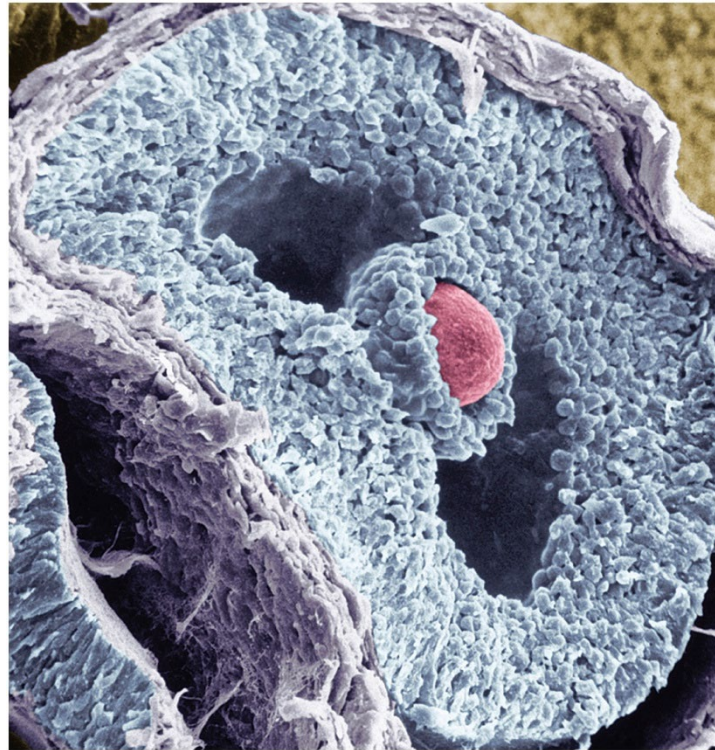
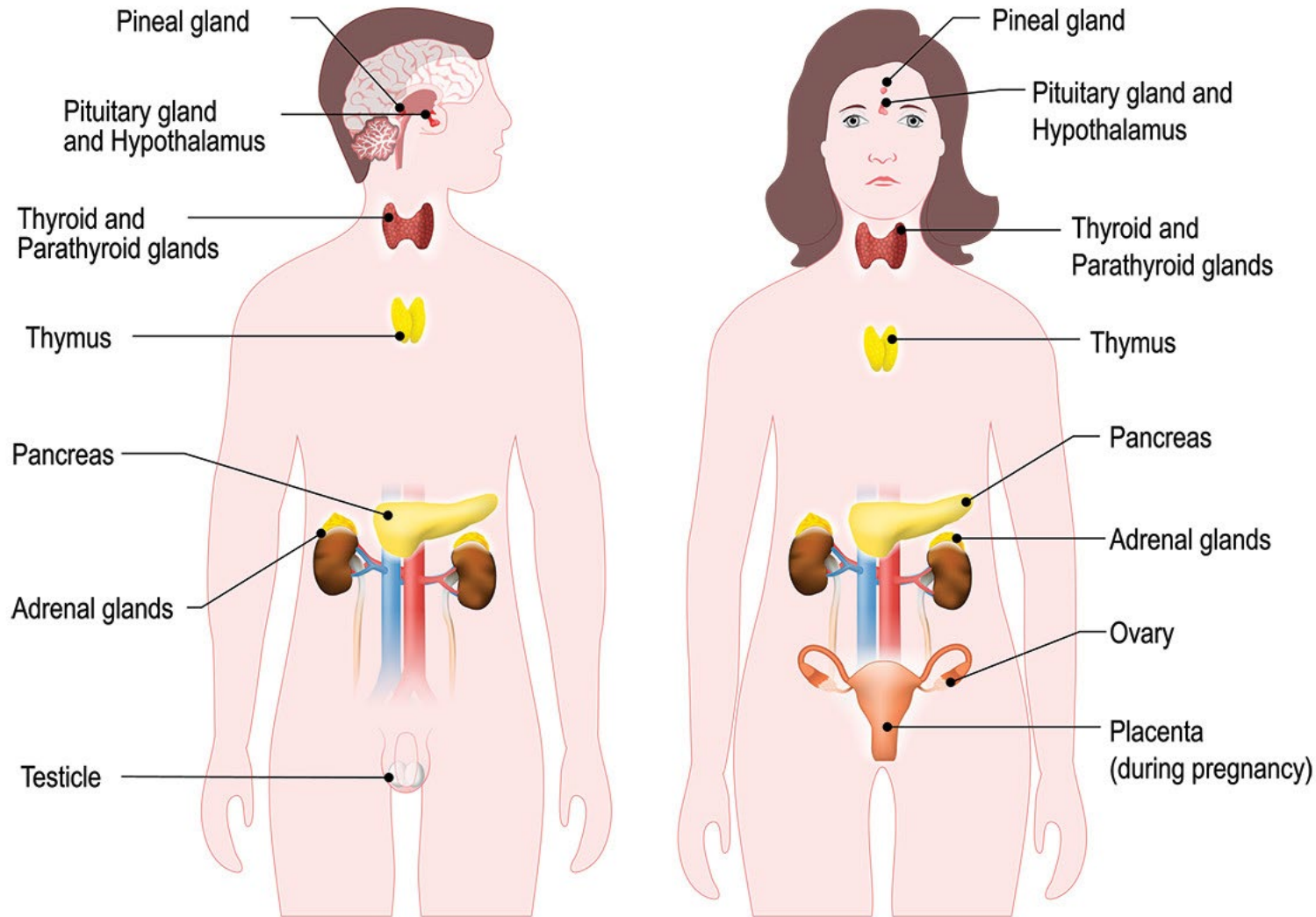


Chapter 17.1

Introduction to the Endocrine System and Hormone Chemistry



ENDOCRINE SYSTEM



The endocrine system is a network of glands that produce and release hormones, which act as chemical messengers to regulate the body's functions.

Its primary function is to control and coordinate the body's metabolism, energy levels, reproduction, growth, development, and response to injury, stress, and mood.

The system works more slowly than the nervous system but has longer-lasting effects on various organs and tissues throughout the body.

Sometimes It's Hard to Classify an Endocrine Gland

Pancreas (mixed gland)

- Exocrine – digestive enzymes
- Endocrine – insulin / glucagon

Hepatocytes (liver cells) defy rigid classification

- releases hormones / endocrine
- releases bile into ducts
- releases albumin and blood-clotting factors into blood (not hormones)

Nervous System VS Endocrine System

Both serve internal communication

- nervous - both electrical and chemical
- endocrine - only chemical

Speed and persistence of response

- nervous - reacts quickly (1-10 msec), stops quickly
- endocrine - reacts slowly (hormone release in seconds or days), effect may continue for weeks

Adaptation to long-term stimuli

- nervous - response declines (adapts quickly)
- endocrine - response persists (adapts slowly)

Area of effect

- nervous - targeted and specific (one organ)
- endocrine – generally more widespread effects (many organs)

Nervous System VS Endocrine System

- Some molecules function as both hormones or neurotransmitters // norepinephrine, cholecystikinin, thyrotropin-releasing hormone, dopamine and antidiuretic hormone
- Some hormones are secreted by neuroendocrine cells (neurons) /// neurons release their secretion into the bloodstream // oxytocin and catecholamines from adrenal gland
- Both systems may affect the same target cells // the neurotransmitter norepinephrine and the hormone glucagon both cause glycogen hydrolysis in liver
- Both systems may influence the function of the other system // neurons trigger hormone secretion or hormones stimulate or inhibit activity of neurons

TABLE 17.2**Names and Abbreviations for Hormones**

Abbreviation	Name	Source
ACTH	Adrenocorticotrophic hormone (corticotropin)	Anterior pituitary
ADH	Antidiuretic hormone (arginine vasopressin)	Posterior pituitary
ANP	Atrial natriuretic peptide	Heart
CRH	Corticotropin-releasing hormone	Hypothalamus
DHEA	Dehydroepiandrosterone	Adrenal cortex
EPO	Erythropoietin	Kidney, liver
FSH	Follicle-stimulating hormone	Anterior pituitary
GH	Growth hormone (somatotropin)	Anterior pituitary
GHRH	Growth hormone–releasing hormone	Hypothalamus
GnRH	Gonadotropin-releasing hormone	Hypothalamus
IGFs	Insulin-like growth factors (somatomedins)	Liver, other tissues
LH	Luteinizing hormone	Anterior pituitary
NE	Norepinephrine	Adrenal medulla
OT	Oxytocin	Posterior pituitary
PIH	Prolactin-inhibiting hormone (dopamine)	Hypothalamus
PRL	Prolactin	Anterior pituitary
PTH	Parathyroid hormone (parathormone)	Parathyroids
T ₃	Triiodothyronine	Thyroid
T ₄	Thyroxine (tetraiodothyronine)	Thyroid
TH	Thyroid hormone (T ₃ and T ₄)	Thyroid
TRH	Thyrotropin-releasing hormone	Hypothalamus
TSH	Thyroid-stimulating hormone (thyrotropin)	Anterior pituitary

TABLE 17.5

Hormones from Sources Other than the Hypothalamus and Pituitary (continued)

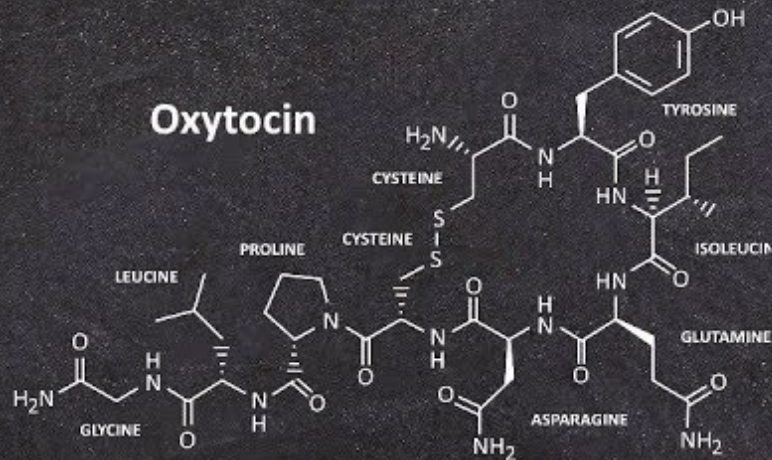
Source	Hormone	Target Organs and Tissues	Principal Effects
Pancreatic islets	Glucagon	Primarily liver	Stimulates amino acid absorption, gluconeogenesis, glycogen and fat breakdown; raises blood glucose and fatty acid levels
	Insulin	Most tissues	Stimulates glucose and amino acid uptake; lowers blood glucose level; promotes glycogen, fat, and protein synthesis
	Somatostatin	Stomach, intestines, pancreatic islet cells	Modulates digestion, nutrient absorption, and glucagon and insulin secretion
	Pancreatic polypeptide Gastrin	Pancreas, gallbladder Stomach	Inhibits release of bile and digestive enzymes Stimulates acid secretion and gastric motility
Ovaries	Estradiol	Many tissues	Stimulates female reproductive development and adolescent growth; regulates menstrual cycle and pregnancy; prepares mammary glands for lactation
	Progesterone	Uterus, mammary glands	Regulates menstrual cycle and pregnancy; prepares mammary glands for lactation
	Inhibin	Anterior pituitary	Inhibits FSH secretion
Testes	Testosterone	Many tissues	Stimulates fetal and adolescent reproductive development, musculoskeletal growth, sperm production, and libido
	Inhibin	Anterior pituitary	Inhibits FSH secretion
Skin	Cholecalciferol	—	Precursor of calcitriol (see kidneys)
Liver	Calcidiol	—	Precursor of calcitriol (see kidneys)
	Angiotensinogen	—	Precursor of angiotensin II (see kidneys)
	Erythropoietin	Red bone marrow	Promotes red blood cell production, increases oxygen-carrying capacity of blood
	Hepcidin Insulin-like growth factor I	Small intestine, liver Many tissues	Promotes iron absorption and mobilization Prolongs and mediates action of growth hormone
Kidneys	Angiotensin I	—	Precursor of angiotensin II, a vasoconstrictor
	Calcitriol	Small intestine	Increases blood calcium level mainly by promoting intestinal absorption of Ca^{2+}
	Erythropoietin	Red bone marrow	Promotes red blood cell production, increases oxygen-carrying capacity of blood
Heart	Atrial natriuretic peptide and brain natriuretic peptide	Kidney	Lower blood volume and pressure by promoting Na^+ and water loss
Stomach and small intestine	Cholecystokinin	Gallbladder, brain	Bile release; appetite suppression
	Gastrin	Stomach	Stimulates acid secretion
	Ghrelin	Brain	Stimulates hunger, initiates feeding
	Peptide YY	Brain	Produces sense of satiety, terminates feeding
	Other enteric hormones	Stomach, intestines	Coordinate secretion and motility in different regions of digestive tract
Adipose tissue	Leptin	Brain	Limits appetite over long term
Osseous tissue	Osteocalcin	Pancreas, adipose tissue	Stimulates pancreatic beta cells to multiply, increases insulin secretion, enhances insulin sensitivity of various tissues, and reduces fat deposition
Placenta	Estrogen, progesterone	Many tissues of mother and fetus	Stimulate fetal development and maternal bodily adaptations to pregnancy; prepare mammary glands for lactation

Learning Objectives

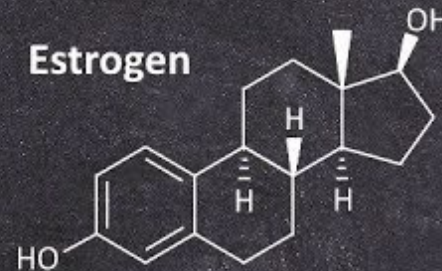
- Hormone chemistry?
- What are the different chemical properties of hormones?
- What are hormones mechanisms of actions?

TYPES OF HORMONES

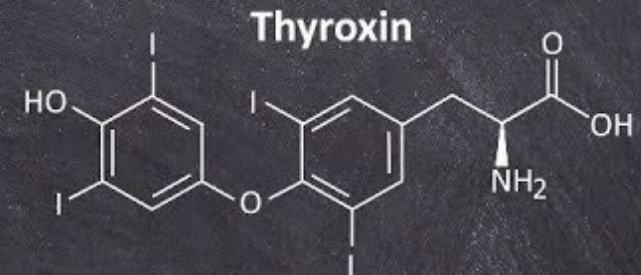
PEPTIDE HORMONES



STEROID HORMONES



AMINE HORMONES



Hormone Chemistry

Three Chemical Classes

Steroids // metabolized from cholesterol

estrogens, progesterone, testosterone, cortisol, corticosterone, aldosterone, DHEA, and calcitriol

Peptides (and glycoproteins) // created from chains of amino acids

secreted by pituitary and hypothalamus

oxytocin, antidiuretic hormone, releasing and inhibiting hormones, and anterior pituitary hormones

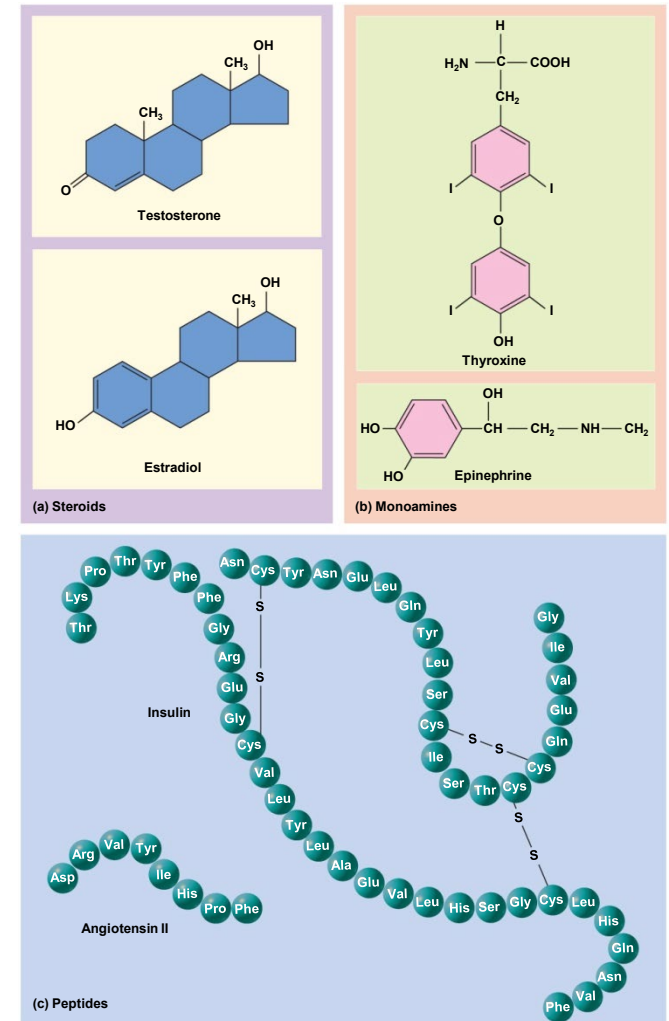
Hormone Chemistry

Three Chemical Classes

Monoamines (biogenic amines)

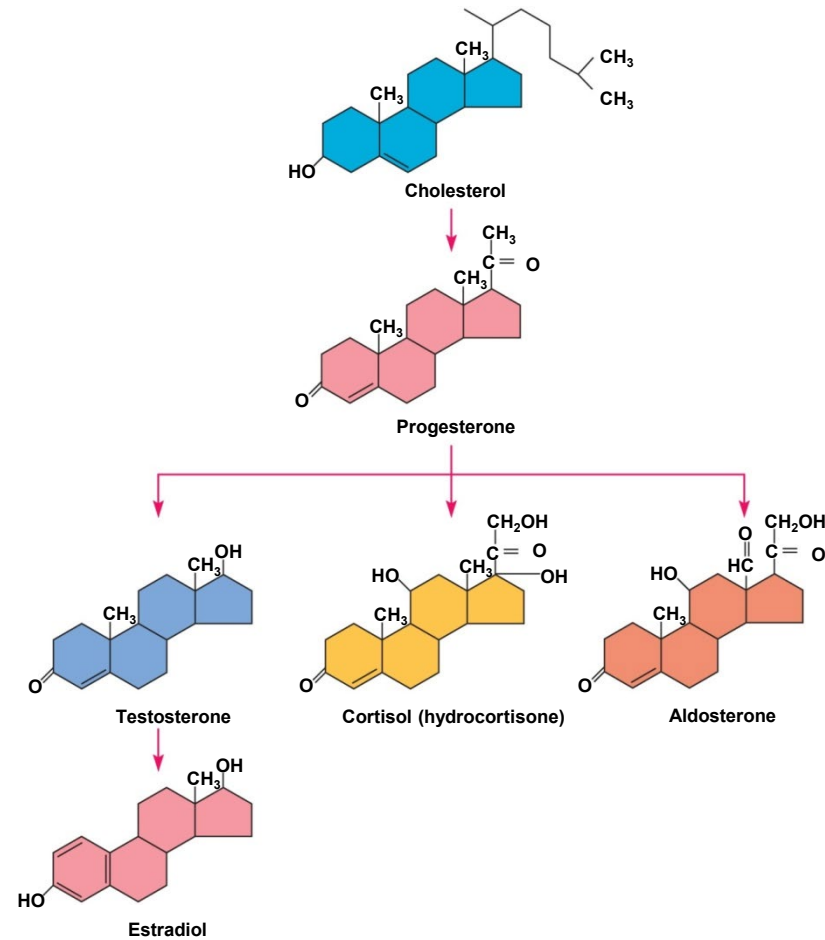
- derived from amino acids
- secreted by adrenal, pineal, and thyroid glands
- epinephrine, norepinephrine, melatonin, and thyroid hormone

Note: all hormones are made either from cholesterol or amino acids (with carbohydrate added to make glycoproteins).



Hormone Synthesis

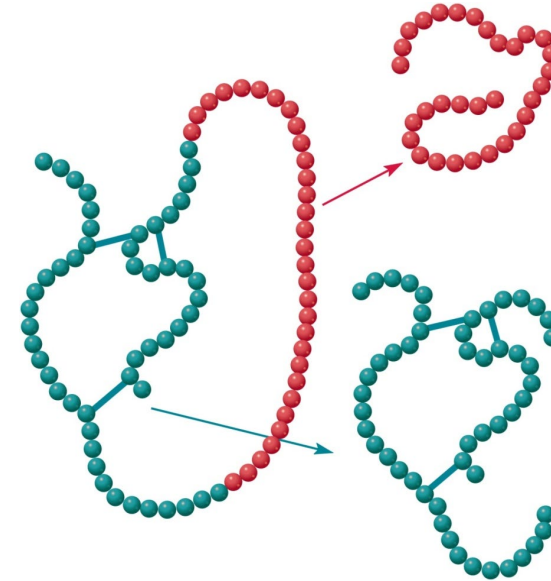
Steroid Hormones



synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone

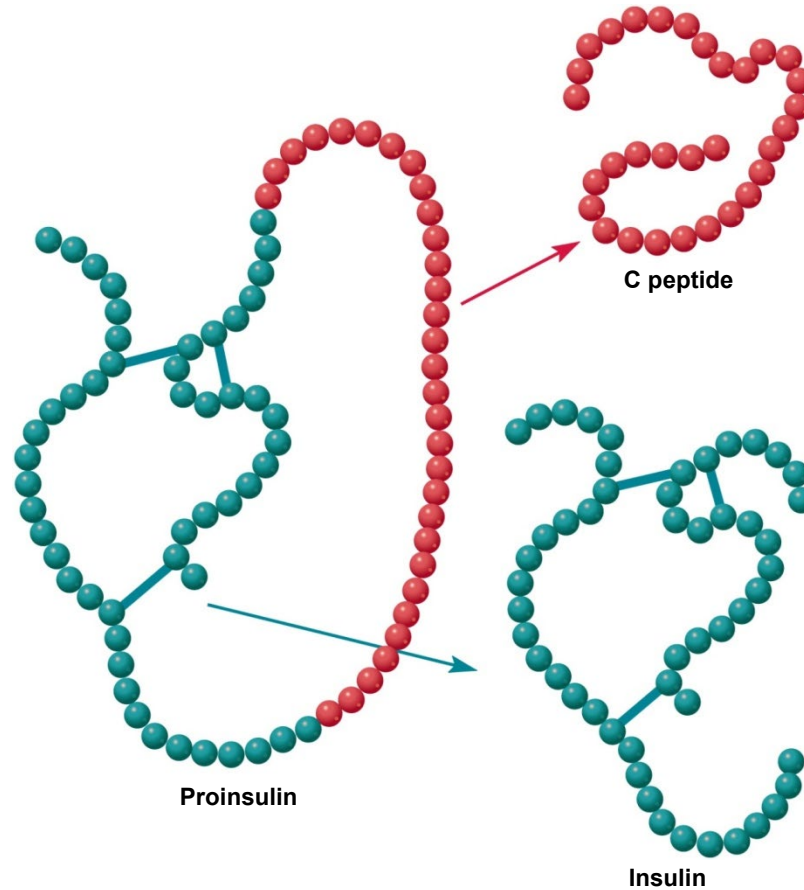
Peptide Hormones

- synthesized using same metabolic pathway used by other protein // example insulin
- first formed as an inactive **pre-prohormone**
- several amino acids in peptide function as a signal that guides it into cisterna of rough endoplasmic reticulum
- signal peptide removed to form **prohormone**
- Golgi apparatus does final transformation to **hormone** then packages hormone for secretion



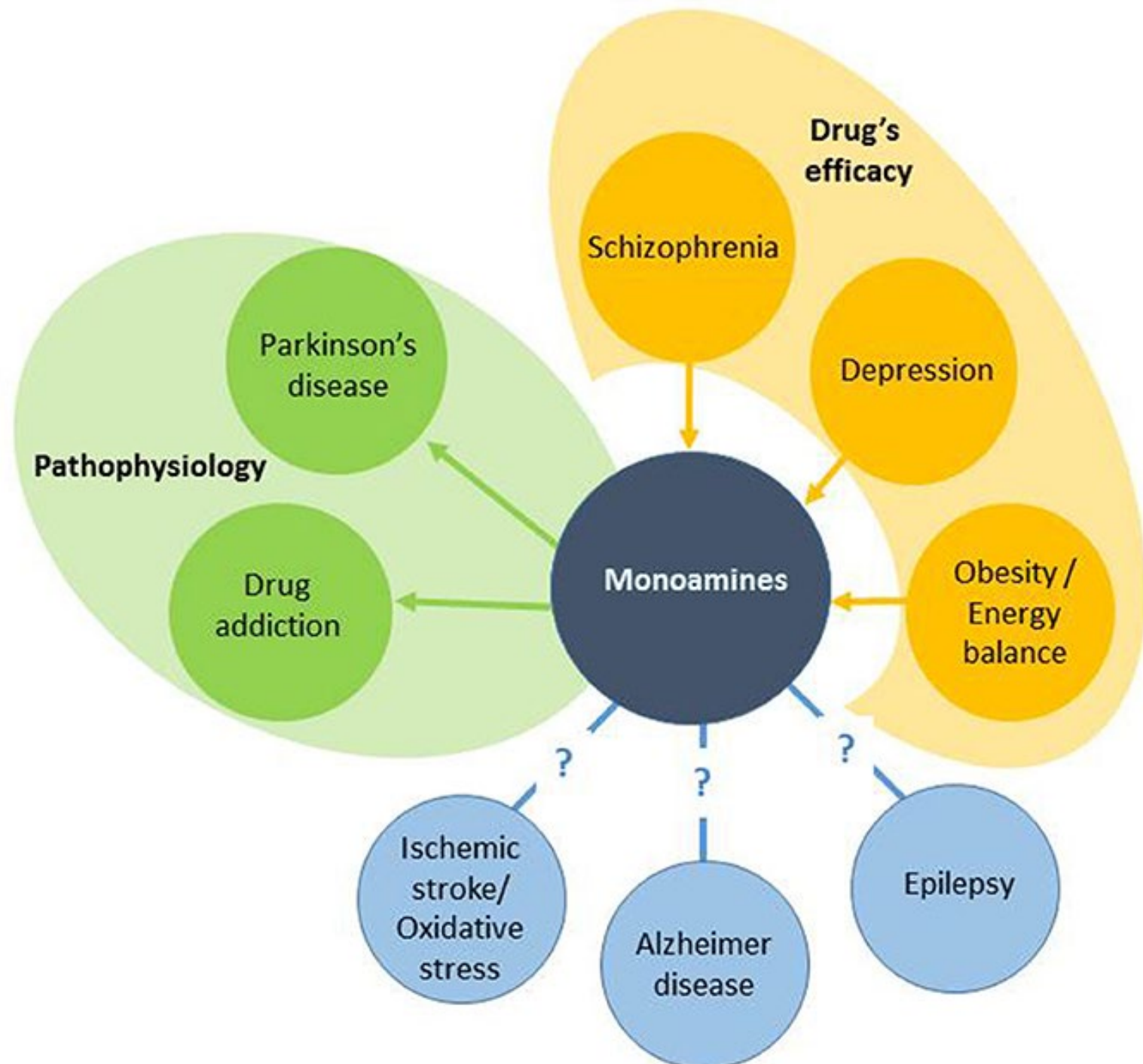
Hormone Synthesis: Insulin

- begins as **pre-proinsulin**, then becomes **proinsulin**
- when connecting peptide is removed, two polypeptide chains are formed that make up insulin

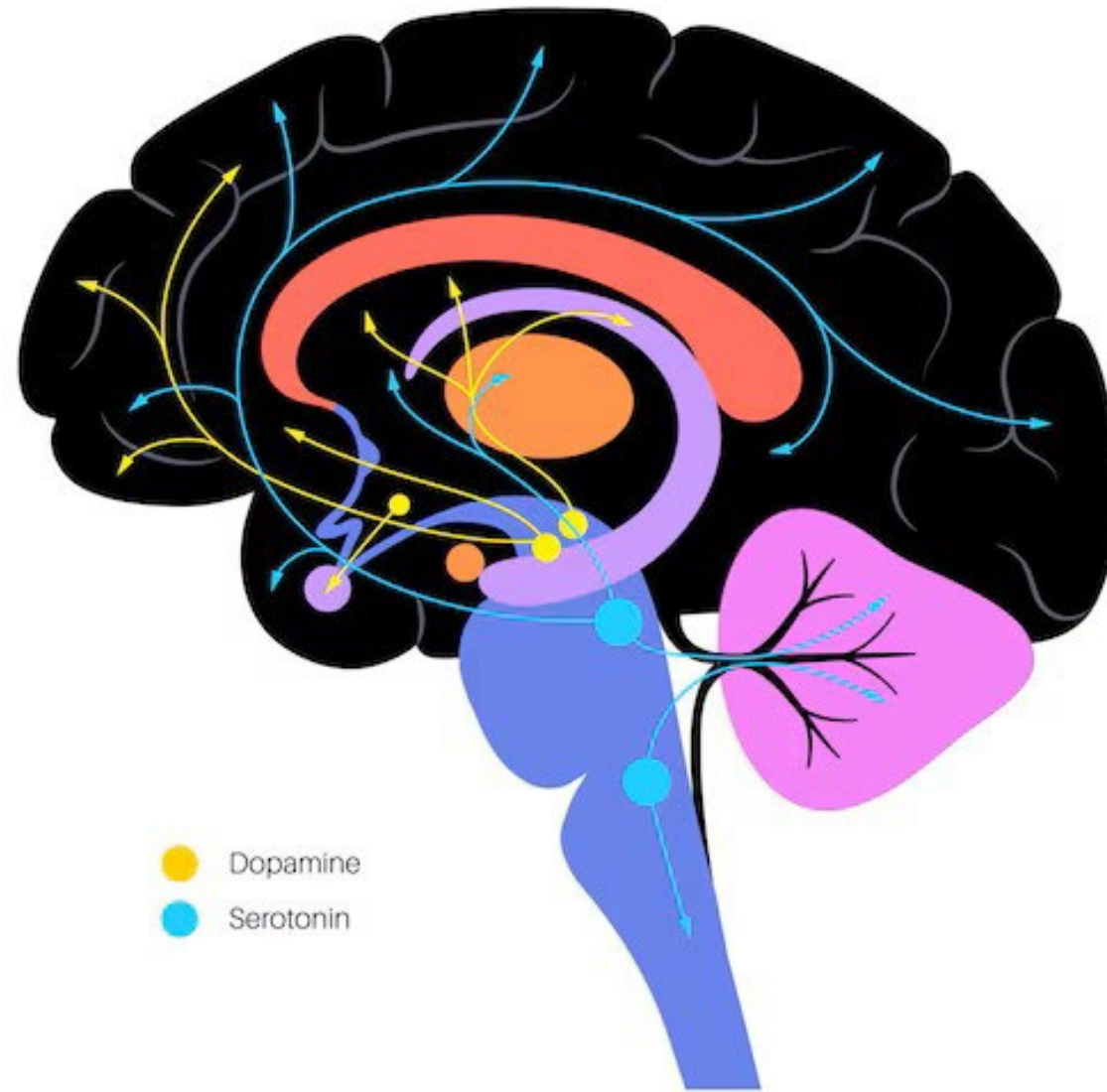


Monoamines

- Dopamine, serotonin, and melatonin are monoamine hormones synthesized from amino acid
- These are important CNS molecules
- **Melatonin** (the hormone released by the pineal gland) is synthesized from the amino acid tryptophan
- What holiday meal has a high concentration of tryptophan?
- Tryptophan is first transformed to the brain neurotransmitter serotonin then serotonin is transformed into melatonin // serotonin major factor affecting mood.



DOPAMIN AND SEROTONIN



Hormone Transport



Most of the monoamine and peptide hormones are **hydrophilic** // mix easily with blood plasma

Steroids and thyroid hormone are **hydrophobic**

Hydrophobic hormones need to bind to transport proteins (albumins and globulins which are synthesized by the liver)

“bound hormones” have certain advantages

- have longer half-life
- protected from liver enzymes
- protected from kidney filtration
- from being broken down by enzymes in the plasma

hydrophobic hormones detach from their transporter in capillaries then the hormone cross capillaries to reach target cell

Hormone Transport

Thyroid hormone is derived from protein, but is the exception to the rule /// hormone made from amino acid but TH is hydrophobic and must bind to transport proteins in the plasma

- Transporters maybe albumin, thyretin and TGB (thyroxine-binding globulin)
- more than 99% of circulating TH is protein bound

Steroid hormones bind to globulins // example - transcortin is the transport protein for cortisol

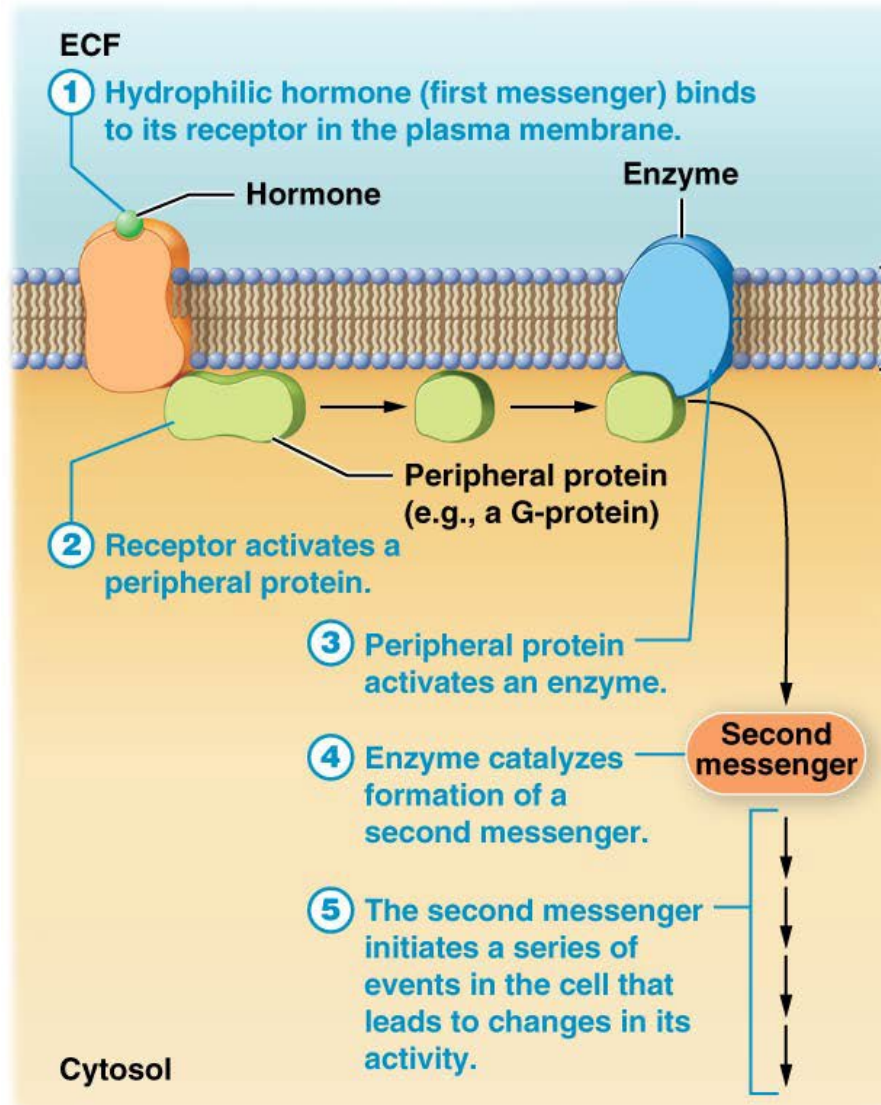
Aldosterone // short half-life

- 85% unbound
- 15% binds weakly to albumin and others

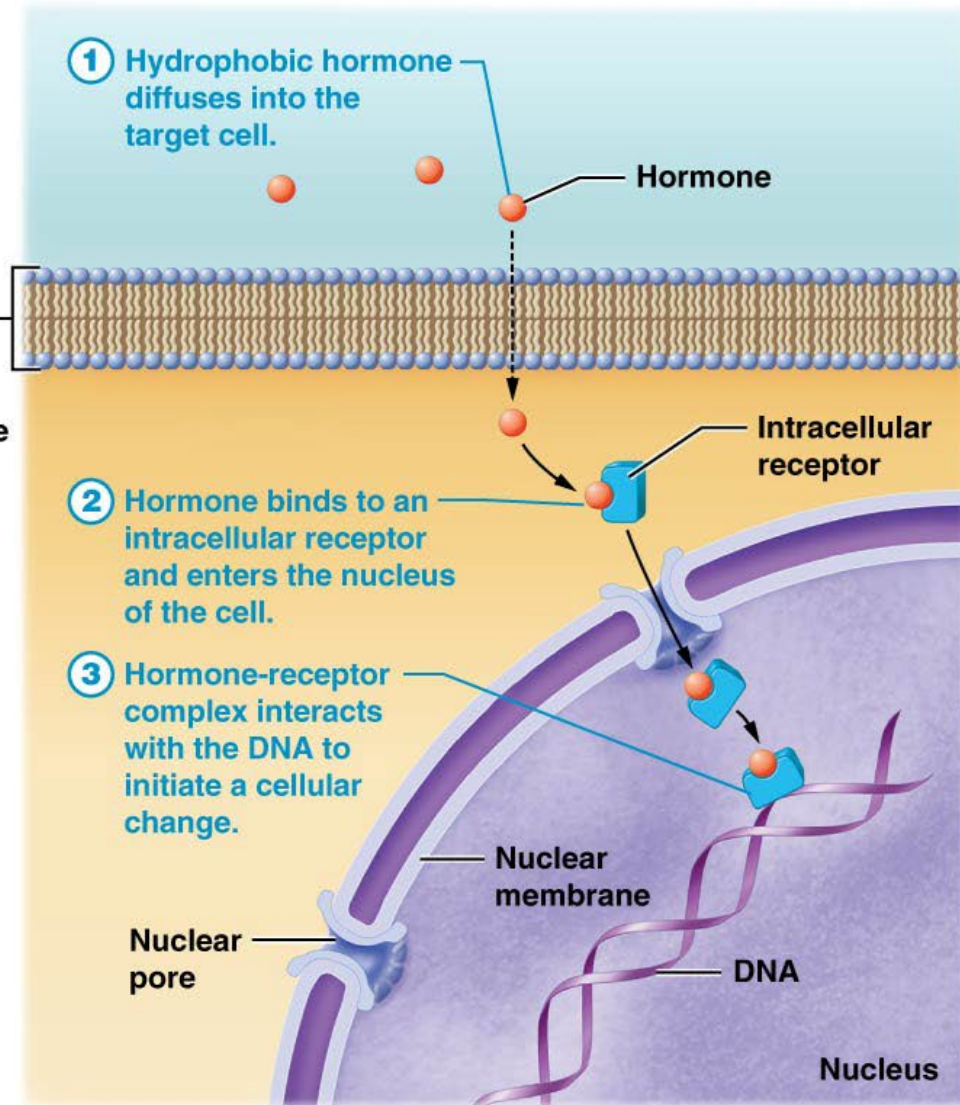
Hormone Receptors

- Hormones stimulate target cells with receptors (docking stations) matched to the hormone (i.e. think lock and key)
- **Receptors** are protein or glycoprotein molecules:
 - located on plasma membrane for hydrophilic hormones
 - located in the nucleoplasm if hormone is hydrophobic
- A receptor functions as a **switch to turn on a metabolic pathway** after the hormone binds to the receptor
- Target cells may have a few thousand receptors for the hormone // concentration of receptors may change (up or down regulated)
- The receptor-hormone interactions exhibit **specificity** and **saturation**
 - each receptor is “**specific**” and matched to only one hormone
 - “**saturated**” when all receptor molecules are occupied by hormone molecules

Mechanisms of action of hydrophilic and hydrophobic hormones. This figure presents examples of how these hormones can work.



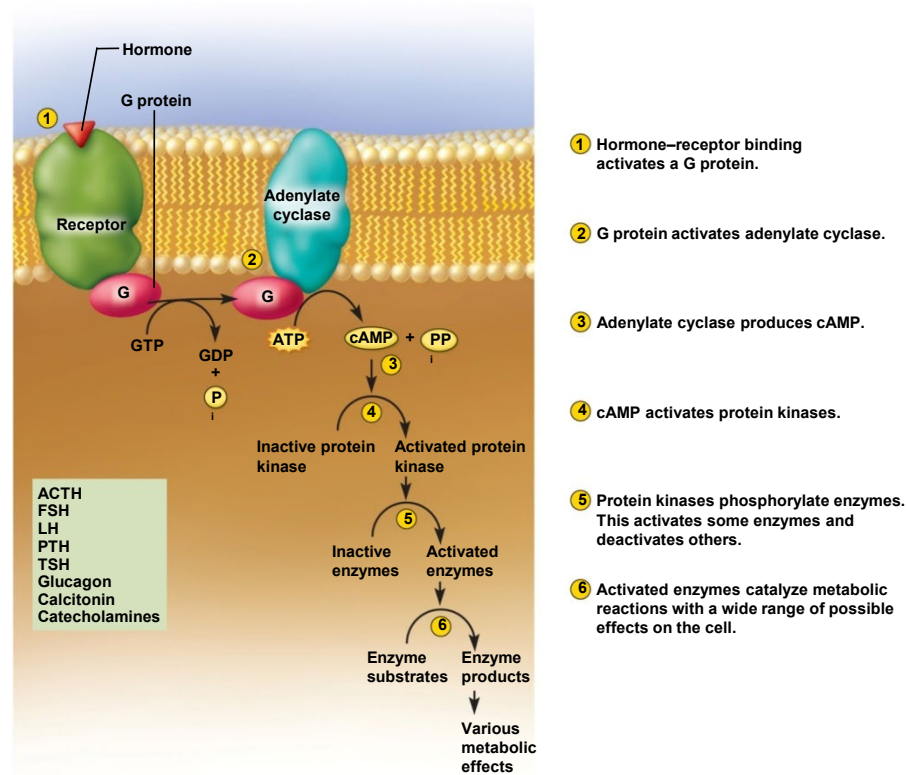
(a) Hydrophilic hormone and second-messenger system



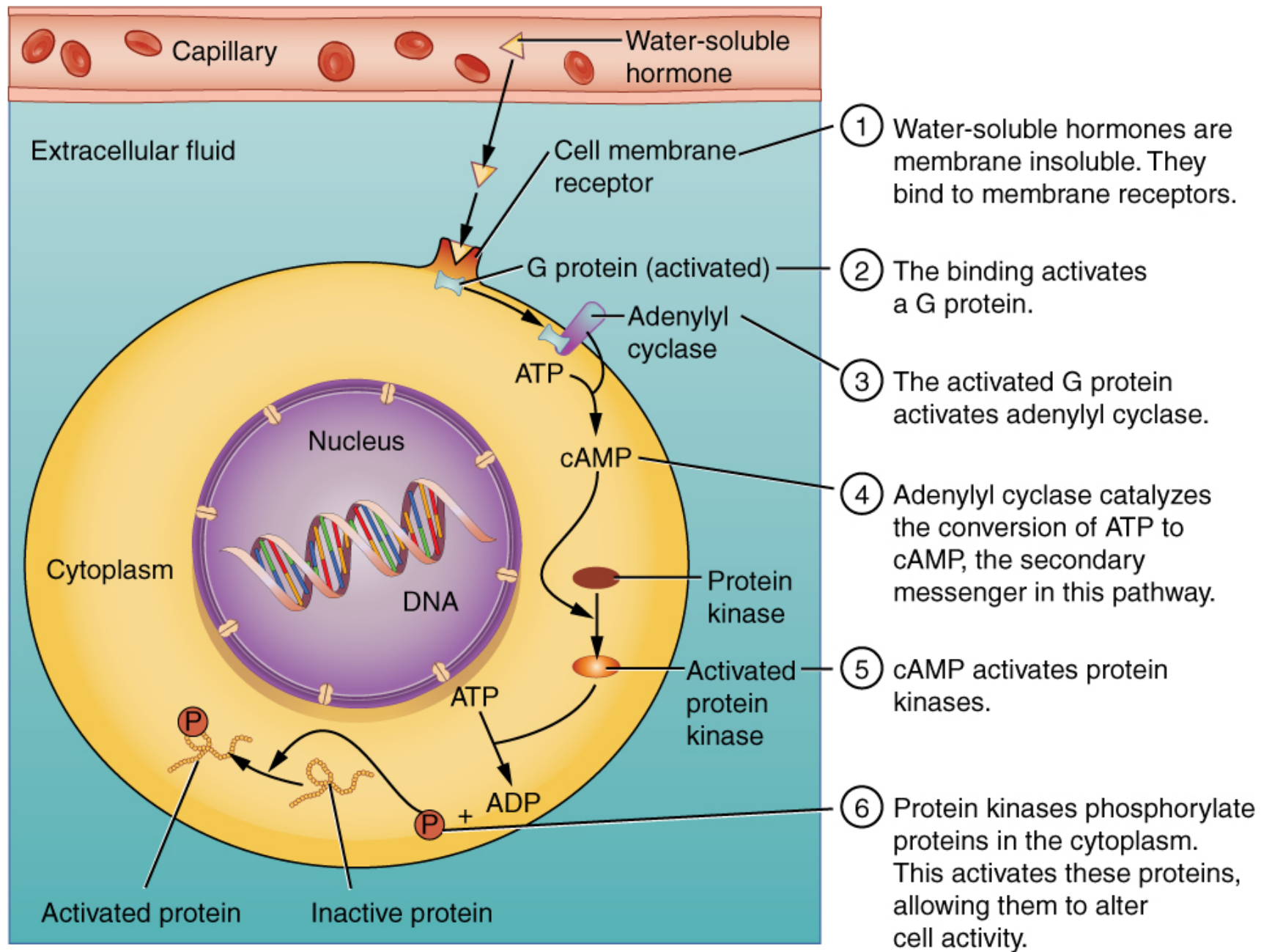
(b) Hydrophobic hormone and intracellular receptor mechanism

Peptides and Catecholamines Are Hydrophilic Molecules (Require Metabotropic Receptors)

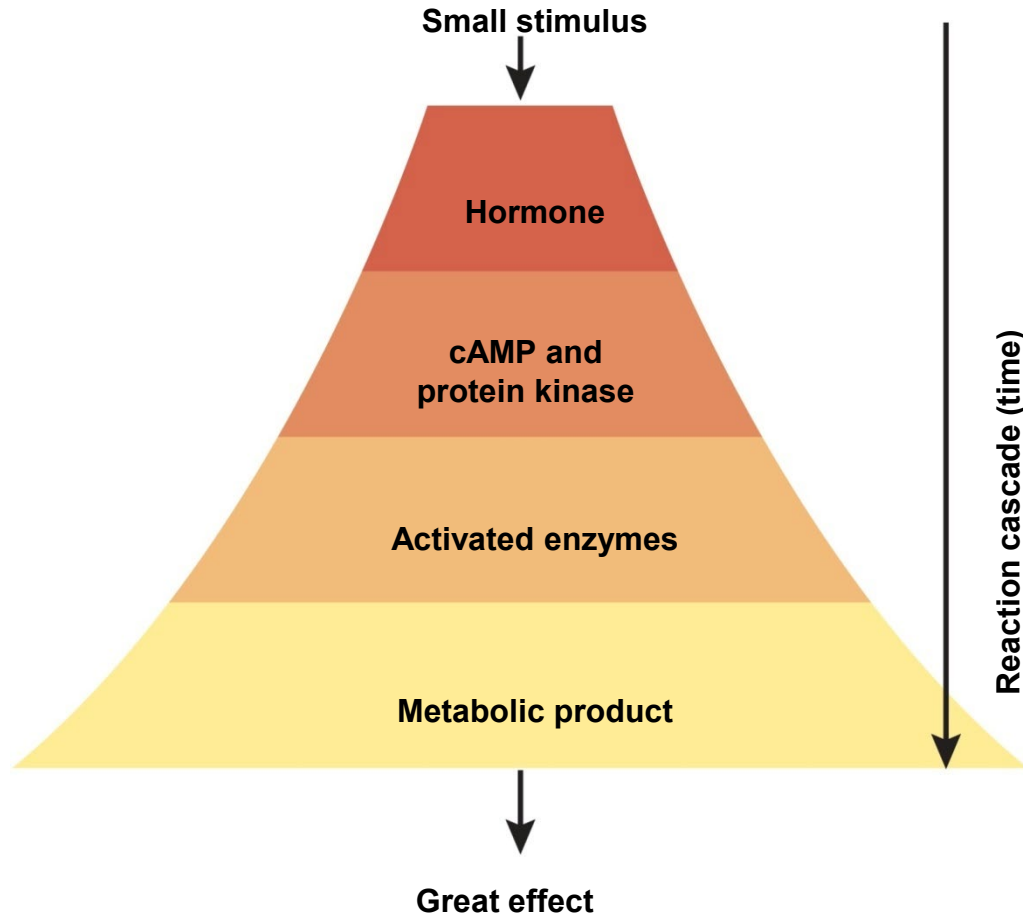
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- Hormone binds to cell-surface receptor
- receptor linked to second messenger system on other side of the membrane
- activates **G protein** which
- activates adenylate cyclase
- produces cAMP /// activates or inhibits enzymes
- possible metabolic reactions:
 - synthesis
 - secretion
 - change membrane potentials



Enzyme Amplification



- hormones are potent molecules
- one hormone molecule can **trigger the synthesis of many enzyme molecules.**
- very small stimulus produces very large effect
- low circulating hormone concentrations may cause great metabolic effect

Control of Pituitary Secretion

Hormone secretion rate is not constant

- regulated by hypothalamus and other brain centers
- negative or positive feedback mechanisms by target organs

Anterior pituitary lobe secretions

- controlled by releasing hormones or inhibiting hormones from hypothalamus

Example = in cold weather, pituitary stimulated by hypothalamus to release TSH // leads to increase in metabolism and more Na-K-ATPase pumps placed in plasma membrane // this results in more heat production // part of the thermoregulation mechanism // **homeostatic mechanism**

Control of Pituitary Secretion

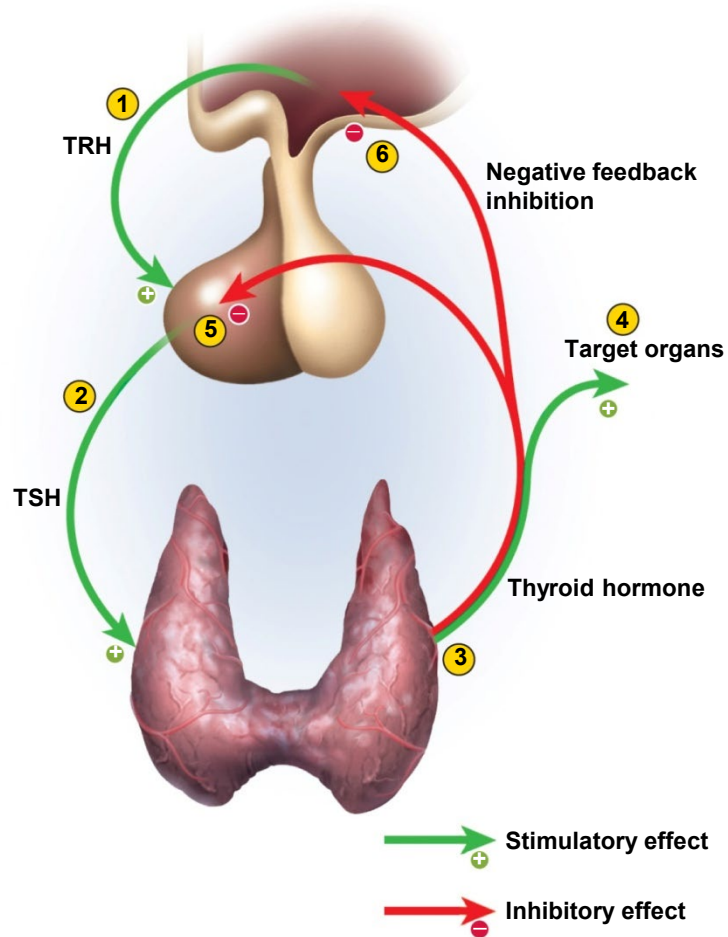
Posterior lobe control – different mechanisms for oxytocin and ADH ///
oxytocin release uses a neuroendocrine reflex // Anti diuretic hormone
release is regulated by increase in blood osmolarity.

Oxytocin: **neuroendocrine reflex** - hormone release in response to nervous
system signals (childbirth and mammary gland's milk discharge)

- **suckling infant** → stimulates nerve endings → hypothalamus →
posterior lobe → oxytocin → milk ejection
- hormone may also be released in response to **higher brain centers** //
milk ejection reflex may be triggered by a baby's cry

Note: neuroendocrine reflex also regulates childbirth (parturition = labor)

Negative and Positive Feedback Regulations



negative feedback // e.g. thyroid regulation

An increased in the target organ's hormone levels inhibits release of TSH

positive feedback // e.g. oxytocin

- childbirth
- stretching cervix
- increases OT release
- more contractions
- self amplifying continues until delivery

Hormonal Interactions

- Permissive effect
 - a second hormone, strengthens the effects of the first
 - thyroid strengthens epinephrine's effect upon lipolysis
- Synergistic effect
 - two hormones acting together for greater effect
 - estrogen & LH are both needed for oocyte production
- Antagonistic effects
 - two hormones with opposite effects
 - insulin promotes glycogen formation & glucagon stimulates glycogen breakdown

Synergistic

Hormones work together to produce greater effect.



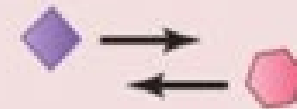
Permissive

First hormone allows action of second hormone.

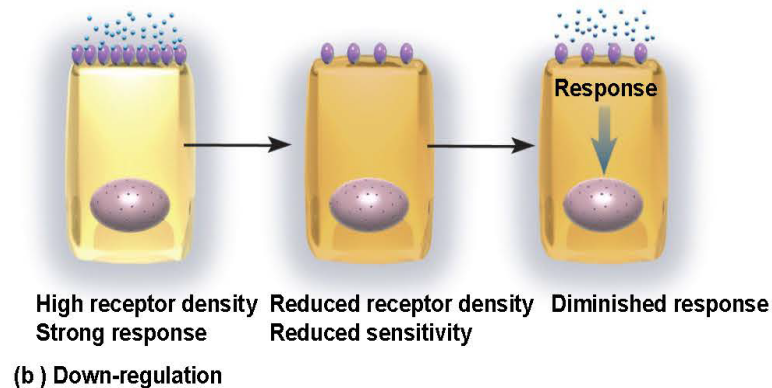
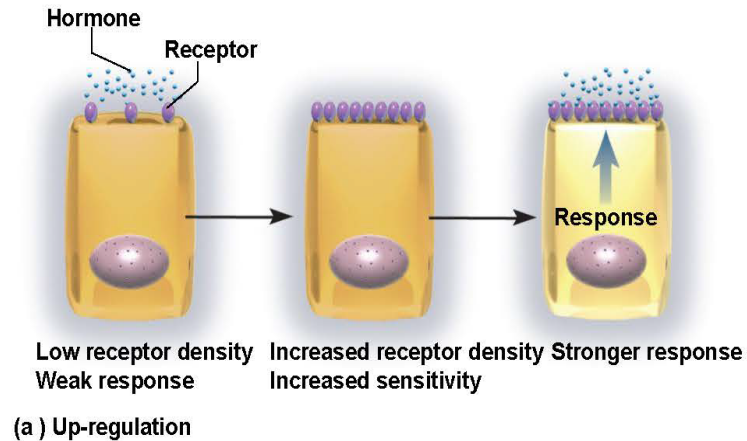


Antagonistic

One hormone causes opposite effect of another hormone.



How Can Target Tissue Change Sensitivity to Hormones?



- target cell sensitivity adjusted by changing the number of receptors
- **up-regulation** means number of receptors is increased
 - sensitivity is increased
- **down-regulation** reduces number of receptors
 - cell less sensitive to hormone
 - may occur with long-term exposure to high hormone concentrations

Hormone Clearance

hormone signal **must be turned off** after the hormone has served its purpose

most hormones are **taken up and degraded** by liver then excreted in the bile

Other hormones **filtered by kidney then excreted in the urine**

metabolic clearance rate (MCR)

- rate of hormone removal from the blood

- half-life** - time required to clear 50% of hormone from the blood

- faster the MCR, the shorter is the half-life