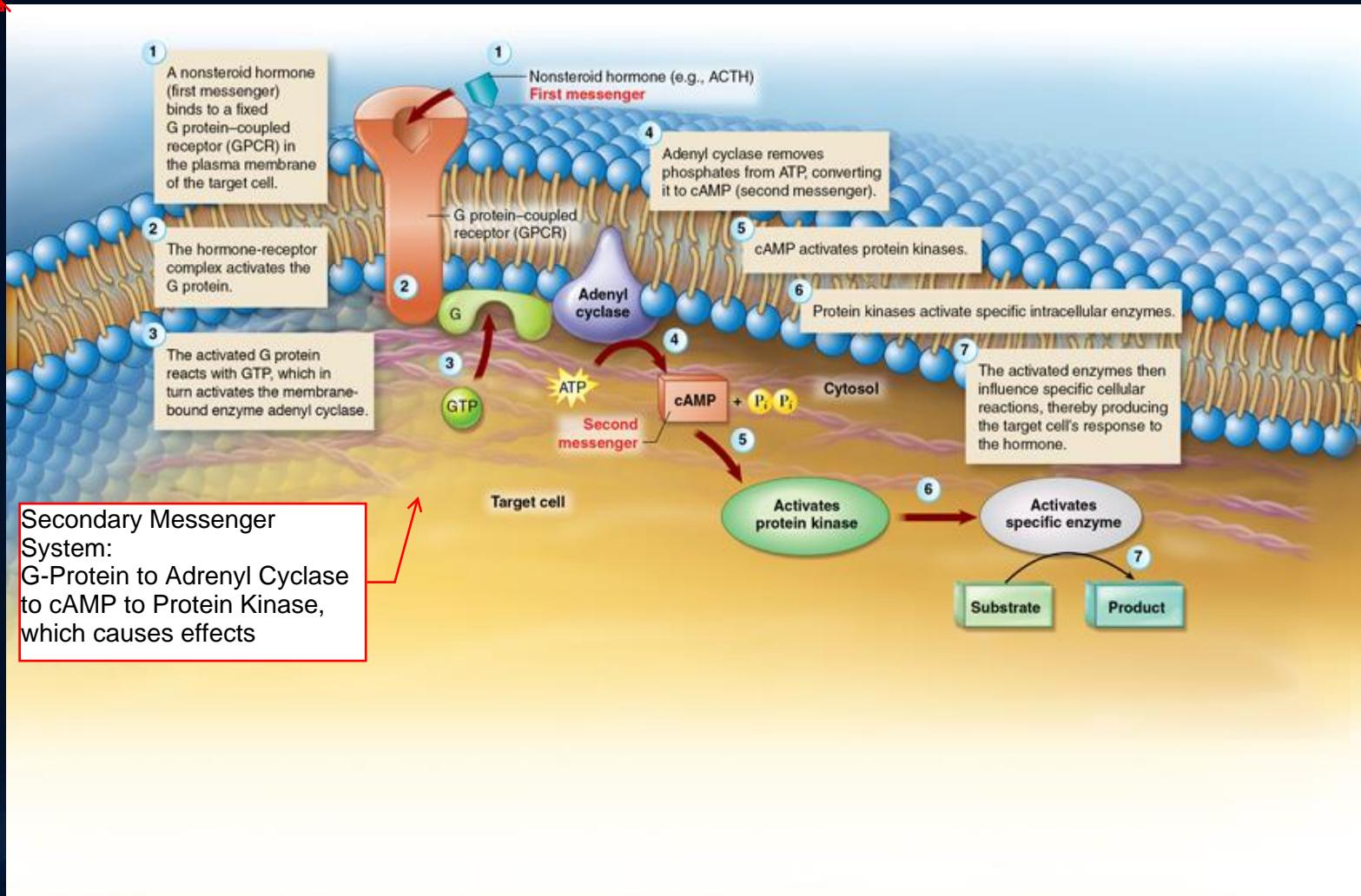
Epinephrine cause calcium intake in cells, resulting in stronger heart contractions

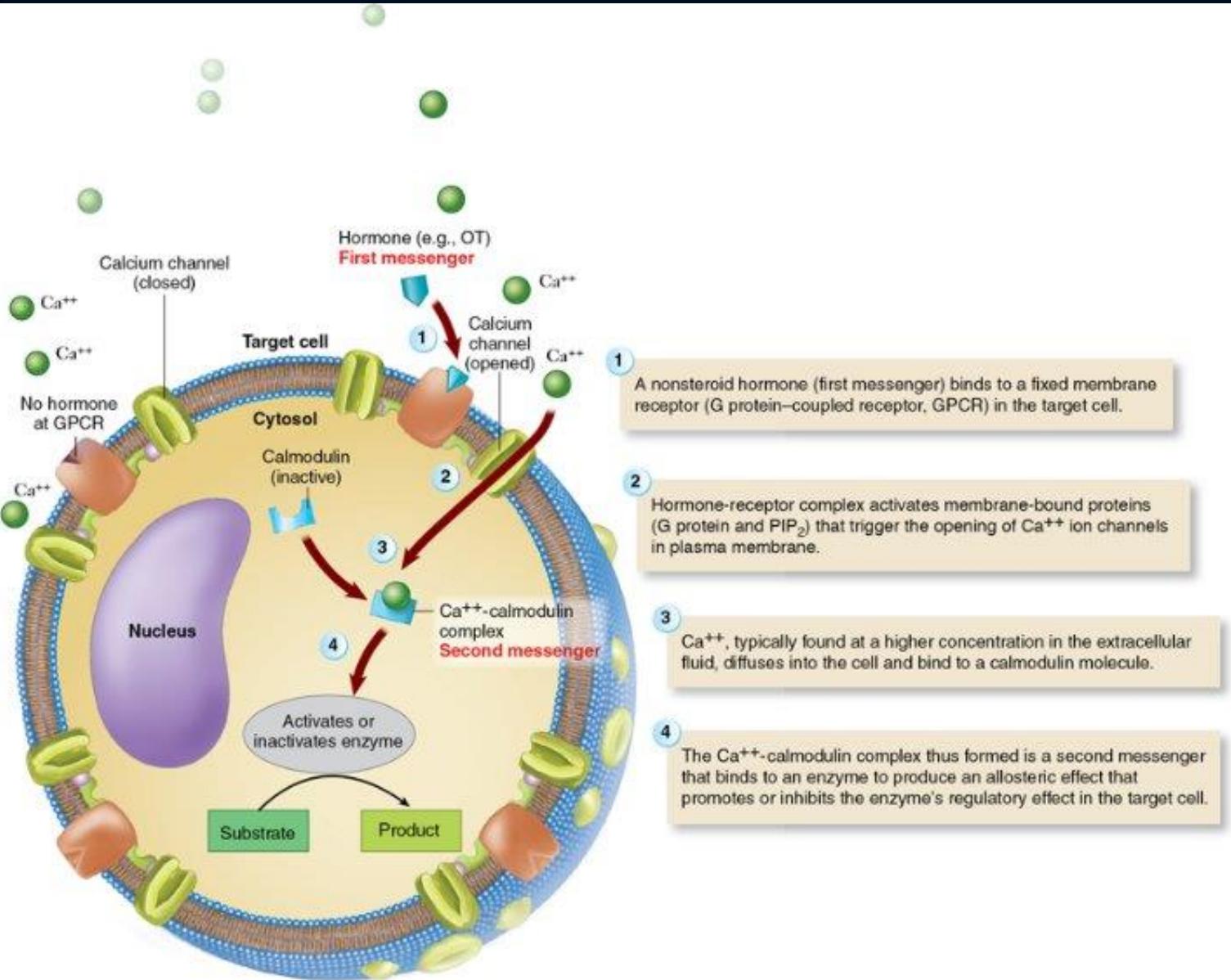
Peptide hormones (H) cannot enter their target cells and must combine with membrane receptors (R) that initiate signal transduction processes.

Epinephrine binds to beta 1 receptors (R) located at the heart, and beta 2 located at the lungs, and alpha at the blood vessels

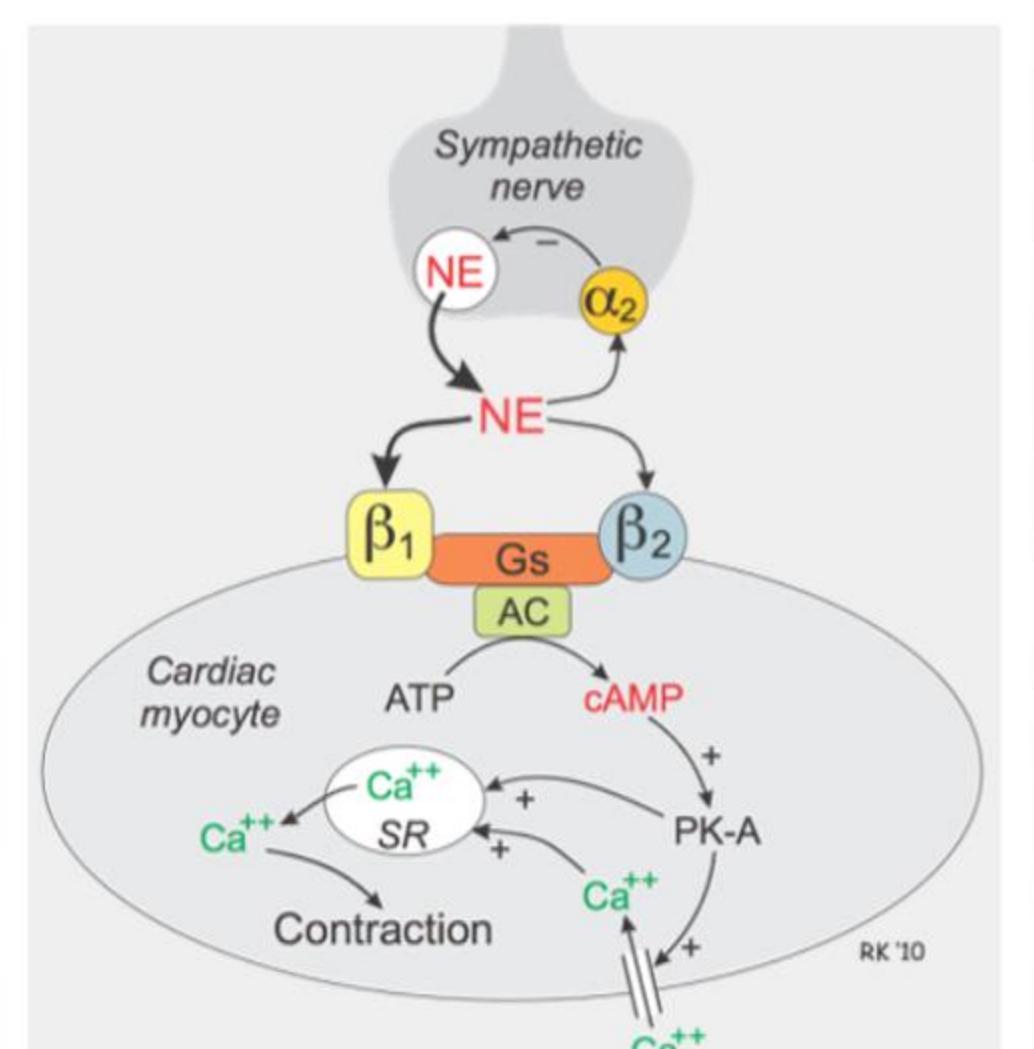


RELEVANT





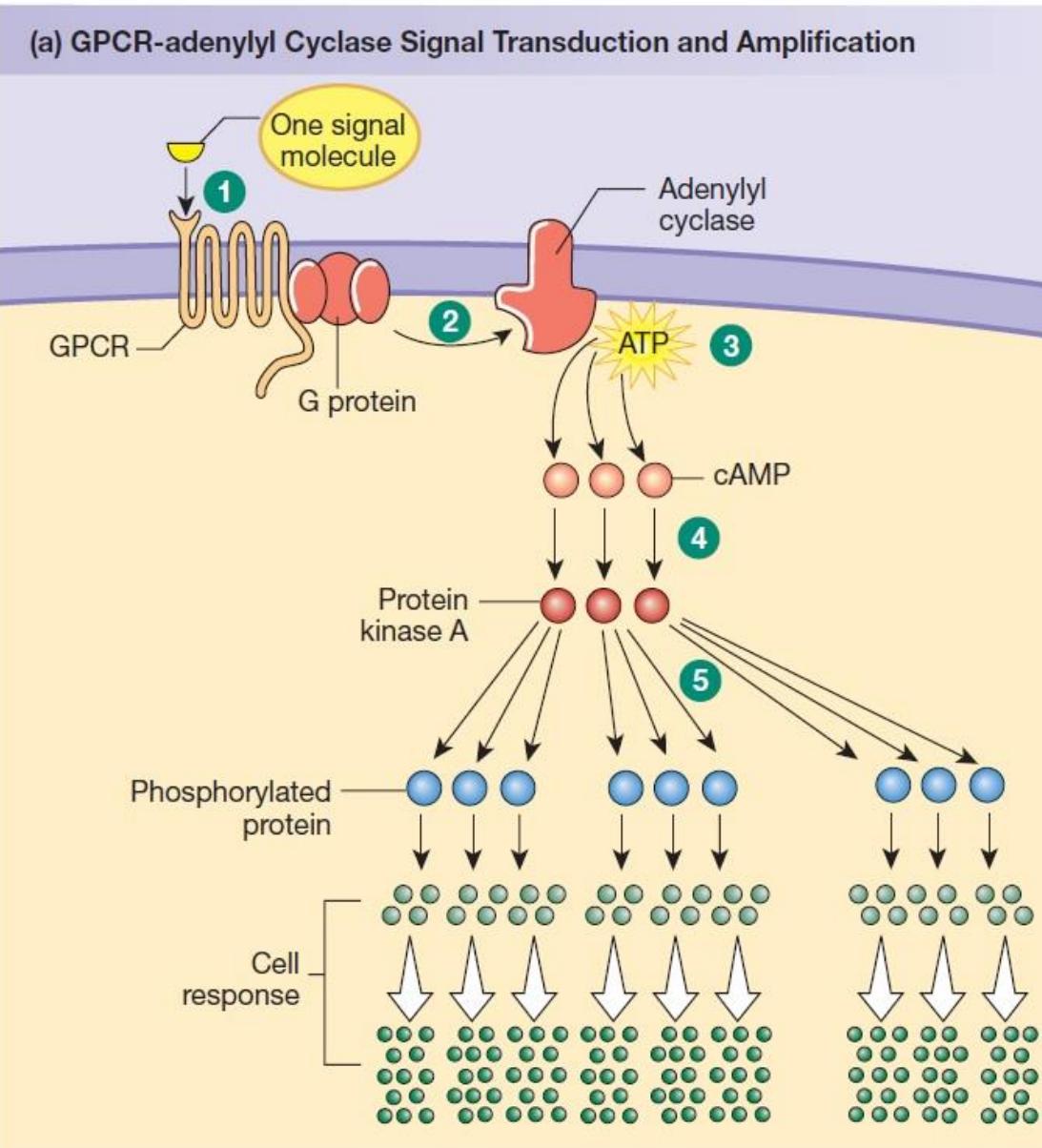
Epinephrine/Norepinephrine



Abbreviations: NE, norepinephrine; Gs, G-stimulatory protein; AC, adenylyl cyclase; PK-A, cAMP-dependent protein kinase; SR, sarcoplasmic reticulum

G Protein Signaling (α s)

(a) GPCR-adenylyl Cyclase Signal Transduction and Amplification



1 Signal molecule binds to G protein-coupled receptor (GPCR), which activates the G protein.

2 G protein turns on adenylyl cyclase, an amplifier enzyme.

3 Adenylyl cyclase converts ATP to cyclic AMP.

4 cAMP activates protein kinase A.

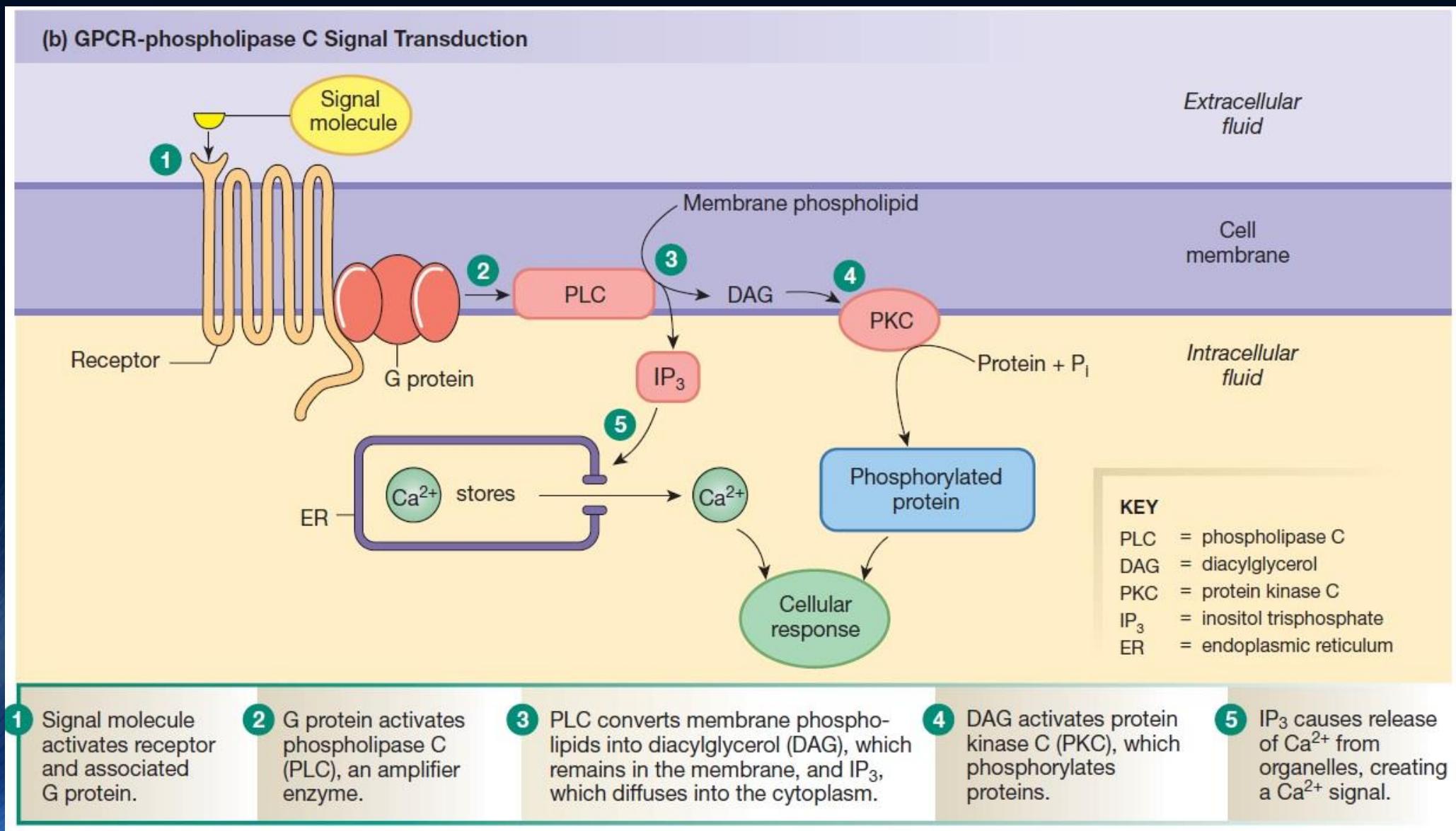
5 Protein kinase A phosphorylates other proteins, leading ultimately to a cellular response.



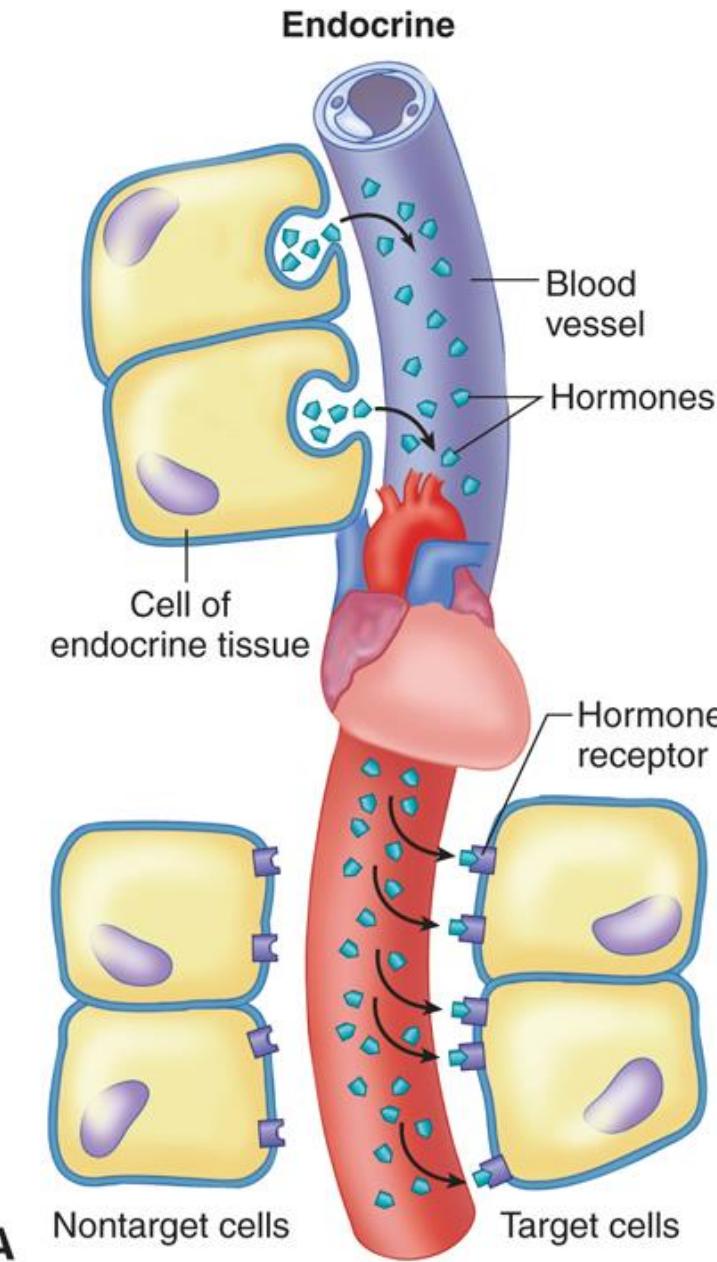
FIGURE QUESTION

Using the pattern shown in Fig. 6.6a, create a cascade that includes ATP, cAMP, adenylyl cyclase, a phosphorylated protein, and protein kinase A.

G Protein Signaling (αq)

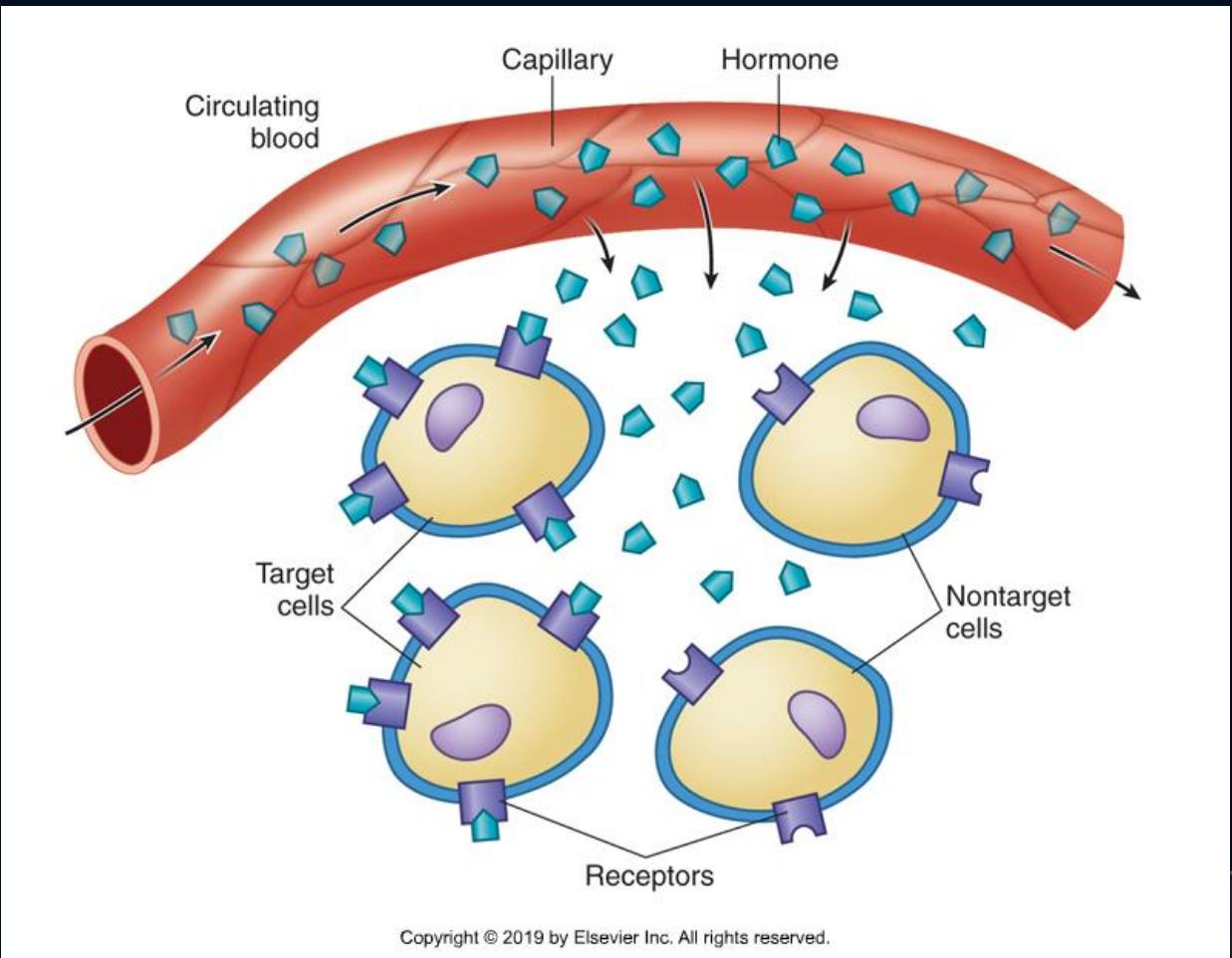


Secretion to Action



Interacting with target tissues

- ▶ Each hormone binds to a specific tissue called a target tissue or organ
- ▶ Target tissue may be close by or far away
- ▶ Some hormones have many targets (more widespread effects)
- ▶ Target cells have specific receptors that hormones bind to
 - ▶ Extracellular receptors (on the cell membrane)
 - ▶ Intracellular receptors (inside the cell)
- ▶ Works on “lock-and-key mechanism”
- ▶ Receptors stimulate secondary messenger production inside the cell (e.g. cyclic adenosine monophosphate (cAMP)) which then activates enzymes in the cell

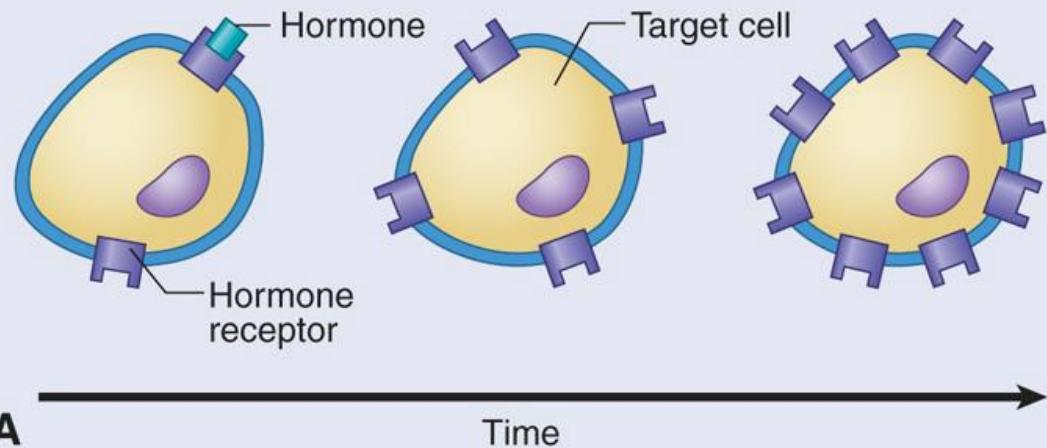


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Receptor Numbers

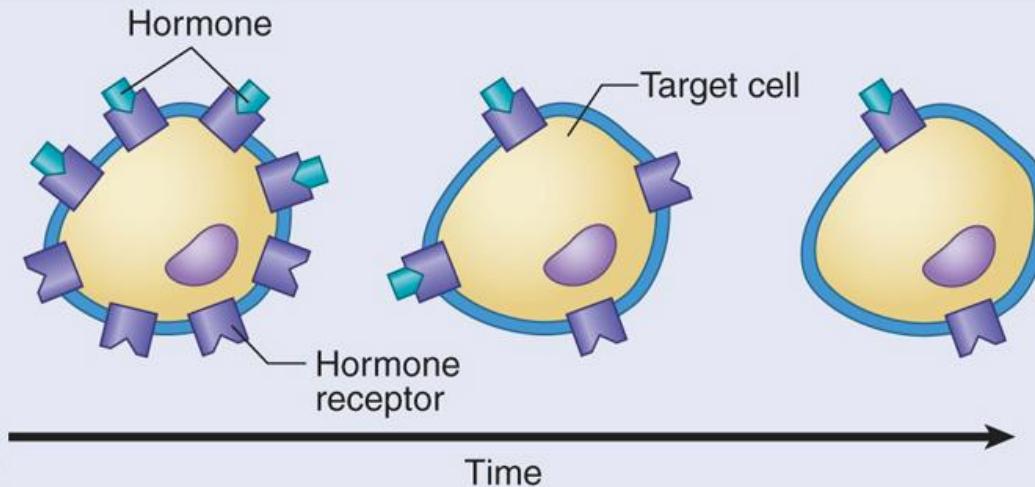
Diabetes (insulin receptors), synthetic steroids

UP-REGULATION



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DOWN-REGULATION



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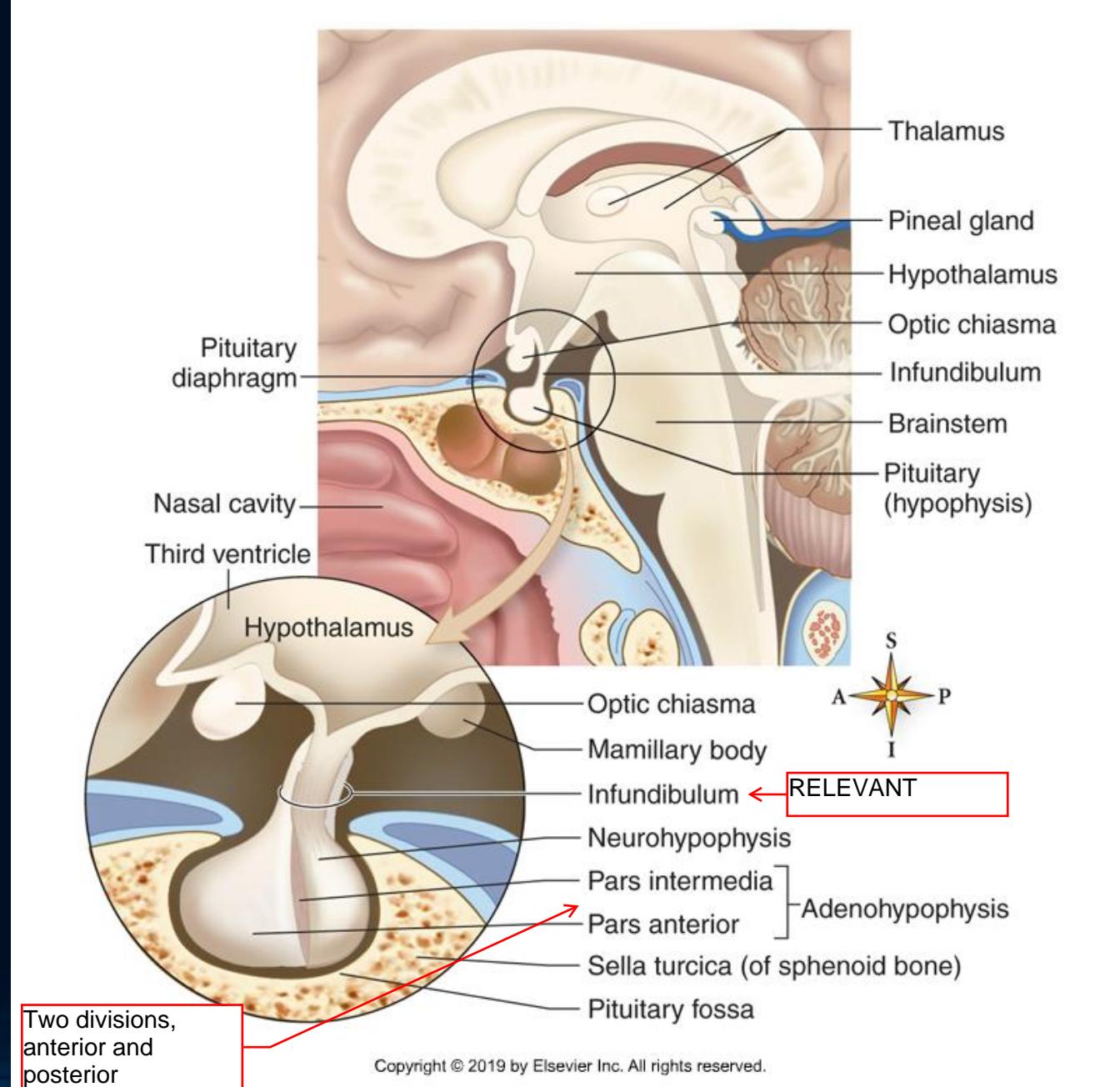
- **Up-regulation:** increases number of receptors
 - Increases sensitivity to hormone
 - Sometimes occurs when blood levels of hormone are *low*
 - Sometimes occurs with changes in development, cell cycle, cell activity

- **Down-regulation:** decreases number of receptors
 - Decreases sensitivity to hormone
 - Sometimes occurs when blood levels of hormone are *high*
 - Sometimes occurs with changes in development, cell cycle, cell activity

Endocrine Part 1

PITUITARY GLAND

Hypothalamus & Pituitary Gland



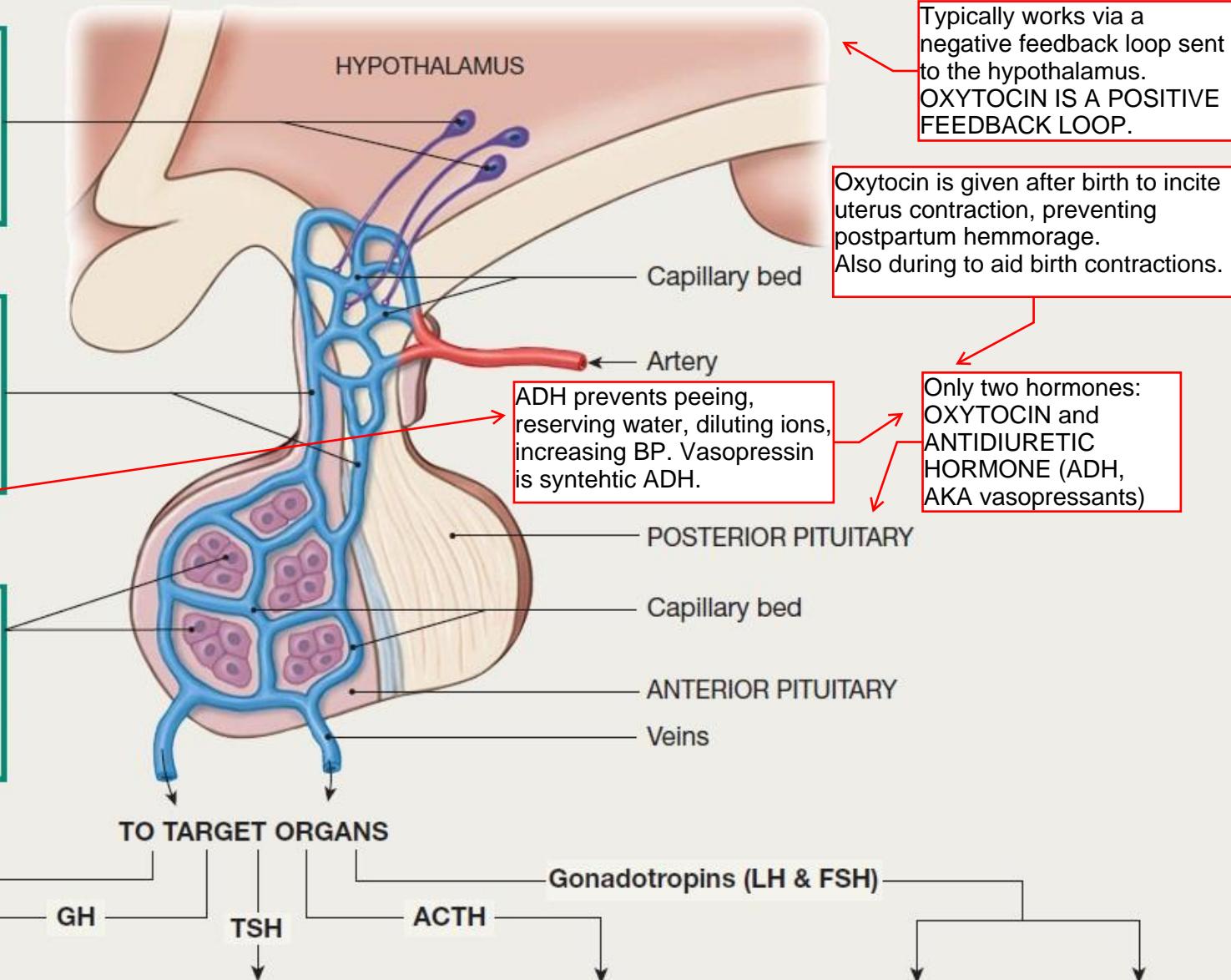
Adenohypophysis (aka Anterior Pituitary Gland)

1 Neurons synthesizing trophic neurohormones release them into capillaries of the portal system.

2 Portal vessels carry the trophic neurohormones directly to the anterior pituitary, where they act on the endocrine cells.

3 Endocrine cells release their peptide hormones into the second set of capillaries for distribution to the rest of the body.

Diabetes insipidus is a lack of ADH causing too much peeing.
Diabetes mellitus causes you to pee from too much sugar.



Hormones Linked to Anterior Pituitary

FLAT GP

Adrenal Glands

Thyroid
stimulating

Mammary glands

HYPOTHALAMIC
HORMONES

growth

Reproductive
hormones

Dopamine

TRH

CRH

GHRH

Somatostatin

GnRH

ANTERIOR
PITUITARY
HORMONES

Prolactin

TSH

ACTH

GH

FSH

LH

ENDOCRINE TARGETS
AND THE HORMONES
THEY SECRETE

Thyroid
gland

Adrenal
cortex

Liver

Thyroid
hormones
(T₃, T₄)

Cortisol

Insulin-like
growth factors
(IGFs)

Breast

Many
tissues

NONENDOCRINE
TARGETS

Neurons in hypothalamus
secreting trophic hormones

Portal system
Anterior pituitary

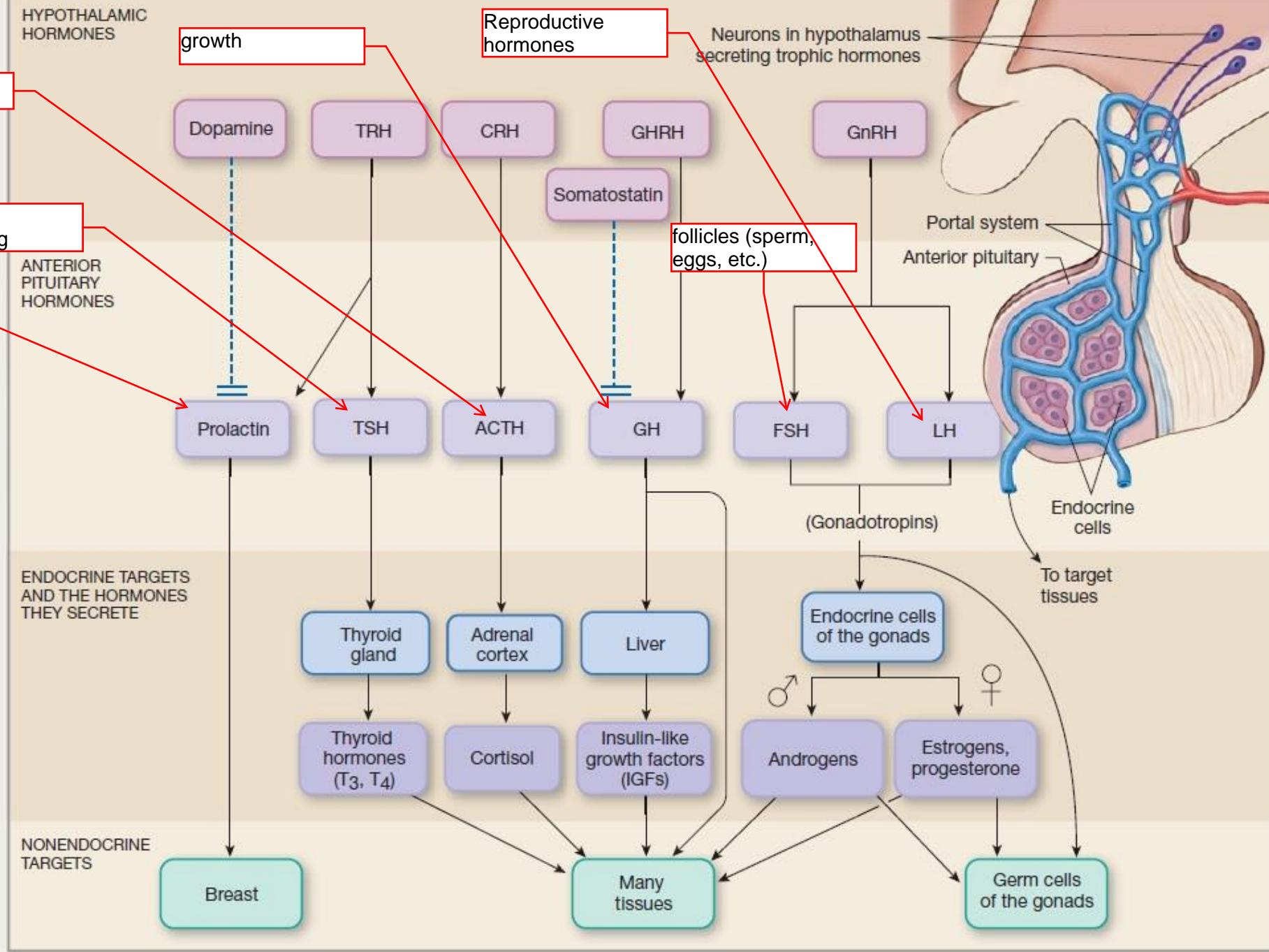
Endocrine
cells

To target
tissues

Endocrine cells
of the gonads

♂ Androgens
♀ Estrogens,
progesterone

Germ cells
of the gonads



Feedback Mechanisms

Short Loop Feedback

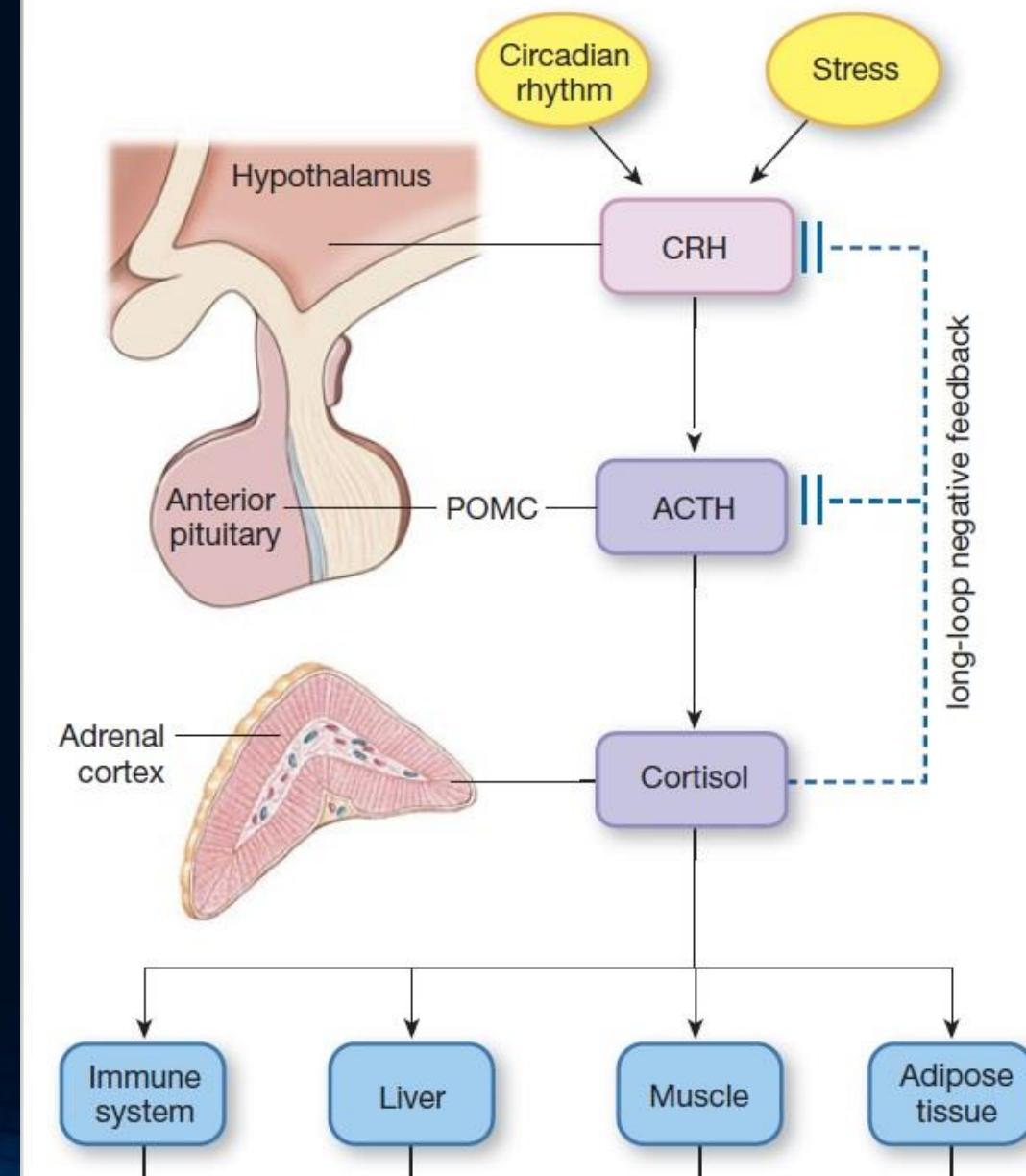
- occurs when pituitary hormone alters secretion of hypothalamic hormone

Long Loop Feedback

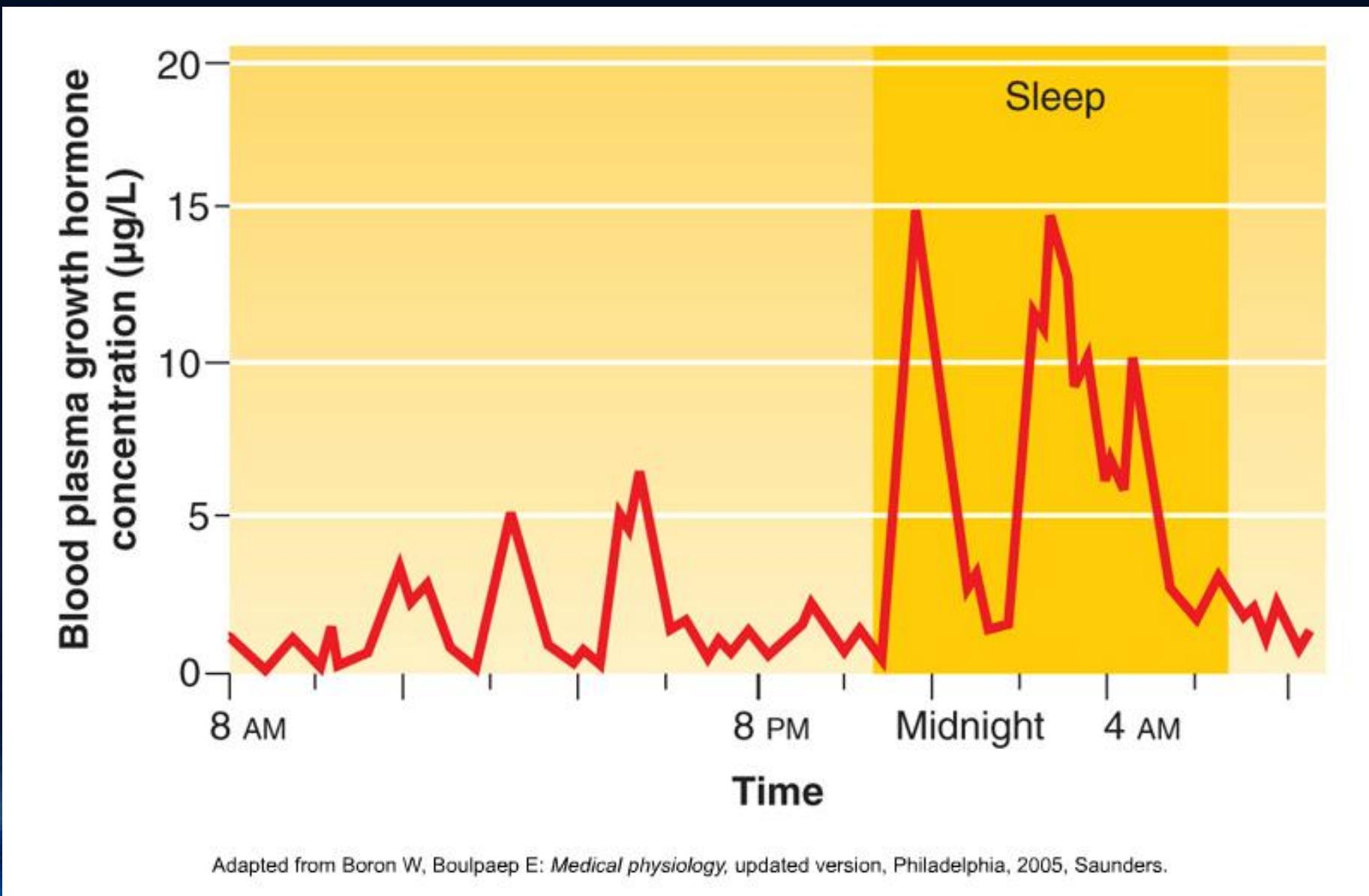
- occurs when target organ hormone alters secretion of hypothalamic or pituitary hormones

THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) PATHWAY

(a) The control of cortisol secretion



Circadian Regulation or Hormone Secretion



Posterior stores hormones instead of making them, as they're made in the hypothalamus

Neurohypophysis (aka Posterior Pituitary)

Vasopressin

- Causes more H₂O to be reabsorbed by kidneys
- Sense of thirst

Oxytocin

- Supports labour & delivery by stimulating contraction of uterus
- Supports letdown reflex for breast feeding
- Love hormone – secreted in higher levels in coupled people than in uncoupled people

