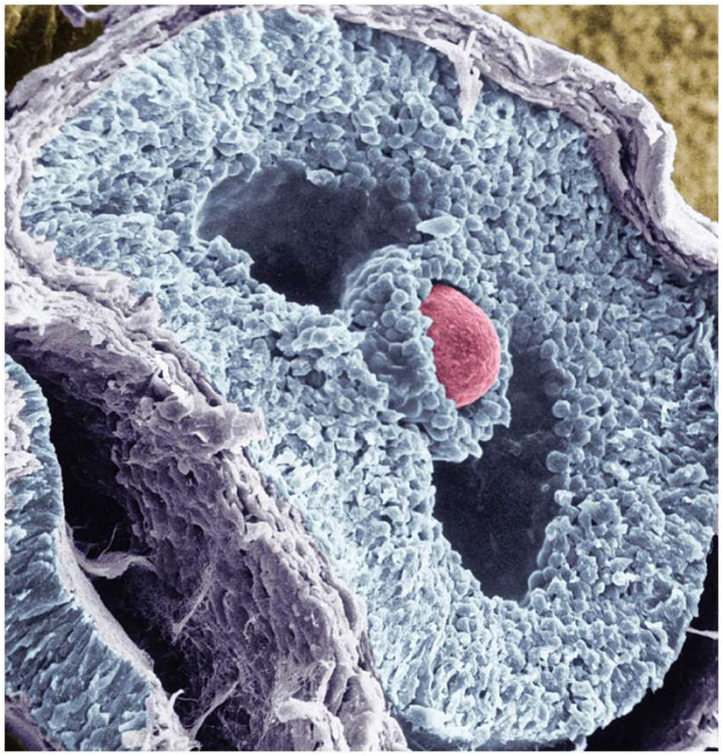
Chapter 18

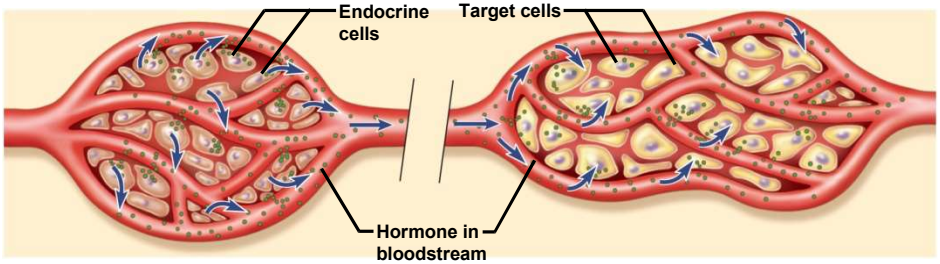
An Introduction to the Endocrine System

Hormone Chemistry



Endocrine System Components

- **endocrine system** – made up of glands that secrete hormones, target tissues with receptors matched to hormones and blood that transports hormones to target tissue



(b) Endocrine system

- **endocrine glands** – organs that are traditional sources of hormones (single cells may secrete hormones)
- **hormones** - chemical messengers that are transported by the bloodstream and change target tissue's cellular metabolism
- **endocrinology** – the study of this system and the diagnosis and treatment of its disorders

Key Steps: Know This!

1. Hormone synthesized by glands.
2. Hormone released into blood.
3. Hormone circulates within circulatory system
4. Hormone leaves blood, diffuse to target tissue.
5. Hormone binds to receptor
6. Hormone changes metabolism of target tissue.

Some Endocrine Organs Hard to Classify

- Pancreas (mixed gland)
  - Exocrine – digestive enzymes
  - Endocrine – insulin / glucagon
- Hepatocytes (liver cells) defy rigid classification
  - releases hormones
  - releases bile into ducts
  - releases albumin and blood-clotting factors into blood (not hormones)

Comparison of Nervous and Endocrine Systems

- **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 - general, widespread effects (many organs)

Comparison of Nervous and Endocrine Systems

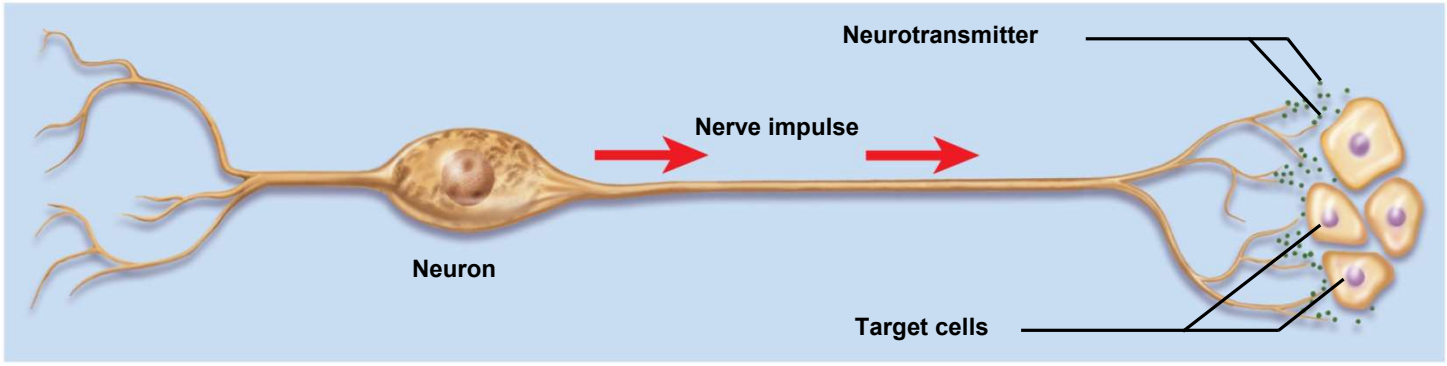
- several chemicals function as both hormones and neurotransmitters // norepinephrine, cholecystokinin, thyrotropin-releasing hormone, dopamine and antidiuretic hormone

- some hormones secreted by neuroendocrine cells (neurons) that release their secretion into the bloodstream // oxytocin and catecholamines

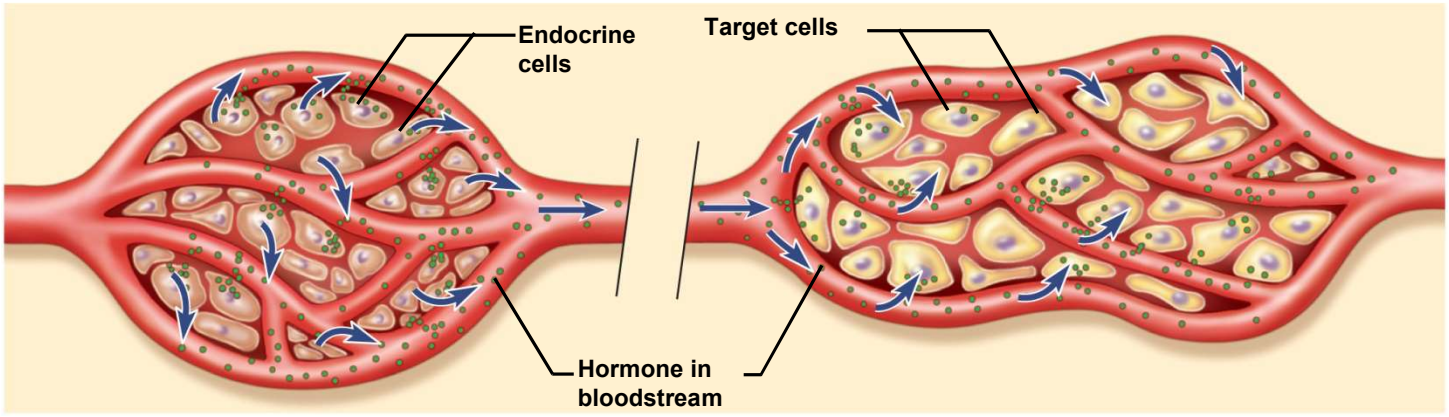
- both systems with overlapping effects on same target cells // norepinephrine and glucagon cause glycogen hydrolysis in liver

- systems regulate each other // neurons trigger hormone secretion // hormones stimulate or inhibit neurons

Communication by the Nervous and Endocrine Systems

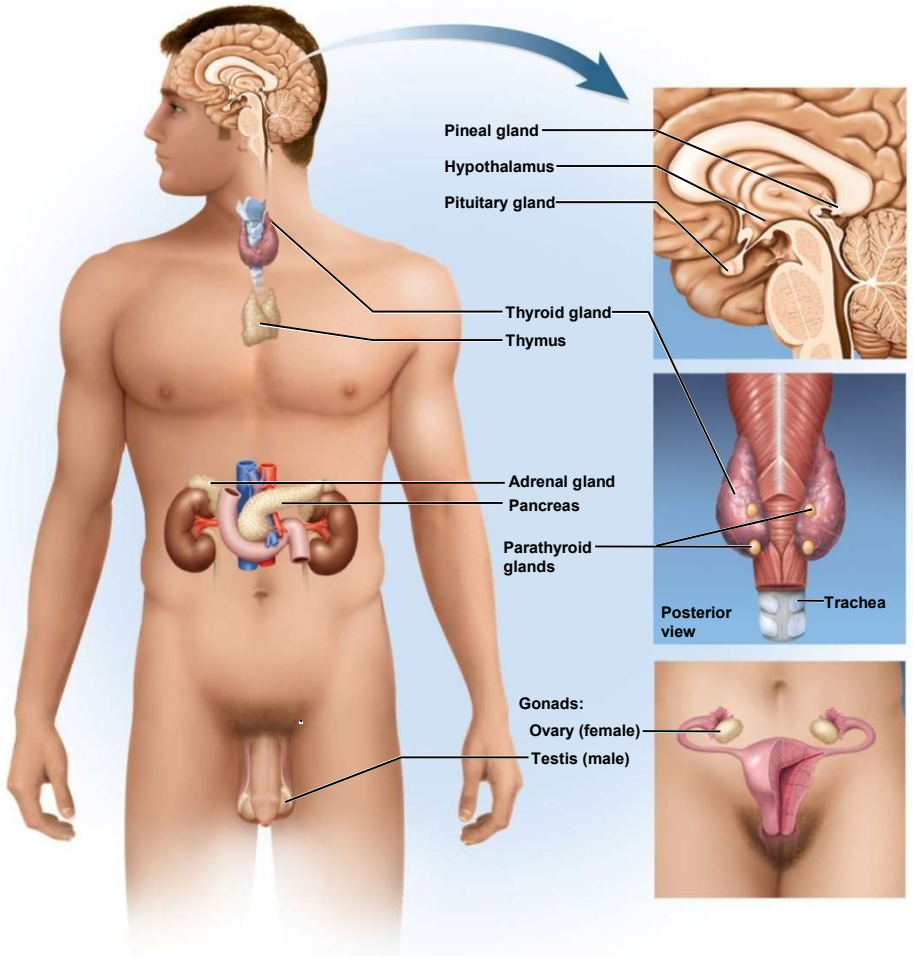


(a) Nervous system



(b) Endocrine system

Major Endocrine Organs



organs of endocrine system / know these (lab & lecture)

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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	Pancreas, gallbladder	Inhibits release of bile and digestive enzymes
	Gastrin	Stomach	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	Small intestine, liver	Promotes iron absorption and mobilization
	Insulin-like growth factor I	Many tissues	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

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TABLE 17.2 Names and Abbreviations for Hormones

Abbreviation	Name	Source
ACTH	Adrenocorticotropic 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

Learning Objectives

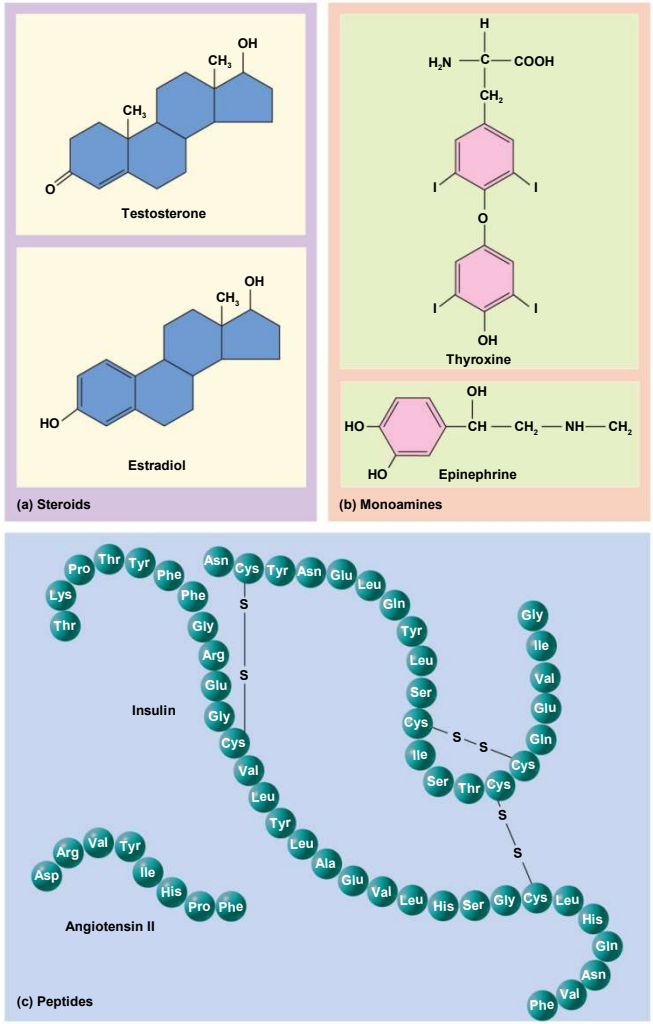
- **Hormone chemistry.**

- **What are the different chemical properties of hormones and what are their mechanisms of actions?**

Hormone Chemistry // Three Chemical Classes

- **steroids**
  - derived from cholesterol
  - secreted by gonads and adrenal glands
  - 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

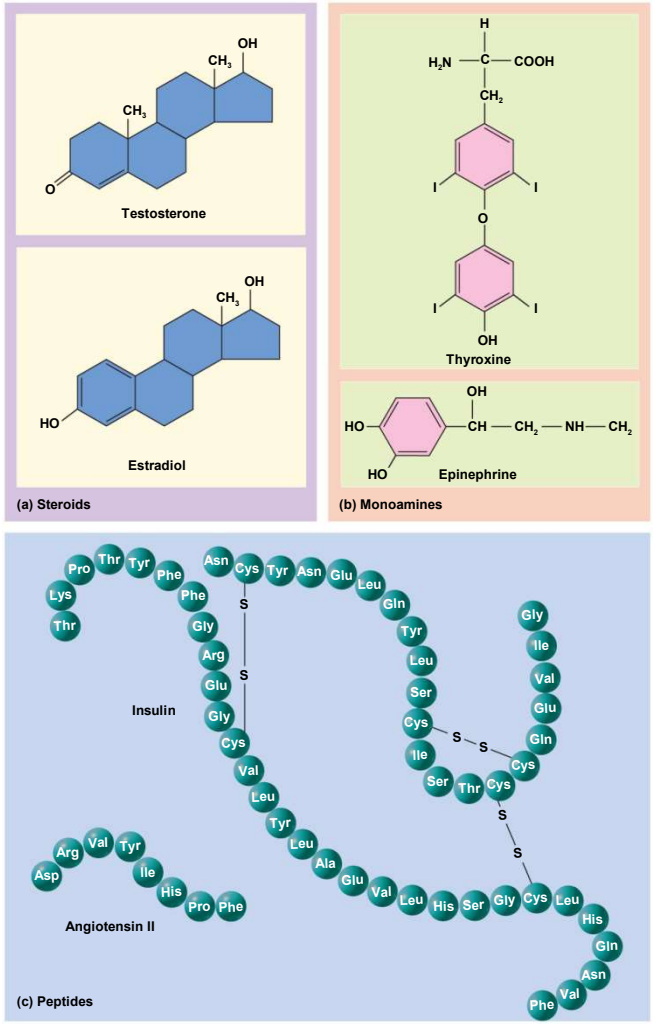


Hormone Chemistry

– **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 from either cholesterol or amino acids (with carbohydrate added to make glycoproteins).*



Hormone Synthesis: Steroid Hormones

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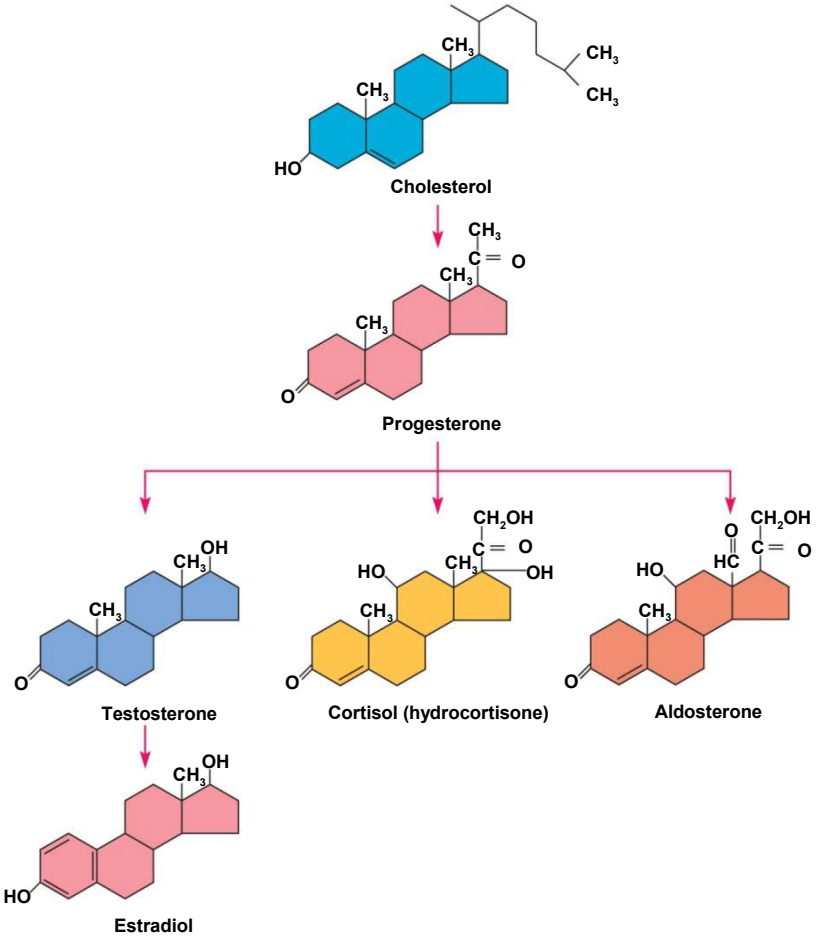

- synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone

Peptides

- synthesized using same metabolic pathways as any other proteinprotein
- 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 does final transformation to **hormone** packaged 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

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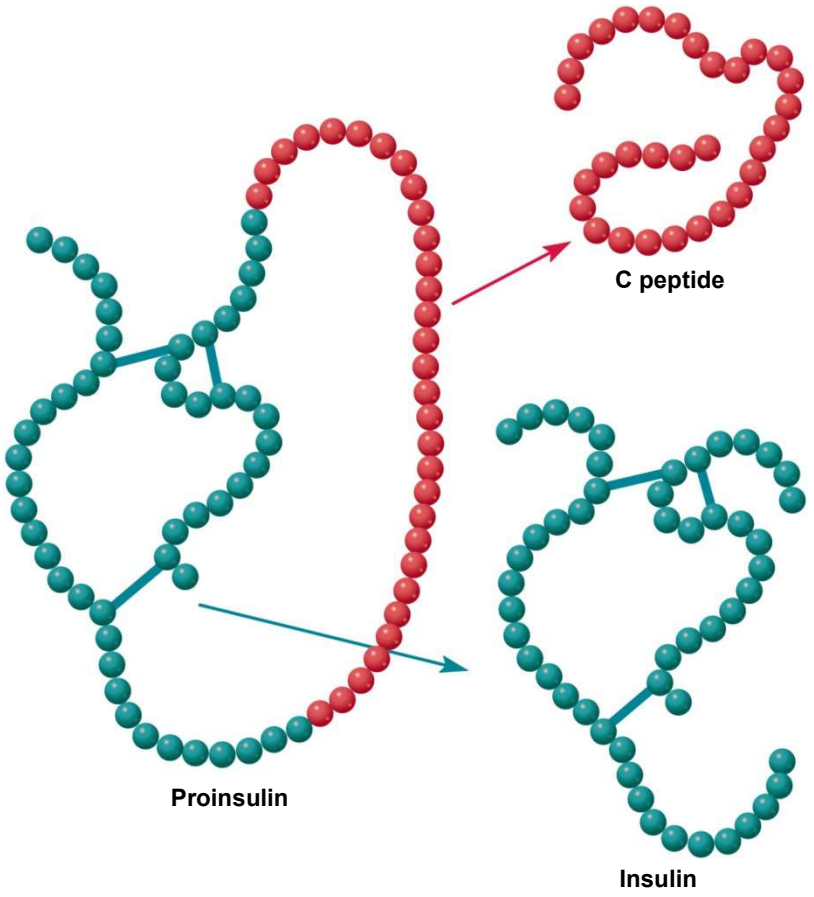


Monoamines

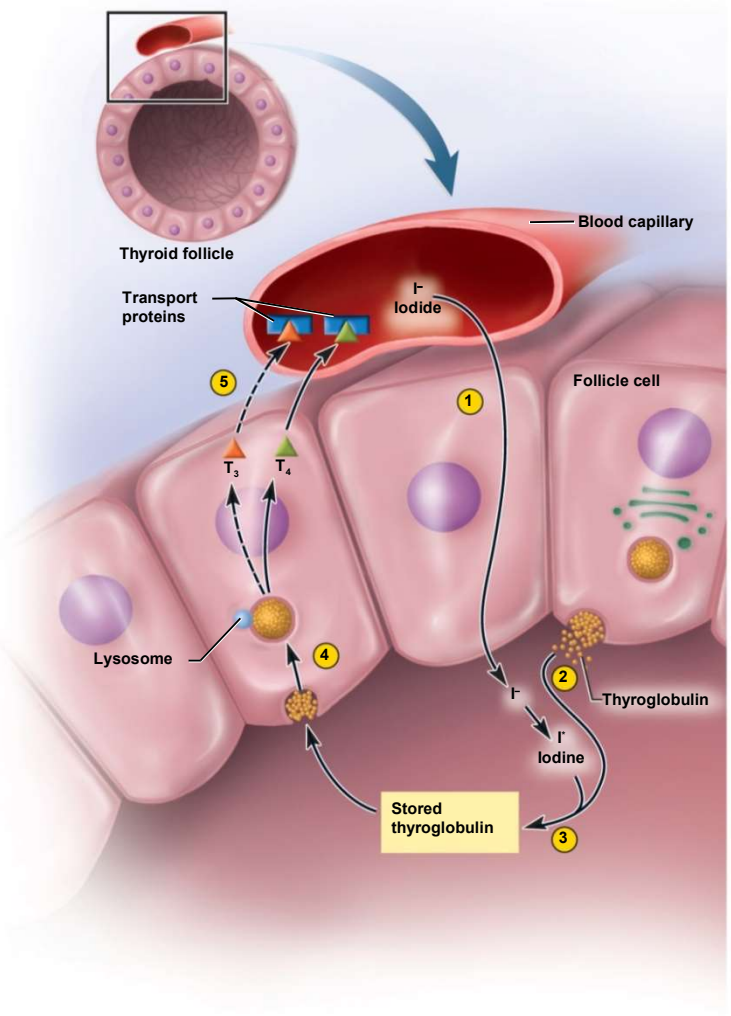
- These are synthesized from amino acid

- E.g. /// **Melatonin** (the hormone released by the pineal gland) is synthesized from the amino acid tryptophan /// tryptophan transformed into the brain neutrotransmitter seratonin which is then transformed into melatonin

- E.g. /// thyroid hormone is composed of 2 tyrosines (tyrosine is an amino acid)

Thyroid Hormone Synthesis

(Note: this is not on exam)



1. Iodide absorption and oxidation
2. Thyroglobulin synthesis and secretion
3. Iodine added to tyrosines of thyroglobulin
4. Thyroglobulin uptake and hydrolysis
5. Release of T_4 and a small amount of T_3 into the blood

T_3 and T_4 Synthesis (not on exam)

- **Follicular cells**
  - absorb **iodide** (I^-) **ions** from blood and store in lumen as a reactive form of iodine
  - synthesize **thyroglobulin** and store in lumen // forms colloid // contains lots of tyrosine
  - tyrosine and iodine combine to form thyroxine (T_4) bound to thyroglobulin
  - stored in follicle

T_3 and T_4 Synthesis (not on exam)

- **TSH**
  - stimulates follicular cells to remove T_4 from thyroglobulin for release into plasma
  - most T_3 is produced in liver or by target cells removing an iodine from circulating T_4
  - 95% T_4 and 5% T_3

Hormone Transport

- most monoamines and peptides 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 longer half-life
    - protected from liver enzymes and kidney filtration
    - transport proteins protect circulating hormones
    - being broken down by enzymes in the plasma and liver
    - being filtered out of the blood by the kidneys
  - only hydrophobic hormones that become unbound are able to leaves capillaries to reach target cell

Hormone Transport

- thyroid hormone /// these are an exception to the rule /// protein based hormone but binds to three transport proteins in the plasma
  - albumin, thyretin and TGB (thyroxine-binding globulin)
  - more than 99% of circulating TH is protein bound
- Some steroid hormones bind to globulins // transcortin is the transport protein for cortisol
  - Aldosterone // short half-life
    - 85% unbound
    - 15% binds weakly to albumin and others

Hormone Receptors

- hormones stimulate only those cells that have receptors for them
- receptors are protein or glycoprotein molecules: // on plasma membrane, in the cytoplasm, or in the nucleus
- receptors act like switches turning on metabolic pathways when hormone binds to them
- usually each target cell has a few thousand receptors for a given hormone
- receptor-hormone interactions exhibit specificity and saturation
  - specific receptor for each hormone
  - saturated when all receptor molecules are occupied by hormone molecules

Hormone Mode of Action

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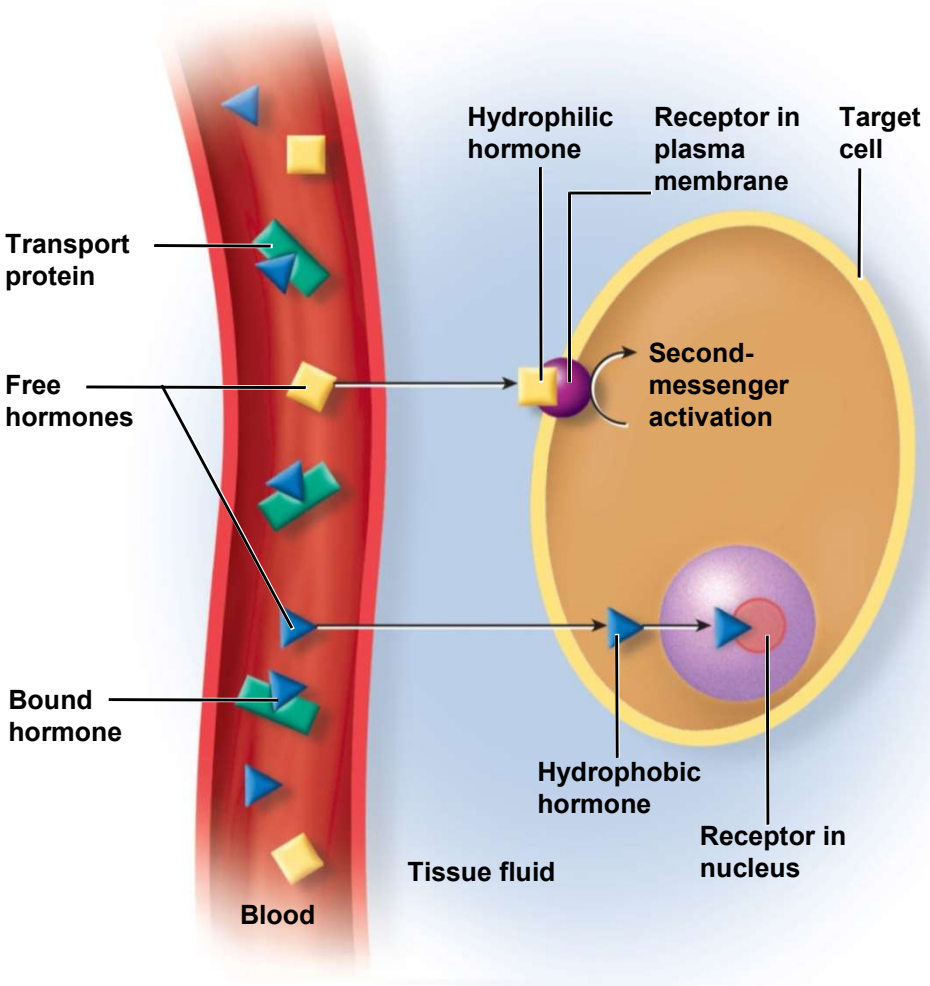

- hydrophobic hormones
  - penetrate plasma membrane and enter nucleus
  - act directly on the genes changing target cell physiology
  - estrogen, progesterone, thyroid hormone act on nuclear receptors
  - take several hours to days to show effect due to lag for protein synthesis

Hormone Mode of Action

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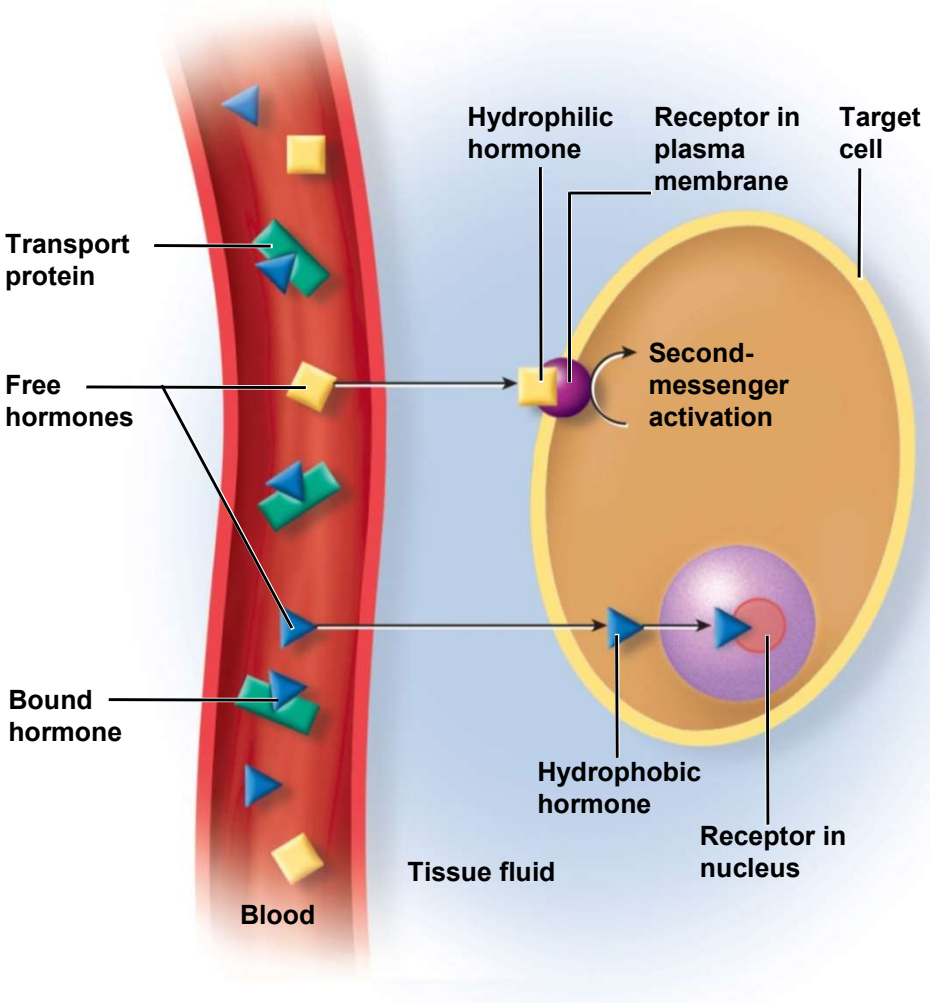
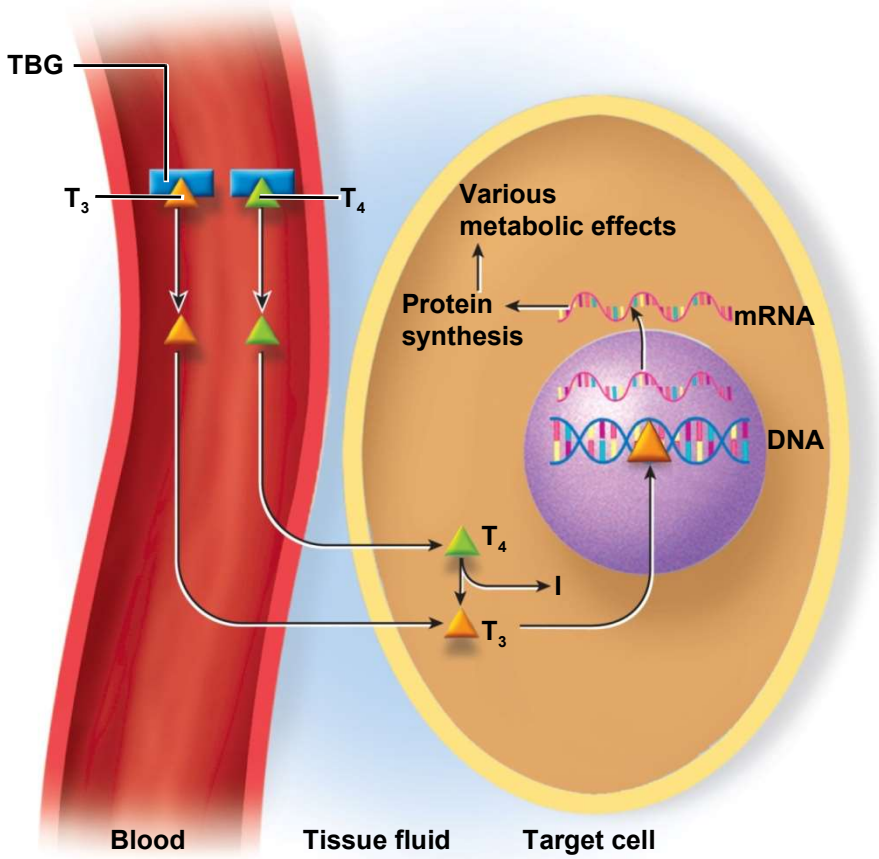


- hydrophilic hormones
  - cannot penetrate into target cell
  - must stimulate physiology indirectly
  - Second messenger systems // also called metabotrophic

Thyroid Hormone



- thyroid hormone <u>enters target cell by diffusion</u> – mostly as T_4 with little metabolic effect
- <u>within target cell, T_4 is converted to more potent T_3</u>
- T_3 enters target cells and binds to receptors in chromatin
- activates genes
  - make a muscle protein (myosin) enhancing cardiac muscle response to sympathetic stimulation
  - strengthening heartbeat

Peptides and Catecholamines: Hydrophilic
(Metabotrophic Mechanism)

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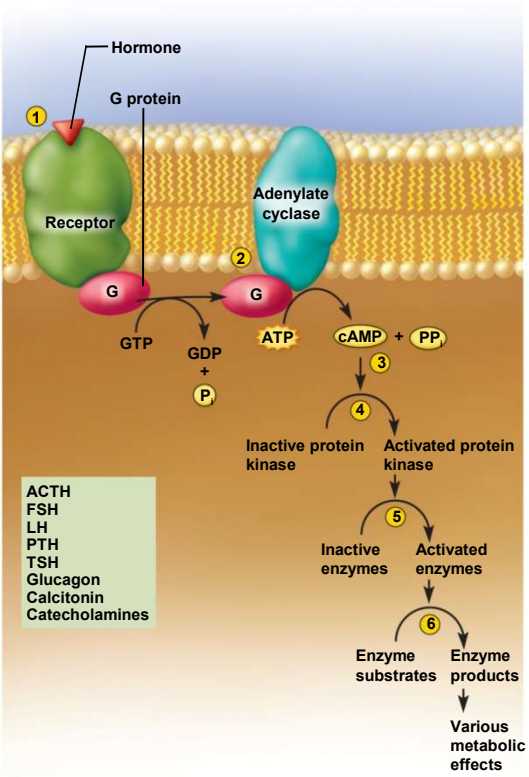
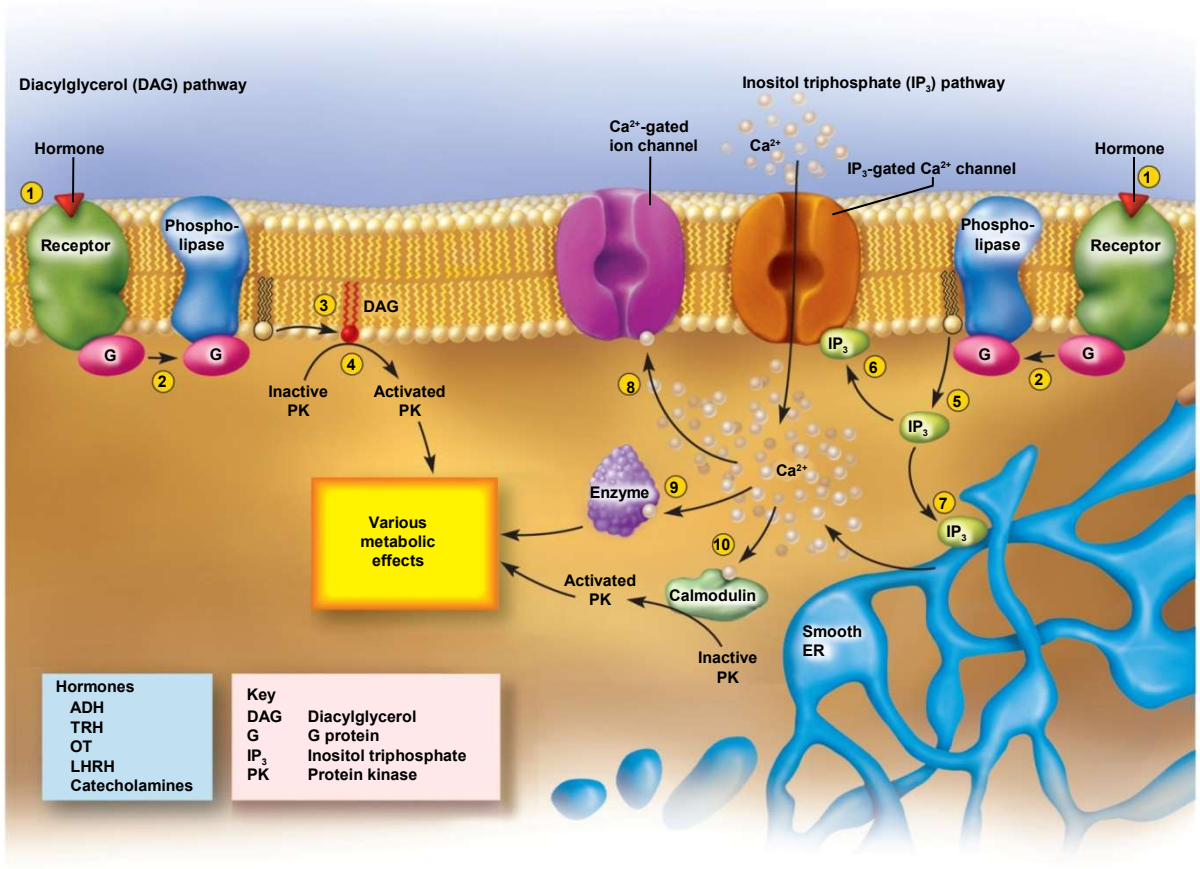


1. Hormone–receptor binding activates a G protein.
2. G protein activates adenylate cyclase.
3. Adenylate cyclase produces cAMP.
4. cAMP activates protein kinases.
5. Protein kinases phosphorylate enzymes. This activates some enzymes and deactivates others.
6. Activated enzymes catalyze metabolic reactions with a wide range of possible effects on the cell.

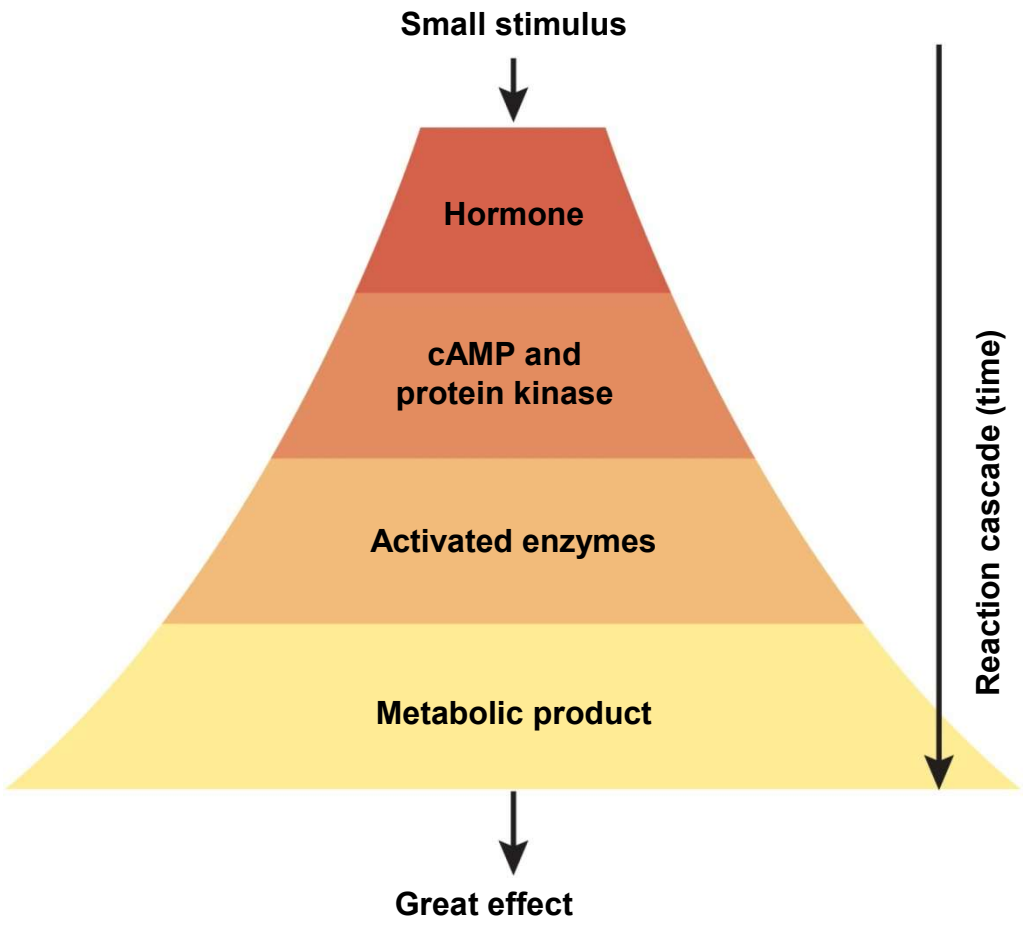
- hormone binds to cell-surface receptor
- receptor linked to second messenger system on other side of the membrane
- activates G protein which
- activates adenylate cyclase
- produces cAMP /// activates or inhibits enzymes
- possible metabolic reactions:
  - synthesis
  - secretion

Other Second Messengers



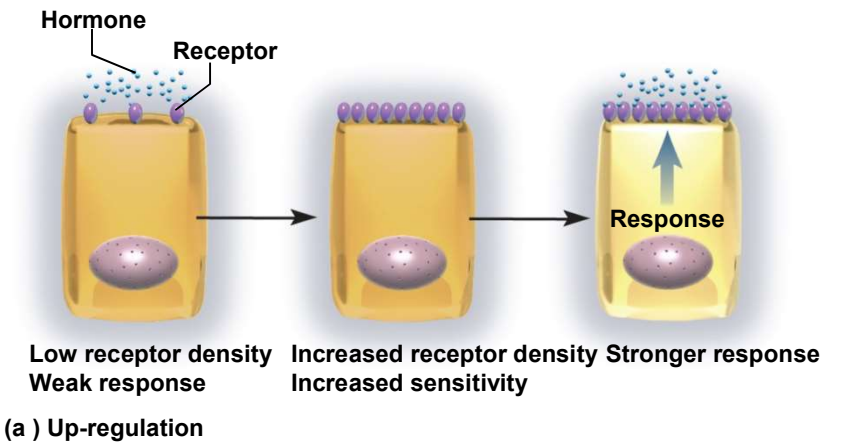
- diacylglycerol (diglyceride) second-messenger system
- inositol triphosphate second-messenger system
- act on cell metabolism in a variety of ways

Enzyme Amplification



- hormones are extraordinarily **potent chemicals**
- one hormone molecule can trigger the synthesis of many enzyme molecules.
- very small stimulus can produce very large effect
- circulating concentrations very low

Modulation of Target Cell Sensitivity



- target cell sensitivity <u>adjusted by changing the number of receptors</u>
- **up-regulation** means number of receptors is increased // sensitivity is increased
- **down-regulation** reduces number of receptors
  - cell less sensitive to hormone
  - happens with long-term exposure to high hormone concentrations
    - bind to other receptors
    - converted to different hormone

Hormone Interactions

- most cells sensitive to more than one hormone and exhibit interactive effects

- synergistic effects
  - multiple hormones act together for greater effect // synergism between FSH and testosterone on sperm production

- permissive effects
  - one hormone enhances the target organ's response to a second later hormone // estrogen prepares uterus for action of progesterone

- antagonistic effects
  - one hormone opposes the action of another // insulin lowers blood glucose and glycogen raises it

Hormone Clearance

- hormone signals must be turned off when they have served their purpose

- most hormones are taken up and degraded by liver and kidney // excreted in bile or 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 MCF, the shorter is the half-life