Endocrine System
M111501302
Fall 2020

Endocrine Physiology

Recommended Text

Guyton and Hall , Textbook of Medical Physiology

Guyton , 14th Edition

Lecture No 1
Introduction to Endocrinology

General Principles of Endocrine Physiology

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More resources

- **Ganong's Review of Medical Physiology, 26e by :**Kim E. Barrett, Susan M. Barman, Heddwen L. Brooks, Jason X.-J. Yuan
- **Physiology: (Costanzo Physiology) 6th Edition** by Linda S. Costanzo PhD .
- **BRS Physiology** Author(s): Linda S. Costanzo Ph.D.
- **USMLE Step 1 Physiology : Kaplan Medical**
-

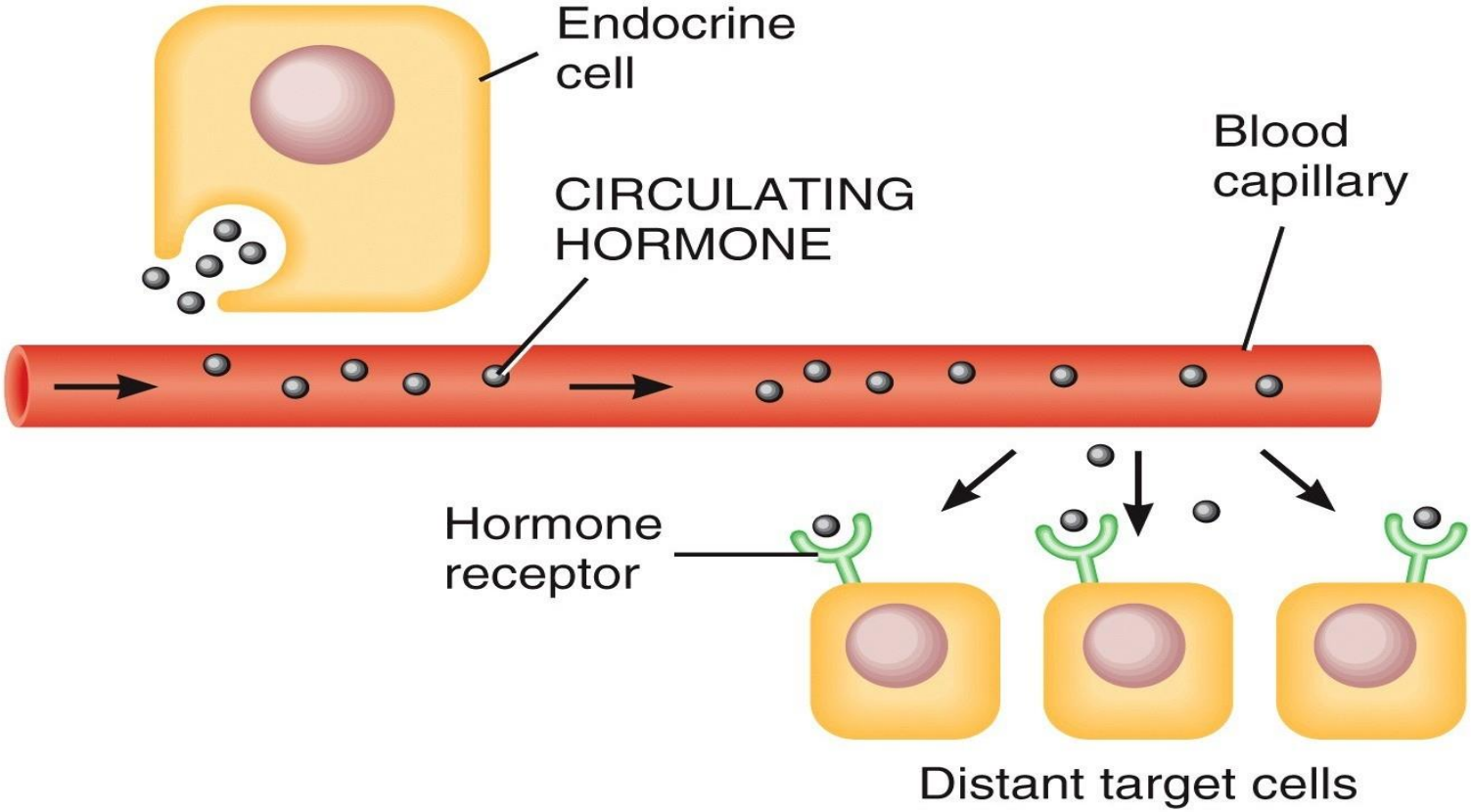
Control Systems of The Body s Nervous and Endocrine Systems

- The nervous and endocrine systems act together to coordinate all systems of the body.
- The nervous system releases neurotransmitters; the endocrine system releases hormones.
- Most hormones circulate through the blood some binds to plasma proteins and bind to receptors on “target cells.” when released
- The action of nervous are rapid whereas the actions of the endocrine system are slower
- The hypothalamus and the pituitary gland coordinates the activity of both systems

Overview of the endocrine system functions

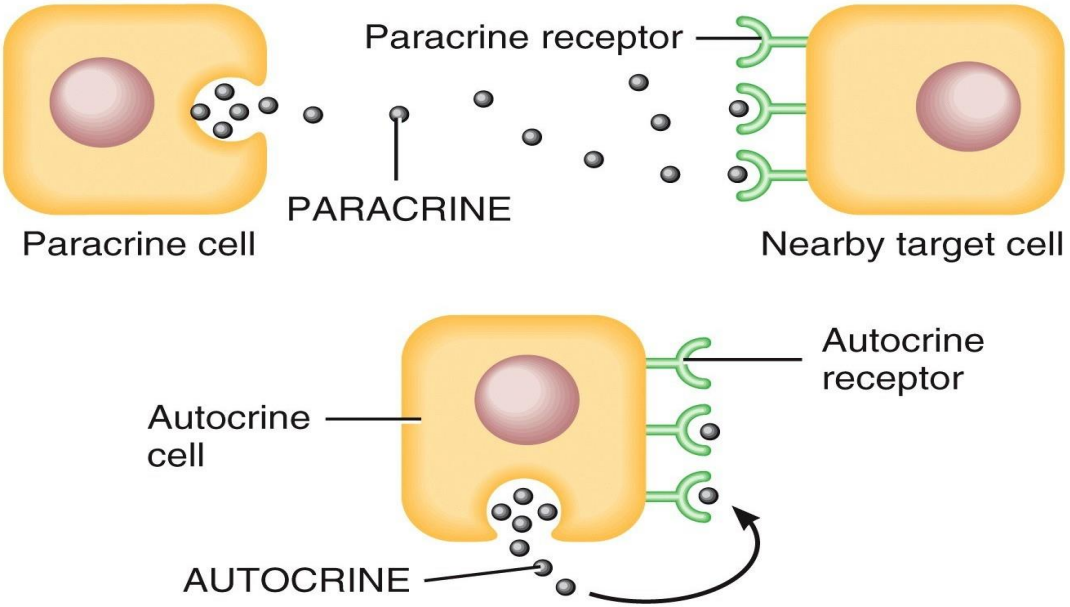
- Maintenance of internal environment
- Regulation of sodium and water balance and control of blood volume and pressure;
- Regulation of calcium and phosphate balance required for cell membrane integrity and intracellular signaling
- sexual and CNS differentiation in the fetus
- Regulation of reproduction functions
- Development and growth
- Adaptation to emergency and stress
- Regulation of energy balance and control of fuel m mobilization, utilization.

Hormone Activity and Intercellular Communication



(a) Circulating hormones

Local Hormones



(b) Local hormones (paracrines and autocrines)

COORDINATION OF BODY FUNCTIONS BY CHEMICAL MESSENGERS

- Endocrine hormone hormones
- Neuroendocrine hormones.
- Paracrine are secreted by cells into the extracellular fluid and affect neighboring target cells of different types.
- Example :
  - cytokine interleukin-1 in monocytes
  - Neurotransmitters across synapses
  - Estrogens produced in the ovaries are crucial for the maturation of ovarian follicles before
  - Ovulation
  - Testosterone in the testis
- Autocrine are secreted by cells into the extracellular fluid and affect the function of the same cells that produced them.
- Cytokines are peptides secreted by cells into the extracellular fluid and can function as autocrine, paracrine, or endocrine hormones.
- Cytokines include the interleukins and other lymphokines that are secreted by T helper cells and act on other cells of the immune system
- Cytokine hormones (e.g., leptin) produced by adipocytes are sometimes called adipokines

Classes of Hormones

- Peptide & Protein Hormones
- Steroid Hormones
- Amine Hormones
- Eicosanoids

Chemical Nature of Hormones

- Amino acid derivatives such as dopamine, catecholamine, and thyroid hormones
- Small neuropeptides GnRH), (TRH), somatostatin, and vasopressin
- large proteins such as insulin, LH, and PTH produced by classic endocrine glands
- Steroid hormones such as cortisol and estrogen vitamin D that are synthesized from cholesterol-based precursors
- Eicosanoids such as leukotriene, lymphokines, prostaglandins and adipokines like leptin

Classification of hormones
Lipid-soluble Hormone

- steroid hormones, thyroid hormones.
- Lipid-soluble hormones circulate bound to transport proteins
- Receptors are Inside the cell, usually in nucleus
- Intracellular action stimulates synthesis of specific new proteins synthesized as needed
- Long half life Long (hours, days) due to affinity for protein carrier

Classification of hormones
Water-soluble hormones

- amine hormones, peptide and protein hormones, eicosanoid hormones).
- Act on membrane bound receptors
- stored in vesicle along with an enzyme that splits off the active hormone
- Mostly dissolved in plasma (free, unbound)
- Short half life

Peptide & Protein Hormones

Gland/Tissue	Hormones	Gland/Tissue	Hormones
Hypothalamus	• TRH, GnRH, CRH GHRH, Somatostatin,	Placenta	• HCG, HCS or HPL
Anterior pituitary	• ACTH, TSH, FSH, LH, PRL, GH	Kidney	• Renin
Posterior pituitary	• Oxytocin, ADH	Heart	• ANP
Thyroid	• Calcitonin	G.I. tract	• Gastrin, CCK, Secretin, GIP, Somatostatin, GLP-1
Pancreas	• Insulin,Glucagon, Somatostatin		
Liver	• Somatomedin C (IGF-1)	Adipocyte	• Leptin
Parathyroid	• PTH		

Peptide Hormone Families

Insulin Family

Insulin
Insulinlike growth factor I (IGF-1, somatomedin C)
Insulinlike growth factor II
Relaxin

Glycoprotein Family

Lutenizing hormone (LH)
Follicle-stimulating hormone (FSH)
Thyroid-stimulating hormone (TSH)
Chorionic gonadotropin (HCG)

POMC Family

Adrenocorticotropic hormone (ACTH)
Melanocyte-stimulating hormone (MSH)

Secretin-Glucagon Family

Secretin
Glucagon
Gastrointestinal polypeptide
Glicentin
Gastric inhibitory polypeptide (GIP)
Glucagon-like peptide 1 (GLP-1)

Growth Hormone Family

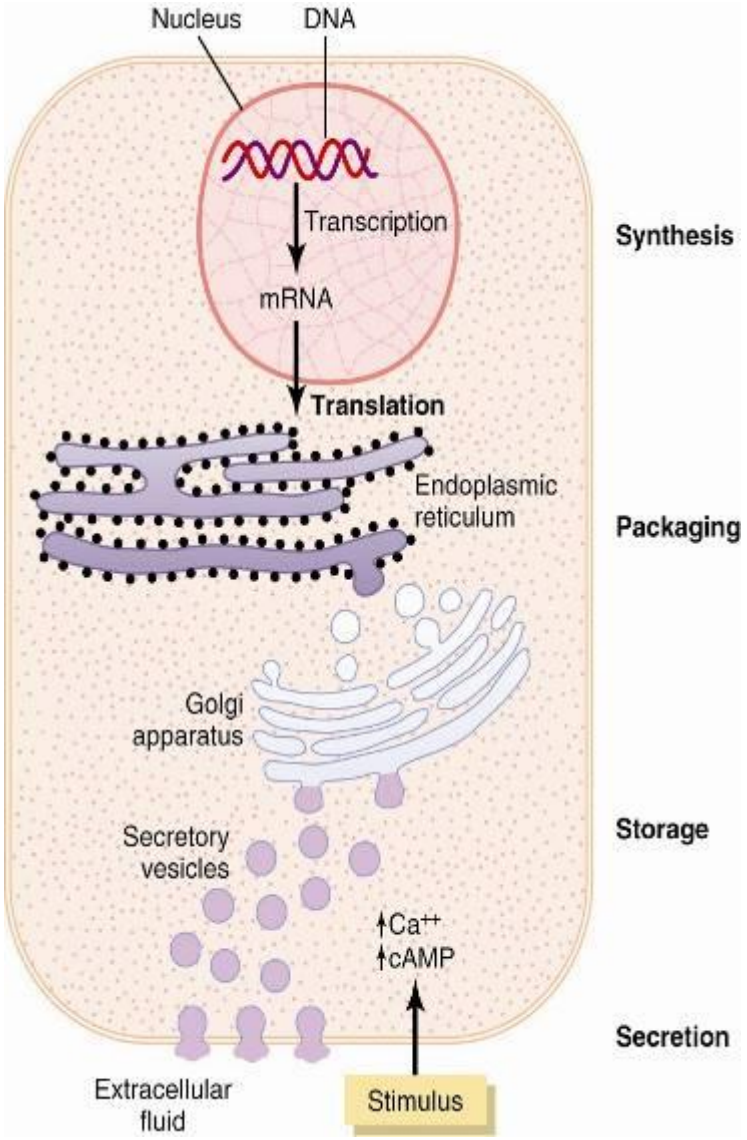
Growth hormone (GH)
Prolactin (PRL)
Chorionic somatomammotrophin (HCS) or Human placental lactogen (HPL)

Neurohypophyseal Family

Antidiuretic hormone (ADH)
Oxytocin

Synthesis & Secretion of Peptide Hormones

The stimulus for hormone secretion often involves changes in intracellular calcium or changes in cyclic adenosine monophosphate (cAMP) in the cell



Peptide hormones synthesis and release

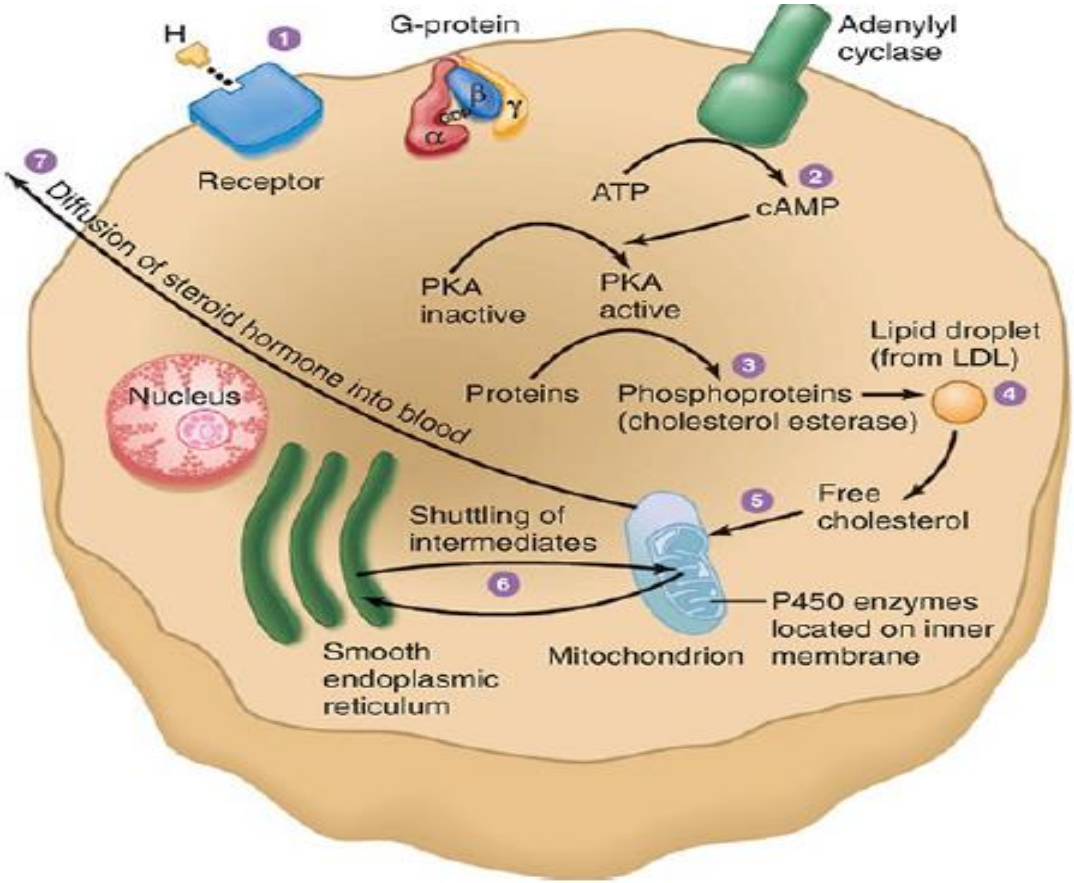
- They are usually synthesized first as larger proteins that are not biologically active (preprohormones)
- and are cleaved to form smaller prohormones in the endoplasmic reticulum.
- These prohormones are then transferred to the Golgi apparatus for packaging into secretory vesicles. In this process, enzymes in the vesicles cleave the prohormones to produce smaller, biologically active hormones and inactive fragments.
- The vesicles are stored within the cytoplasm, and many are bound to the cell membrane until their secretion is needed.
- Secretion of the hormones and the inactive fragments by exocytosis.

Amine Hormones : synthesis and release

- Amine hormones (thyroid hormones, epinephrine, norepinephrine) are derivatives of tyrosine
- NE and Epi are released by exocytosis
- Thyroid hormones are released by diffusion when the split from thyroglobulin

Gland/Tissue	Hormones
Hypothalamus	• Dopamine
Thyroid	• T_3, T_4
Adrenal medulla	• NE, EPI

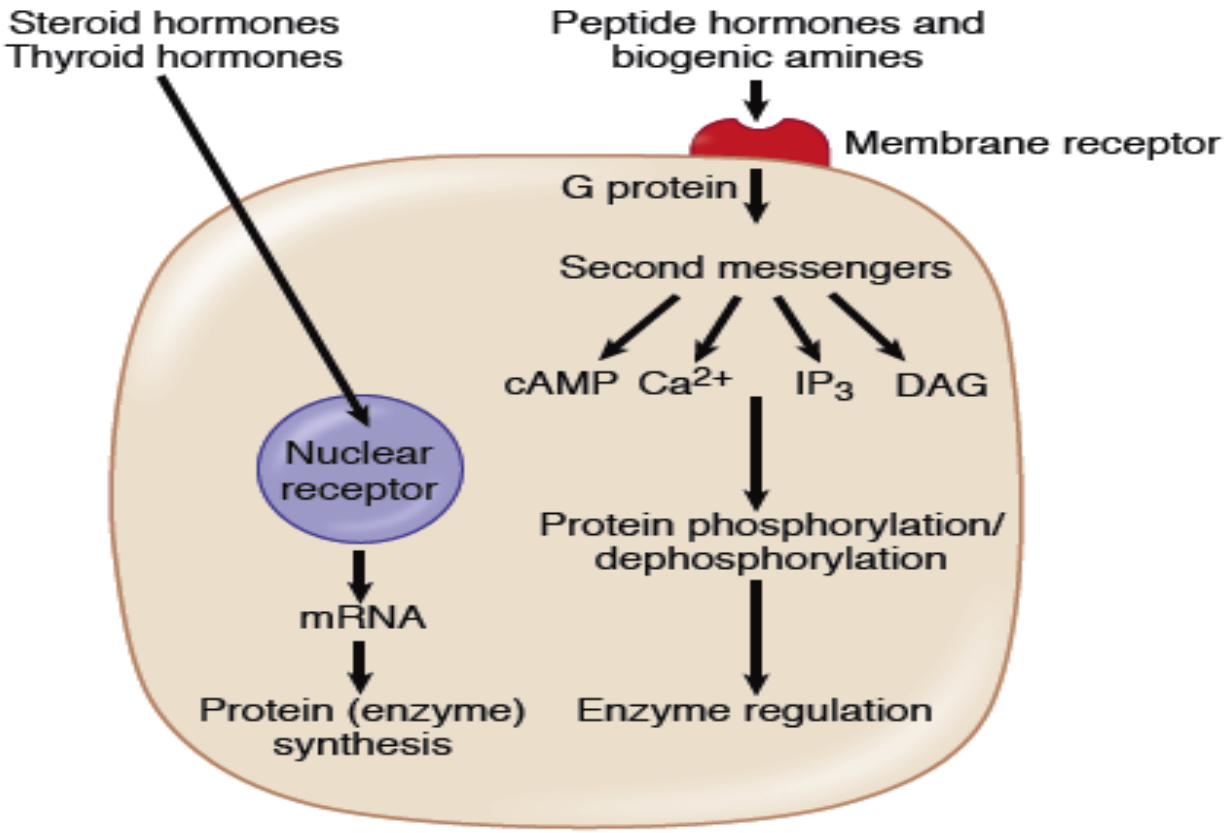
Steroid hormones : Synthesis and release



Synthesis and secretion of Steroid Hormones

- **Are Usually Synthesized From Cholesterol and are not stored.**
- The chemical structure of steroid hormones is similar to that of cholesterol, and in most instances
- Although there is usually very little hormone storage in steroid-producing endocrine cells
- large stores of cholesterol esters in cytoplasm vacuoles can be rapidly mobilized for steroid synthesis after a stimulus.
- Much of the cholesterol in steroid-producing cells comes from the plasma, but there is also de novo synthesis of cholesterol in steroid-producing cells.
- Because the steroids are highly lipid soluble, once they are synthesized, they can simply diffuse across the cell membrane and enter the interstitial fluid and then the blood.

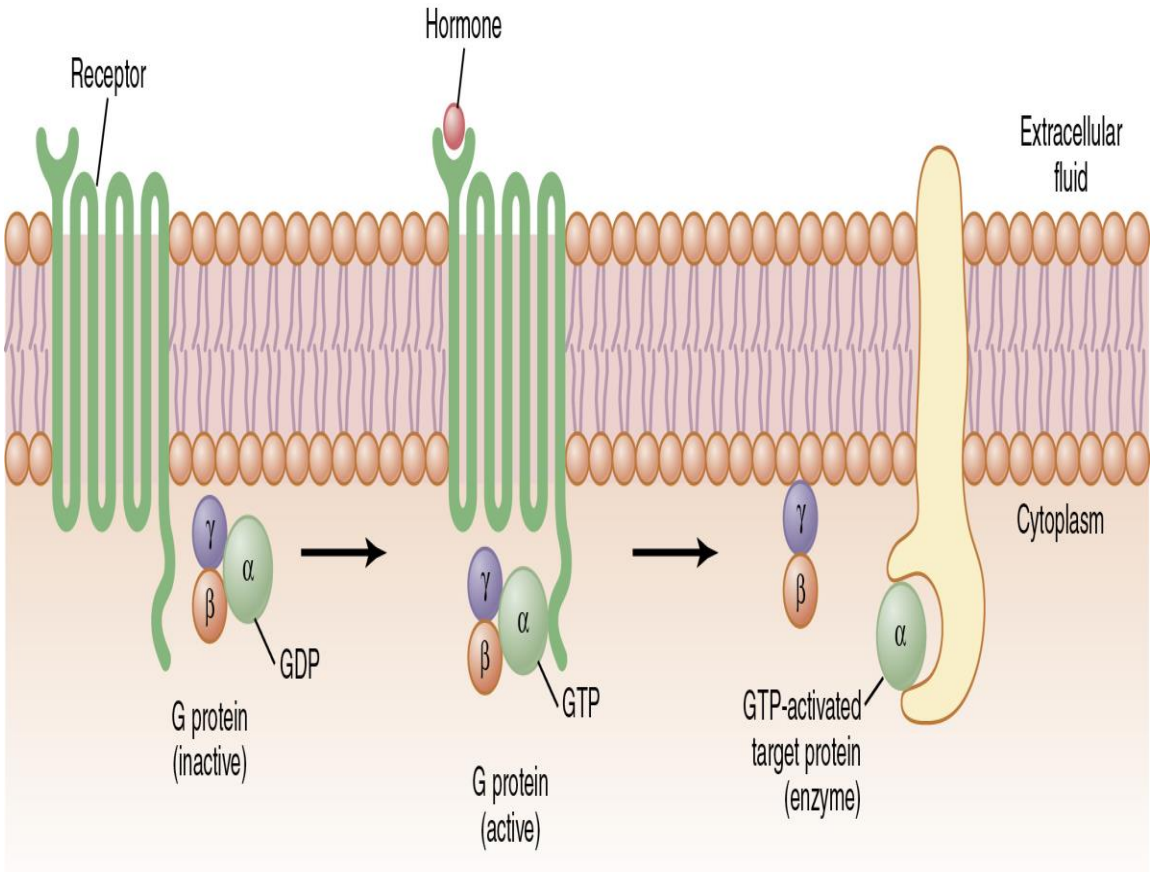
Hormonal signal transduction



Mechanism of Hormone action
G Protein-Coupled Receptors

1.hormone activates the receptor. Inactive α, β, and γ G protein complex associates
2.with the receptor and is activated, exchange of guanosine triphosphate *(GTP)* for guanosine diphosphate *(GDP)*.

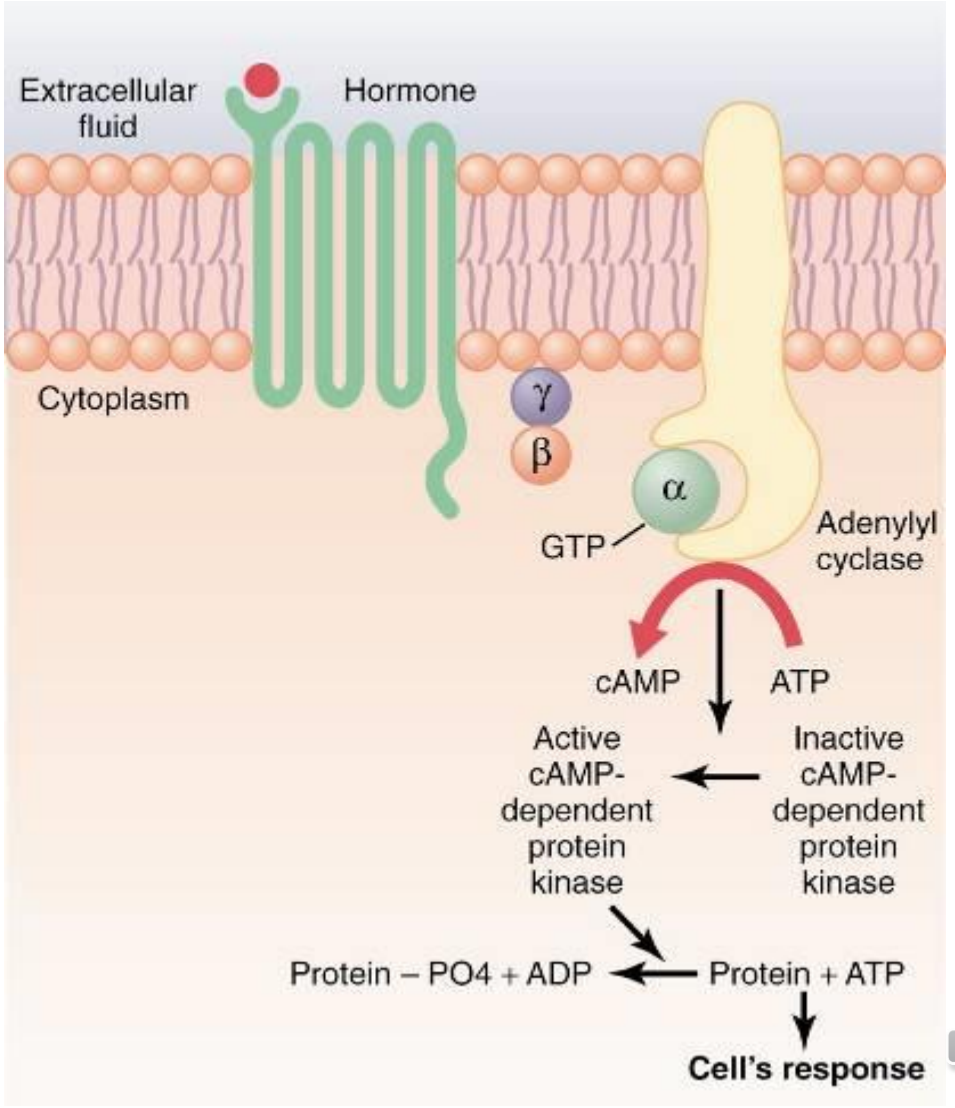
3 This process causes the α subunit (to which the GTP is bound) to dissociate from the β and γ subunits of the G protein and to interact with membrane-bound target proteins (enzymes, for example Adenyl cyclase) that initiate intracellular signals



Cyclic Adenosine Monophosphate (cAMP) Second Messenger Mechanism

intrinsic GTPase activity in the G protein converts GTP back to GDP, and the αs subunit returns to its inactive state.

Intracellular cAMP is degraded to an inactive metabolite, 5′ AMP, by the enzyme phosphodiesterase



CELL MECHANISMS OF HORMONE ACTION AND SECOND MESSENGERS
Summary

G proteins coupled receptors properties

- Are guanosine triphosphate (GTP)-binding proteins that couple hormone receptors to adjacent effector molecules.
- For example, in the cyclic adenosine monophosphate (cAMP) second messenger system G proteins couple the hormone receptor to adenylate cyclase.
- The G protein couples the hormone to inositol 1,4,5-triphosphate (IP3) second messenger systems
- have intrinsic GTPase activity.
- have three subunits: α, β, and γ.
- The α subunit can bind either guanosine diphosphate (GDP) or GTP.
- When GDP is bound to the α subunit, the G protein is inactive. When GTP is bound, the G protein is active.
- G proteins can be either stimulatory (Gs) or inhibitory (Gi).

Effects cAMP

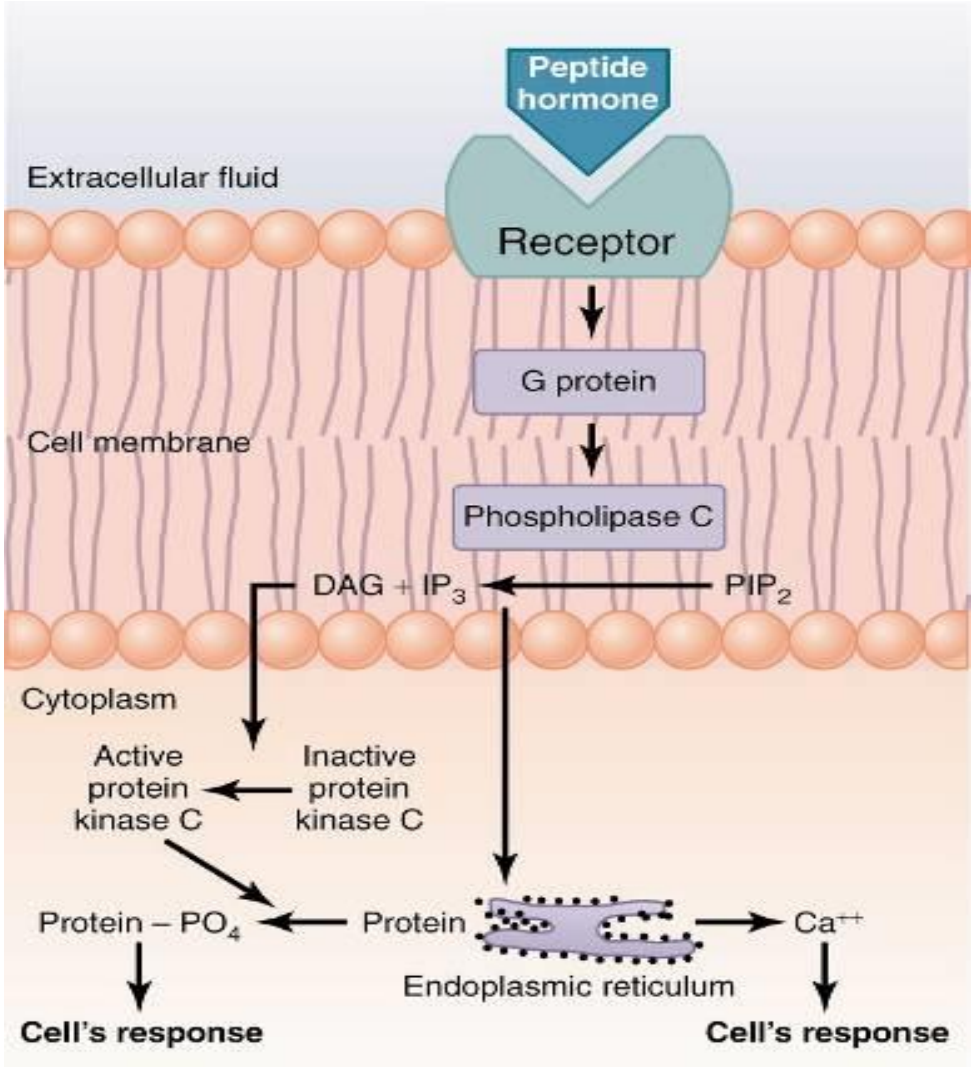
- The specific action that occurs in response to increases or decreases of cAMP in each type of target cell depends on the nature of the intracellular machinery some cells
- Therefore, different functions are elicited in different target cells, such as initiating synthesis of specific intracellular chemicals, causing
  - muscle contraction or relaxation
  - initiating secretion by the cells,
  - altering cell permeability to ions
  - Synthesis and secretion of hormones example thyroid
  - increases water channels epithelial cells of the distal and collecting tubules of the kidney leading to permeability to water.

Hormones That Use the Adenylyl Cyclase–cAMP Second Messenger System

- Adrenocorticotropic hormone (ACTH)
- Angiotensin II (epithelial cells)
- Calcitonin
- Catecholamines (β receptors)
- Corticotropin-releasing hormone (CRH)
- Follicle-stimulating hormone (FSH)
- Glucagon
- Growth hormone–releasing hormone (GHRH)
- Human chorionic gonadotropin (hCG)
- Luteinizing hormone (LH)
- Parathyroid hormone (PTH)
- Secretin
- Somatostatin
- Thyroid-stimulating hormone (TSH)
- Vasopressin (V2 receptor, epithelial cells in collecting duct of neoprene

Cell Membrane Phospholipid Second Messenger System

Phospholipase C attached to the inside projections of the receptors
.This enzyme catalyzes the breakdown of phospholipids
PIP2 phosphatidylinositol 4,5-diphosphate



Summary IP3 mechanism

- Hormone binds to a receptor in the cell membrane and, via a G protein activates phospholipase C
- Phospholipase C liberates diacylglycerol and IP3 from membrane lipids
- IP3 mobilizes Ca2+ from the endoplasmic reticulum
- Together, Ca2+ and diacylglycerol activate protein kinase , which phosphorylates proteins and causes specific physiologic actions
- Lipid portion of DAG is *arachidonic acid,* which is the precursor for the *prostaglandins* and other local hormones that cause multiple effects in tissues throughout the body.

Hormones That Use the Phospholipase C Second Messenger System

- Angiotensin II (vascular smooth muscle)
- Catecholamines (α receptors)
- Gonadotropin-releasing hormone (GnRH)
- Parathyroid hormone (PTH)
- Oxytocin
- Thyrotropin-releasing hormone (TRH)
- Vasopressin (V1 receptor, vascular smooth muscle)

Hormones That Use the guanylate cyclase Second Messenger System cGMP

- Atrial natriuretic peptide (ANP)
- Nitric oxide

Ca calmodulin system

- Intracellular calcium ion *(Ca++)* concentration increases
  - when Ca++ enters the cell through calcium channels in the cell membrane
  - released from the sarcoplasmic reticulum.
- The Ca++ binds to *(CaM)* to form a Ca++-CaM complex, which then activates myosin light chain kinase *(MLCK)*.
- The active MLCK phosphorylates the myosin light chain leading to attachment of the myosin head with the actin filament and contraction of the smooth muscle.

(Receptor Tyrosine Kinase Signaling)
Tyrosine Kinases receptors

- **Receptor tyrosine kinases** have *intrinsic* tyrosine kinase activity within the receptor molecule.

- **Tyrosine kinase associated receptors** do not have intrinsic tyrosine kinase activity but *associate* noncovalently with proteins known as associated Janus kinase (JAK) which have tyrosine kinase activity

Receptor tyrosine kinases

- One type of receptor tyrosine kinase is a monomer(e.g., **nerve growth factor [NGF] and epidermal growth factor receptors,**).
- In this monomeric type, binding of ligand to the extracellular domain results in dimerization of the receptor,
- activation of intrinsic tyrosine kinase, and phosphorylation of tyrosine moieties on itself and other proteins, leading to its physiologic actions.
- Another type of receptor tyrosine kinase is already a dimer (e.g., **insulin and insulin-like growth factor [IGF] receptors** binding of the ligand (e.g., insulin) activates intrinsic tyrosine kinase and leads to phosphorylation of itself and other proteins and ultimately the hormone's physiologic actions. The mechanism of

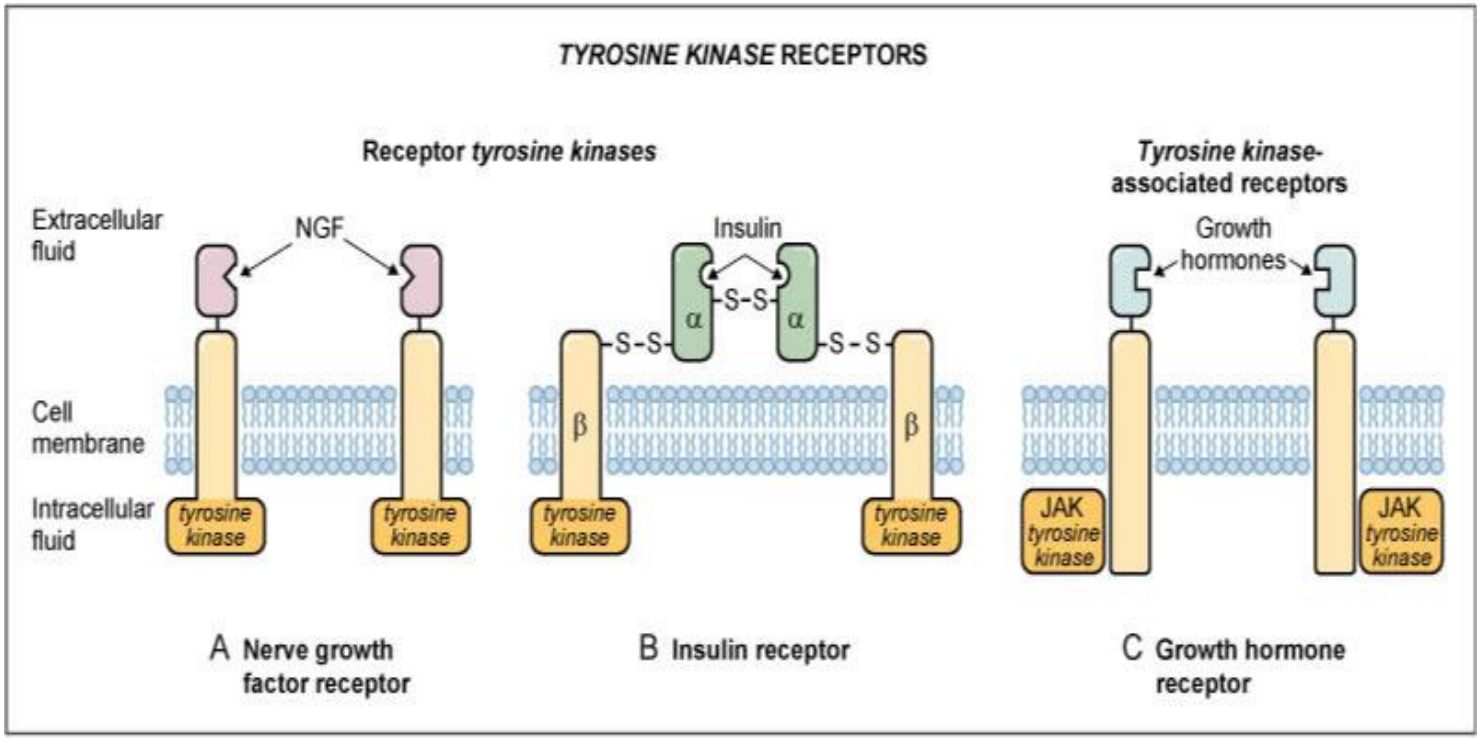


Fig. 9-6. **Tyrosine kinase receptors.** Nerve growth factor **(A)** and insulin **(B)** utilize receptor tyrosine kinases that have intrinsic tyrosine kinase activity. Growth hormone **(C)** utilizes a tyrosine kinase–associated receptor. NGF, nerve growth factor; JAK, Janus family of receptor-associated tyrosine kinase.

The Insulin Receptor & Mechanisms of Insulin Action

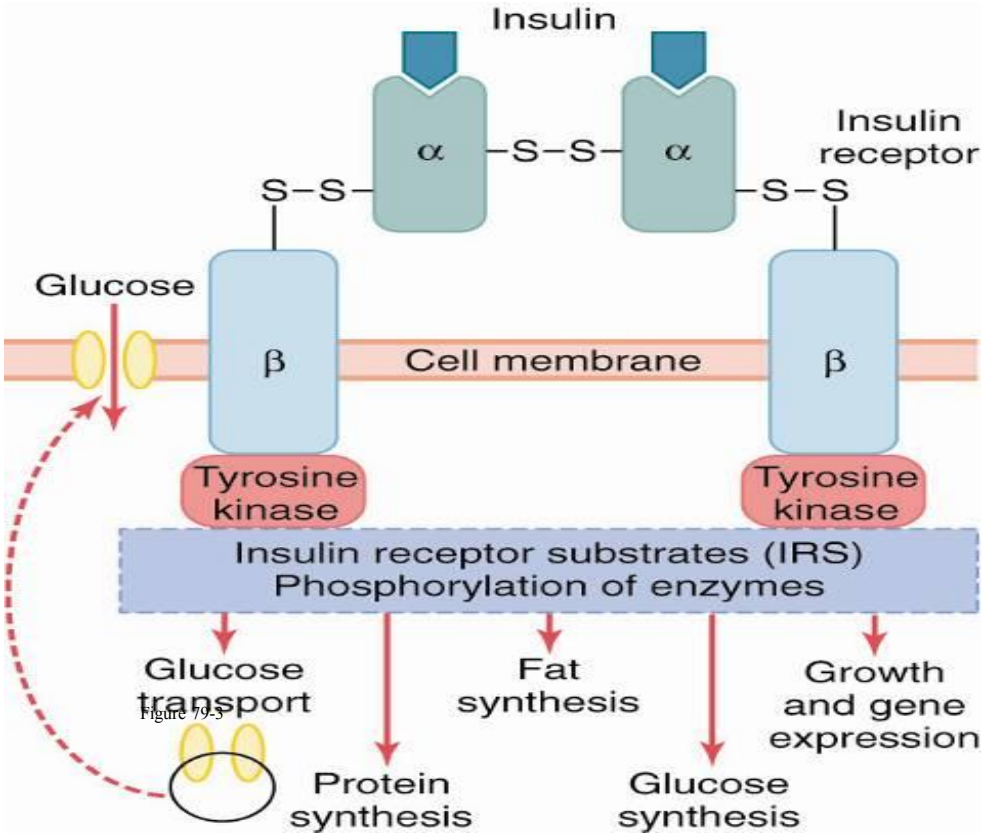


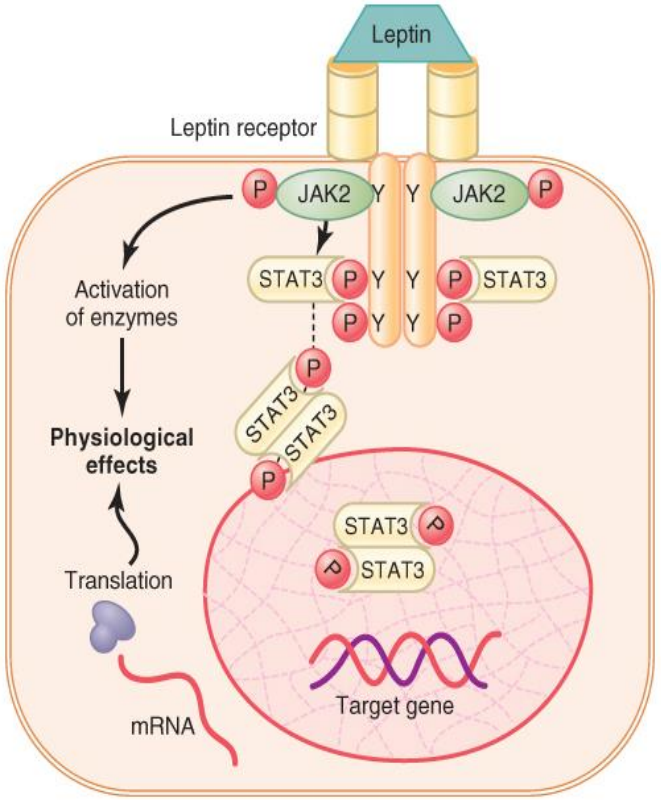
Figure 79-3

Tyrosine kinase-associated receptors (e.g., **growth hormone receptors)**

- The intracellular domain of the receptor domain does not have tyrosine kinase activity
- is noncovalently “associated” with tyrosine kinase such as those in the Janus kinase family (**JAK** Janus family of receptor-associated tyrosine kinase, or “just another kinase”). **)**,
- Hormone binds to the extracellular domain, leading to receptor dimerization and activation of tyrosine kinase in the associated protein (e.g., JAK).
- The associated tyrosine kinase phosphorrylates tyrosine moieties on itself, the hormone receptor, and other proteins.
- Downstream targets of JAK include members of the **STAT** (signal transducers and activators of transcription) family, which cause transcription of mRNAs and ultimately new proteins involved in the hormone’s physiologic actions.

An enzyme-linked receptor—the leptin receptor.

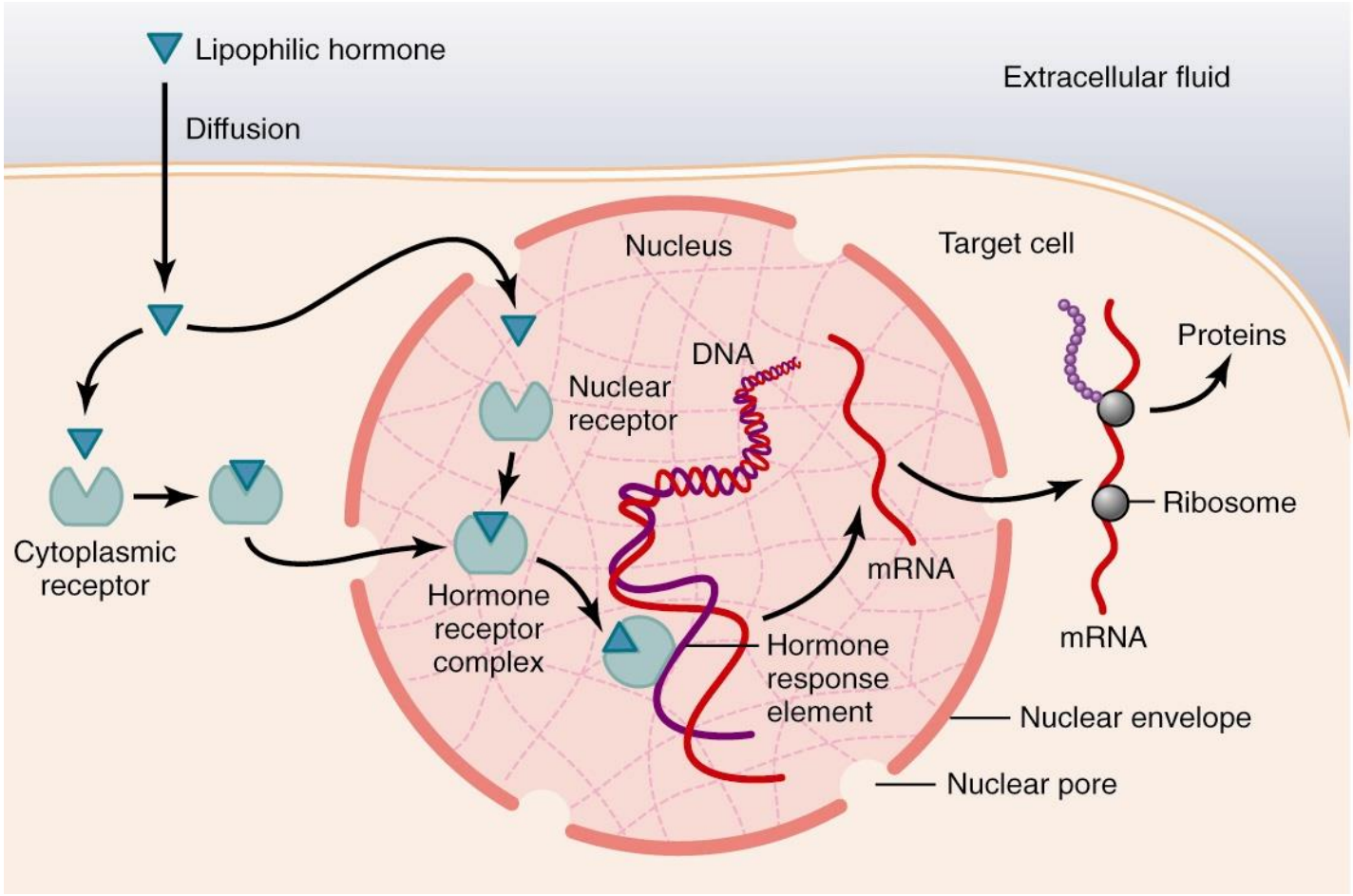
The receptor exists as a homodimer (two identical parts), and leptin binds to the extracellular part of the receptor, causing phosphorylation *(P)* and activation of the intracellular associated Janus kinase 2 *(JAK2)*. This mechanism causes phosphorylation of signal transducer and activator of transcription *(STAT)* proteins, which then activates the transcription of target genes and the synthesis of proteins



Hormones That Use Receptor Tyrosine Kinase Signaling

- Growth hormone
- Insulin
- Insulin-like growth factor-1
- Leptin
- Prolactin

Steroid & Thyroid Hormones - Mechanism of Action Intracellular Hormone Receptors and Activation of Genes.



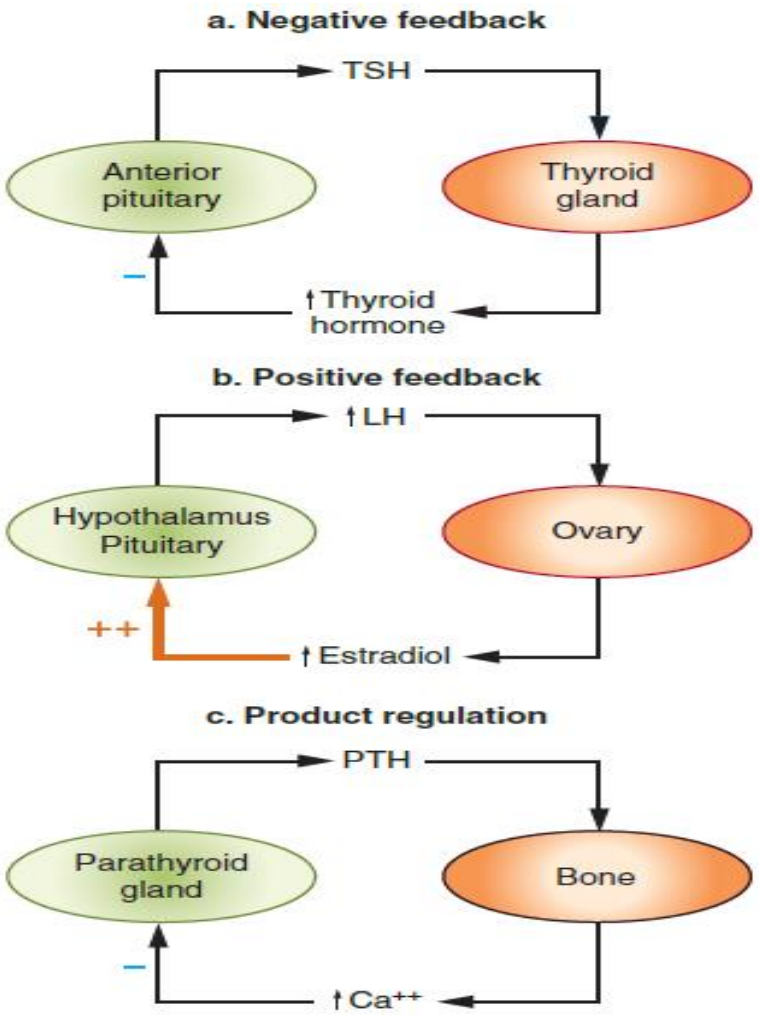
Steroid hormone mechanism of action

- Steroid (or thyroid) hormone diffuses across the cell membrane and binds to its **receptor**
- The hormone–receptor complex enters the nucleus and dimerizes (step 2).
- The **hormone–receptor dimers** are transcription factors that **bind to steroid-responsive elements (SREs)** of DNA and initiate DNA transcription
- **New messenger RNA** is produced, leaves the nucleus, and is translated to synthesize new proteins
- The **new proteins** that are synthesized have specific physiologic actions. For example
    - For example, Aldosterone induces the synthesis of Na+ channels in the renal principal cells and thus increases Na reabsorption

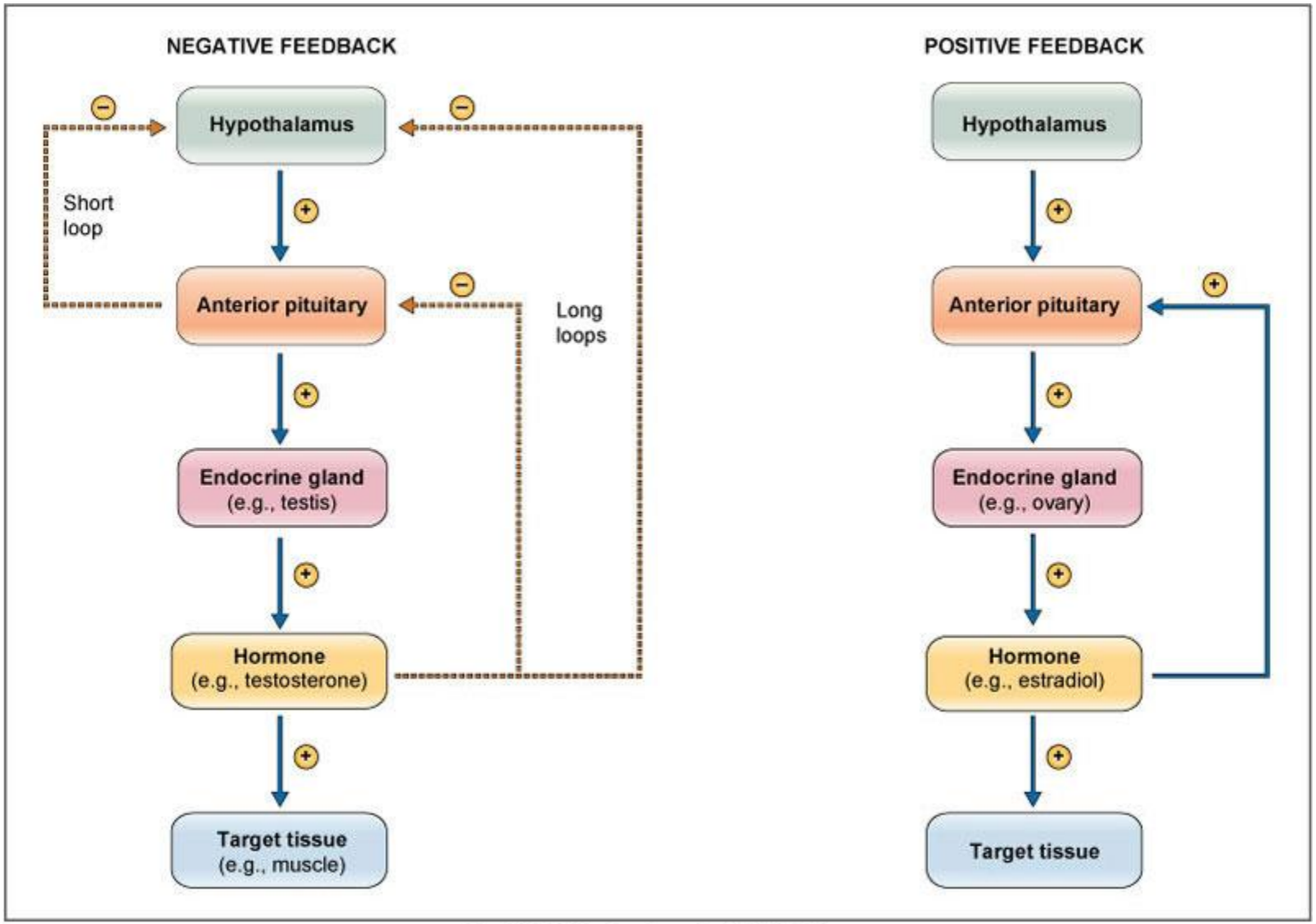
Control of hormone secretion

- Feedback Mechanisms
- Hormonal Rhythms
- Product mechanism

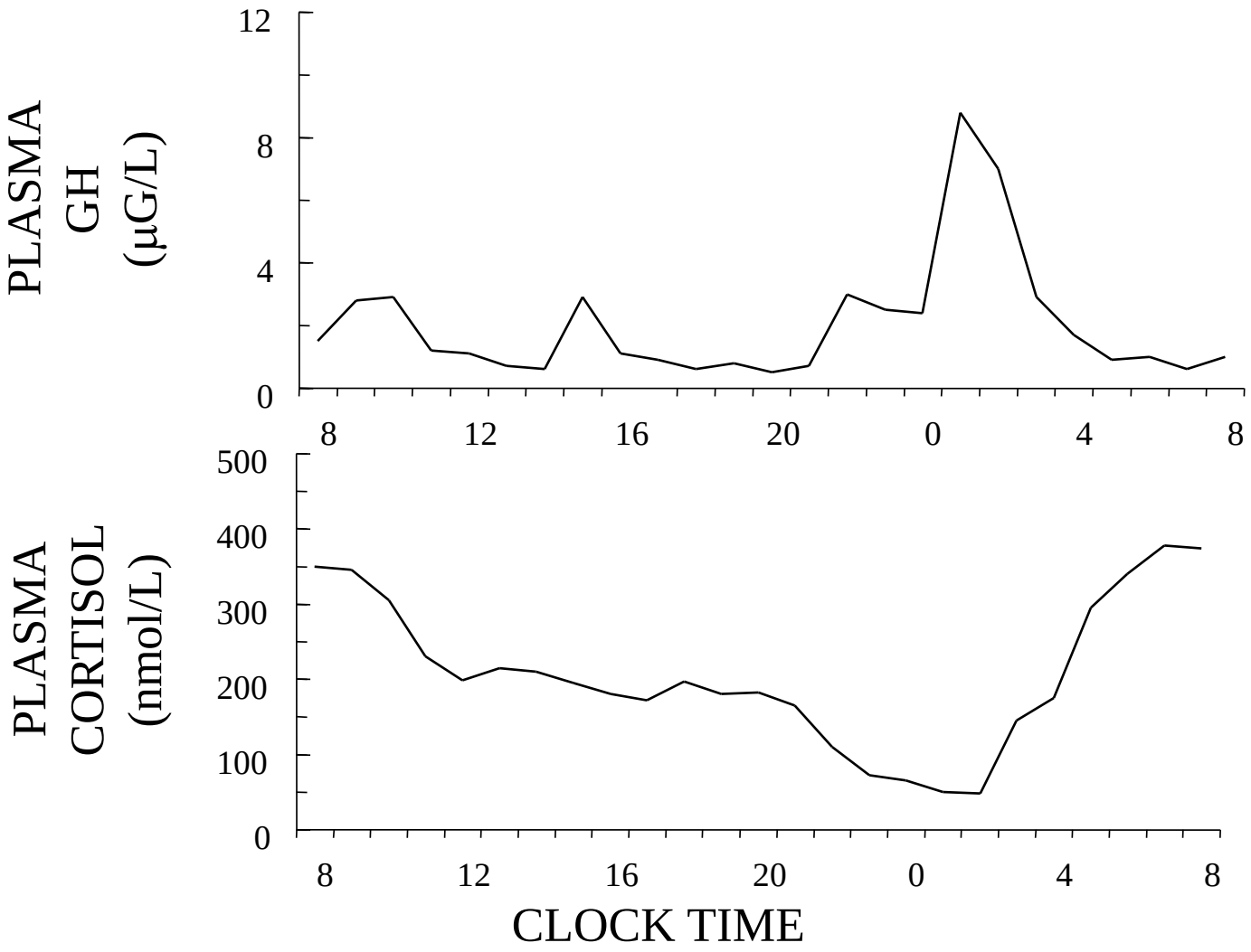
General mechanisms of hormonal regulation



Feedback Mechanisms



Hormonal Rhythms



Patterns of hormone release.

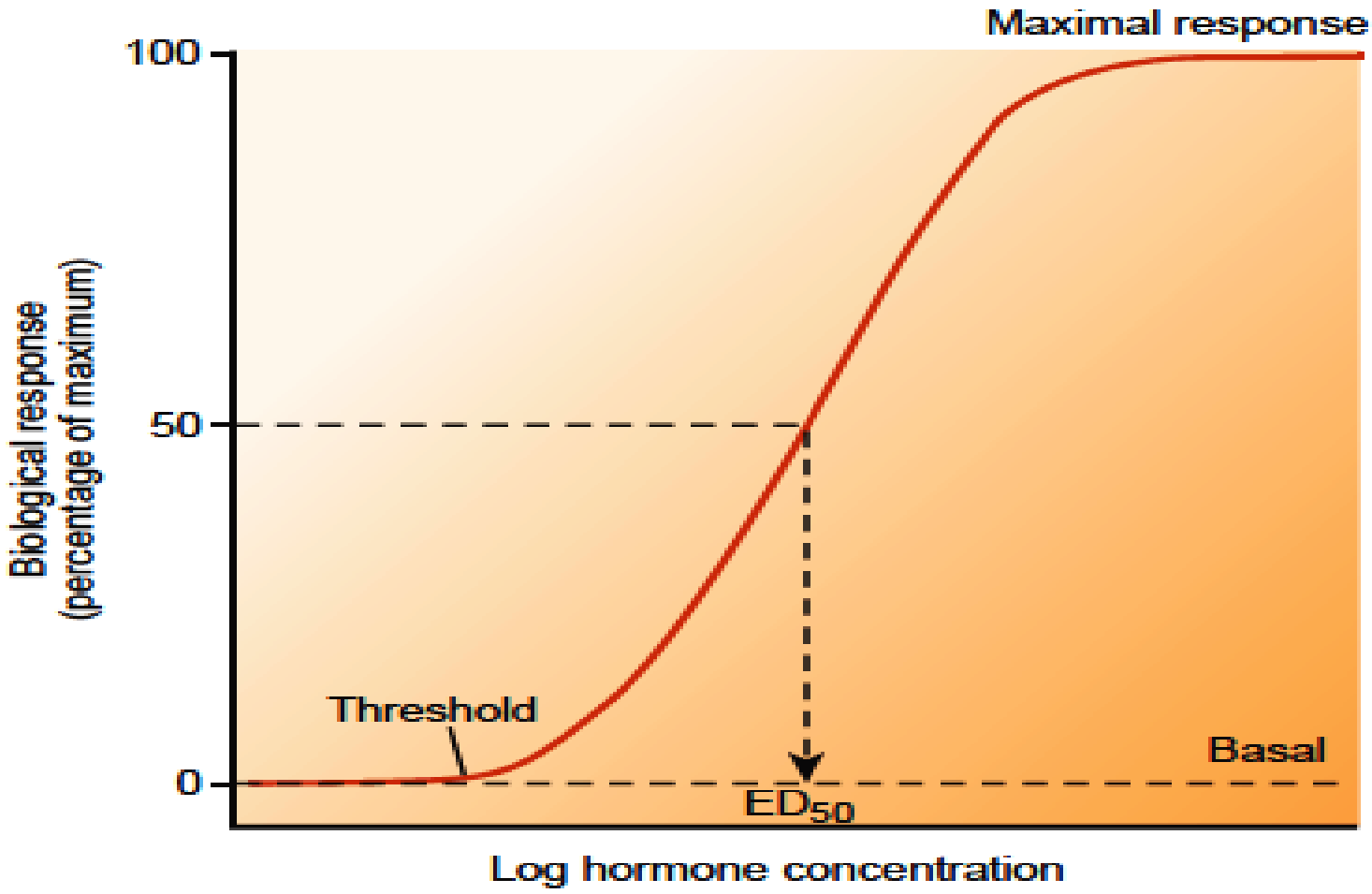
Plasma hormone concentrations fluctuate throughout the day.

- Plasma hormone measurements do not always reflect the function of a given endocrine system.
- Both cortisol and growth hormone show considerable variations in blood levels throughout the day.
- These levels can also be affected by sleep deprivation, light, stress, and disease, night work, sleep patterns
- Levels of hormones are dependent on their secretion rate, rates of metabolism and excretion, metabolic clearance rate, circadian pattern, fluctuating environmental stimuli

Regulation of hormones receptors and responsiveness of target tissue hormones

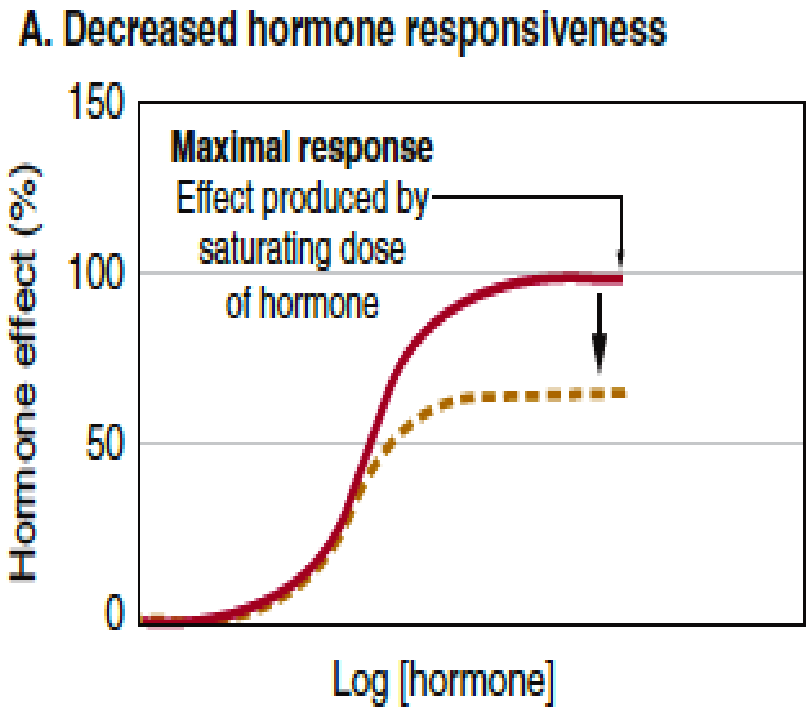
- Responsiveness
  - is expressed in the dose-response relationship in which the magnitude of response is correlated with hormone concentration.
  - As the hormone concentration increases, the response usually increases and then levels off.
- Sensitivity is defined as the hormone concentration that produces 50% of the maximal response.
  - If more hormone is required to produce 50% of the maximal response, then there has been a decrease in sensitivity of the target tissue.
  - If less hormone is required, there has been an increase in sensitivity of the target tissue.

Dose response curve of hormone action



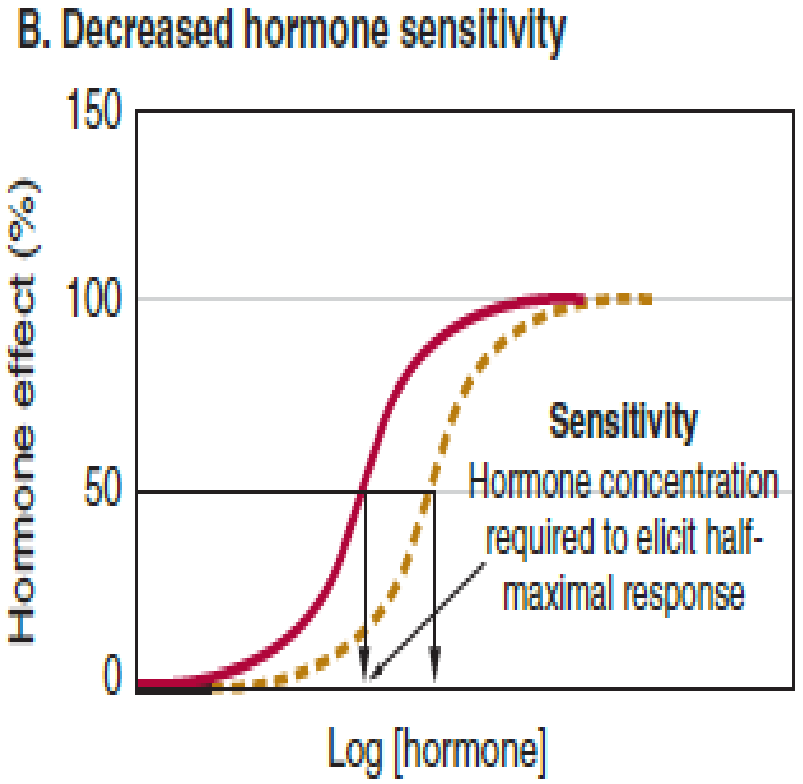
A Hormone responsiveness.

- Decreased responsiveness to hormone effects and can be due
- decreased number of hormone receptors
- decreased number of target cells.
- When responsiveness is decreased, then no matter how high the hormone concentration is, a maximal response will not be achieved



Hormone sensitivity.

- A decrease in hormone sensitivity requires higher hormone concentrations to produce 50% of the maximal response.
- Decreased sensitivity can be due to decreased
  - hormone–receptor affinity
  - Decreased hormone–receptor number
  - Hormone receptor resistance



- *Resistance to hormone action*
- Abnormalities in receptors or events distal to the ligand-receptor interaction, often due to chronic elevation of circulating hormone (e.g., type II diabetes) or drug therapy.
- Receptors are often saturated.

- *Permissive action* A phenomenon in which one type of hormone must be present before another hormone can act; for example, cortisol must be present for glucagon to carry out gluconeogenesis and prevent hypoglycemia.
- Thyroxine increases responsiveness to catecholamines

Regulation of receptors

■ **Hormones determine the sensitivity of the target tissue by regulating the number or sensitivity of receptors.**

Down-regulation of receptors

- A hormone **decreases the number or affinity of receptors** for itself or for another hormone.
- Is a mechanism in which a hormone decreases the number or affinity of its receptors in a target tissue.
- The purpose of down-regulation is to reduce the sensitivity of the target tissue when hormone levels are high for an extended period
  - in the uterus, progesterone down-regulates its own receptor and the receptor for estrogen.
  - T4 or T3, decreases the sensitivity of thyrotropin-releasing hormone (TRH) r receptors in the anterior pituitary.

Mechanisms of down regulation

- inactivation of some of the receptor molecules
- inactivation of some of the intracellular protein signaling molecules
- degradation of the receptors by lysosomes after they are internalized;
- Decreased synthesis of new receptors.

Regulation of receptors

Up-regulation of receptors

- a hormone increases the number or affinity of its receptors or for another hormone .
- Up-regulation may occur by
  - increasing synthesis of new receptors
  - decreasing degradation of existing receptors
- **Examples :**
  - **I**n the ovary, estrogen up-regulates its own receptor and the receptor for LH
  - prolactin increases the number of its receptors in the breast
  - growth hormone increases the number of its receptors in skeletal muscle and liver
  - estrogen increases the number of its receptors in the uterus.
  - In the uterus, estrogen up-regulates the receptors for LH in the ovaries

Metabolic clearance rate of hormones

- Metabolic clearance rate of hormones:

  Rate of disappearance of hormone from the plasma (nanograms per minute) /Concentration of hormone (nanograms per milliliter of plasma)

Ways of hormone clearance from plasma

- metabolic destruction by the tissues : Endocytosis of hormone receptor complex into the cell and metabolization of the complex usually receptors are recycled
- excretion by the liver into the bile, and
- excretion by the kidneys into the urine.
- The rate of clearance of water-soluble molecules is faster than hormones bound to plasma proteins
- The rate of steroid hormones is decreased and their levels in blood increase when the liver is diseased because these hormones are conjugated mainly in the liver and then “cleared” into bile

Hormonal transport

- Dissolved in plasma
- Bound to plasma proteins

Circulating Transport Proteins

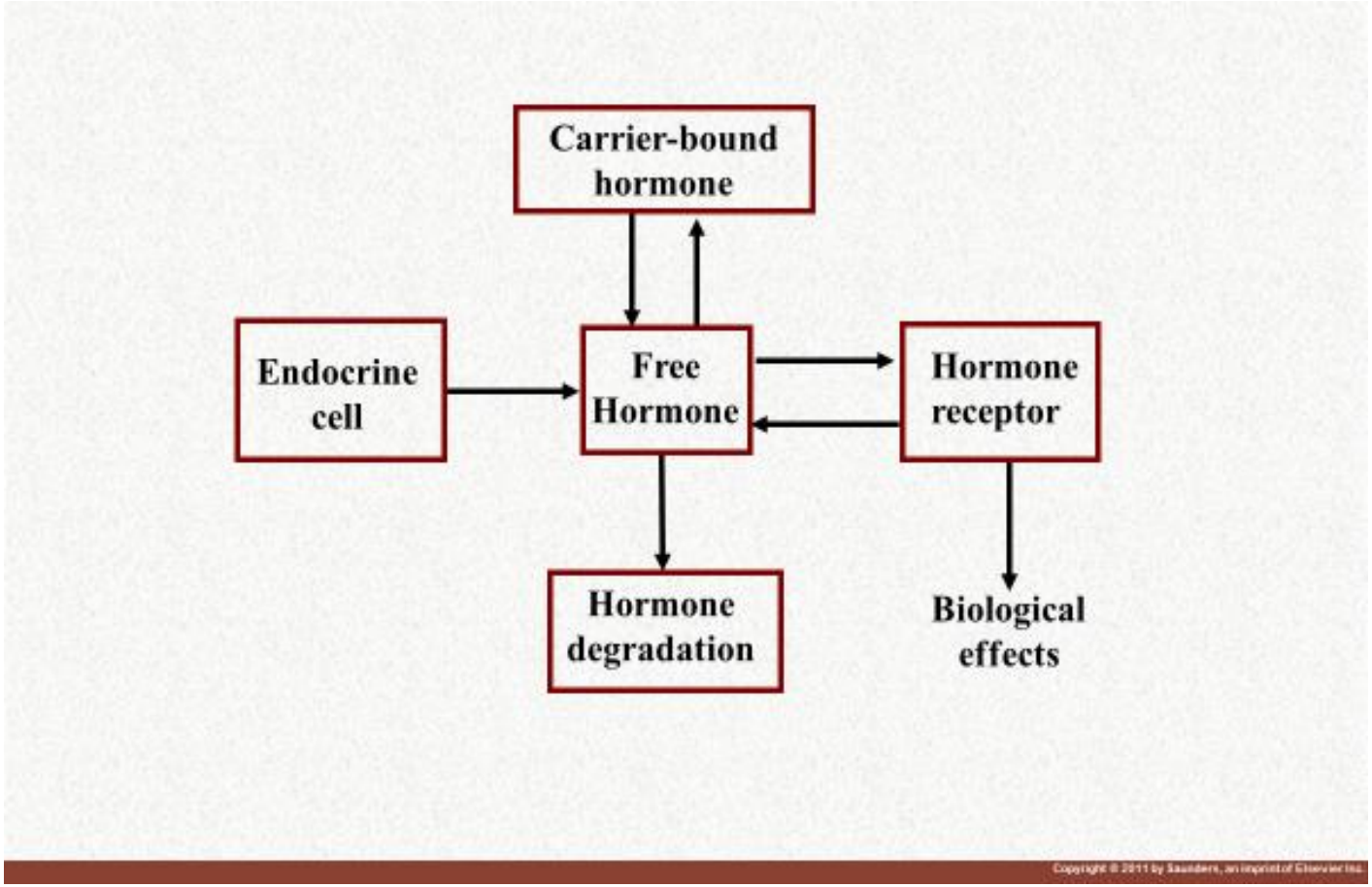
Transport Protein	Principle Hormone Transported
Specific	
Corticosteroid binding globulin (CBG, transcortin)	Cortisol, aldosterone
Thyroxine binding globulin (TBG)	Thyroxine, triiodothyronine
Sex hormone-binding globulin (SHBG)	Testosterone, estrogen
Nonspecific	
Albumin	Most steroids, thyroxine, triiodothyronine
Transthyretin (prealbumin)	Thyroxine, some steroids

Hormones with Degree of Protein Binding of

Hormone	Protein binding (%)	Plasma half-life	Metabolic clearance (ml/minute)
Thyroid			
Thyroxine	99.97	6 days	0.7
Triiodothyronine	99.7	1 day	18
Steroids			
Cortisol	94	100 min	140
Testosterone	89	85 min	860
Aldosterone	15	25 min	1100
Proteins			
Thyrotropin	little	50 min	50
Insulin	little	8 min	800
Antidiuretic hormone	little	8 min	600

MCR = (mg/minute removed)/(mg/ml of plasma) = ml cleared/minute

The relationship between hormone secretion, carrier protein binding, and hormone degradation.



Measurement of Hormone Levels

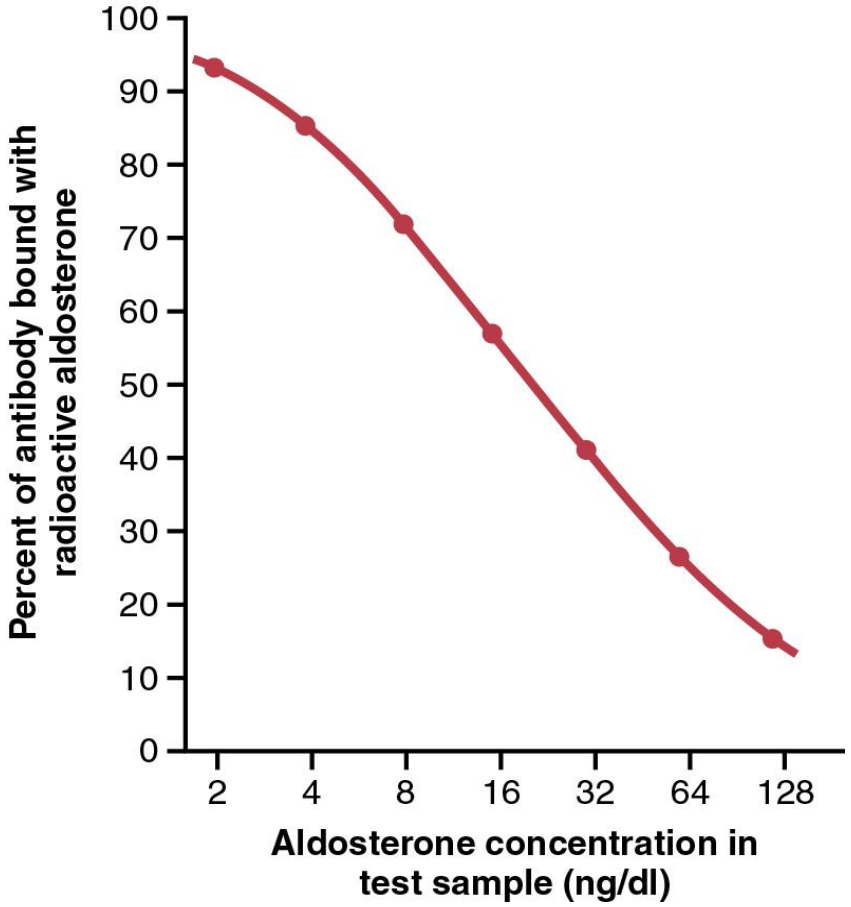
Plasma analysis

- Provides information at the time of sampling only and may not reflect the overall secretion rate
- When hormone secretion is episodic (pulsatile), a single sampling may reflect peaks (erroneous hyperfunction) or nadirs (erroneous hypofunction).
- Pulsatile secretion, diurnal and cyclic variation, age, sleep entrainment, and hormone antagonism must all be considered in evaluating circulating levels.
- Growth hormone is secreted in pulses and mainly at night. Such peak is not observed or reflected a fasting morning sample.
- However, growth hormone stimulates the secretion of IGF-I which circulates attached to protein and has a long half-life (20 hours). Plasma IGF-I measured at any time during the day is usually a good index of overall growth hormone secretion.
- Thyroid is a fairly constant system (no pulsatile) release and T4 has a half-life of about 6–7 days. Thus, a random measurement of total T4 is usually a good estimate of daily plasma levels.

Hormonal measurements
Urine analysis

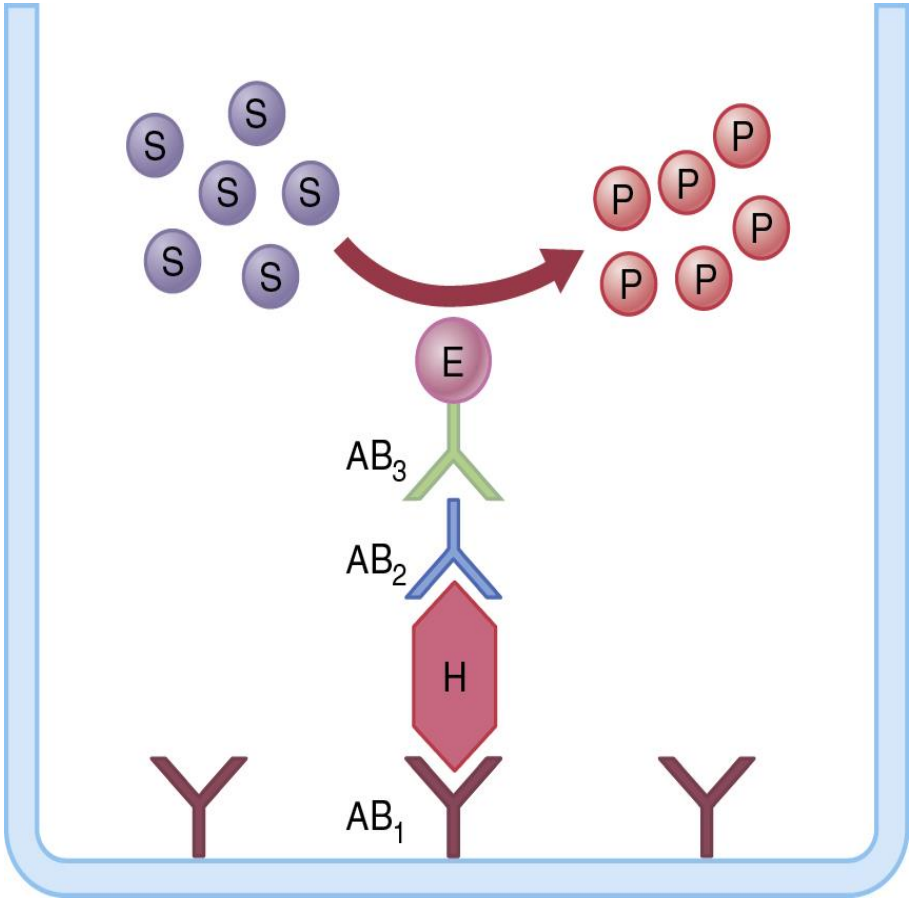
- restricted to the measurement of catecholamines , steroid hormones (Cortisol for example) , and water-soluble hormones such as hCG and LH.
- A distinct advantage of urine analysis is that it provides an integrated sample.
- – A “24-hour urine free cortisol” is often necessary to pick up a low-level in Cushing’s syndrome and to eliminate the highs and lows of the normal circadian rhythm.
- Please note steroid levels can be estimated in blood as well

Principles of Radioimmunoassay



Principles of the ELISA

(Enzyme-Linked Immunosorbent Assay)



DISORDERS OF THE ENDOCRINE SYSTEM
Primary versus Secondary Disorders

- A primary disorder

means dysfunction originating in the endocrine gland itself, ither hyper- or hypo-function.

Examples of a primary disorder include:

- excess cortisol from an adrenal adenoma (Conn's disease)
- pheochromocytoma
- decreased thyroid secretion (Hashimoto's thyroiditis)
- reduced ADH secretion (central diabetes insipidus)

DISORDERS OF THE ENDOCRINE SYSTEM
Primary versus Secondary Disorders

- A secondary disorder
  - indicates that a disturbance is secondary to diseases of other organs causing the gland to secrete more or less of the hormone.
- Examples of a secondary disorder :
  - hyperparathyroidism that develops in chronic renal failure
  - Cushing disease (pituitary adenoma secreting ACTH) resulting in hypercortisolism
  - SIADH: ectopic secretion of ADH by tumors cancers
  - Secondary adrenal insufficiency is adrenal hypofunction due to a lack of adrenocorticotropic hormone (ACTH)
  - Pituitary hypothyroidism

Suppression and stimulating test

Suppression tests : usually used to test hyperfunctions

- Failure of glucose to suppress growth hormone diagnostic for acromegaly
- Overnight Dexamethasone Suppression Test :
- Failure of dexamethasone (low dose) to suppress cortisol diagnostic for hypercortisolism

Stimulating tests : usually used to test hypofunction

- Hypothalamic hormones test anterior pituitary reserve
- Injection of the pituitary trophic hormone (e.g., ACTH) tests target gland reserve.
- Failure of growth hormone release after arginine injection

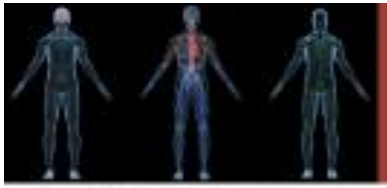
Hypofunction

- Can be caused by autoimmune disease (Hashimoto thyroiditis)
- primary adrenal insufficiency
- gonadal failure, hemorrhage,
- Infection
- damage by neoplasms
- Evaluated by a stimulation test
- Hypothalamic hormones test anterior pituitary
- Injection of the pituitary trophic hormone (e.g., ACTH) tests target gland reserve.
- Failure of growth hormone release after arginine injection

Hyperfunction

- Caused by hormone-secreting tumors, hyperplasia, autoimmune stimulation, ectopically produced peptide hormones (e.g., ACTH)
- Evaluated by a suppression test
- Multiple endocrine neoplasia
  - hyperparathyroidism, endocrine pancreas, and pituitary Adenomas
  - medullary carcinoma of the thyroid, pheochromocytoma,

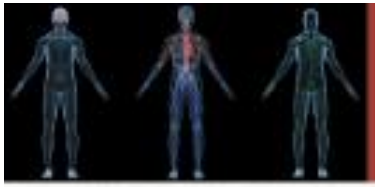
,



Causes of Decreased Endocrine Function

- Hypofunction
  - Autoimmune: Hashimoto's thyroiditis, type I DM, Addison's disease
  - Iatrogenic: radiation-induced hypopituitarism, hypothyroidism, surgical
  - Infectious/Inflammatory: adrenal insufficiency
  - Hormone mutations: GH, AVP
  - Enzyme defects: 21-hydroxylase deficiency
  - Nutritional/vitamin deficiency: vitamin D deficiency, iodine deficiency
  - Hemorrhage/infarction: Sheehan's syndrome, adrenal insufficiency

- Hormone resistance
  - Receptor mutations: GH, AVP
  - Postreceptor mutations: type II DM



Causes of Endocrine Hyperfunction

- Neoplastic
  - Benign: pituitary adenomas, hyperparathyroidism, autonomous thyroid or adrenal nodules
  - Malignant: adrenal and thyroid cancer
  - Ectopic: ACTH, SIADH
- Autoimmune
  - Graves' disease
- Iatrogenic
  - Cushing's syndrome, hypoglycemia
- Infectious/Inflammatory
  - Subacute thyroiditis
- Activating receptor mutations
  - TSH