

ENDOCRINE PHYSIOLOGY

PROF. ABDULMAJEED AL-DREES

OBJECTIVES

- **By the end of this lecture, students should be able to describe :**
- **Hormones**
 - Definition
 - Chemical structure
 - Paracrine and autocrine
- **Secretion and clearance of hormones**
- **Mechanism of action of hormones**
 - Hormone receptors, down-regulation and up-regulation
 - Intracellular signaling
 - Second messenger mechanism (cAMP, IP₃)

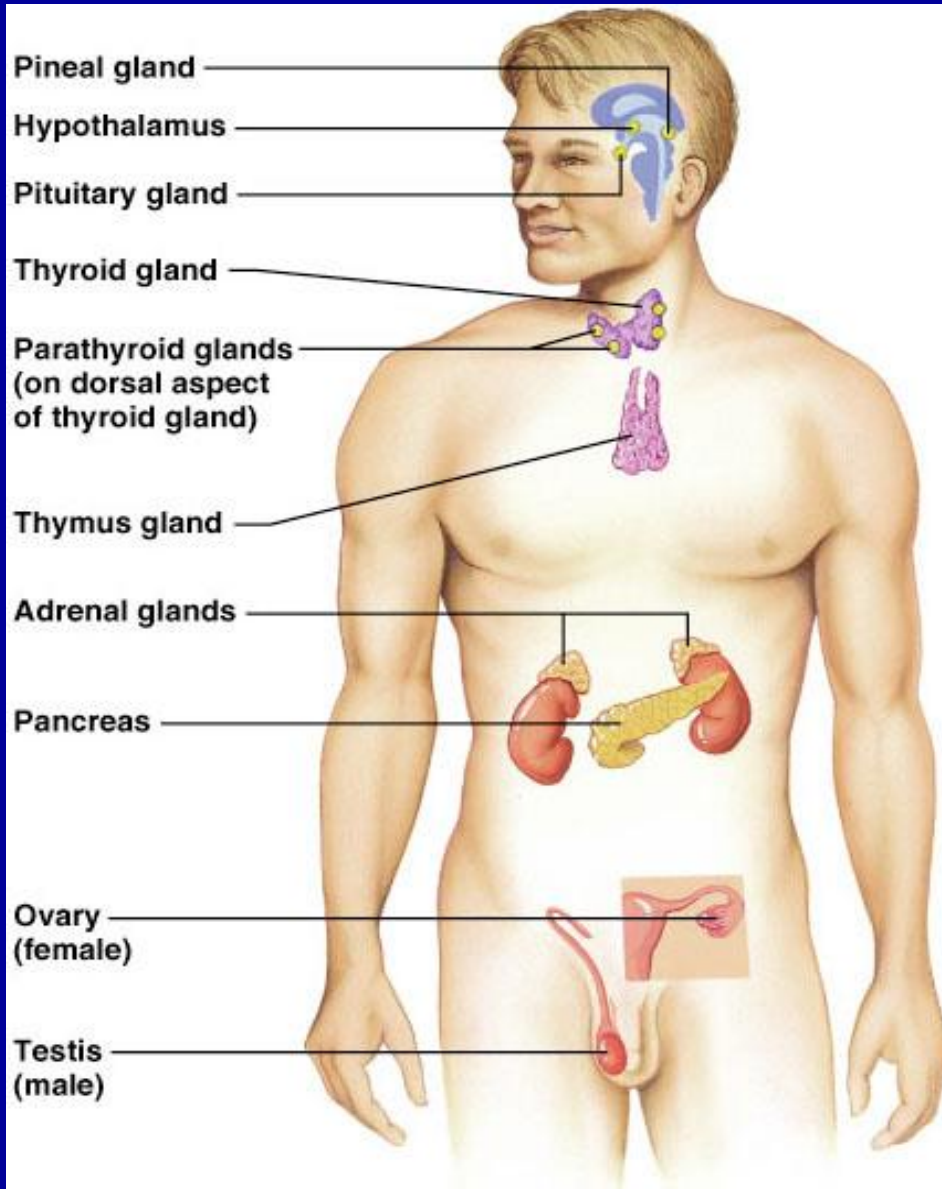
GLANDS

- **Exocrine gland.**
- **Endocrine gland.**

What is hormone?.

- **Chemical substance** secreted in a small amount from endocrine gland directly to the blood stream in response to **stimulus** to cause physiological responses at the **target tissues**.

ENDOCRINE GLANDS



HYPOTHALAMUS

TRH CRH GnRH GHRH Somatostatin Dopamine

ANTERIOR PITUITARY

TSH FSH LH ACTH MSH Growth hormone Prolactin

POSTERIOR PITUITARY

Oxytocin ADH

THYROID

T₃, T₄ Calcitonin

PARATHYROID

PTH

PANCREAS

Insulin Glucagon

ADRENAL MEDULLA

Norepinephrine Epinephrine

KIDNEY

Renin 1,25-Dihydroxycholecalciferol

ADRENAL CORTEX

Cortisol Aldosterone Adrenal androgens

TESTES

Testosterone

OVARIES

Estradiol Progesterone

CORPUS LUTEUM

Estradiol Progesterone

PLACENTA

HCG HPL
Estriol Progesterone

Table 9-1 Commonly Used Abbreviations in Endocrine Physiology

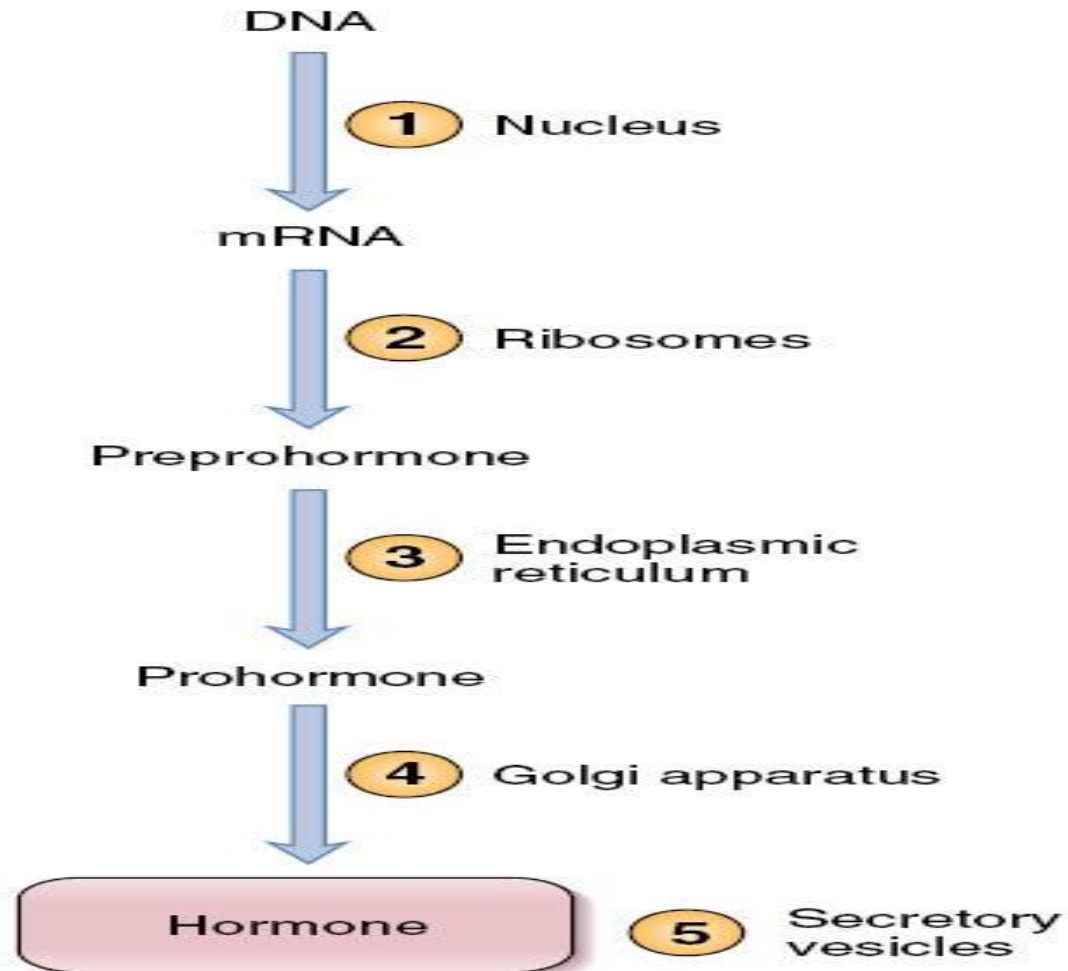
Abbreviation	Hormone	Abbreviation	Hormone
ACTH	Adrenocorticotrophic hormone	LH	Luteinizing hormone
ADH	Antidiuretic hormone	MIT	Monoiodotyrosine
CRH	Corticotropin-releasing hormone	MSH	Melanocyte-stimulating hormone
DHEA	Dehydroepiandrosterone	PIF	Prolactin-inhibiting factor
DIT	Diiodotyrosine	POMC	Pro-opiomelanocortin
DOC	11-Deoxycorticosterone	PTH	Parathyroid hormone
FSH	Follicle-stimulating hormone	PTU	Propylthiouracil
GHRH	Growth hormone-releasing hormone	SRIF	Somatotropin release-inhibiting factor
GnRH	Gonadotropin-releasing hormone	T ₃	Triiodothyronine
HCG	Human chorionic gonadotropin	T ₄	Thyroxine
HGH	Human growth hormone	TBG	Thyroxine-binding globulin
HPL	Human placental lactogen	TRH	Thyrotropin-releasing hormone
IGF	Insulin-like growth factor	TSH	Thyroid-stimulating hormone

CHEMICAL CLASSIFICATION OF HORMONES

- **Peptides or proteins hormones.**
- **Steroid hormones.**
- **Amine hormones.**

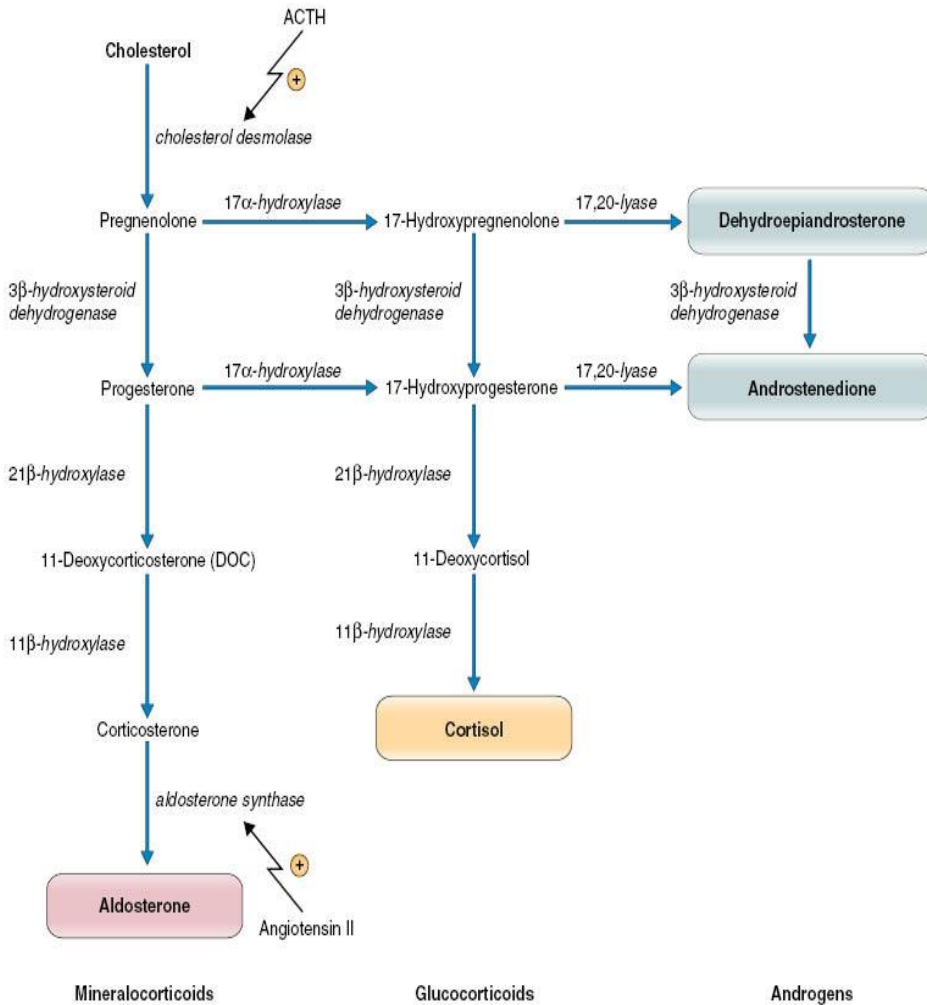
HORMONES SYNTHESIS

PEPTIDE HORMONE SYNTHESIS

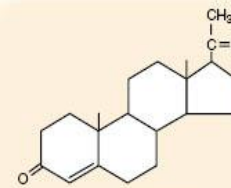
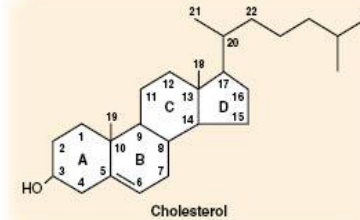


STEROIDS HORMONES

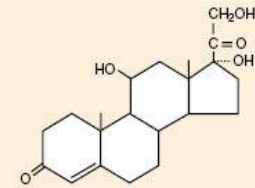
BIOSYNTHESIS OF ADRENOCORTICAL HORMONES



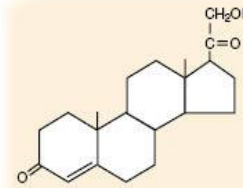
ADRENOCORTICAL STEROIDS



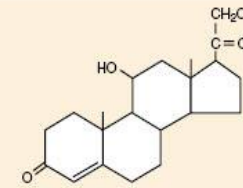
Progesterone



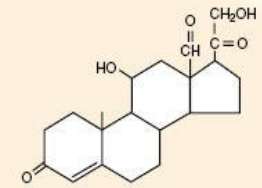
Cortisol



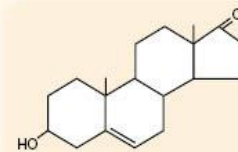
11-Deoxycorticosterone (DOC)



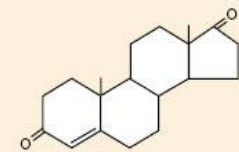
Corticosterone



Aldosterone

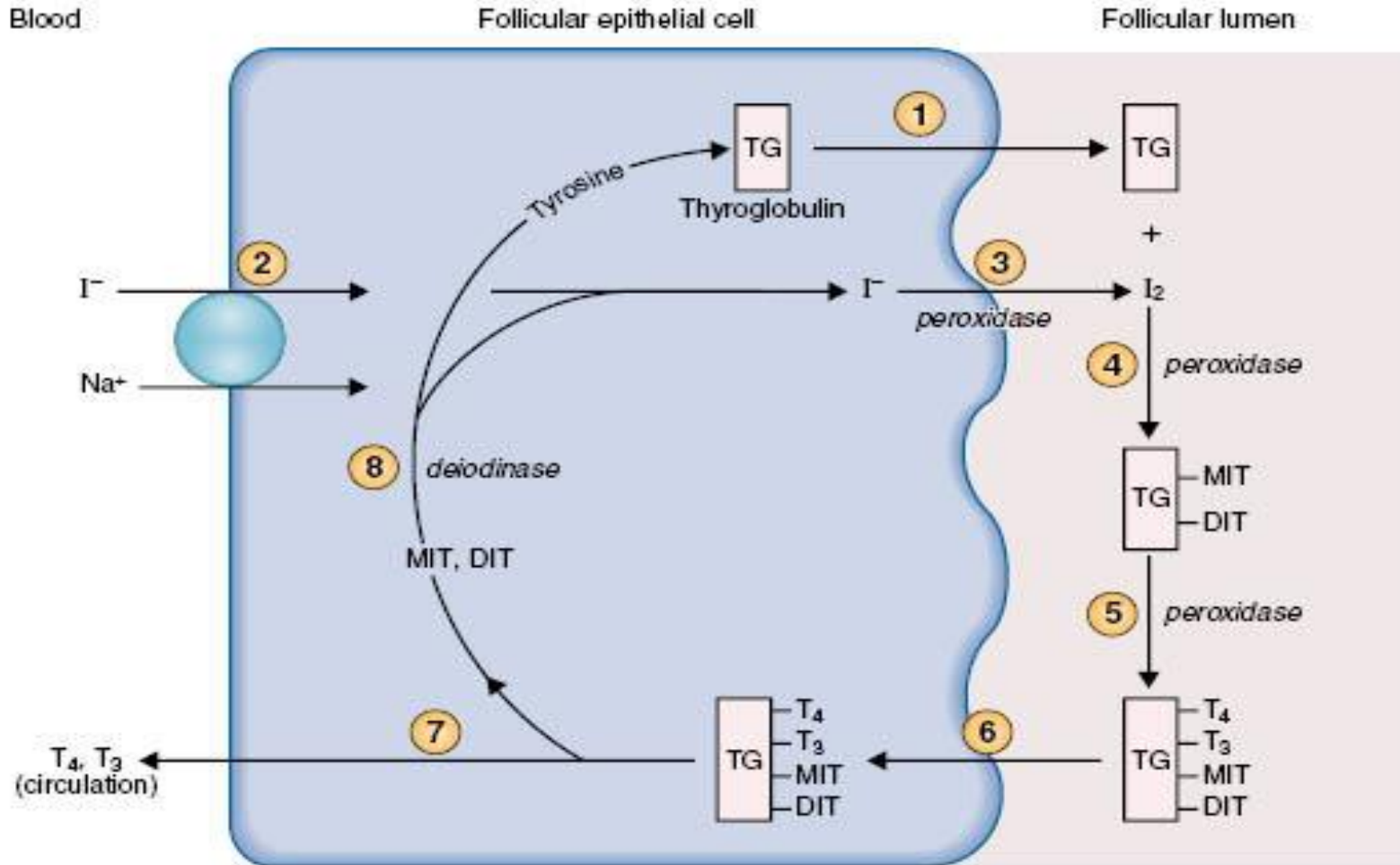


Dehydroepiandrosterone (DHEA)



Androstenedione

AMINE HORMONE

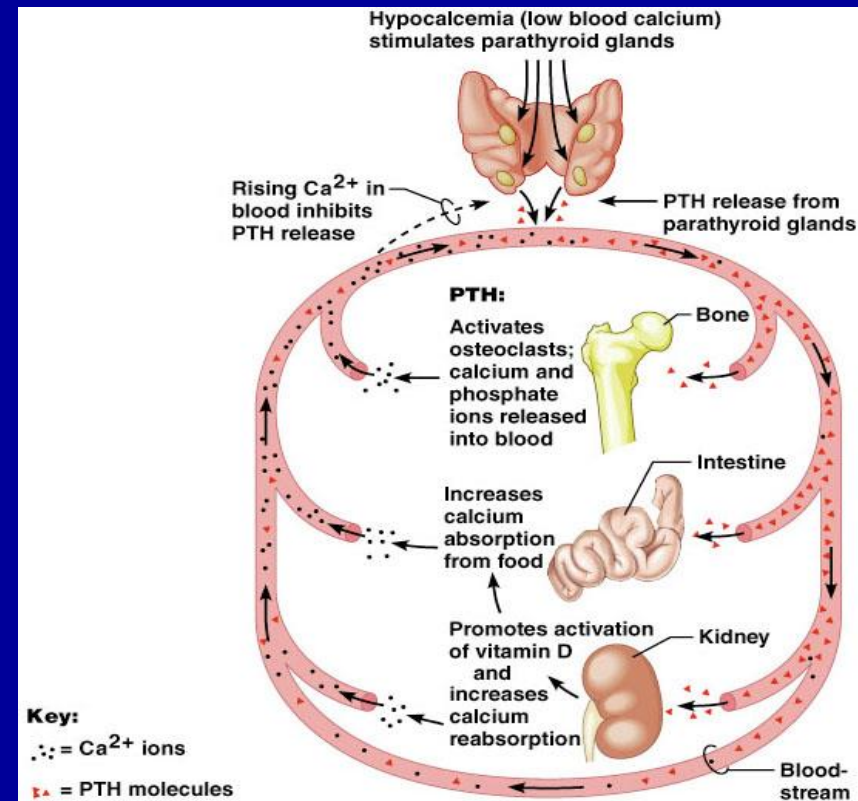
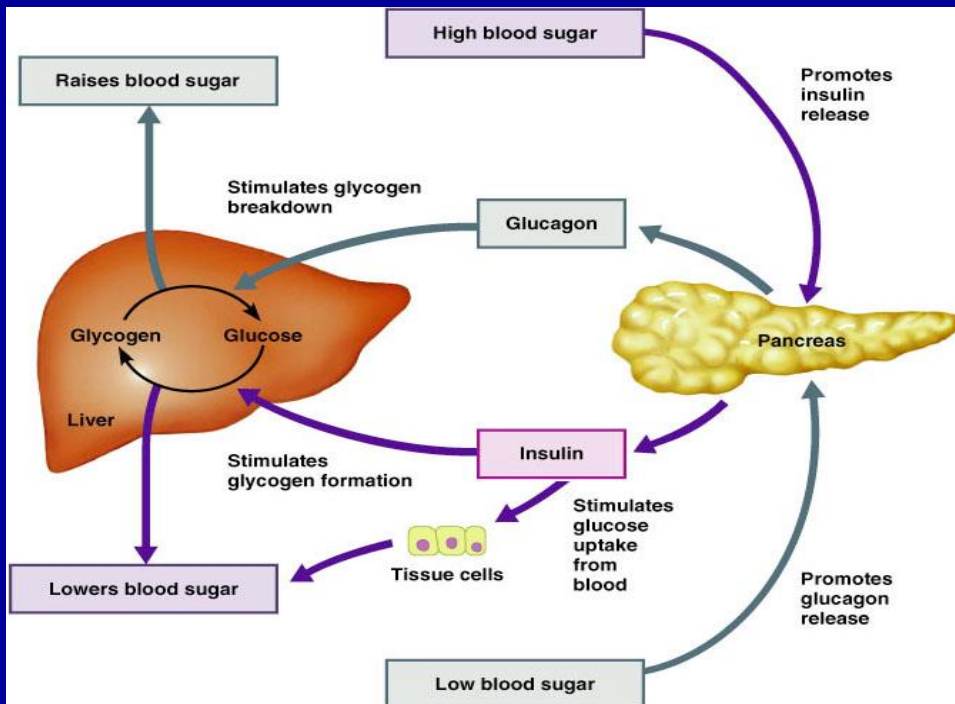


CLASSIFICATION OF STIMULI

- **Humoral Stimuli.**
- **Neural Stimuli.**
- **Hormonal Stimuli.**

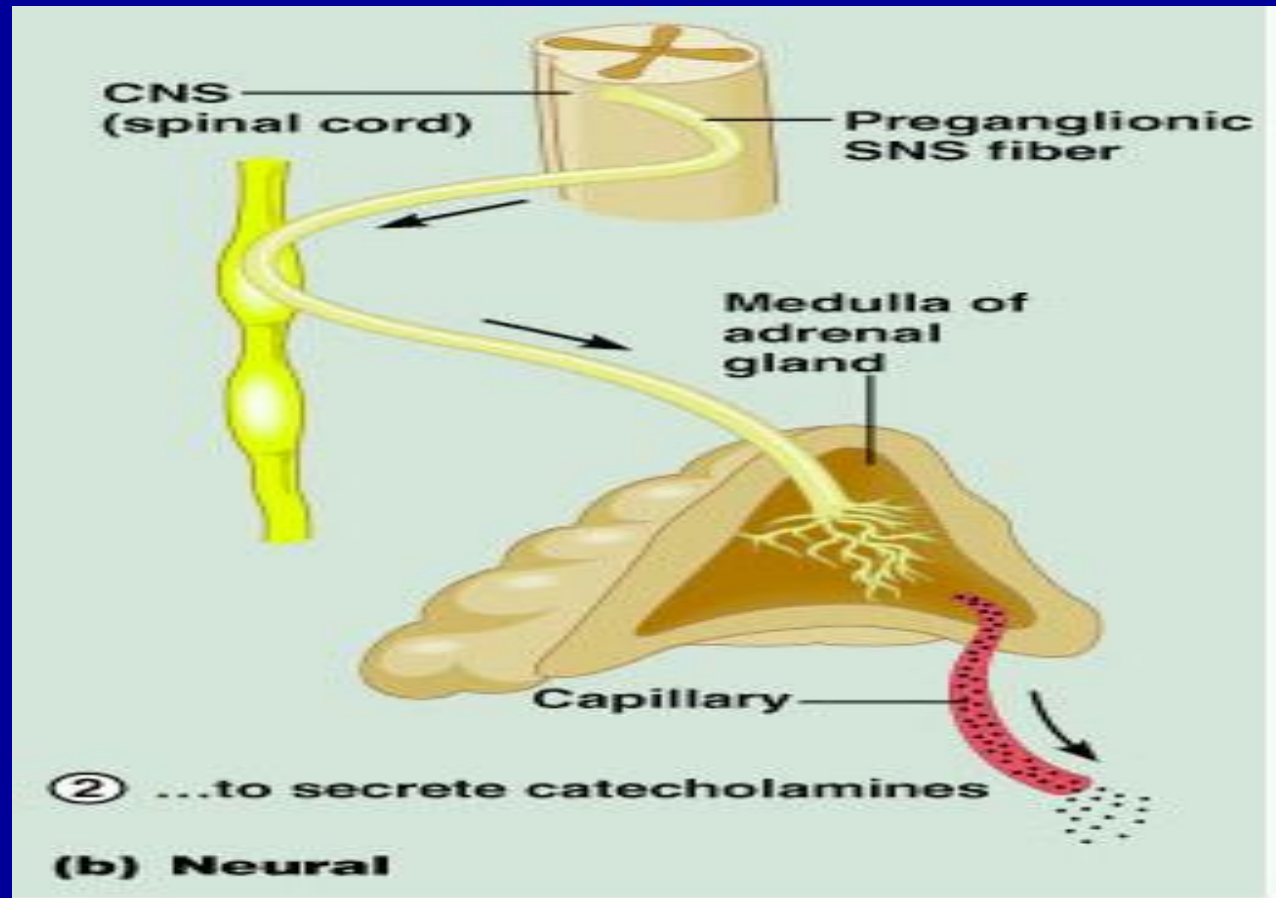
Humoral Stimuli

- Secretion of **hormones** in direct response to **changing** in blood levels of **ions** and **nutrients**



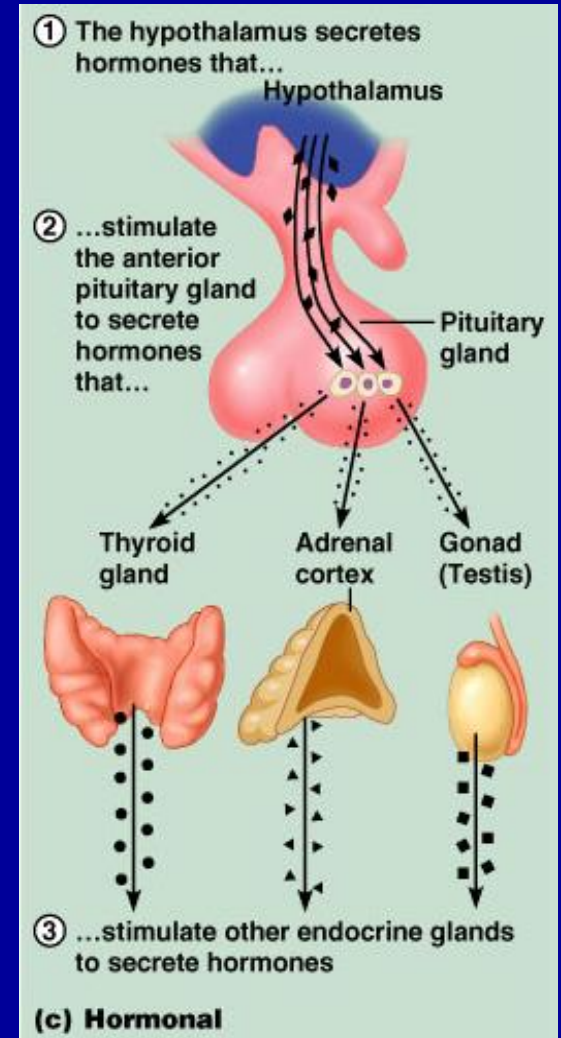
Neural Stimuli

- **Nerve** fibers stimulate **hormone** release.



Hormonal Stimuli

- Release of **hormones** in response to **hormones** produced by other endocrine gland.

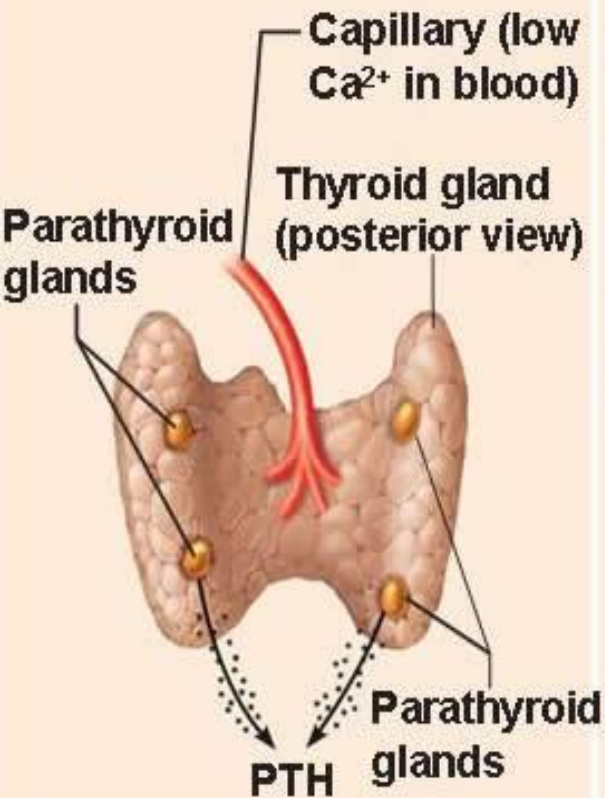


(a) Humoral Stimulus

(b) Neural Stimulus

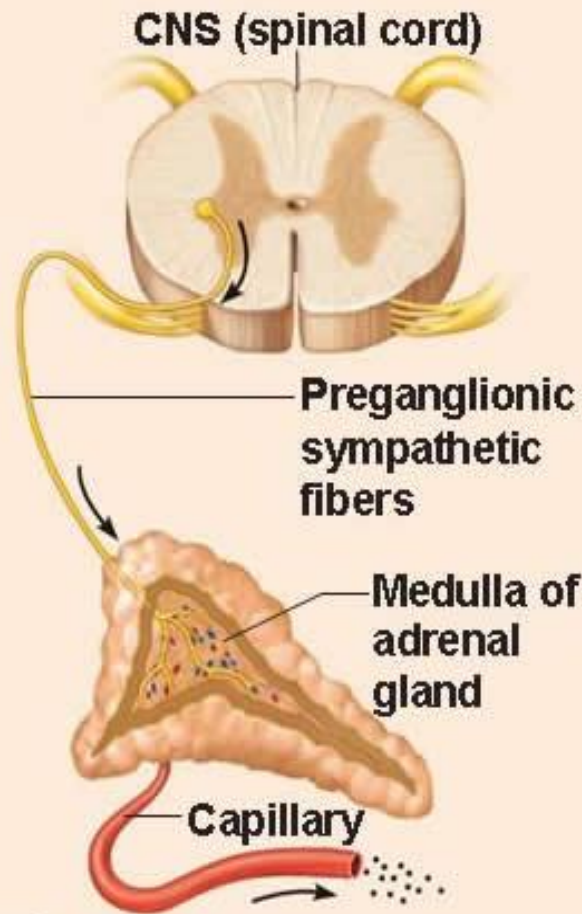
(c) Hormonal Stimulus

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



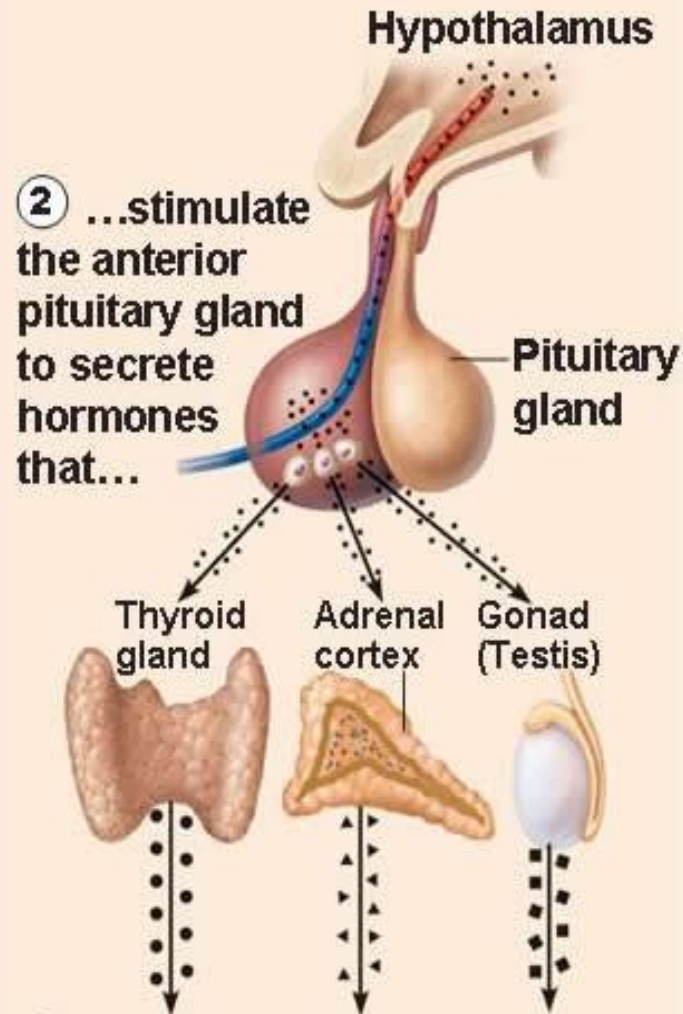
② ...secretion of parathyroid hormone (PTH) by parathyroid glands*

① Preganglionic sympathetic fibers stimulate adrenal medulla cells...



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

① The hypothalamus secretes hormones that...



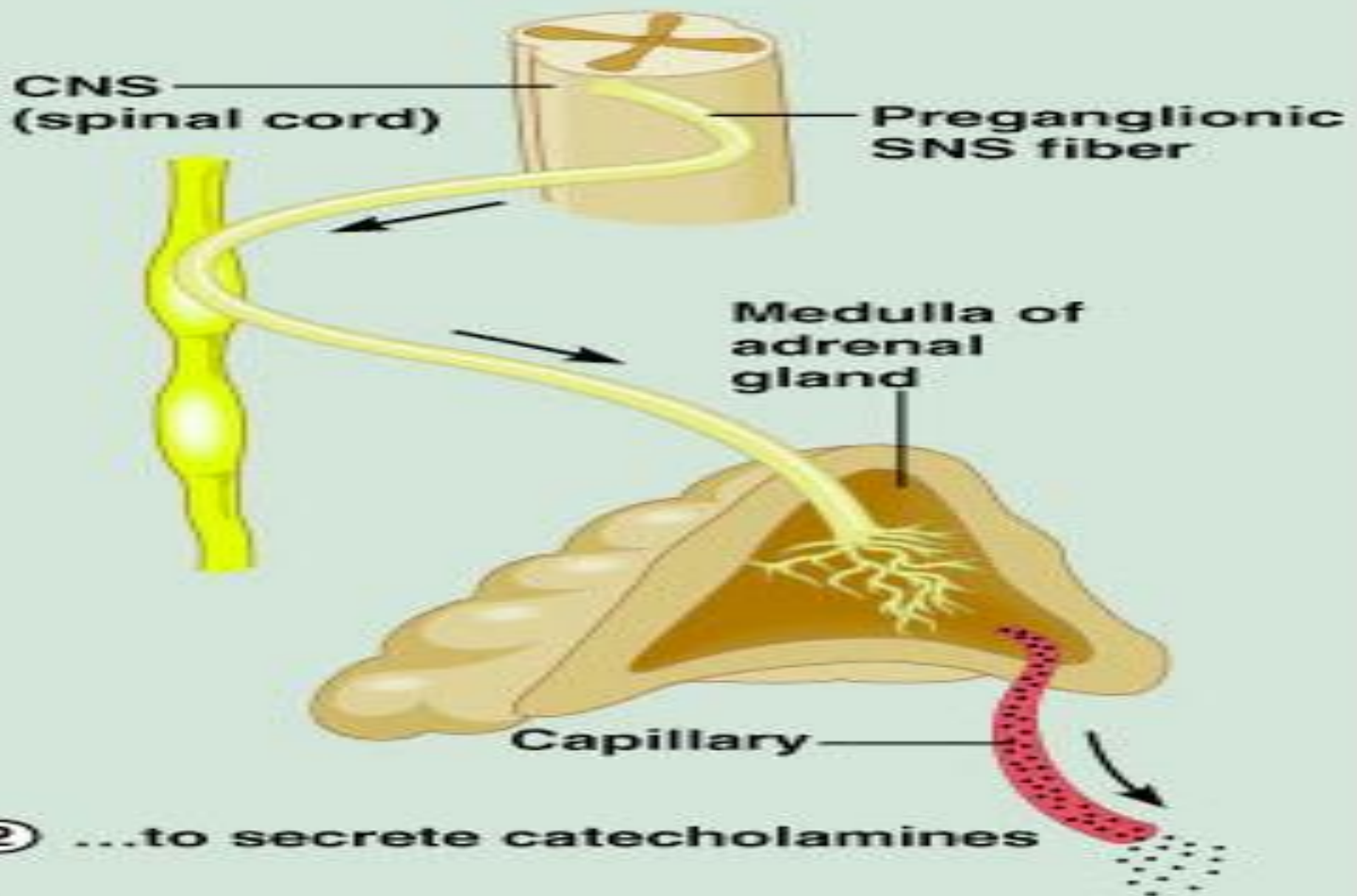
② ...stimulate the anterior pituitary gland to secrete hormones that...

③ ...stimulate other endocrine glands to secrete hormones

REGULATION OF HORMONE SECRETION

- **Neural mechanism.**
- **Feedback mechanism.**

NEURAL MECHANISM

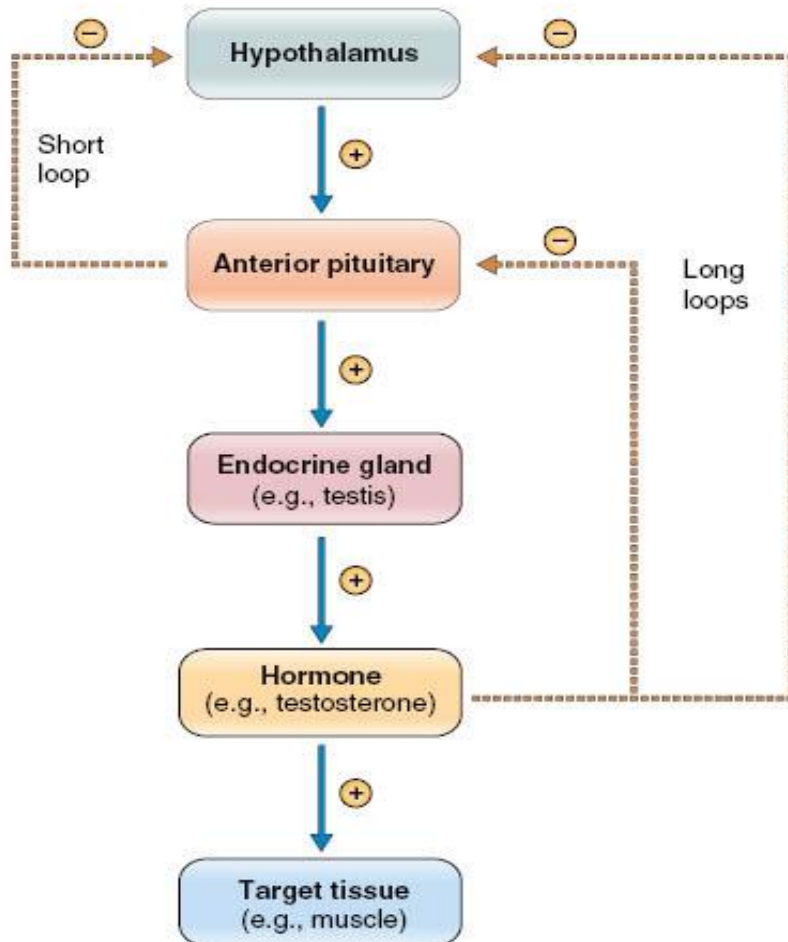


② ...to secrete catecholamines

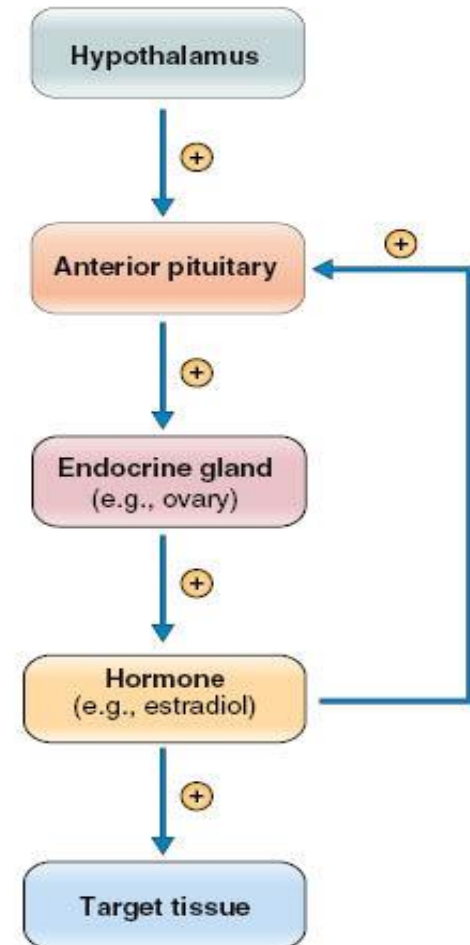
(b) Neural

FEEDBACK MECHANISM

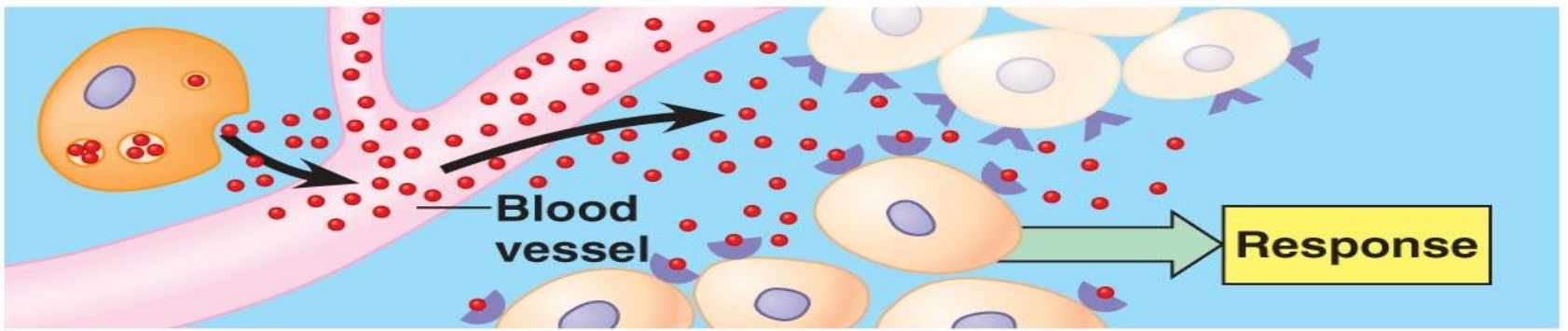
NEGATIVE FEEDBACK



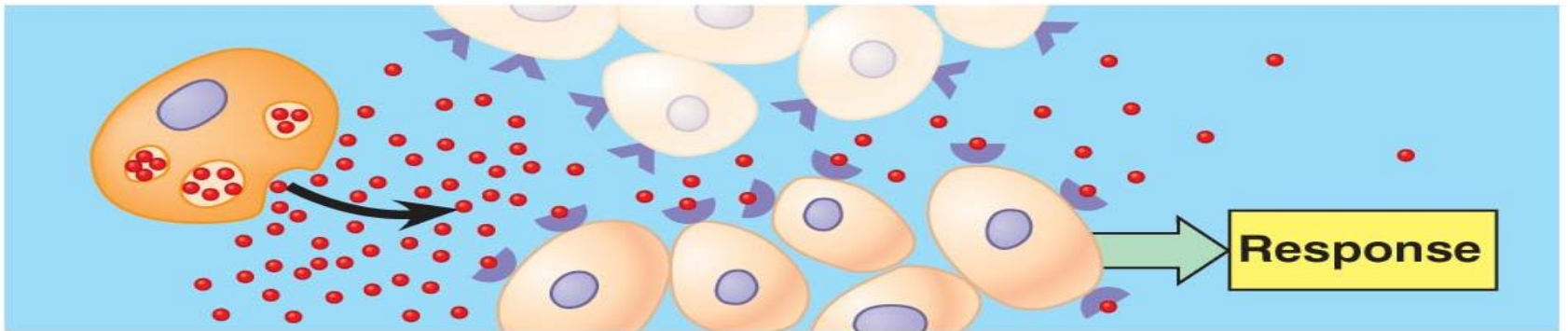
POSITIVE FEEDBACK



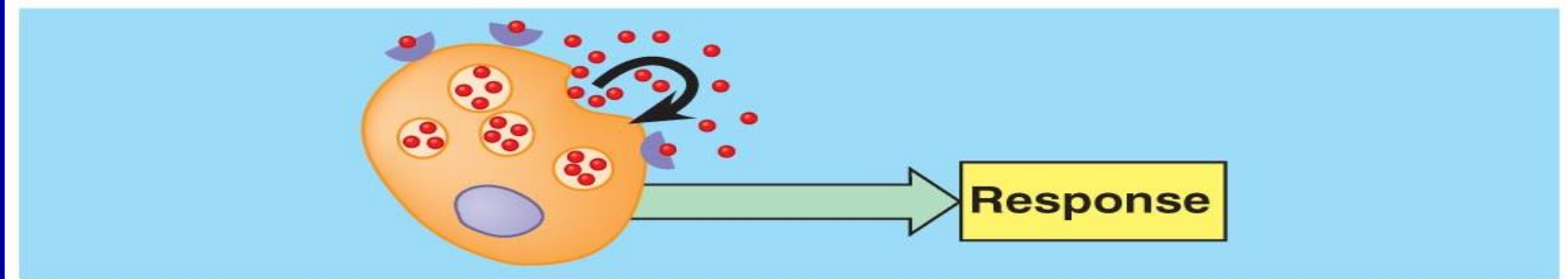
- **Autocrines** – chemicals that exert their effects on the same cells that secrete them.
- **Paracrines** – locally acting chemicals that affect cells other than those that secrete them.



(a) Endocrine signaling



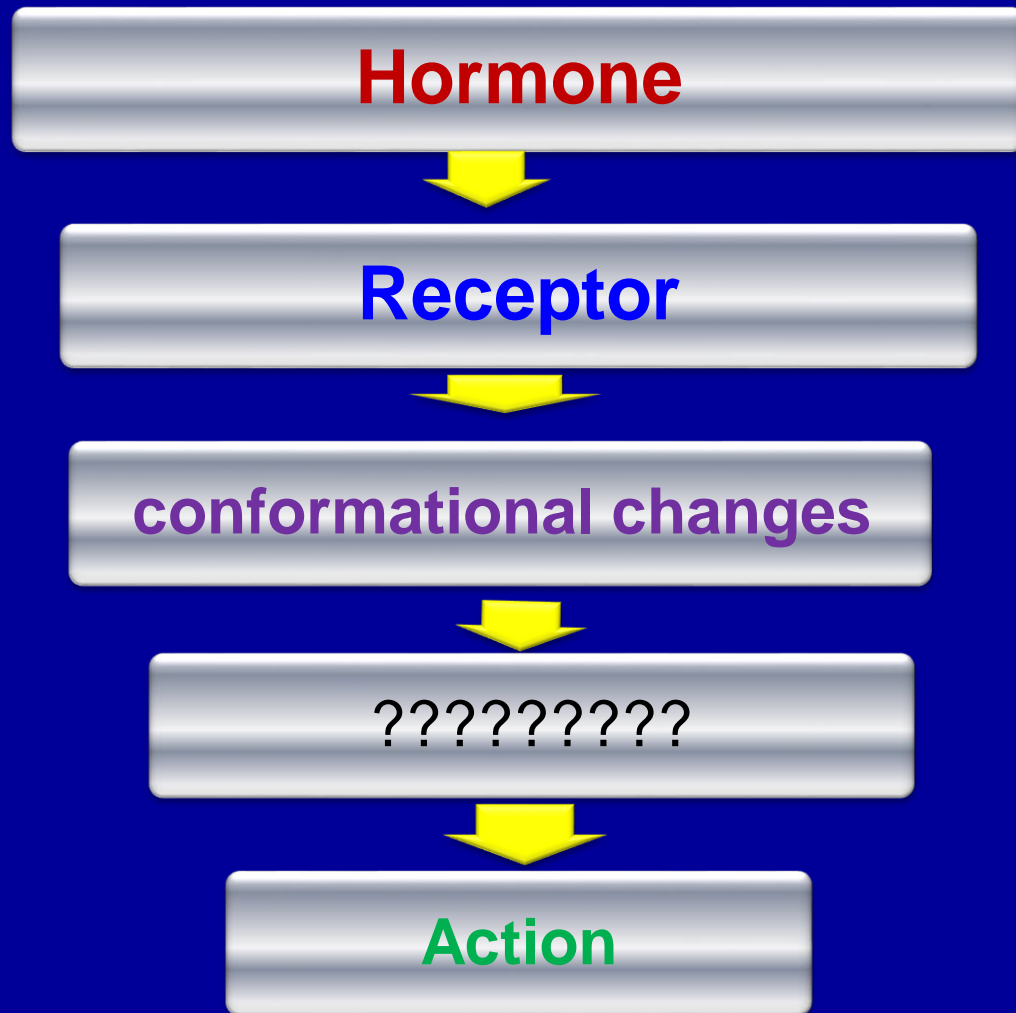
(b) Paracrine signaling



(c) Autocrine signaling

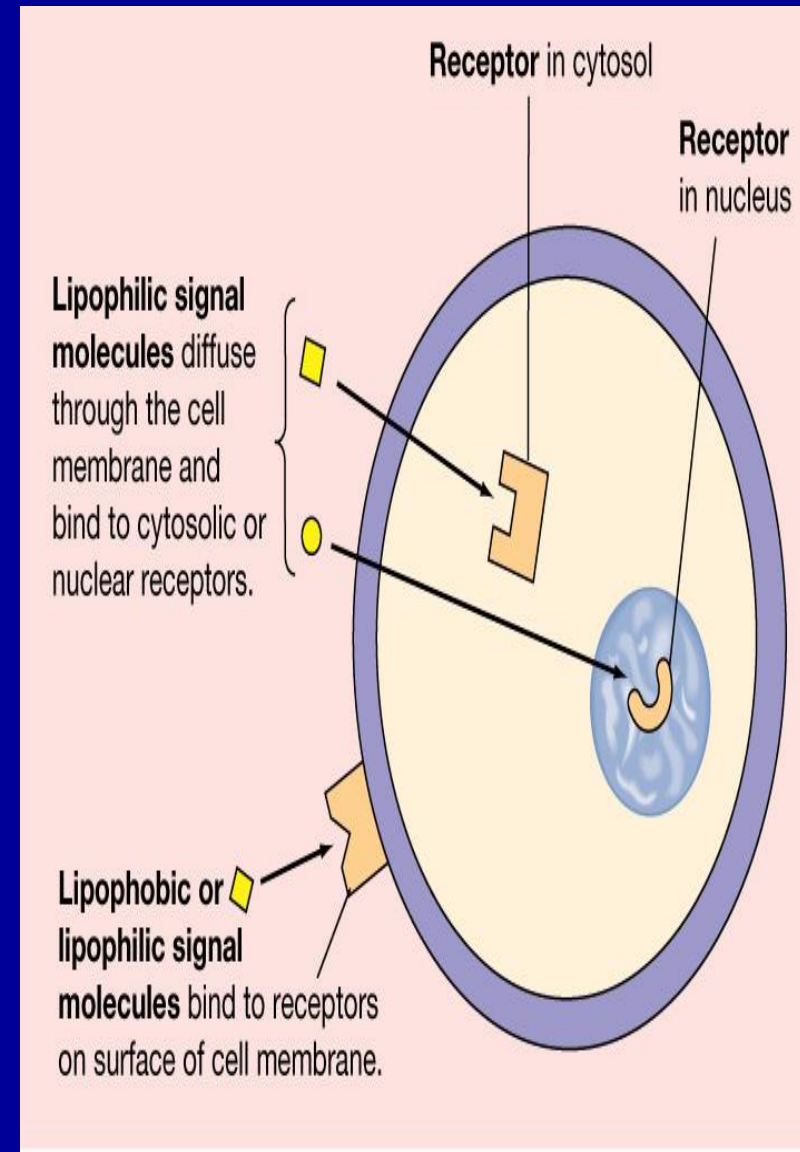
TARGET TISSUE

MECHANISM OF ACTION



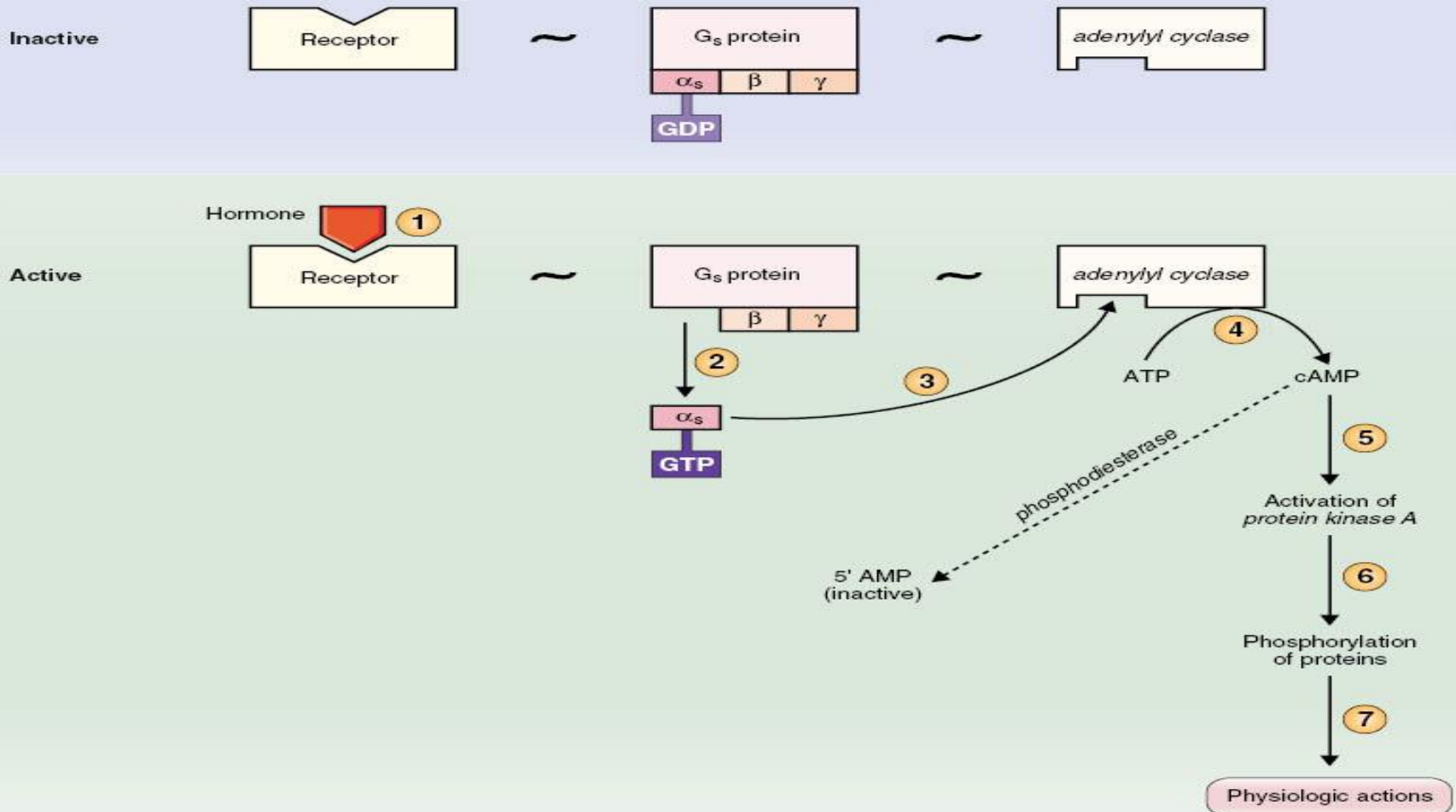
RECEPTOR LOCATIONS

- **Cytosolic or Nuclear**
 - **Lipophilic ligand enters cell**
 - **Often activates gene**
 - **Slower response**
- **Cell membrane**
 - **Lipophobic ligand can't enter cell**
 - **Outer surface receptor**
 - **Fast response**

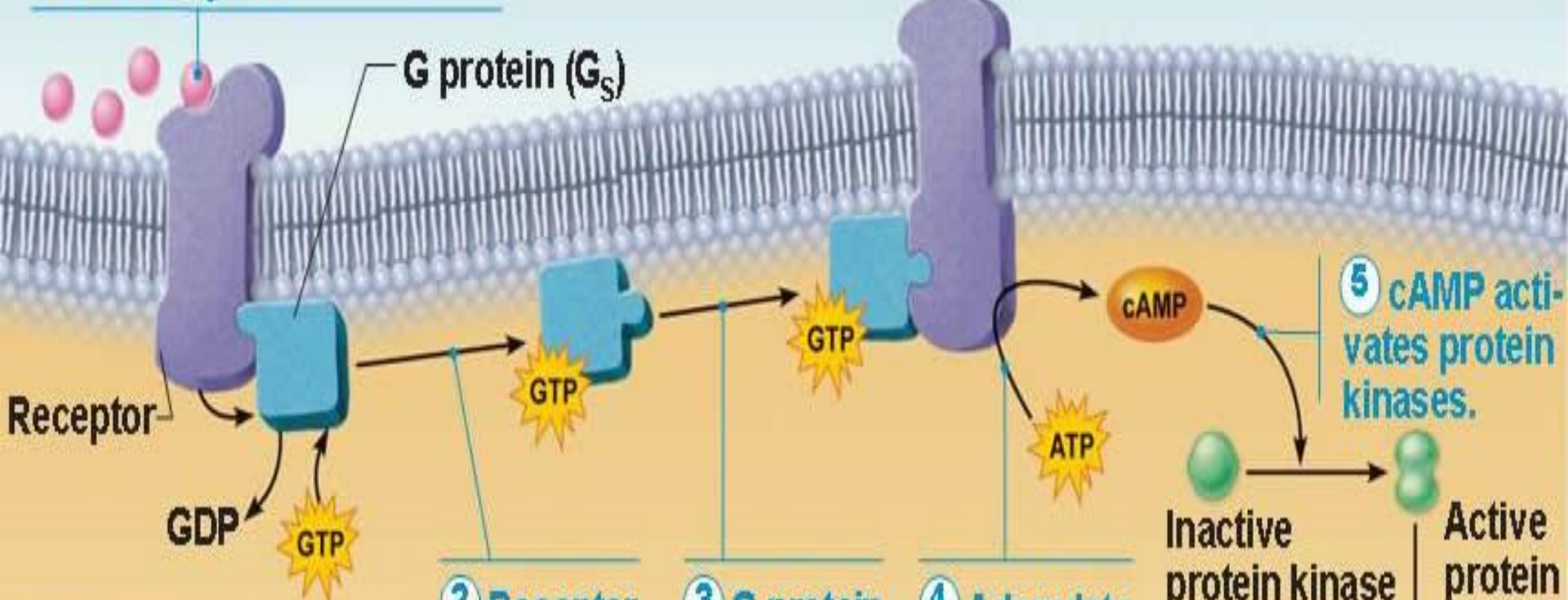


SECOND MESSENGER

ADENYLYL CYCLASE MECHANISM



1 Hormone (1st messenger) binds receptor.



2 Receptor activates G protein (G_s)

3 G protein activates adenylate cyclase.

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

5 cAMP activates protein kinases.

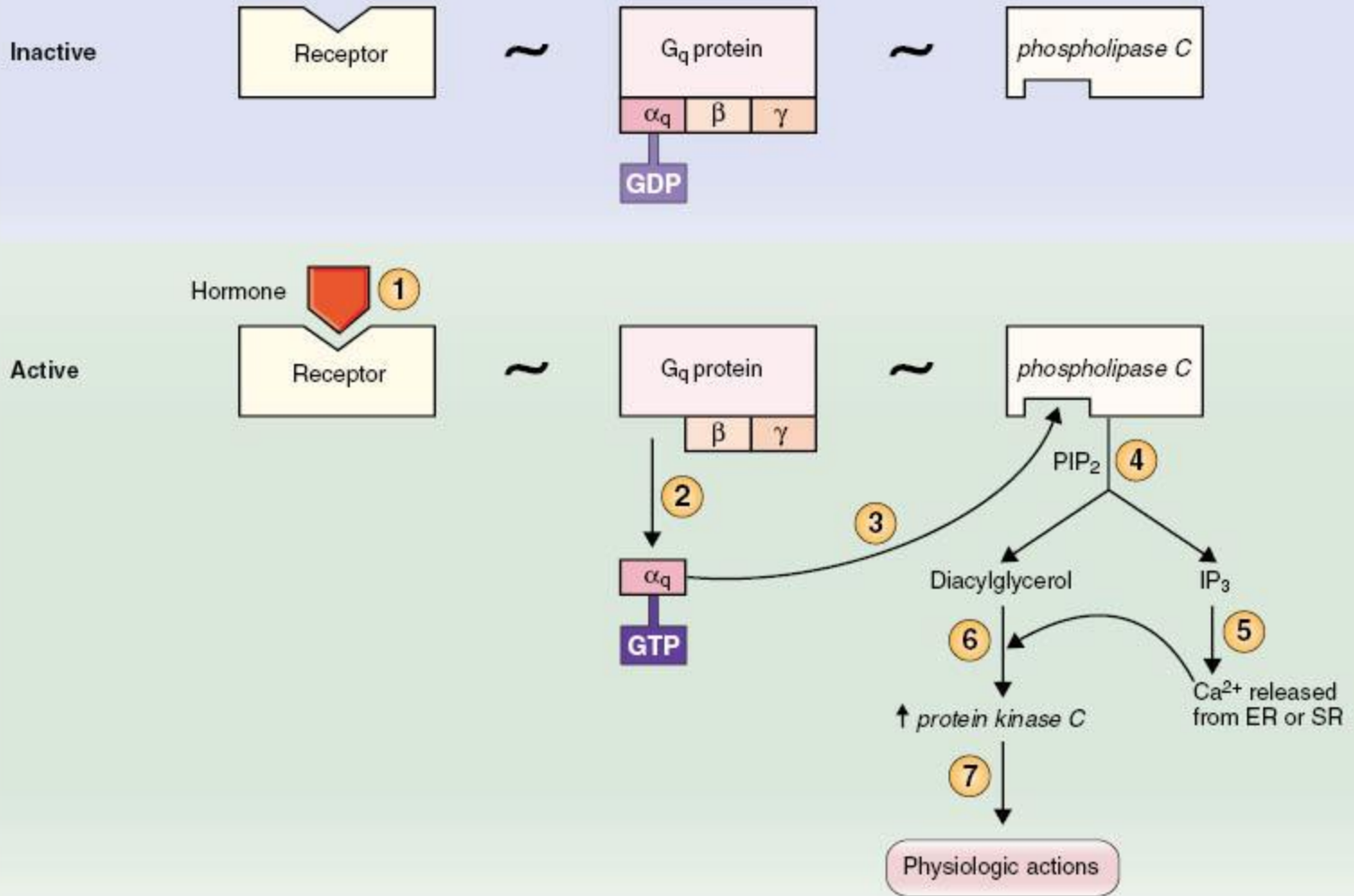
Inactive protein kinase → Active protein kinase

Triggers responses of target cell (activates enzymes, stimulates cellular secretion, opens ion channel, etc.)

Cytoplasm

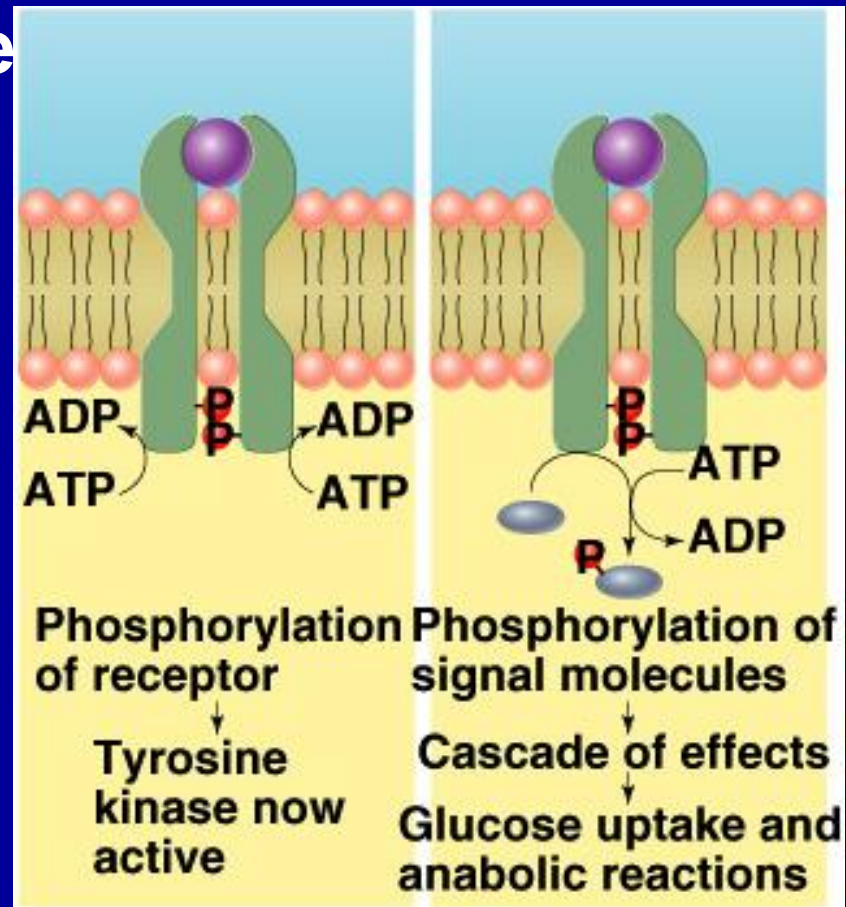
- Hormones that act via cAMP mechanisms:**
- | | |
|-------------|------------|
| Epinephrine | Glucagon |
| ACTH | PTH |
| FSH | TSH |
| LH | Calcitonin |

PHOSPHOLIPASE C MECHANISM

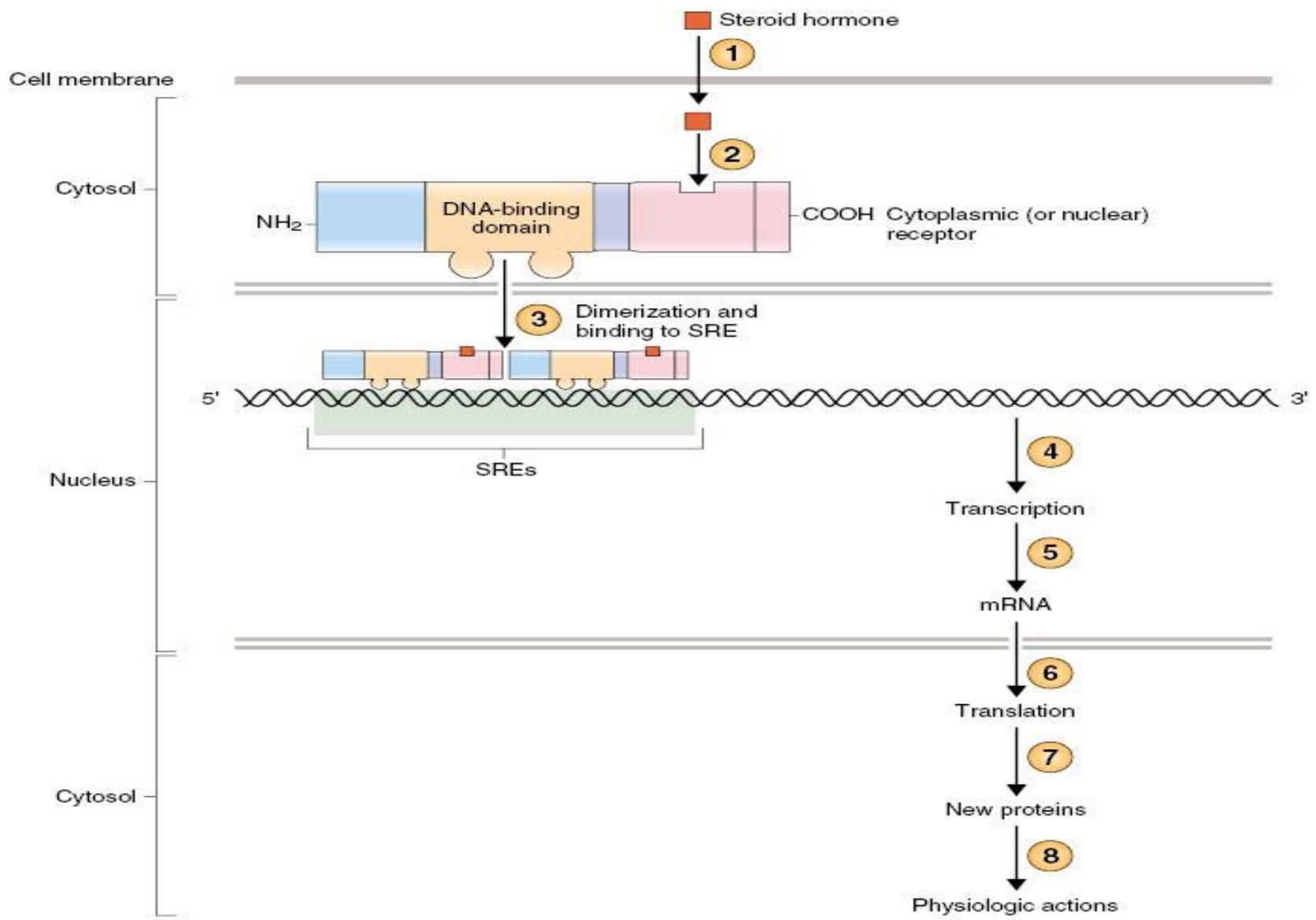


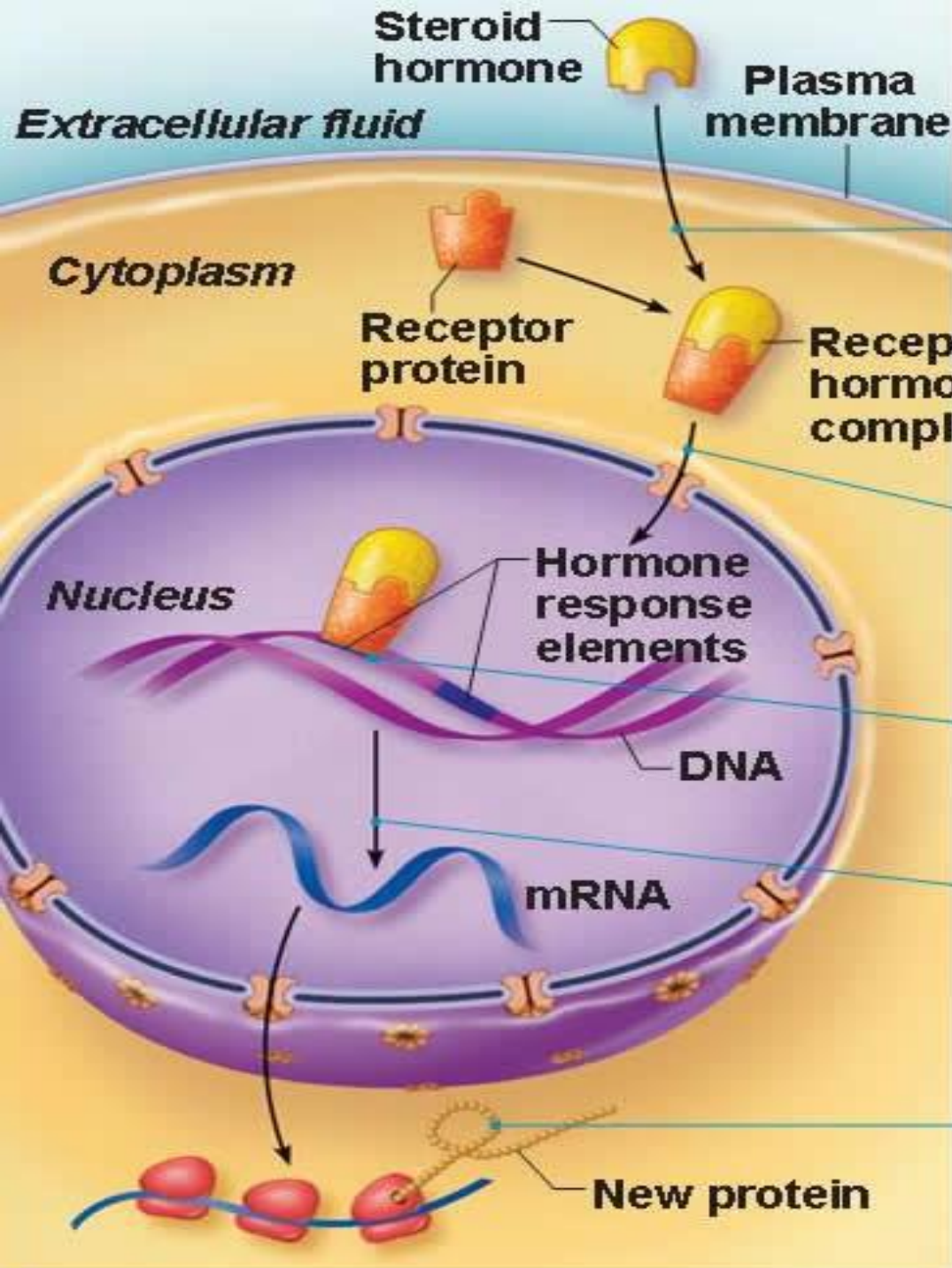
Tyrosine Kinase System

- Activated tyrosine kinase phosphorylates signaling molecules
- Induction of hormone/growth factor effects



STERIOD AND THYROID HORMONE MECHANISM





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.

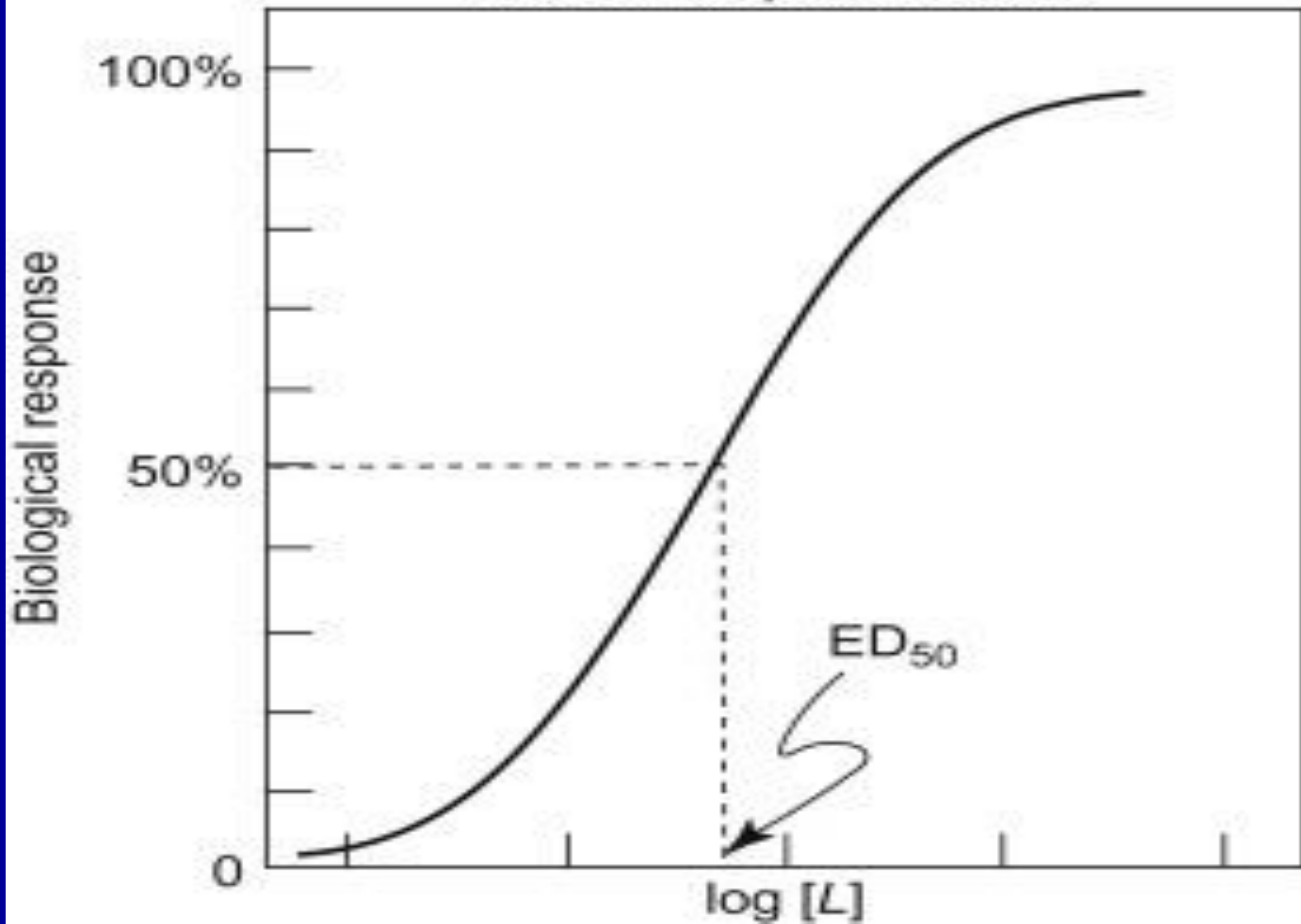
Table 9-3 Mechanisms of Hormone Action

Adenylyl Cyclase Mechanism (cAMP)	Phospholipase C Mechanism (IP ₃ /Ca ²⁺)	Steroid Hormone Mechanism	Tyrosine Kinase Mechanism
ACTH	GnRH	Glucocorticoids	Insulin
LH	TRH	Estrogen	IGF-1
FSH	GHRH	Progesterone	
TSH	Angiotensin II	Testosterone	
ADH (V ₂ receptor)	ADH (V ₁ receptor)	Aldosterone	
HCG	Oxytocin	1,25-Dihydroxycholecalciferol	
MSH	α ₁ Receptors	Thyroid hormones	
CRH			
Calcitonin			
PTH			
Glucagon			
β ₁ and β ₂ receptors			

REGULATION OF HORMONE RECEPTORS

- **Dose-response relationship.**
- **Sensitivity.**
- **Number.**
- **Affinity.**

Dose-Response curve



DOWN-REGULATION

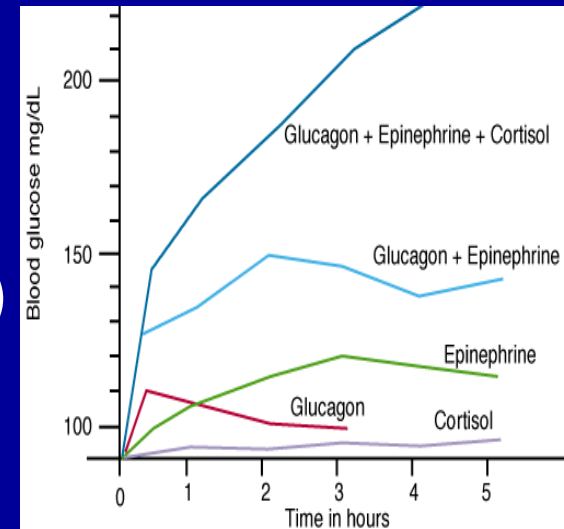
- **Decrease synthesis.**
- **Increase degradation.**
- **Inactivation .**
- **T3.**

UP-REGULATION

- **Increase synthesis.**
- **Decrease degradation.**
- **Activation .**
- **prolactin.**

INTERACTION OF HORMONES AT TARGET CELLS

- **Permissiveness** (Thyroid hormone have permissive effect on growth hormone action)
- **Synergism** (glucagon, cortisol and epinephrine)
- **Antagonism** (Glucagon /insulin)



HORMONE CONCENTRATIONS IN THE BLOOD

- Concentrations of circulating hormone reflect:
 - Rate of release
 - Speed of inactivation and removal from the body
- Hormones are removed from the blood by:
 - Degrading enzymes
 - The kidneys
 - Liver enzyme systems

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