

# Endocrine Part 1

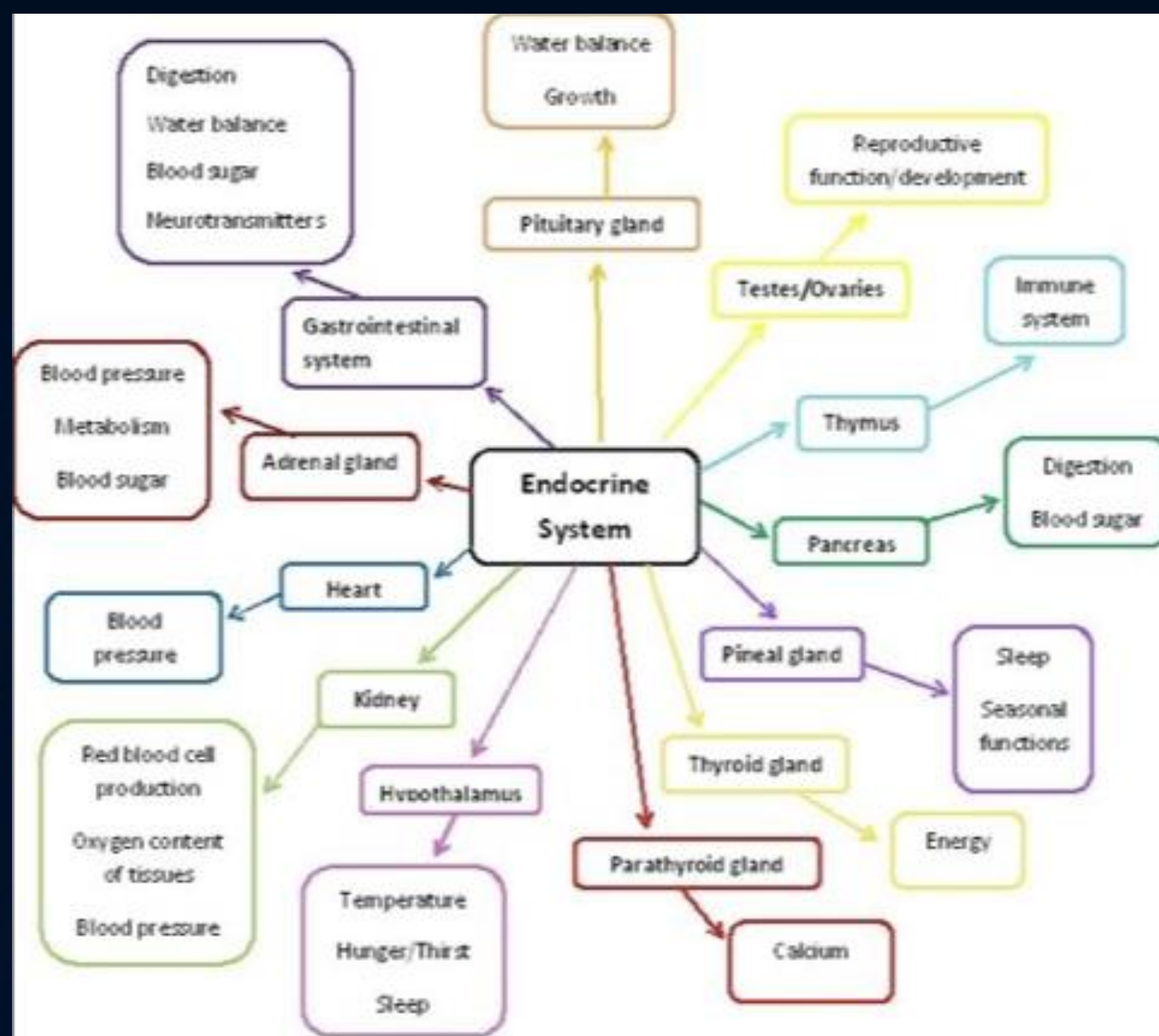
INTRO TO THE ENDOCRINE SYSTEM

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.

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

Exocrine system on the other hand has ducts, 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

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)

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

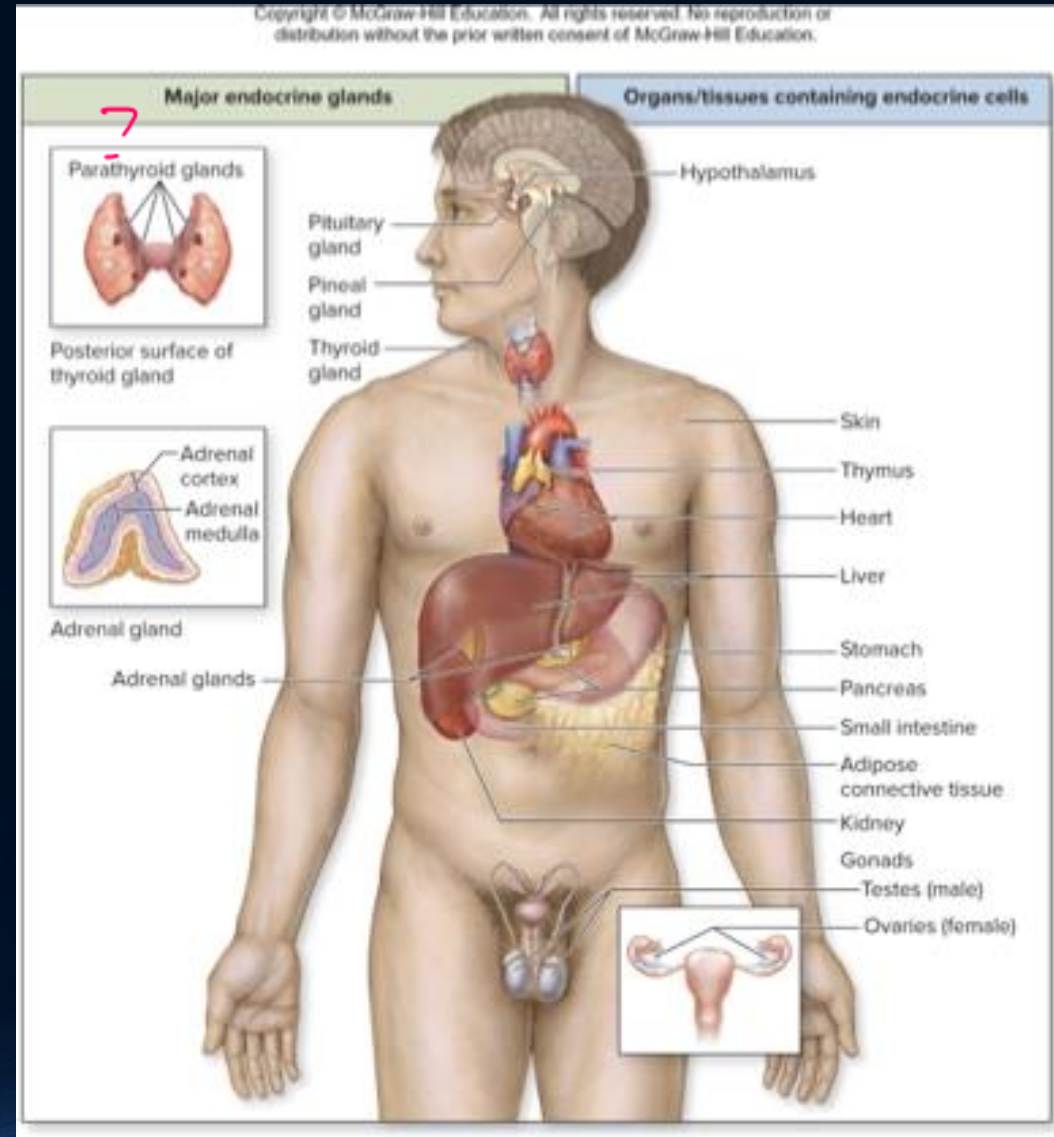
# Endocrine System – General Function

- **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



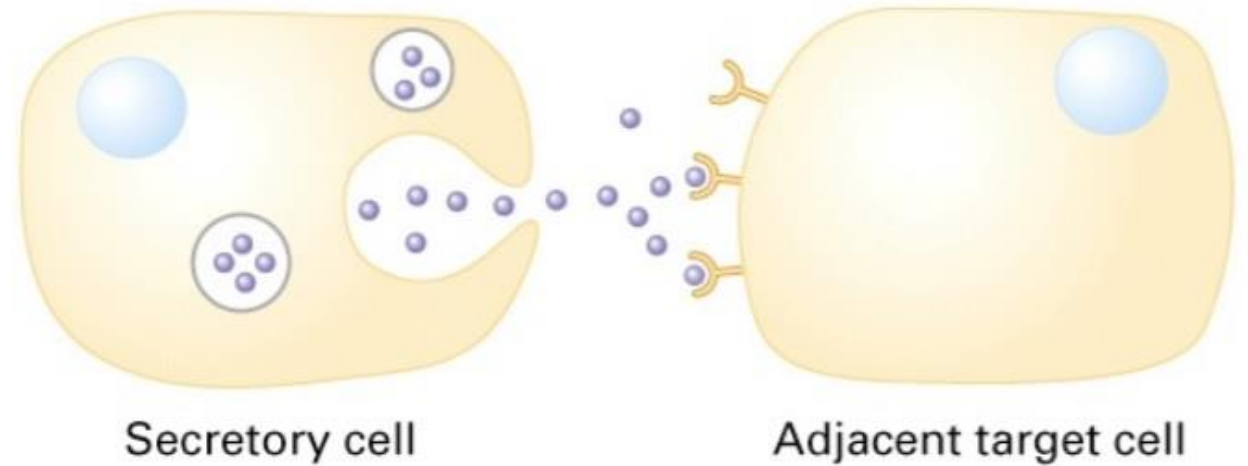
## 3 Types of Signalling

1. Endocrine – somewhere else in body via bloodstream

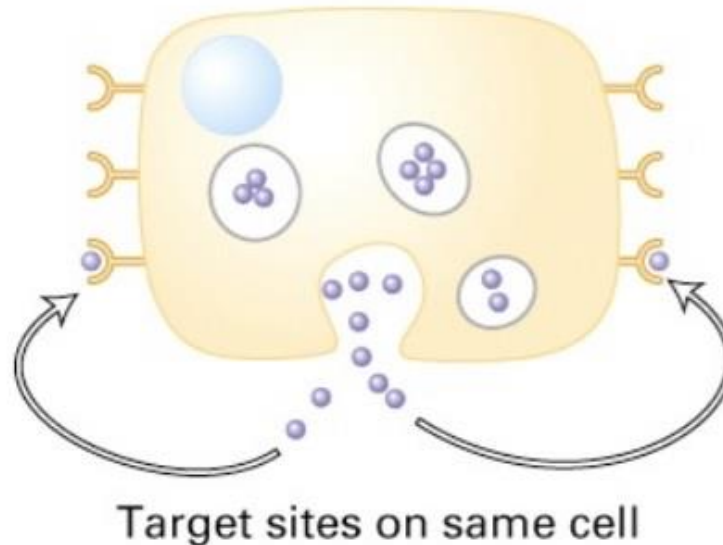
2. Autocrine – self signalling

3. Paracrine – neighbouring cells

(b) Paracrine signaling



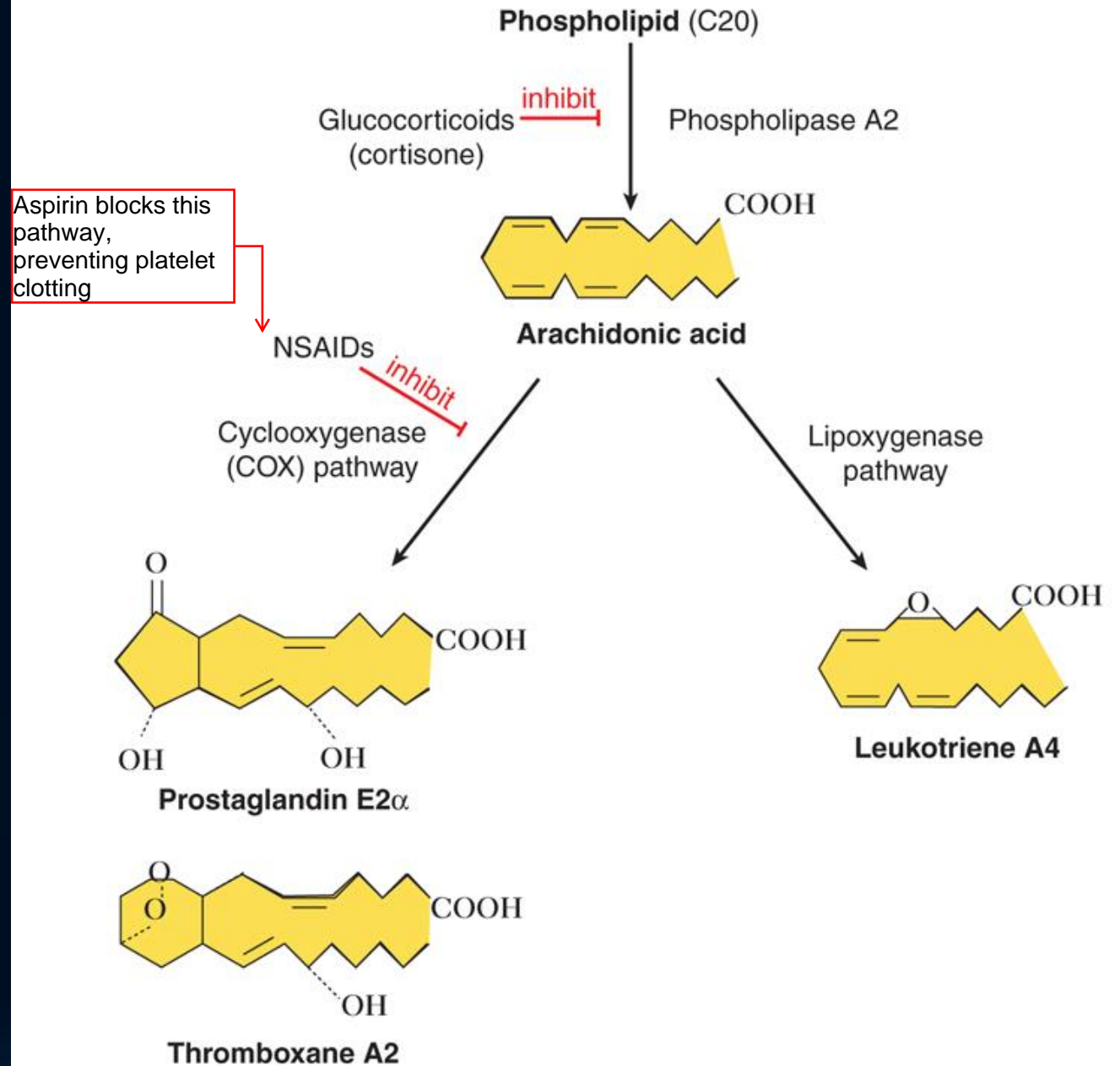
(c) Autocrine signaling



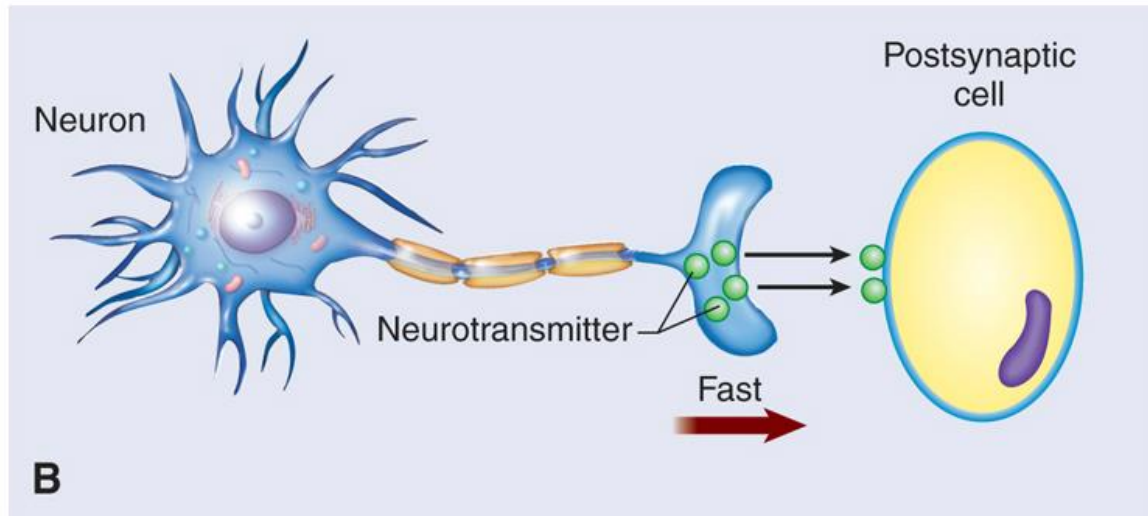
Key:

- Extracellular signal
- Y Receptor
- Membrane-attached signal

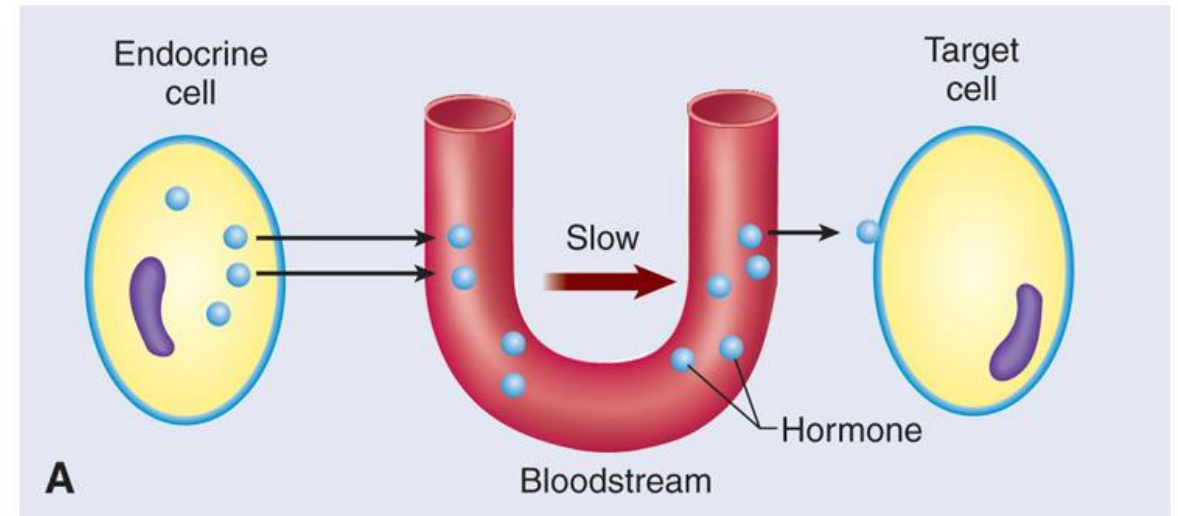
# Local regulators – eicosanoids



# Nervous vs Endocrine Communication

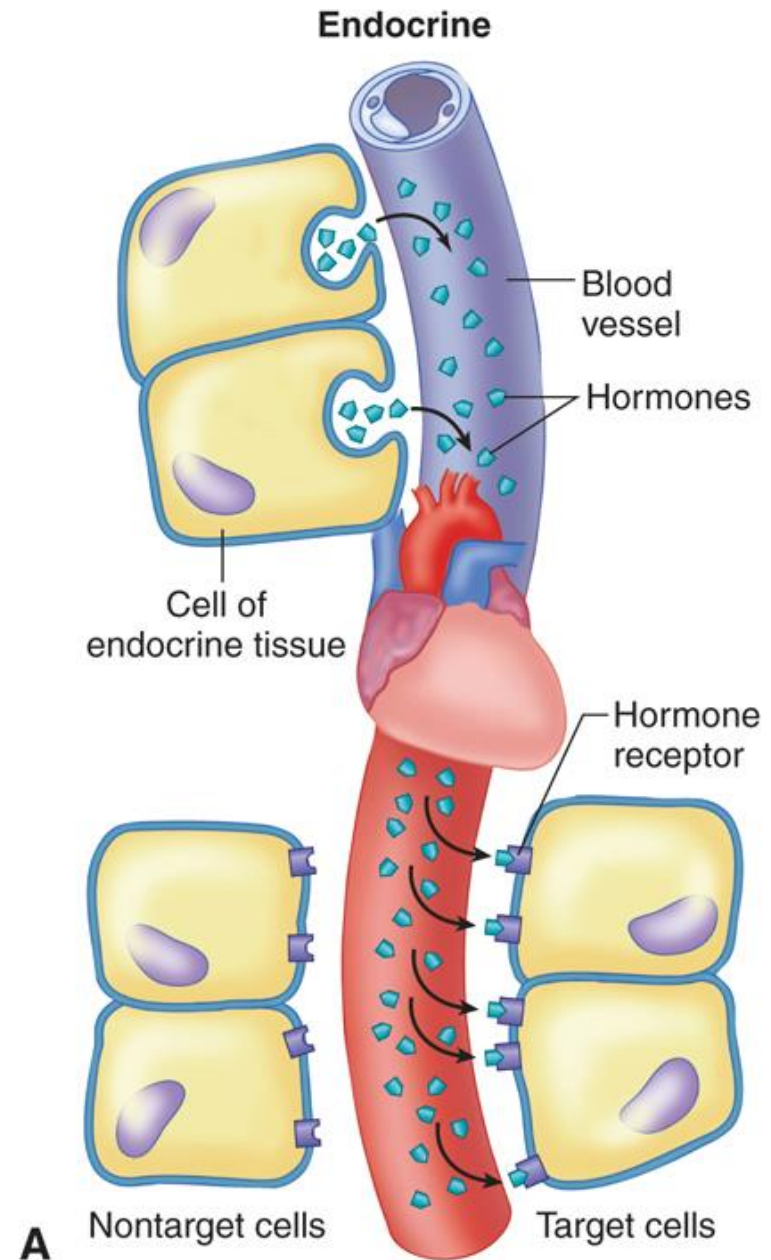


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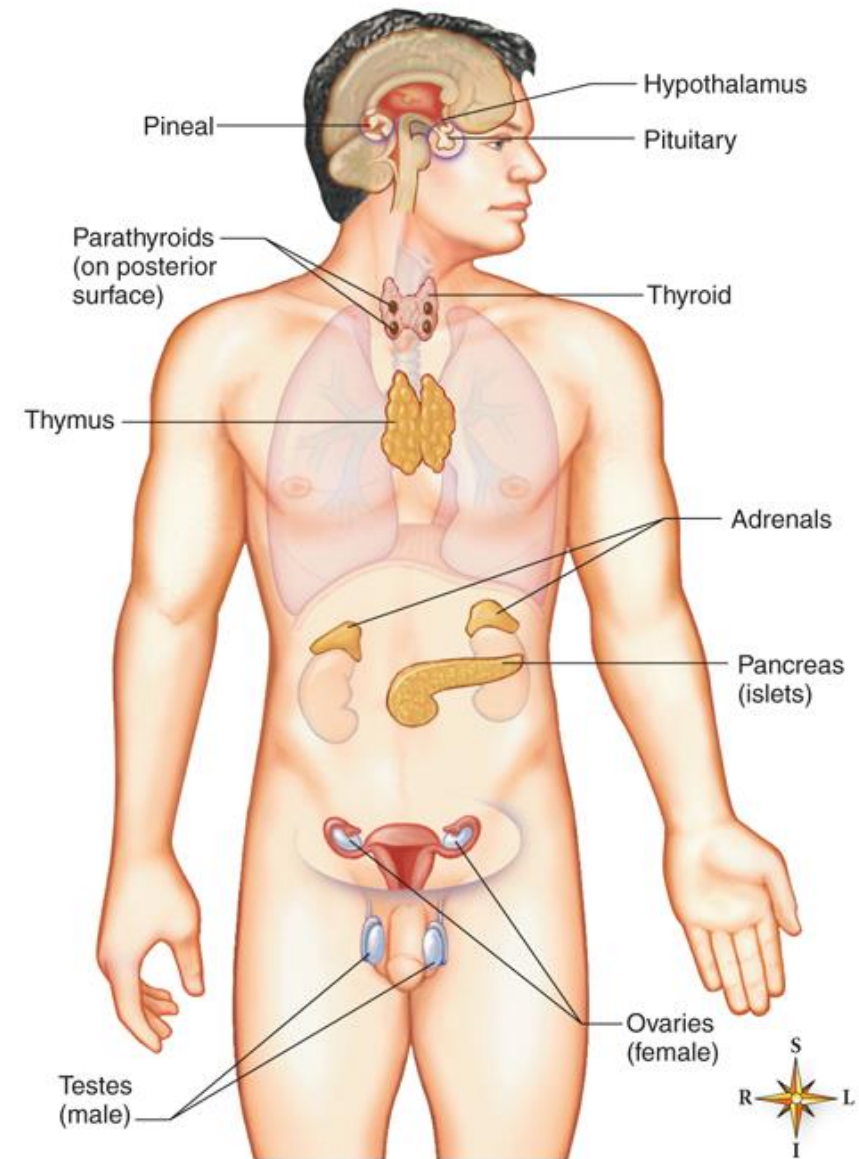


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# Secretion to Action



# Primary Endocrine Glands



# Endocrine Part 1

HORMONE CLASSIFICATION & SIGNALING MECHANISMS

All begin as cholesterol, with different side chains added on

**Steroid**

- Cortisol (hydrocortisone)
- Aldosterone
- Estrogens
- Progesterone
- Testosterone

Primary difference. Steroids can enter cell membrane, non-steroids require facilitated entry

All chains of amino acids backbones

**Nonsteroid**

Sugars added to amino acids

**Proteins**

- Growth hormone (GH)
- Prolactin (PRL)
- Parathyroid hormone (PTH)
- Calcitonin (CT)
- Adrenocorticotrophic hormone (ACTH)
- Insulin
- Glucagon

**Glycoproteins**

- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Thyroid-stimulating hormone (TSH)
- Human chorionic gonadotropin (hCG)

**Peptides**

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

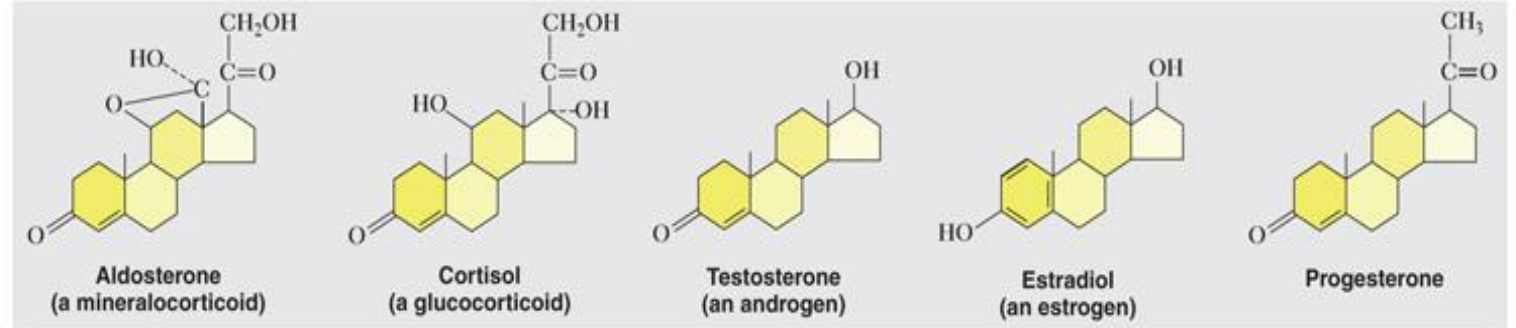
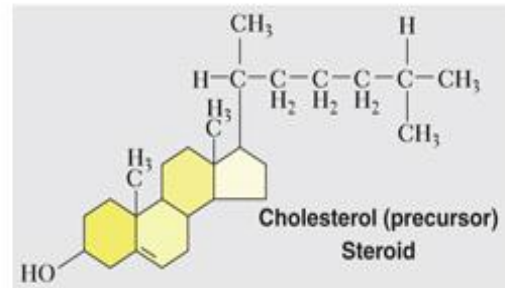
**Amino acid derivatives**

- Amines**
  - Norepinephrine (NE)
  - Epinephrine (Epi)
  - Melatonin
- Iodinated amino acids**
  - Thyroxine ( $T_4$ )
  - Triiodothyronine ( $T_3$ )

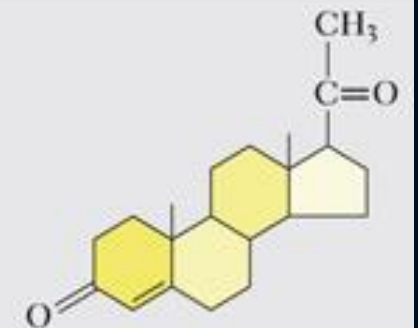
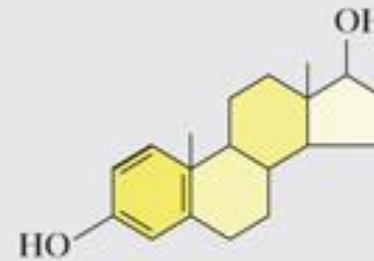
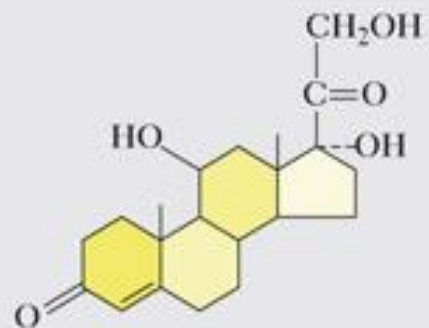
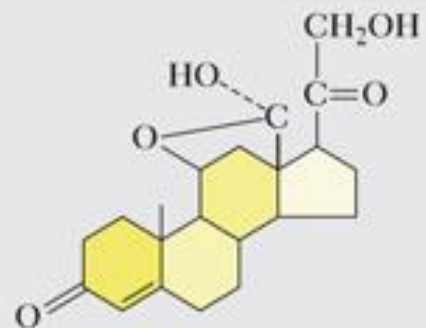
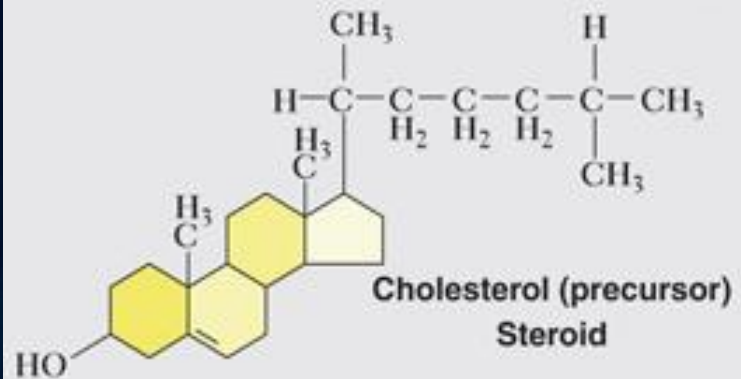
## Structural classifications of hormones

# Steroid hormones

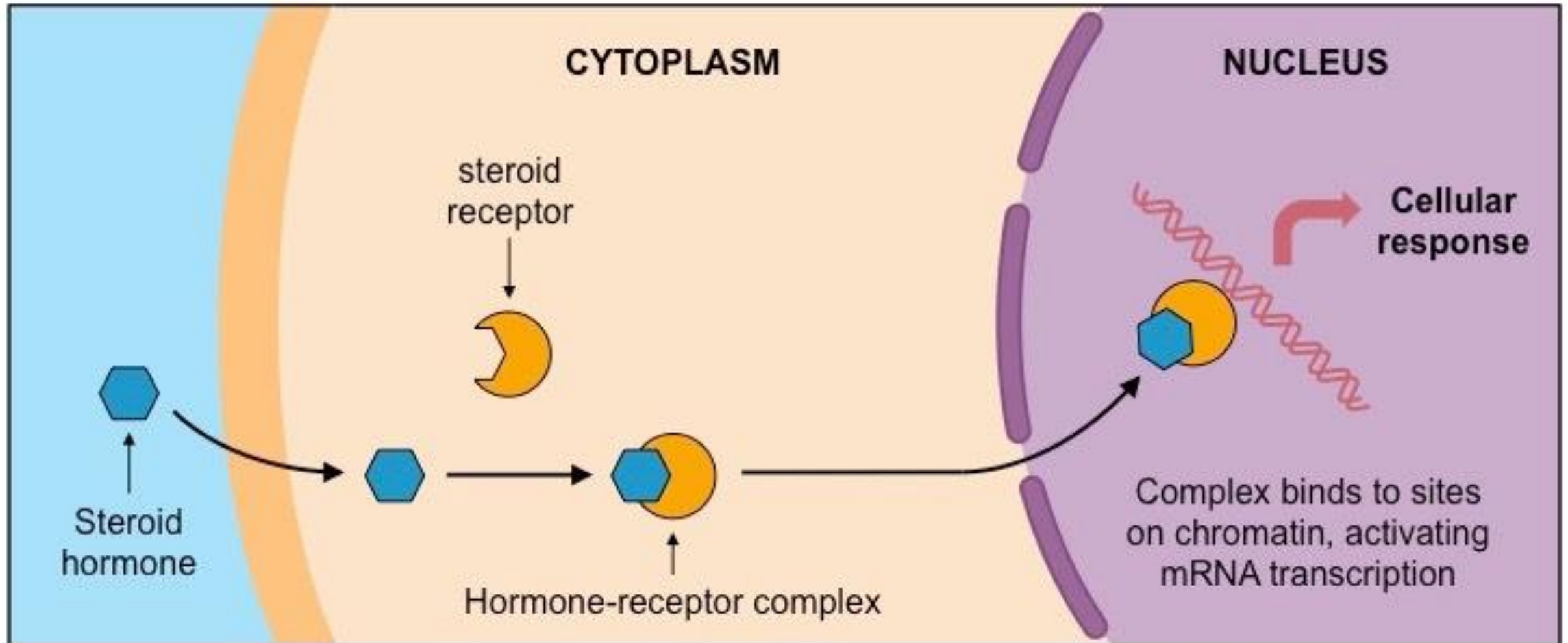
- Lipid-soluble molecules synthesized from cholesterol
- Includes gonadal steroids (e.g., estrogen)
- Includes steroid synthesized by adrenal cortex (e.g., cortisol)
- Calcitriol sometimes classified in this group, but more accurately called a *sterol*



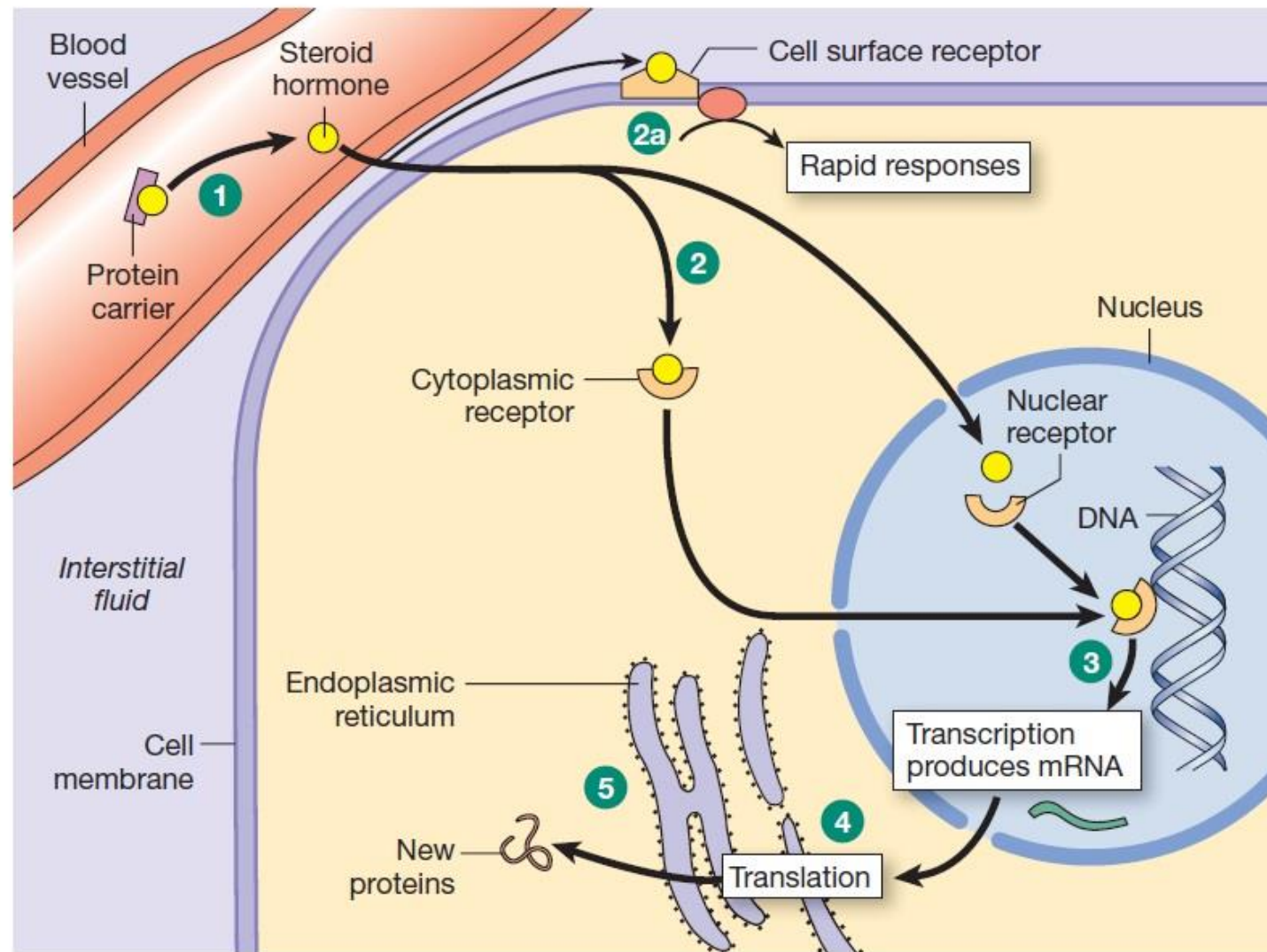
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# Steroid Hormone Receptors



# 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.

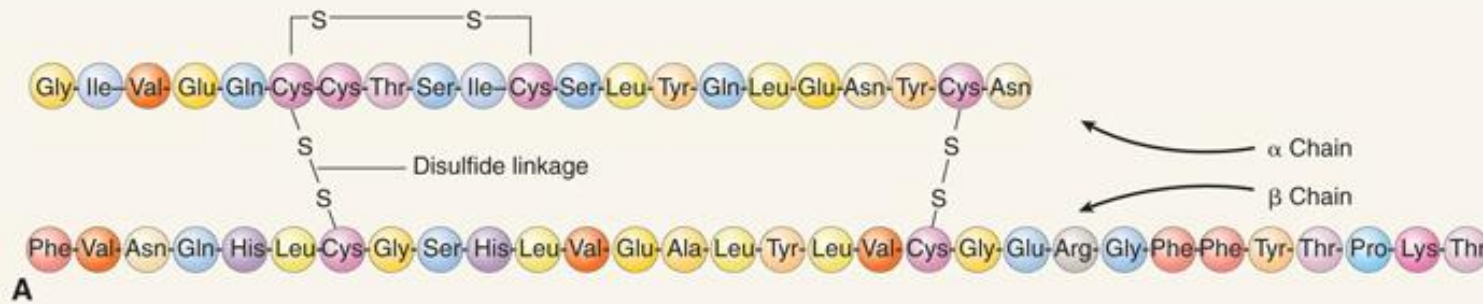
3 The receptor-hormone complex binds to DNA and activates or represses one or more genes.

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)

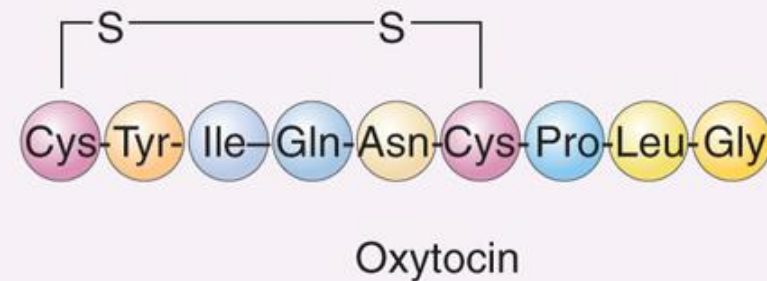
## PROTEIN HORMONE (INSULIN)



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

## PEPTIDE HORMONE (OXYTOCIN [OT])

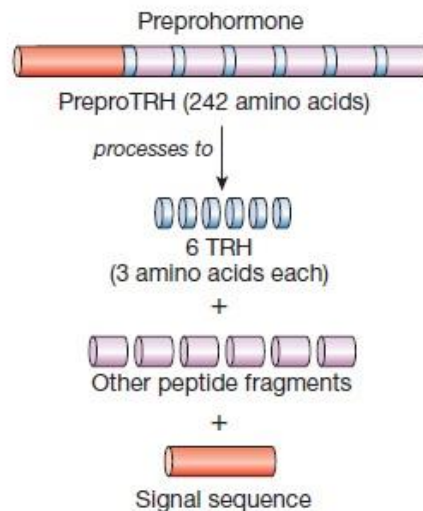


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# Protein & Peptide Hormone Synthesis

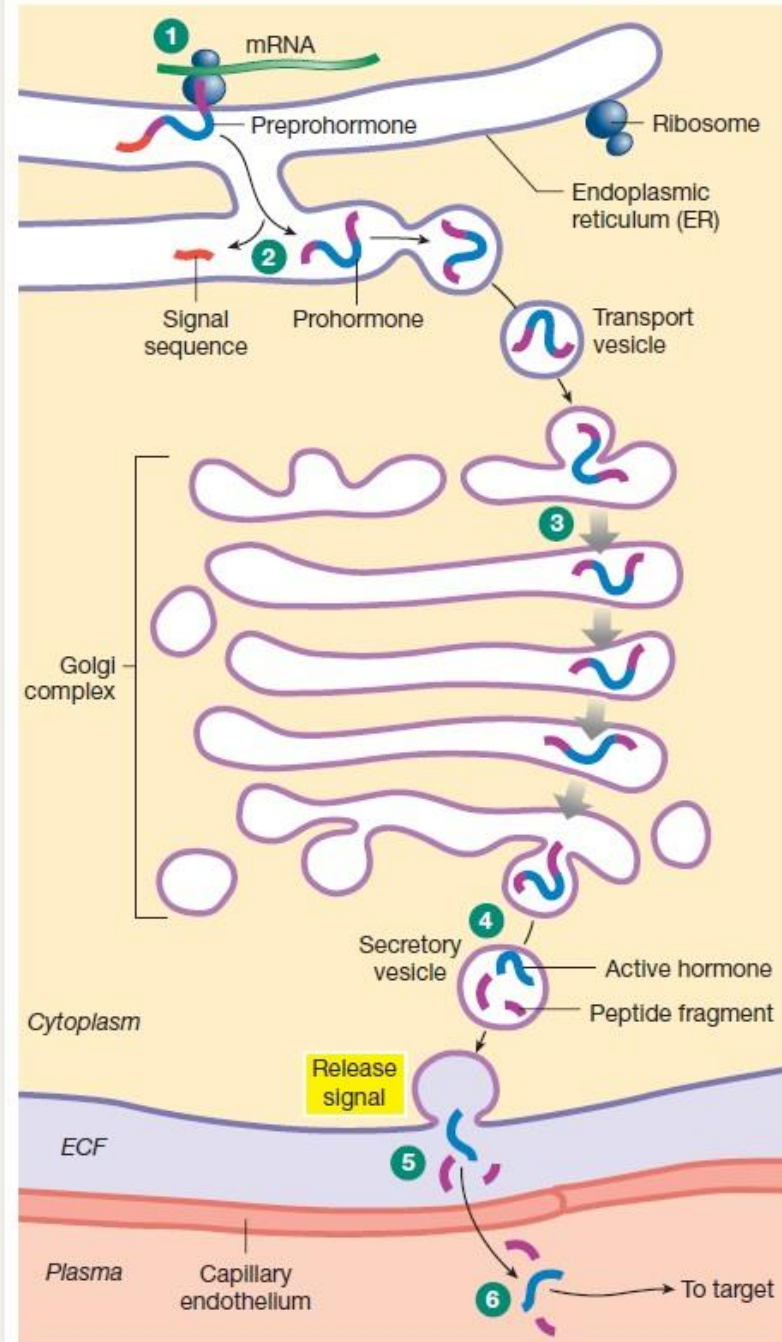
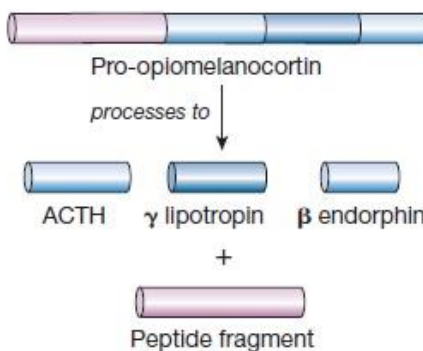
## (a) Preprohormones

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.

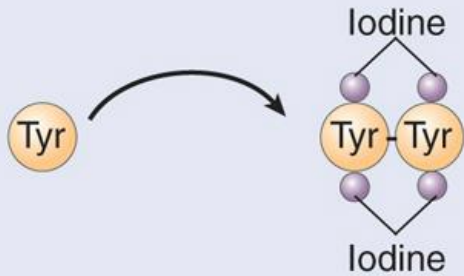
**4** Secretory vesicles containing enzymes and prohormone bud off the Golgi. The enzymes chop the prohormone into one or more active peptides plus additional peptide fragments.

**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.

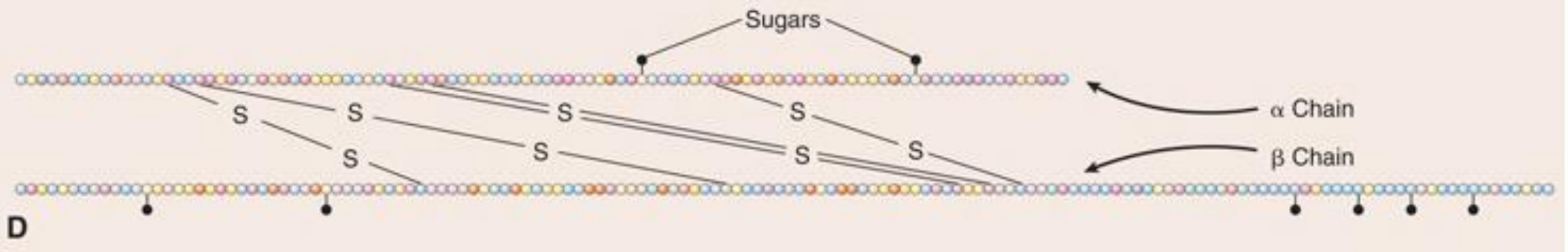
# Amino Acid Derivative & Glycoprotein Hormones

## AMINO ACID DERIVATIVE (THYROXINE [T<sub>4</sub>])



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

## GLYCOPROTEIN HORMONE (HUMAN CHORIONIC GONADOTROPIN [hCG])

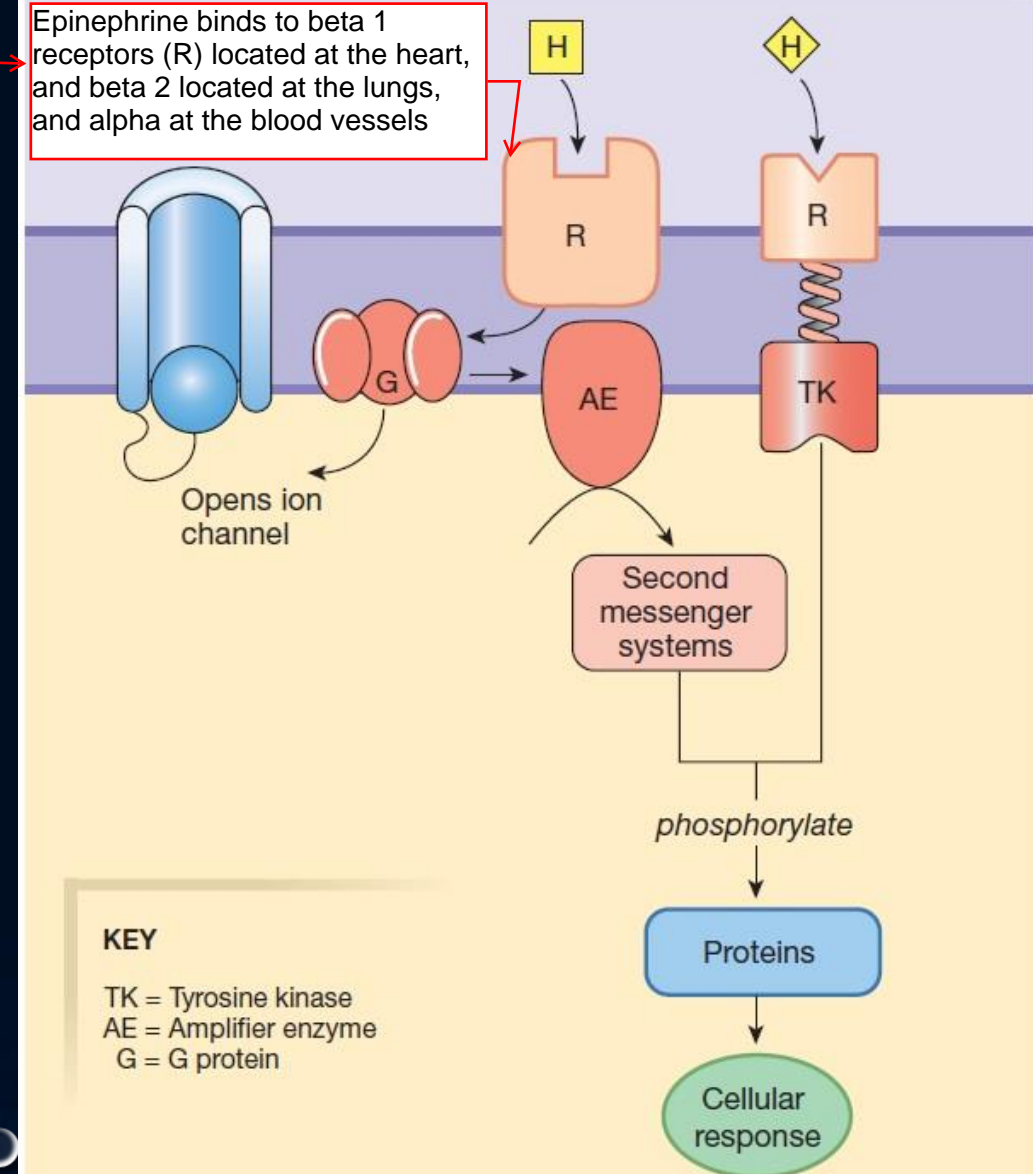


# Non-steroid Hormone Signaling

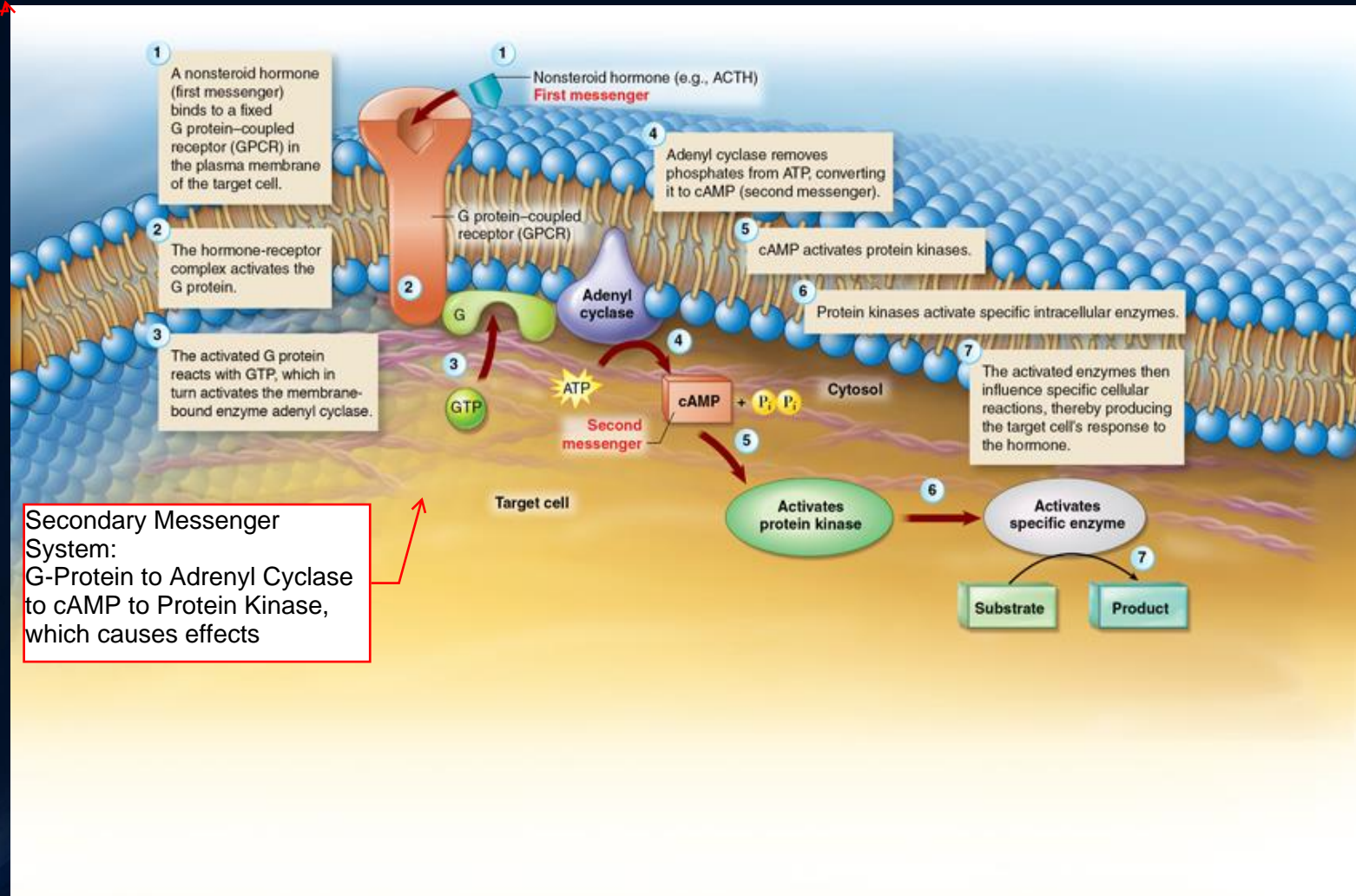
Epinephrine cause calcium intake in cells, resulting in stronger heart contractions

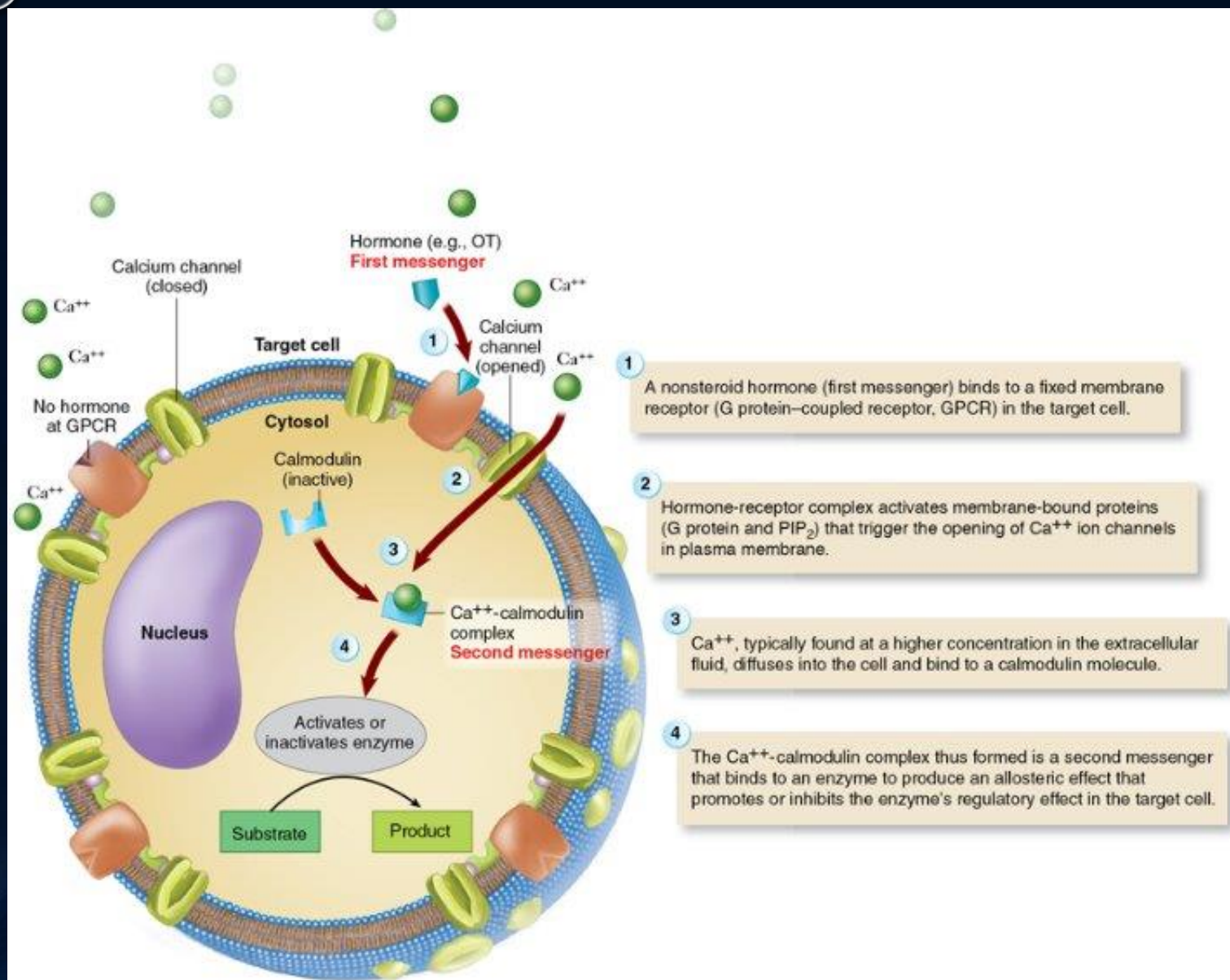
Peptide hormones (H) cannot enter their target cells and must combine with membrane receptors (R) that initiate signal transduction processes.

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

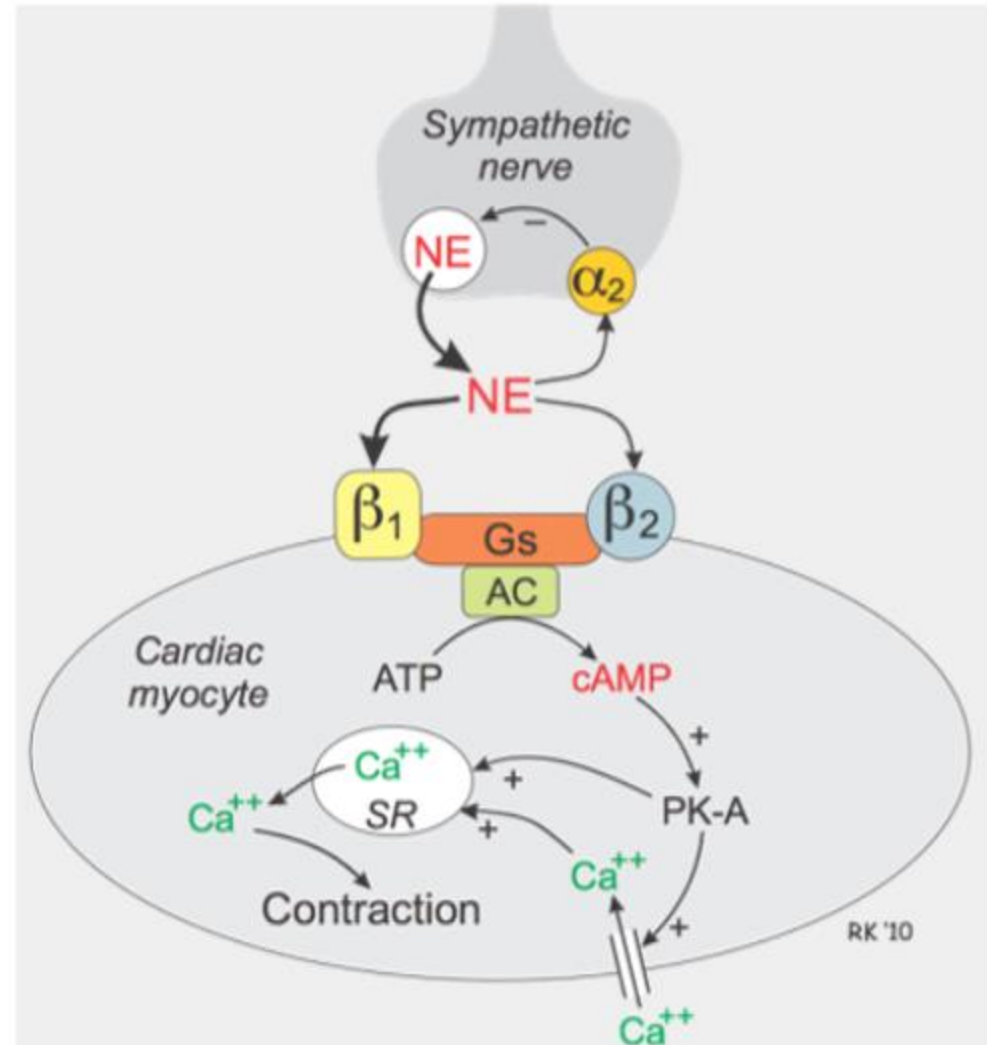


RELEVANT





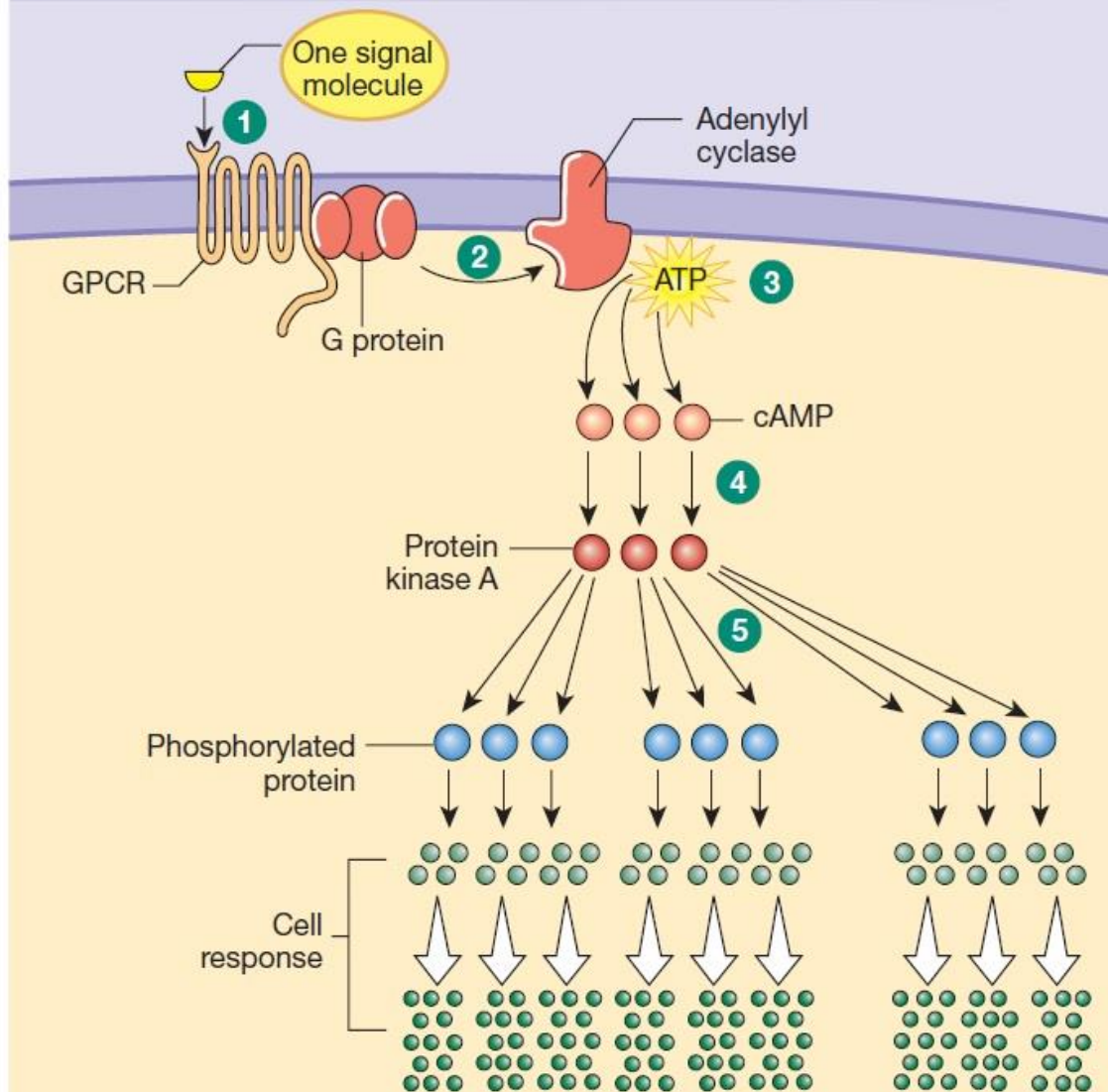
# Epinephrine/Norepinephrine



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

# G Protein Signaling ( $\alpha$ 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.

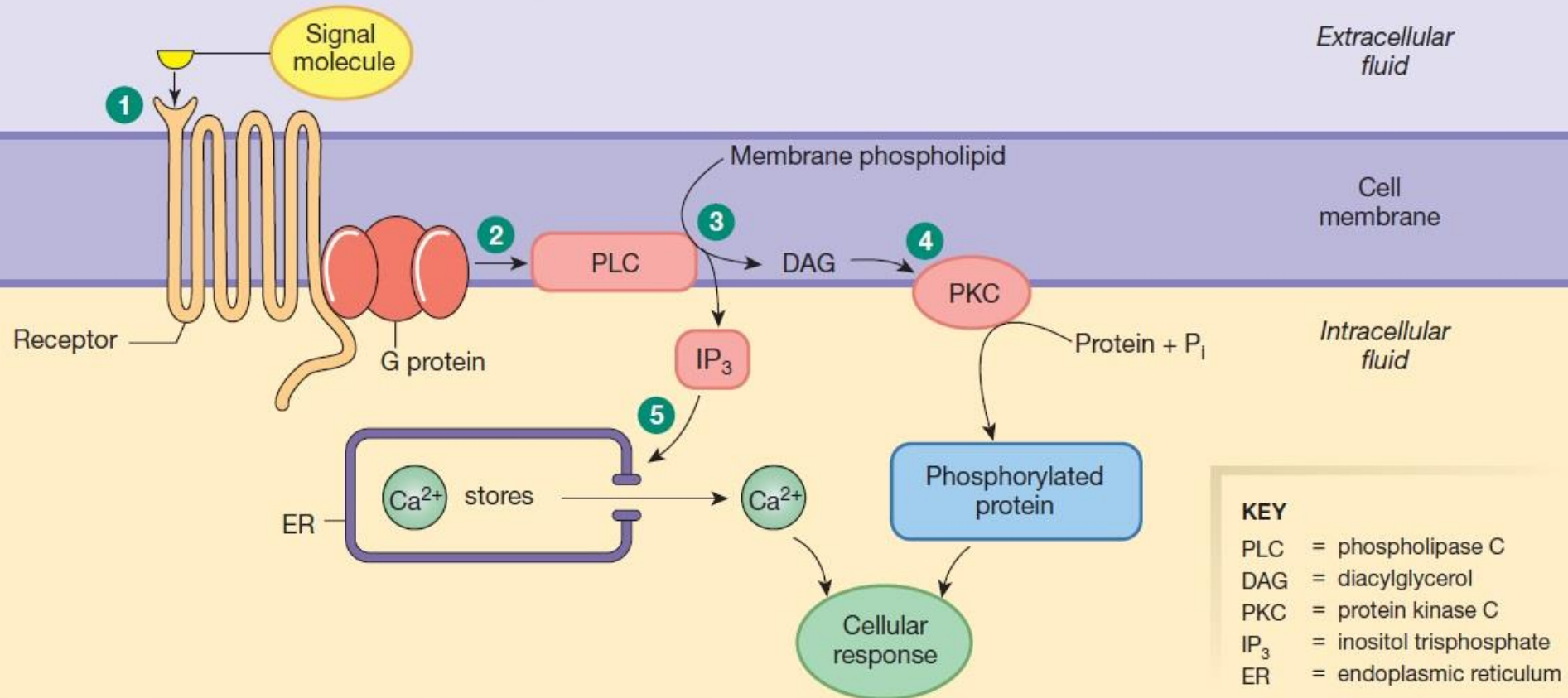


## FIGURE QUESTION

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 ( $\alpha_q$ )

(b) GPCR-phospholipase C Signal Transduction



**1** Signal molecule activates receptor and associated G protein.

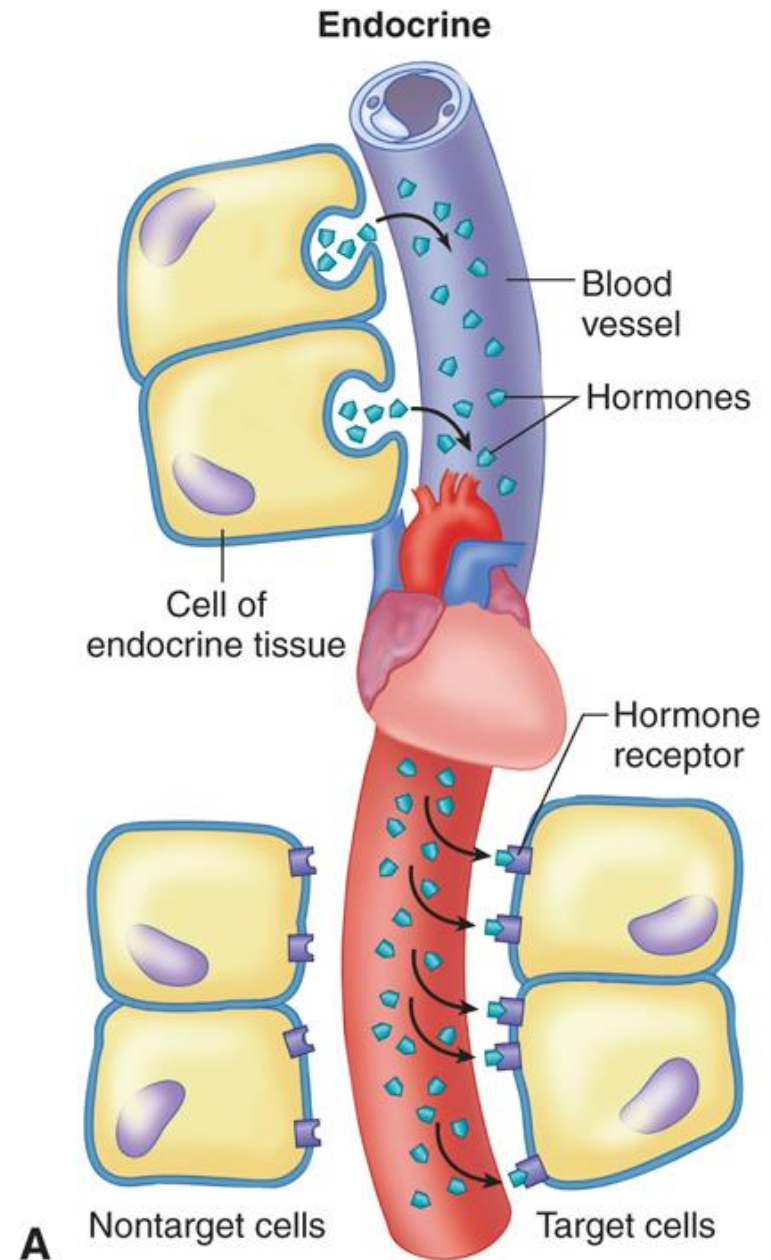
**2** G protein activates phospholipase C (PLC), an amplifier enzyme.

**3** PLC converts membrane phospholipids into diacylglycerol (DAG), which remains in the membrane, and  $IP_3$ , which diffuses into the cytoplasm.

**4** DAG activates protein kinase C (PKC), which phosphorylates proteins.

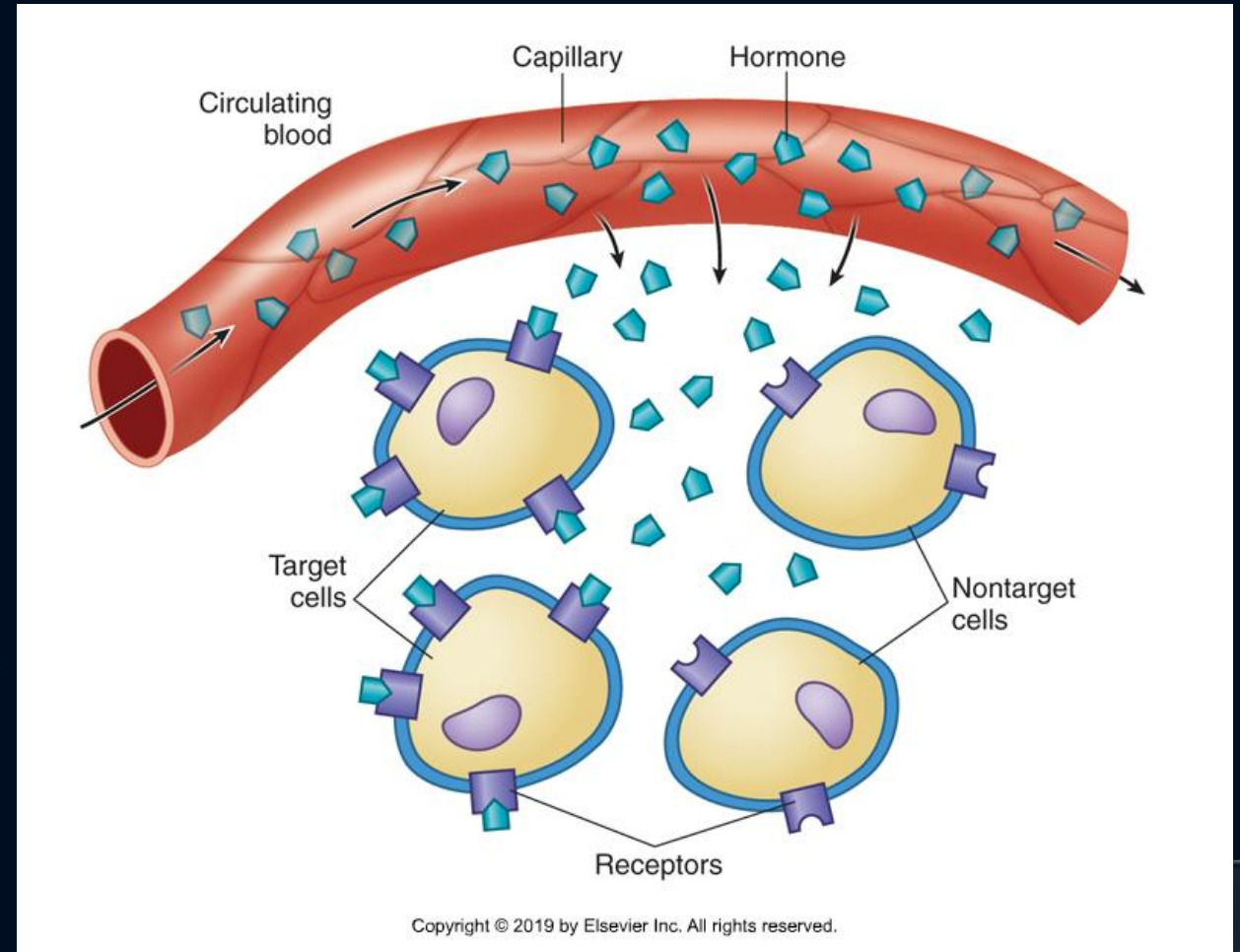
**5**  $IP_3$  causes release of  $Ca^{2+}$  from organelles, creating a  $Ca^{2+}$  signal.

# Secretion to Action



# Interacting with target tissues

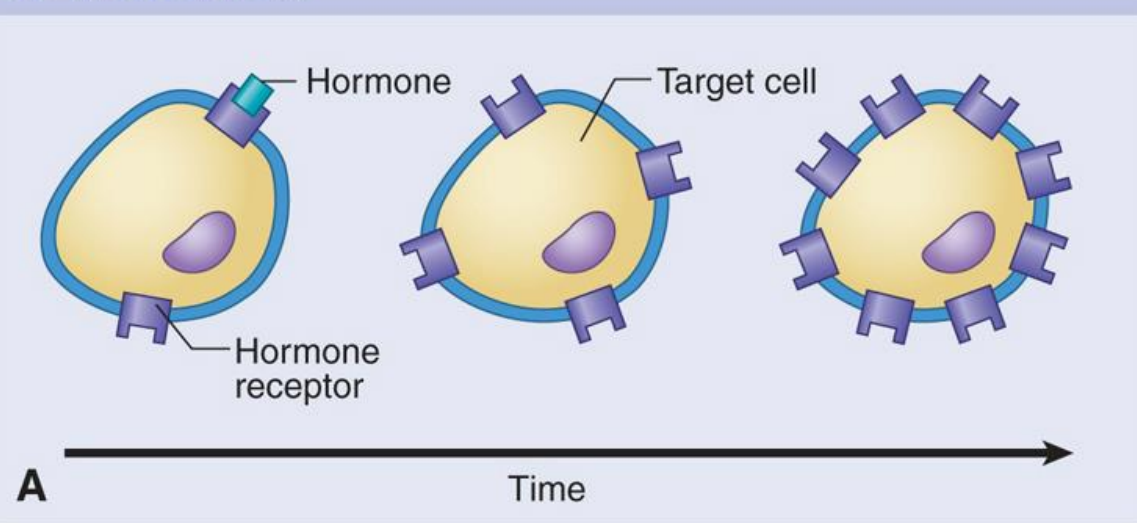
- ▶ Each hormone binds to a specific tissue called a target tissue or organ
- ▶ Target tissue may be close by or far away
- ▶ Some hormones have many targets (more widespread effects)
- ▶ Target cells have specific receptors that hormones bind to
  - ▶ Extracellular receptors (on the cell membrane)
  - ▶ 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



# Receptor Numbers

Diabetes (insulin receptors),  
synthetic steroids

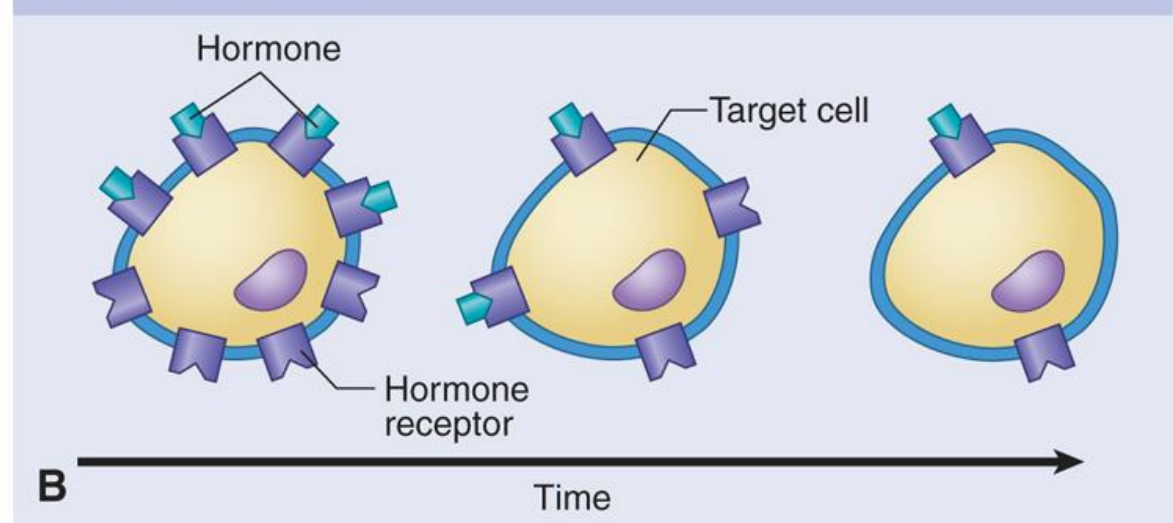
## UP-REGULATION



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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



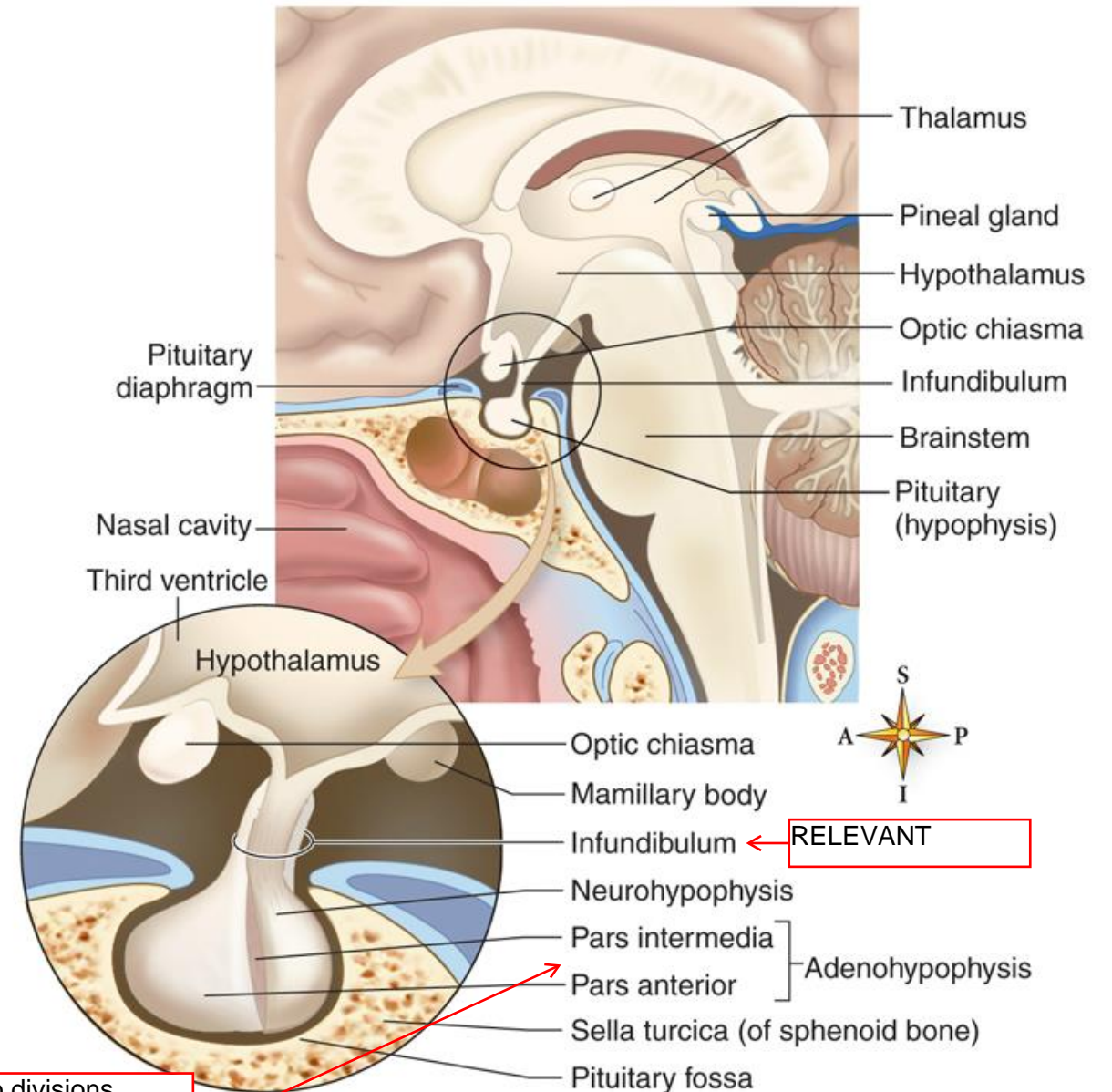
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- **Down-regulation:** decreases number of receptors
  - Decreases sensitivity to hormone
    - Sometimes occurs when blood levels of hormone are *high*
    - Sometimes occurs with changes in development, cell cycle, cell activity

# Endocrine Part 1

PITUITARY GLAND

# Hypothalamus & Pituitary Gland

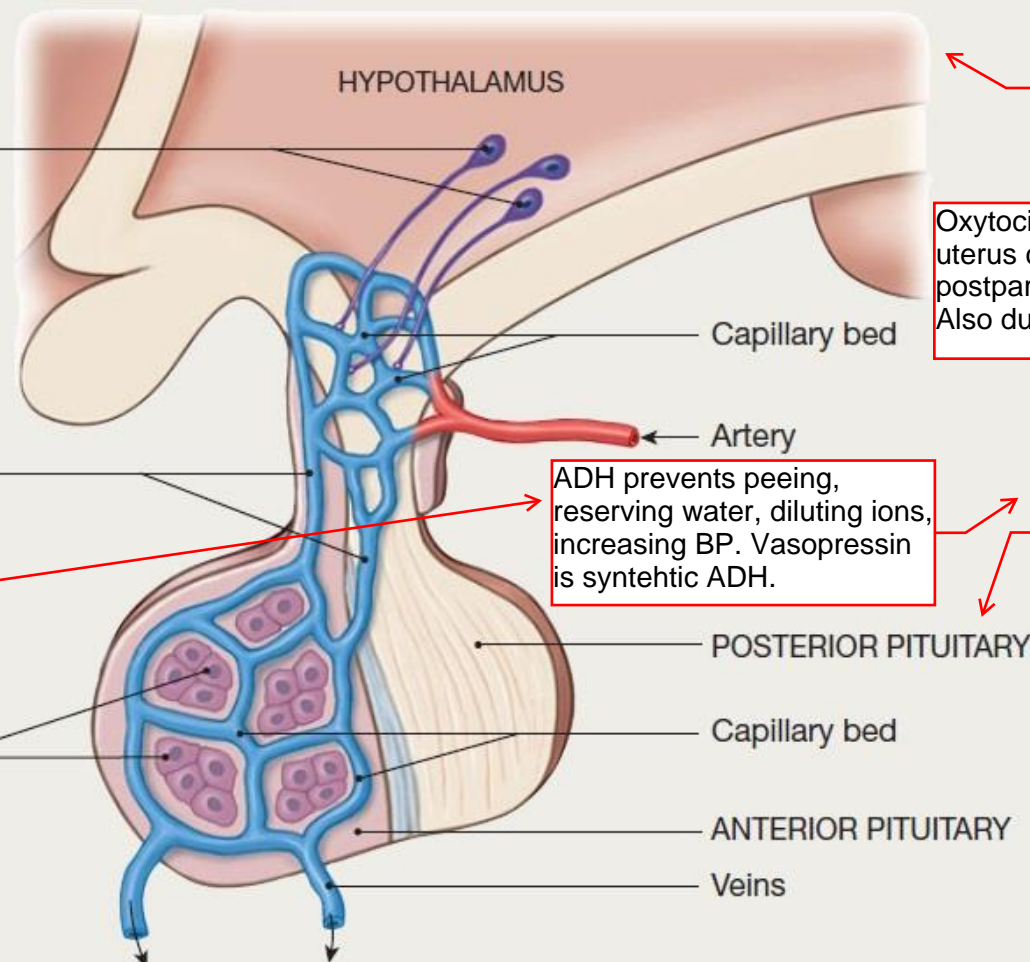


# Adenohypophysis (aka Anterior Pituitary Gland)

**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.



Typically works via a negative feedback loop sent to the hypothalamus. **OXYTOCIN IS A POSITIVE FEEDBACK LOOP.**

Oxytocin is given after birth to incite uterus contraction, preventing postpartum hemorrhage. Also during to aid birth contractions.

ADH prevents peeing, reserving water, diluting ions, increasing BP. Vasopressin is syntehtic ADH.

Only two hormones: **OXYTOCIN** and **ANTIDIURETIC HORMONE (ADH, AKA vasopressants)**

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

Prolactin

GH

TSH

ACTH

Gonadotropins (LH & FSH)

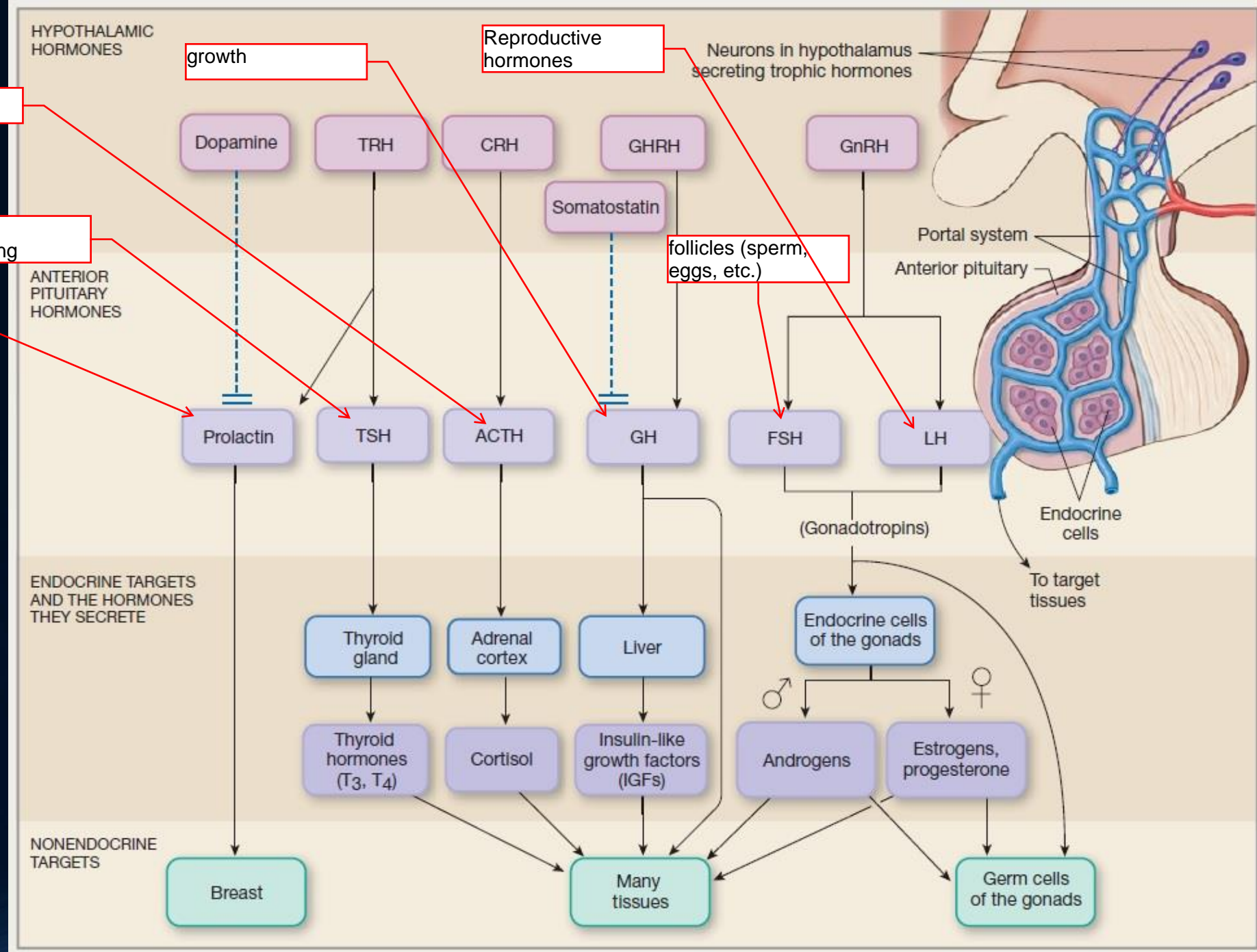
FLAT GP

Adrenal Glands

Thyroid stimulating

Mammary glands

# Hormones Linked to Anterior Pituitary



# Feedback Mechanisms

## Short Loop Feedback

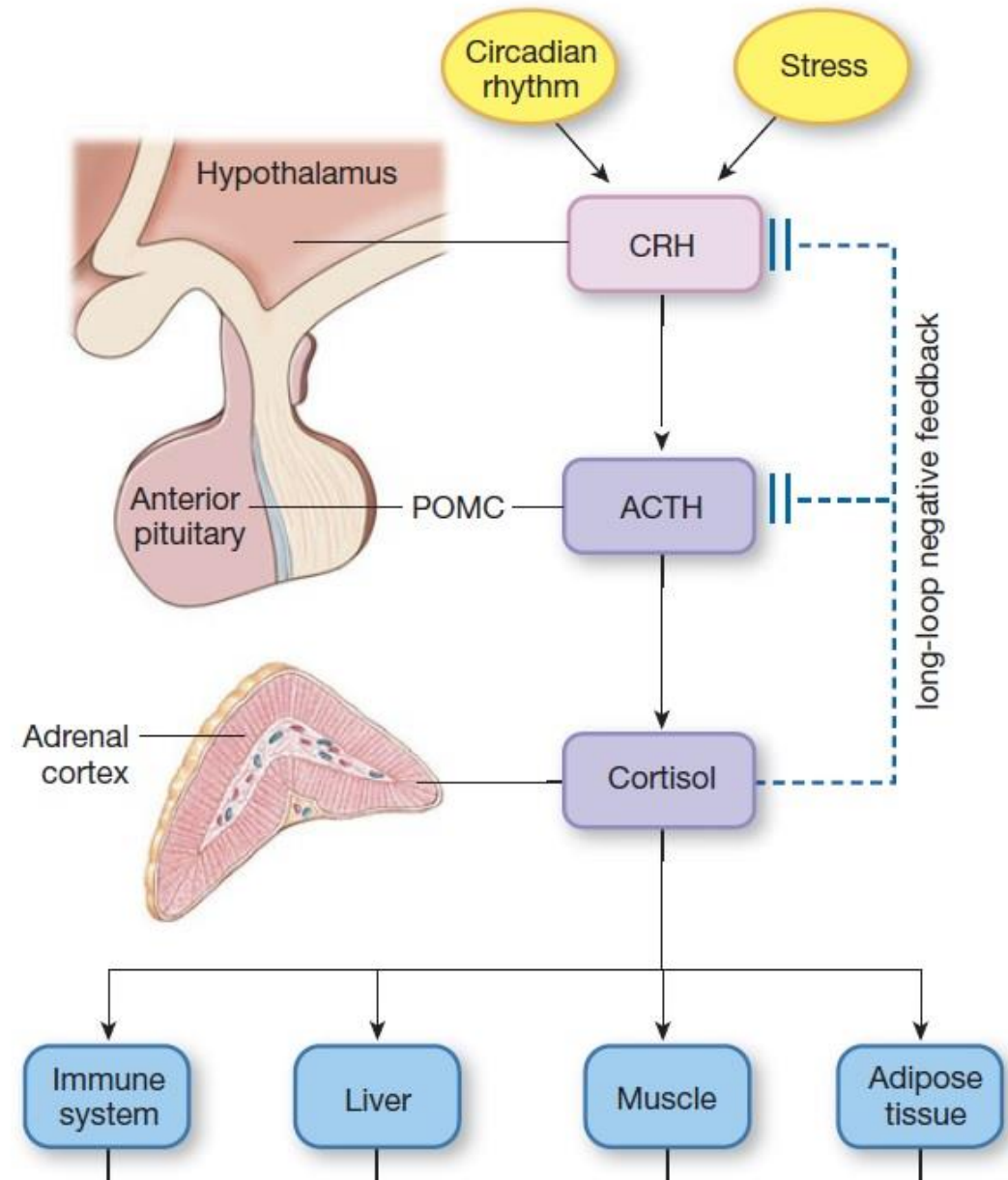
- occurs when pituitary hormone alters secretion of hypothalamic hormone

## Long Loop Feedback

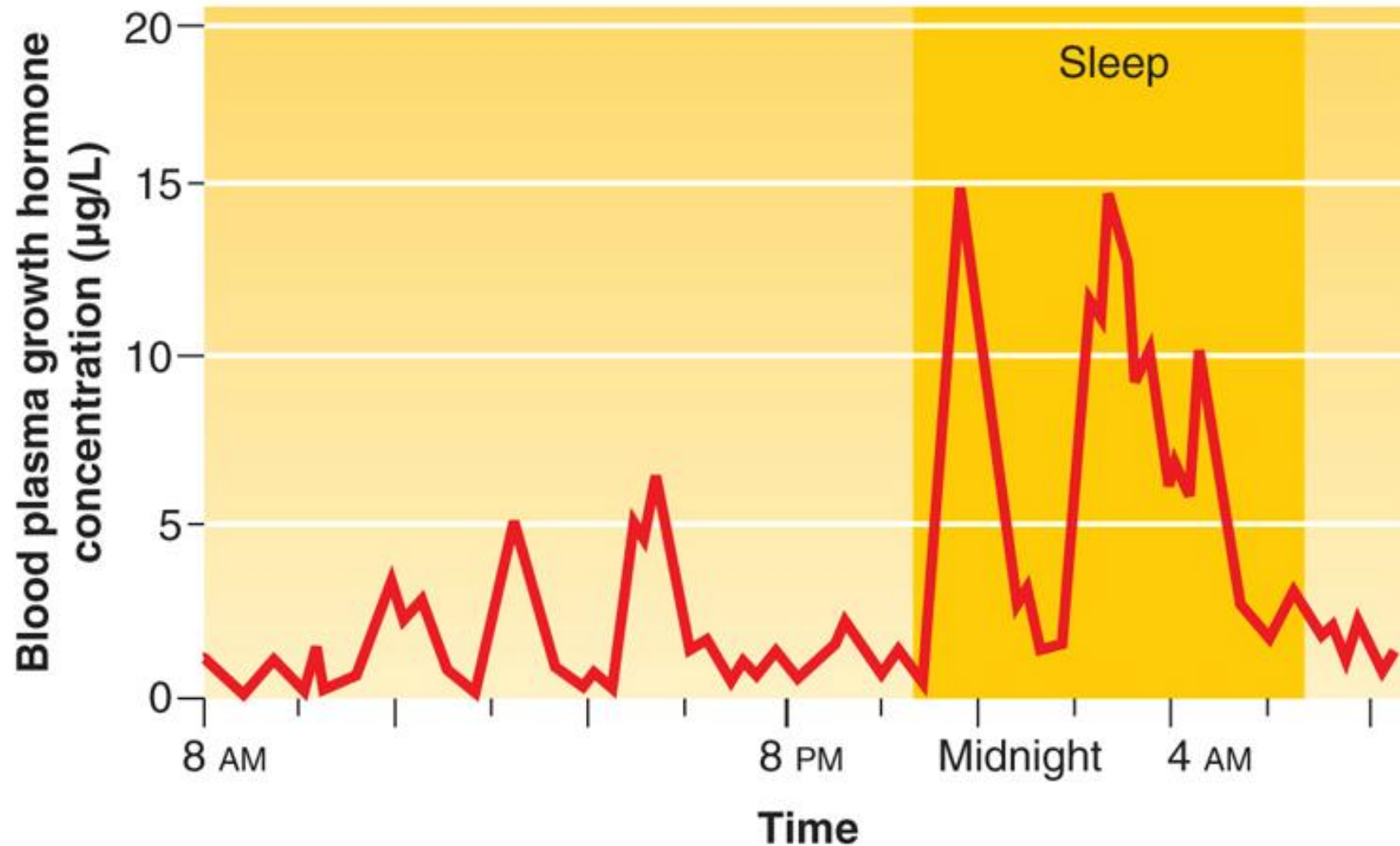
- occurs when target organ hormone alters secretion of hypothalamic or pituitary hormones

### THE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) PATHWAY

#### (a) The control of cortisol secretion



# Circadian Regulation or Hormone Secretion



Adapted from Boron W, Boulpaep E: *Medical physiology*, updated version, Philadelphia, 2005, Saunders.

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

# Neurohypophysis (aka Posterior Pituitary)

## Vasopressin

- Causes more H<sub>2</sub>O 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

