Endocrine glands role in regulation of physiological functions of oral cavity.

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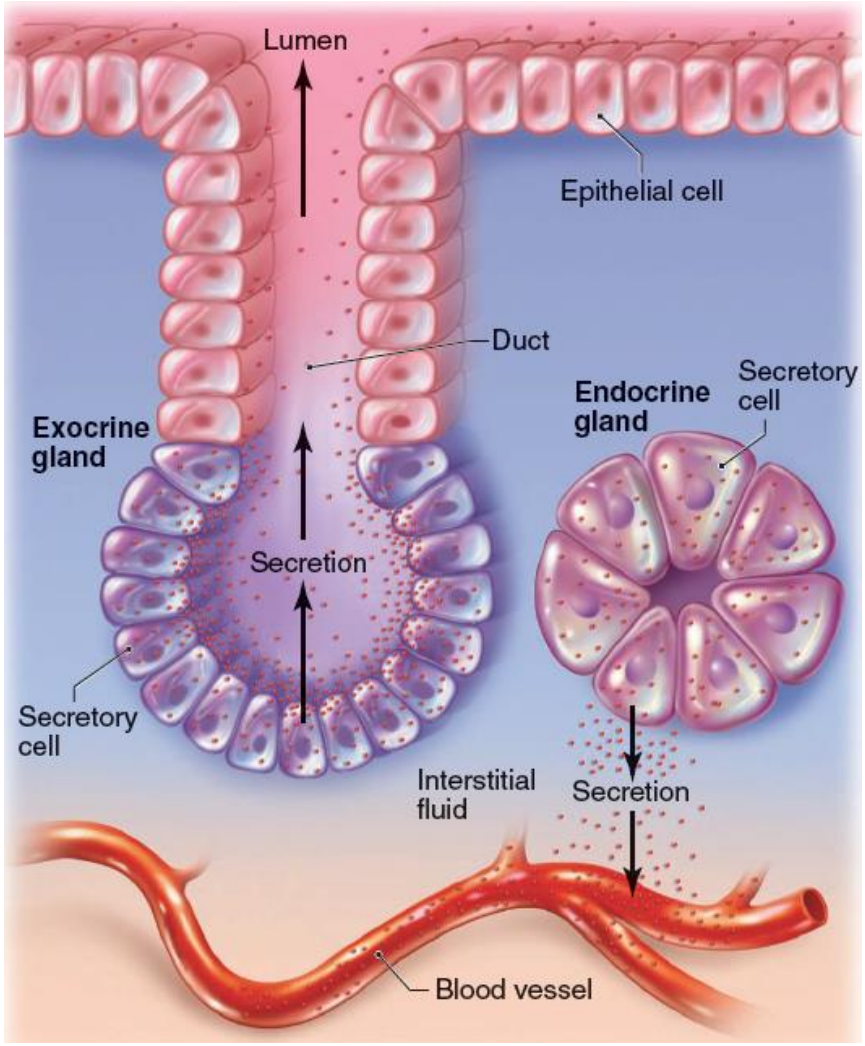
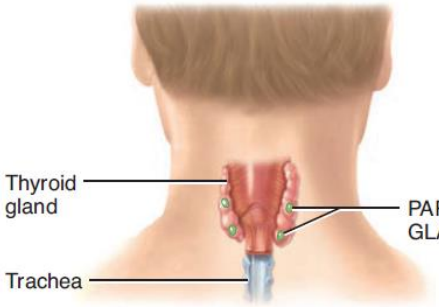
Hormones

- Hormones are chemical messengers secreted into the circulation by ductless glands.
- Hormones maintain homeostasis by regulating processes such as development, metabolism, and reproduction.



Endocrine system



PARATHYROID GLANDS (behind thyroid glands)

FUNCTIONS OF HORMONES

1. Help regulate:
   - Chemical composition and volume of internal environment (interstitial fluid).
   - Metabolism and energy balance.
   - Contraction of smooth and cardiac muscle fibers.
   - Glandular secretions.
   - Some immune system activities.
2. Control growth and development.
3. Regulate operation of reproductive systems.
4. Help establish circadian rhythms.

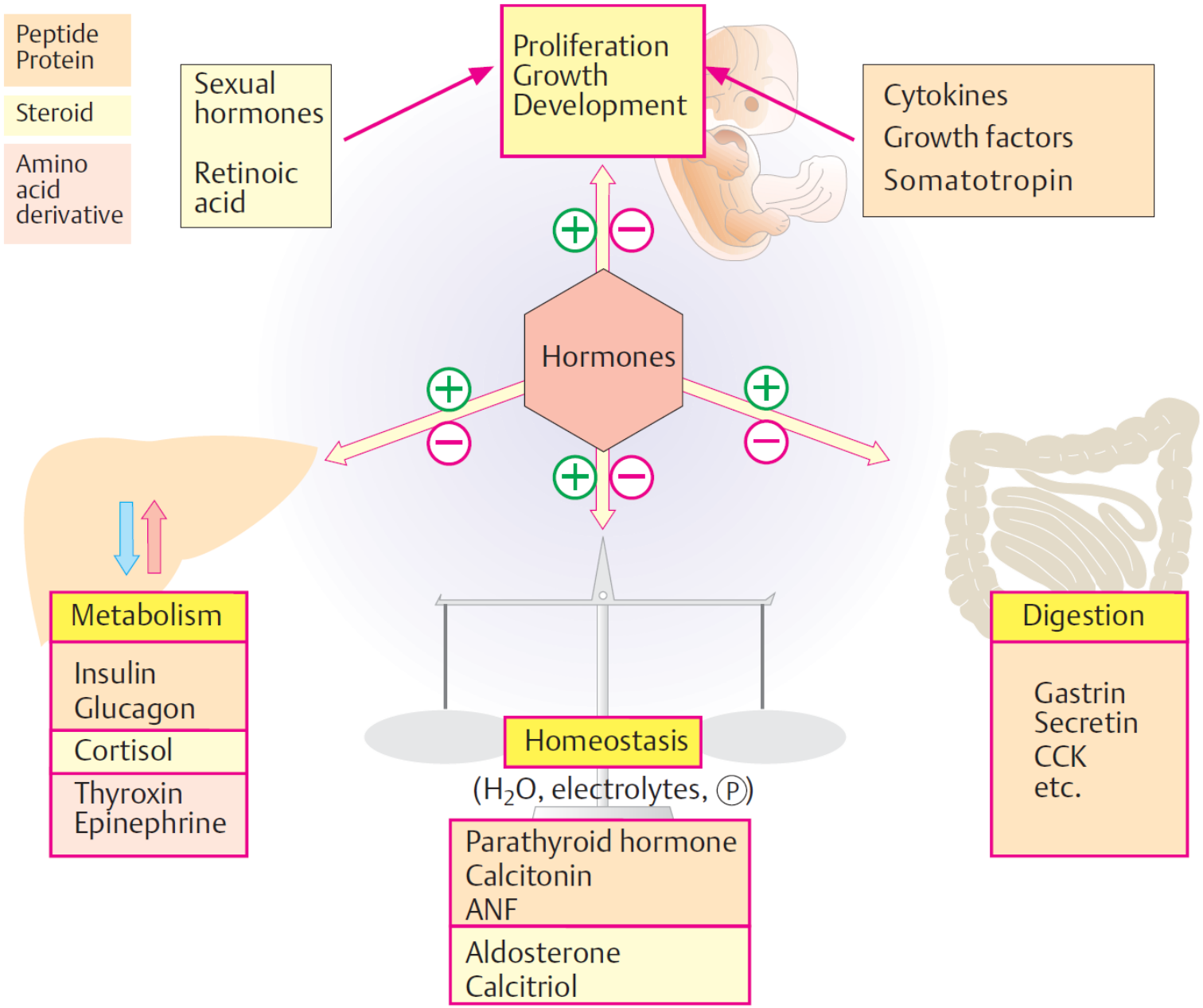
Endocrine Glands

Gland	Hormone
anterior pituitary gland	thyroid-stimulating hormone, growth hormone, gonadotropins, prolactin, adrenocorticotropic hormone
posterior pituitary gland	antidiuretic hormone, oxytocin
thyroid gland	thyroxine, triiodothyronine, calcitonin
parathyroid gland	parathyroid hormone
islets of Langerhans	insulin, glucagon, somatostatin
adrenal medulla	epinephrine, norepinephrine
adrenal cortex	cortisol, aldosterone
the ovaries	estrogen, progesterone
the testes	testosterone

Organs with Endocrine function

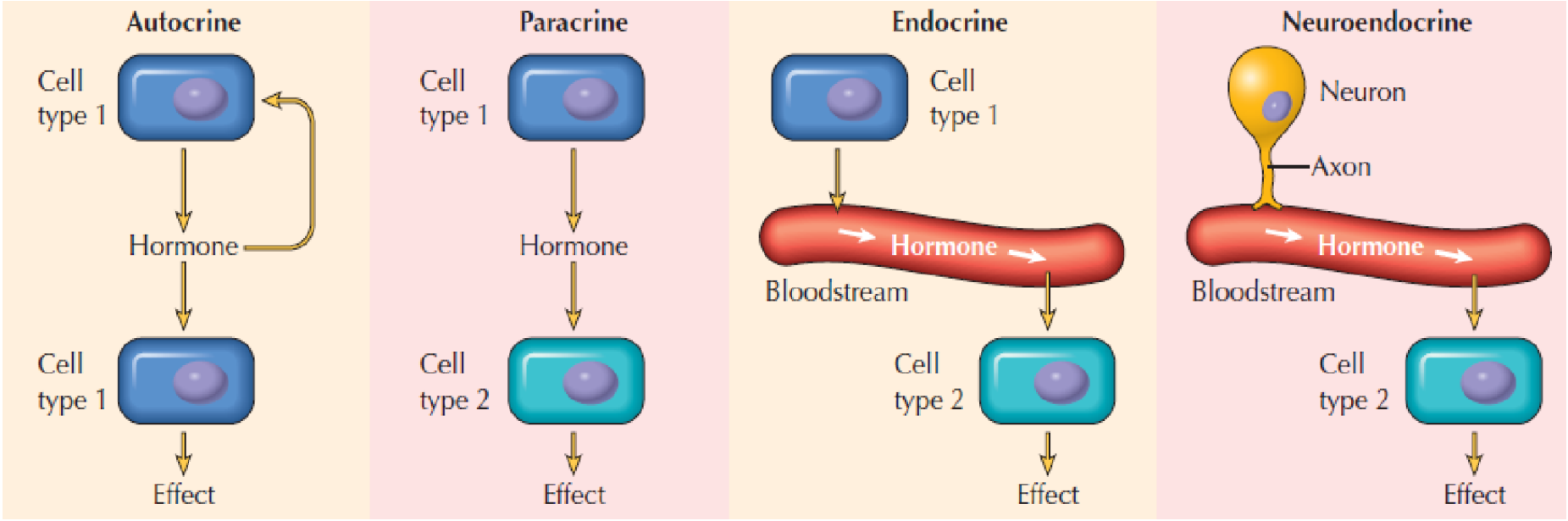
Gland	Hormone
hypothalamus	releasing hormones
pineal gland	melatonin
heart	atrial natriuretic peptide
kidneys	erythropoietin
adipose tissue	leptin, adiponectin
stomach	gastrin, ghrelin
intestines	secretin, cholecystokinin, gastrin inhibitory peptide, motilin
thymus	thymosin
liver	insulin-like growth factor 1

Role of Hormones



Types of hormone action

1. **Autocrine** (cells act on themselves);
2. **Paracrine** (target cells are located nearby);
3. **Endocrine** (distant action);
4. **Neuroendocrine** (hormones are released by neurons into the blood).



Chemical classification of hormones

1. **Derivates of amino acids:**
- **tyrosine**: thyroxine and triiodothyronine, epinephrine, and norepinephrine;
- **tryptophan**: melatonin.

2. **Proteins and polypeptides** (preprohormone):
- releasing hormones;
- thyroid-stimulating hormone, growth hormone, gonadotropins, prolactin, adrenocorticotropic hormone;
- antidiuretic hormone, oxytocin;
- insulin and glucagon;
- parathyroid hormone;
- calcitonin.

3. **Steroid hormones** (derived from cholesterol):
- cortisol, aldosterone;
- estrogen, progesterone, testosterone.

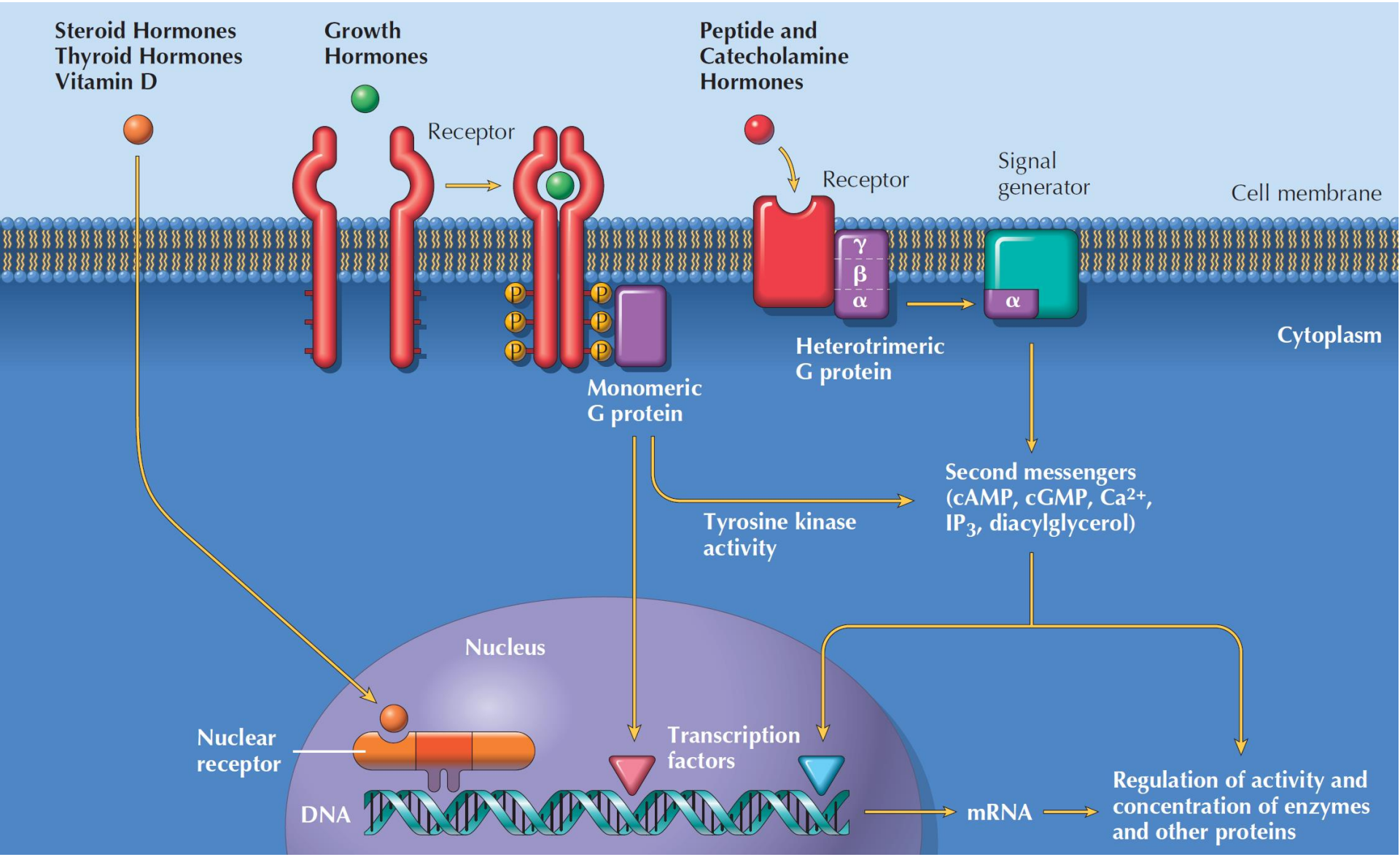
Comparison of hormones

			TYROSINE DERIVATIVES	
	PEPTIDE HORMONES	STEROID HORMONES	Catecholamines	Thyroid Hormones
Synthesis and storage	Made in advance; stored in secretory vesicles	Synthesized on demand from precursors	Made in advance; stored in secretory vesicles	Made in advance; precursor stored in secretory vesicles
Release from parent cell	Exocytosis	Simple diffusion	Exocytosis	Simple diffusion
Transport in blood	Dissolved in plasma	Bound to carrier proteins	Dissolved in plasma	Bound to carrier proteins
Half-life	Short	Long	Short	Long
Location of receptor	Cell membrane	Cytoplasm or nucleus; some have membrane receptors also	Cell membrane	Nucleus
Response to receptor-ligand binding	Activation of second messenger systems; may activate genes	Activation of genes for transcription and translation; may have nongenomic actions	Activation of second messenger systems	Activation of genes for transcription and translation
General target response	Modification of existing proteins and induction of new protein synthesis	Induction of new protein synthesis	Modification of existing proteins	Induction of new protein synthesis
Examples	Insulin, parathyroid hormone	Estrogen, androgens, cortisol	Epinephrine, norepinephrine	Thyroxine (T_4)

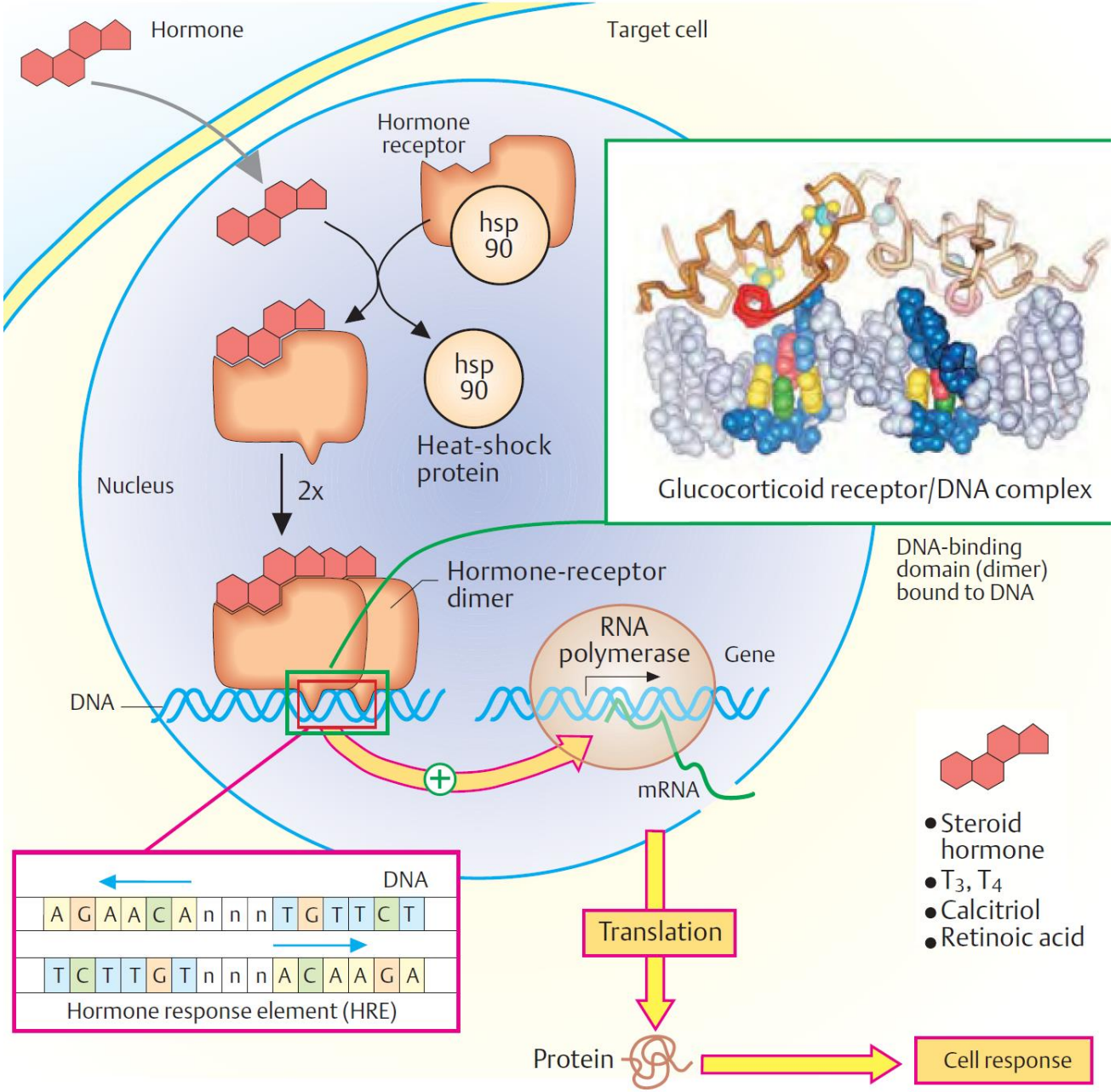
Hormone-binding proteins

Plasma protein	Hormone
Albumin	Multiple lipophilic hormones
Transthyretin	Thyroxine
Transcortin	Cortisol, aldosterone
Thyroxine-binding globulin	Thyroxine, triiodothyronine
Sex hormone-binding globulin	Testosterone, estrogen

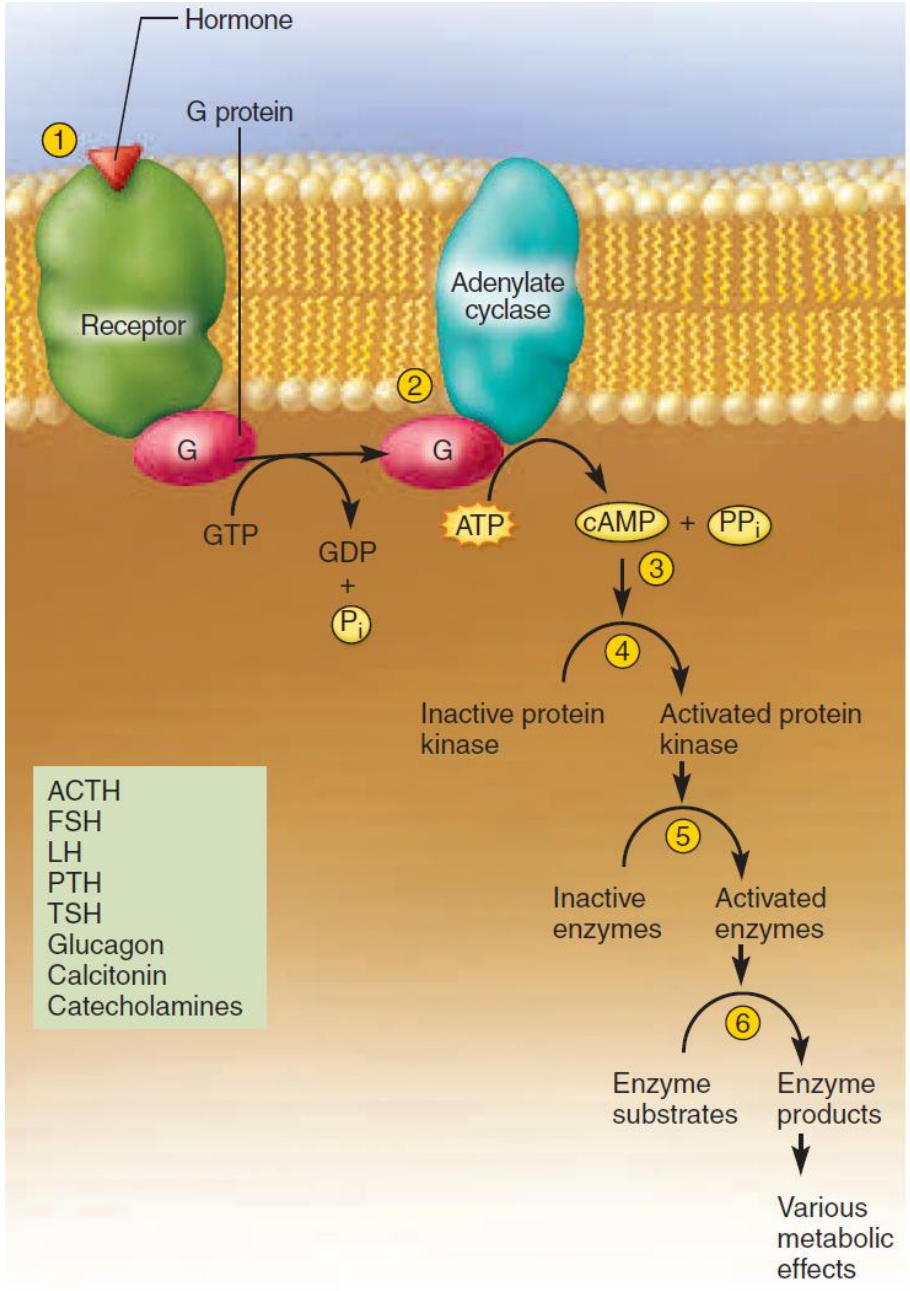
Mechanisms action of hormones



Mechanisms action of lipophilic hormones

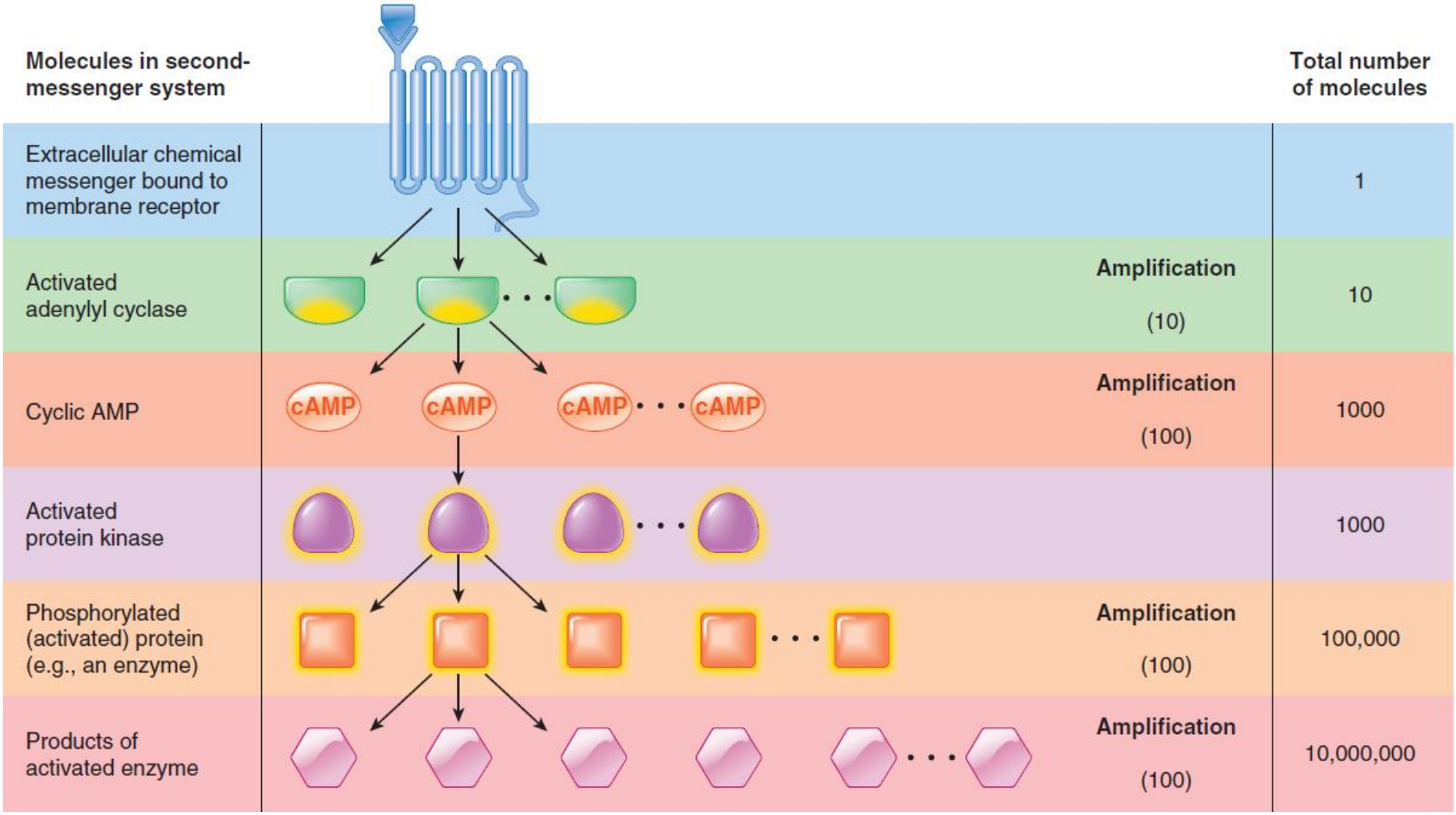


cAMP Mechanism

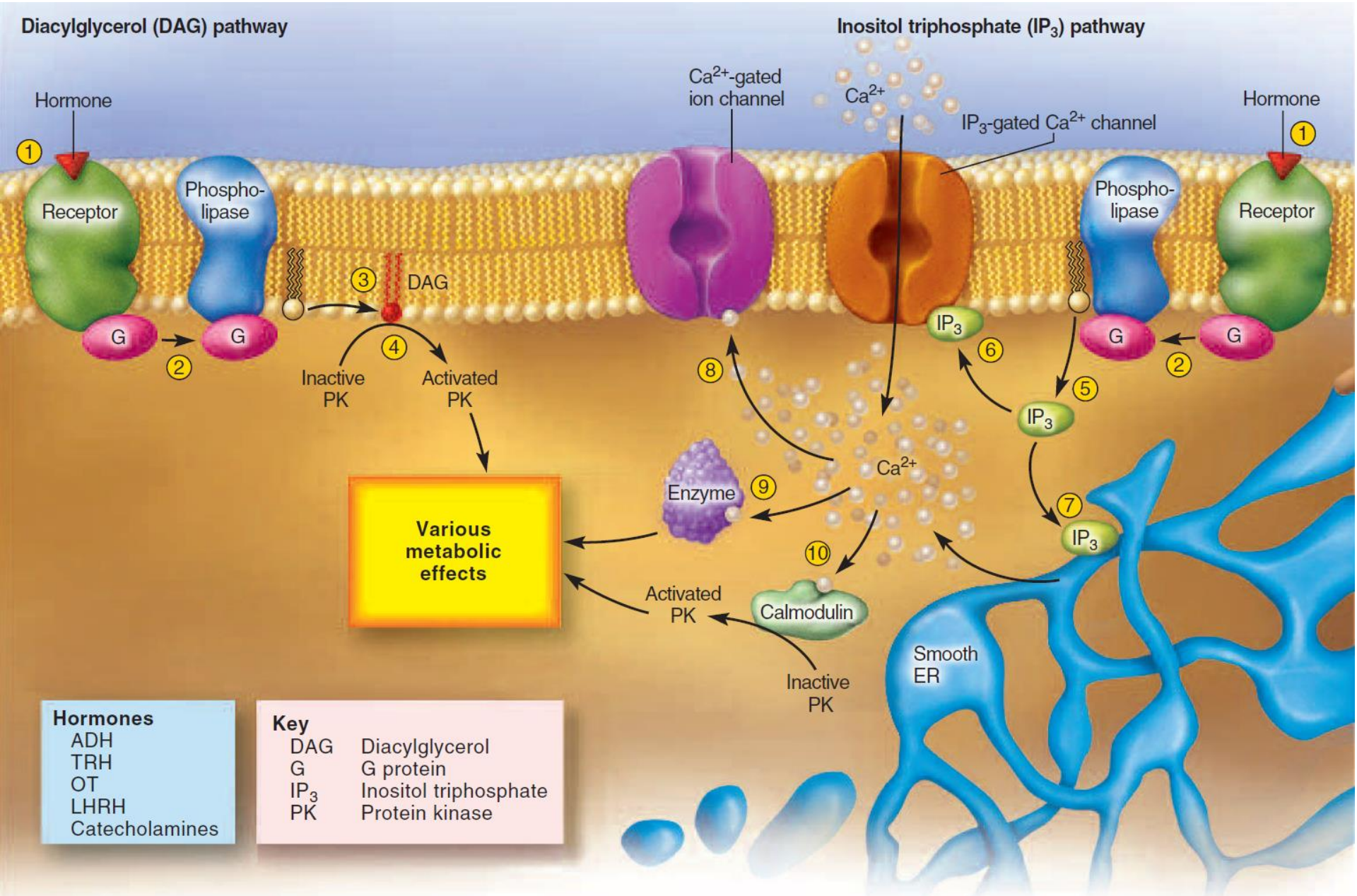


1. Hormone–receptor binding activates a G protein.
2. G protein activates adenylate cyclase.
3. Adenylate cyclase produces cAMP.
4. cAMP activates protein kinases.
5. Protein kinases phosphorylate enzymes. This activates some enzymes and deactivates others.
6. Activated enzymes catalyze metabolic reactions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

Amplification of initial signal



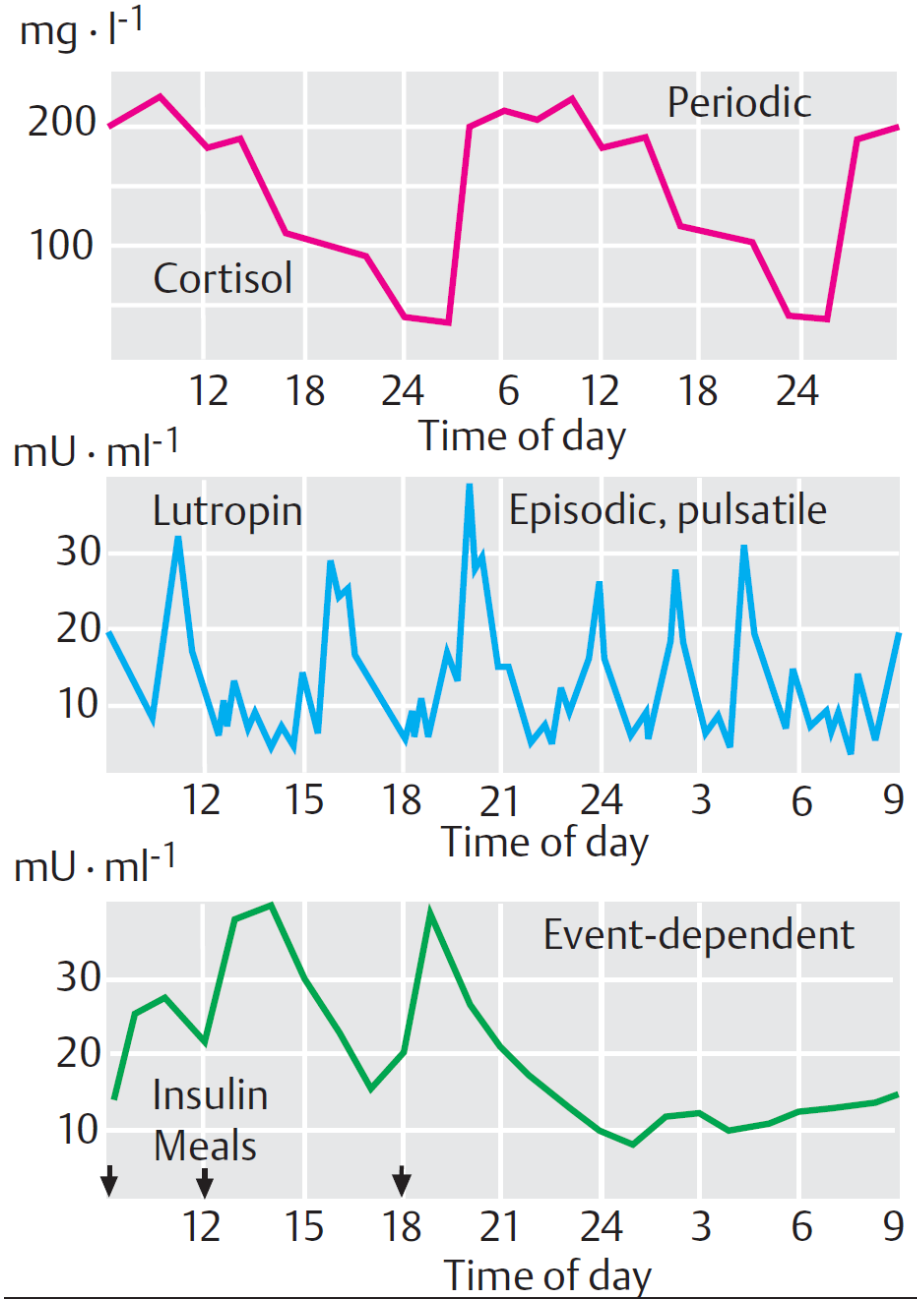
IP_3 Mechanism



Mechanisms of hormone action

cAMP mechanism	IP_3 mechanism	Intracellular mechanism	Tyrosine kinase
ACTH	GnRH	Cortisol	Insulin
LH and FSH	TRH	Estrogen	IGF-1
TSH	GHRH	Testosterone	
ADH (V2)	Angiotensin II	Progesterone	
HCG	ADH (V1)	Aldosterone	
MSH	Oxytocin	T_3 and T_4	
CRH	α_1 AR	Vitamin D	
β_1 and β_2 AR			
Calcitonin			
PTH			
Glucagon			

Secretion of hormones

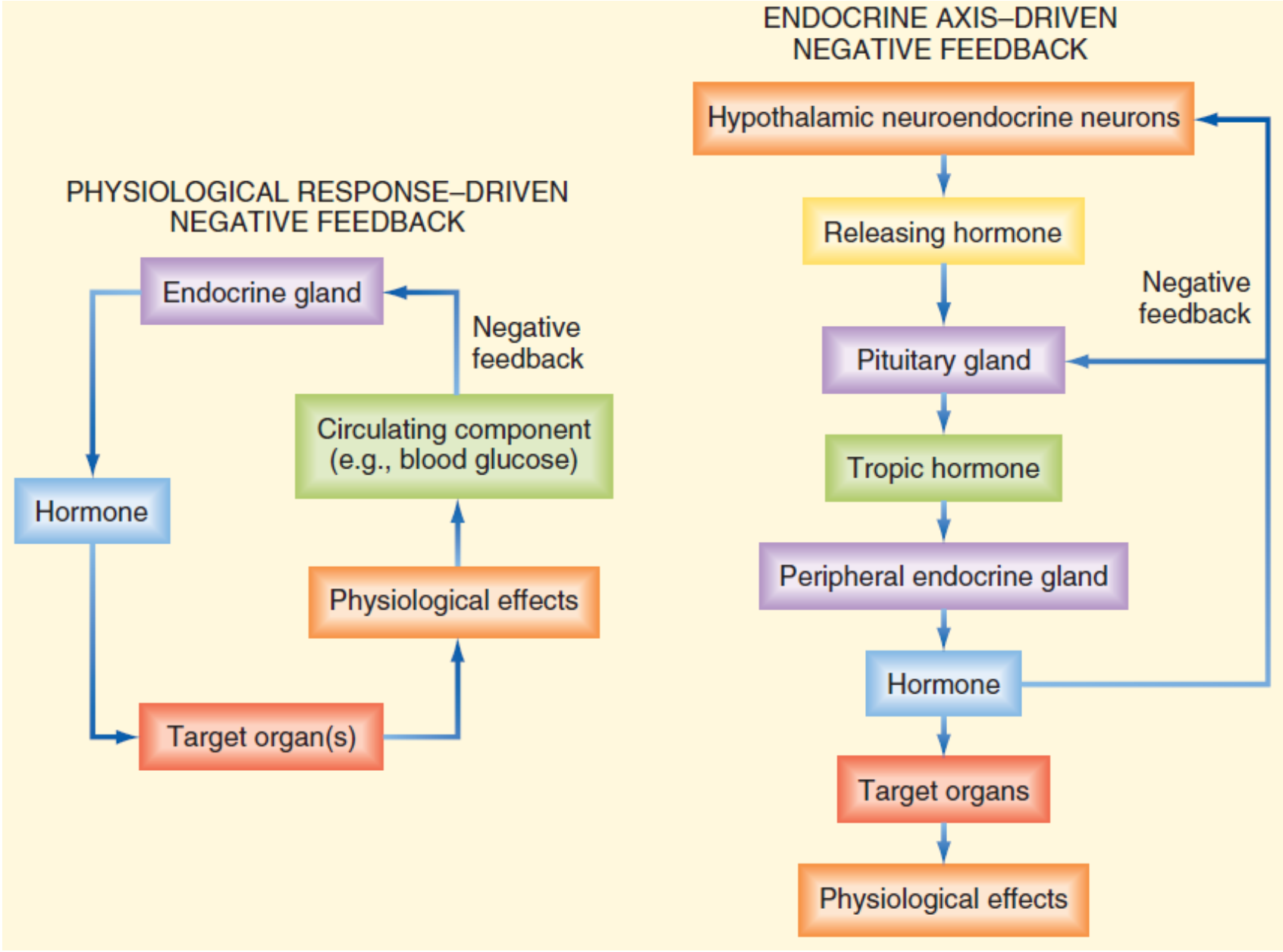


Hormones plasma level depends on time of day (circadian rhythm), month, year, or on physiological cycles.

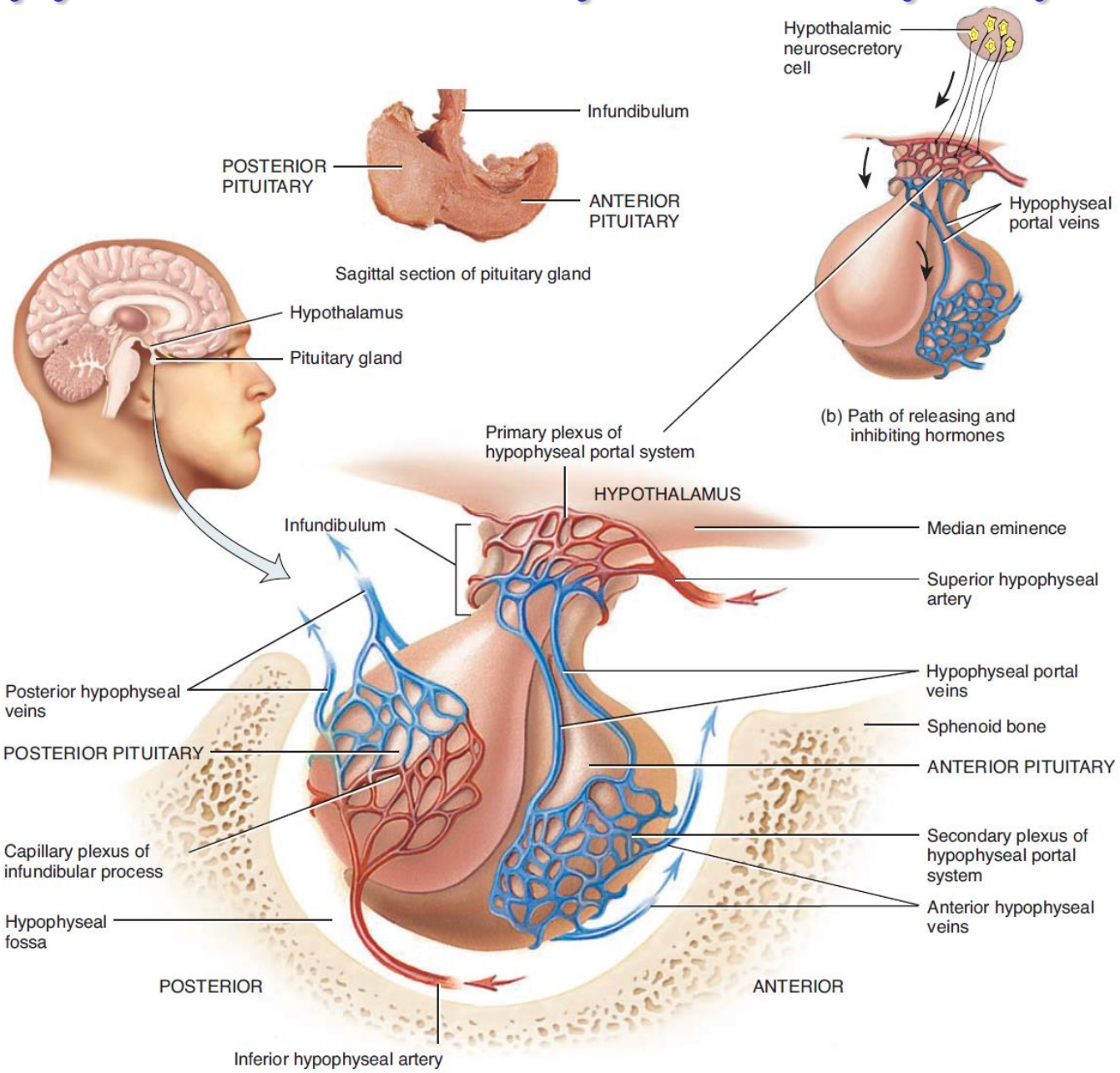
Types of secretion:

- Periodic;
- Episodic or pulsatile;
- Event-regulated.

Regulation of hormone secretion



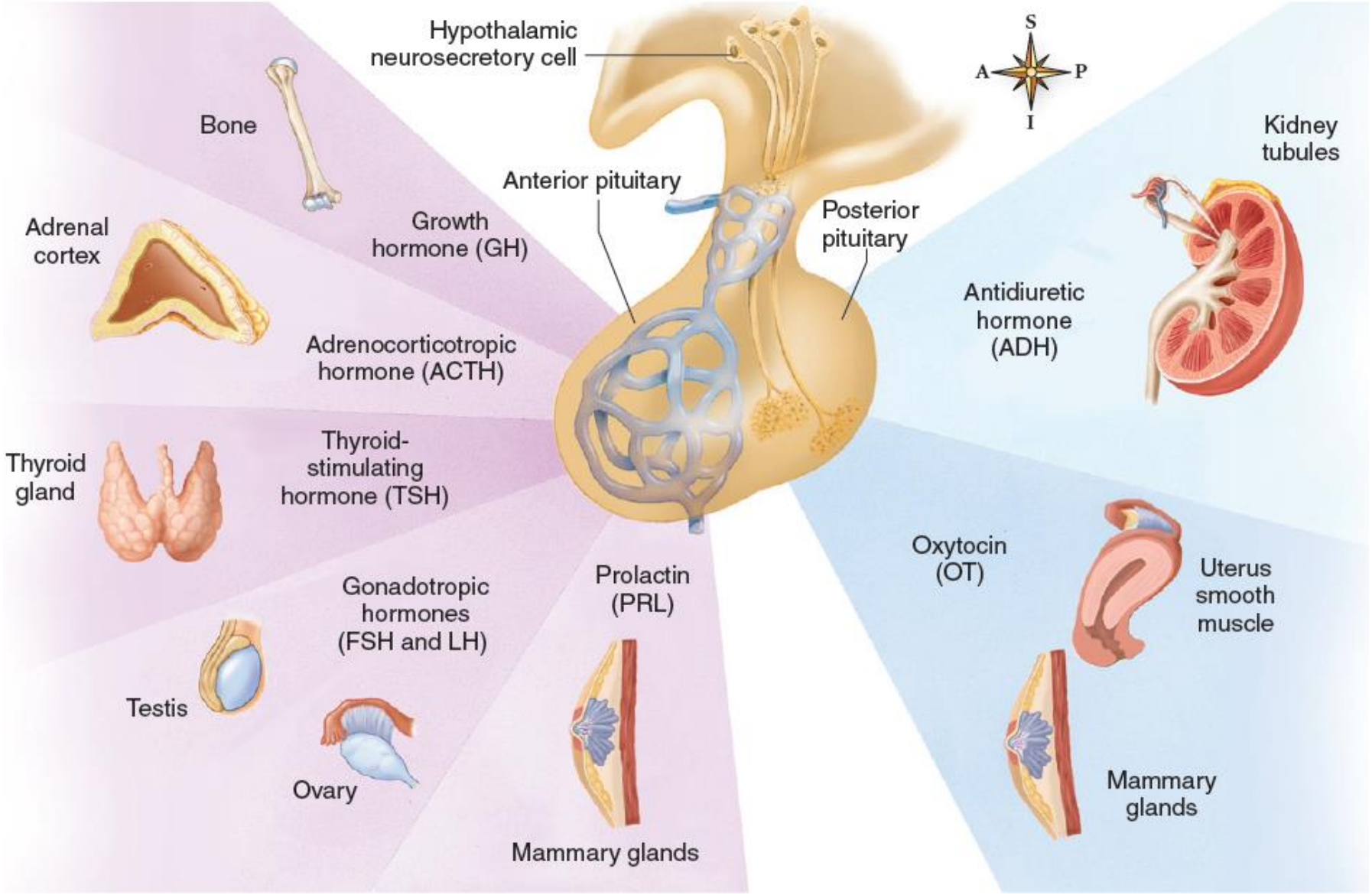
Hypothalamus-pituitary system



Hypothalamic releasing hormones

Hormone	Principal Effect
Growth hormone-releasing hormone (GHRH)	Promotes secretion of growth hormone
Growth hormone-inhibitory hormone (GHIH) or somatostatin (SS, SRIF)	Inhibits secretion of growth hormone
Corticotropin-releasing hormone (CRH)	Promotes secretion of ACTH
Thyrotropin-releasing hormone (TRH)	Promotes secretion of TSH and prolactin
Gonadotropin-releasing hormone (GnRH)	Promotes secretion of FSH and LH
Prolactin-inhibitory hormone (PIH) or dopamine	Inhibits secretion of prolactin

Hormones of Pituitary gland



Hormones of the Anterior Pituitary

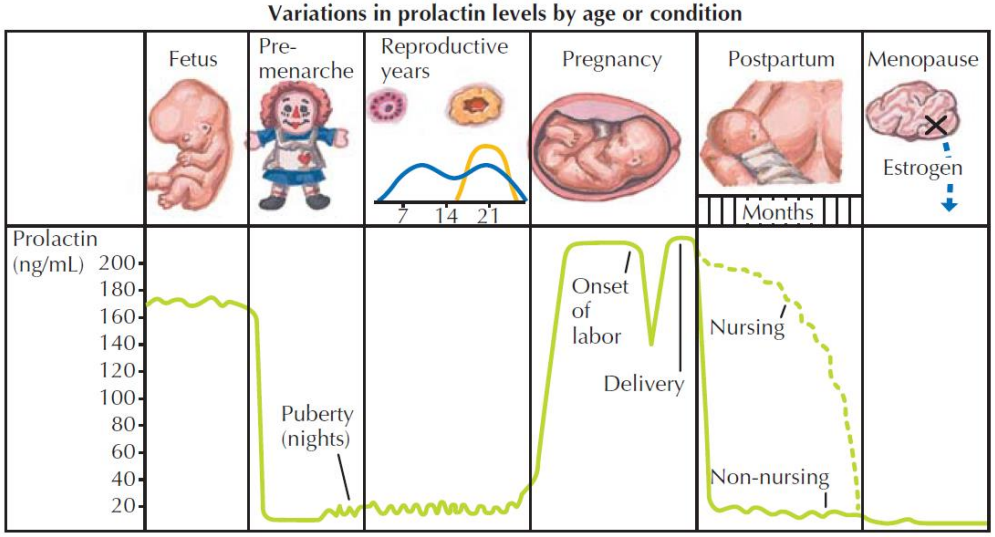
Hormone	Principal Effect	Regulation of secretion
Adrenocorticotropic hormone (ACTH)	↑ secretion of glucocorticoids and androgens; maintain size of adrenal cortex	+ CRH; - glucocorticoids
Thyroid-stimulating hormone (TSH)	↑ secretion of thyroid hormones; maintain size of follicular cells	+ TRH; - thyroid hormones
Follicle-stimulating hormone (FSH)	gamete production; estrogen production in females	+ GnRH; - sex steroids, inhibin
Luteinizing hormone (LH)	ovulation and formation of corpus luteum; ↑ estrogen and progesterone secretion by ovaries; ↑ testosterone secretion by testes	+ GnRH; - sex steroids
Growth hormone (GH)	↑protein synthesis and body growth; lipolysis; ↑ blood glucose	+ GHRH; - somatostatin
Prolactin (PRL)	milk production by lactating mammary glands, breast development	+ TRH; - PIH

Prolactin (PRL)

Actions of PRL:

- a. stimulates development of the breast (with estrogens and progesterone) at puberty and during pregnancy;
- b. stimulates milk production (↑ synthesis lactose, lactalbumin, casein, and milk fats);
- c. suppresses ovulation by ↓ GnRH release (lactational amenorrhea);
- d. Inhibits spermatogenesis.

- **Secretion is increased** by TRH, estrogen (inhibits lactogenic effect), pregnancy, breast-feeding, sleep, stress;
- **Secretion is decreased** by dopamine, bromocriptine (dopamine agonist), somatostatin.

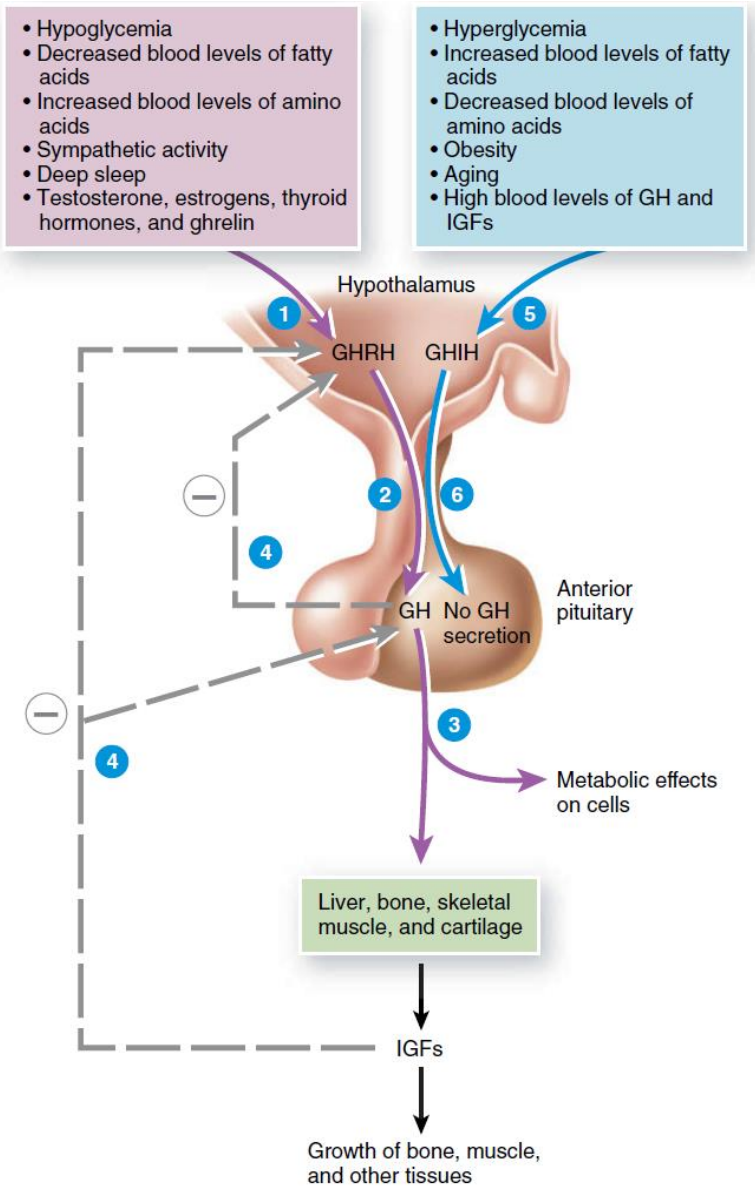


Clinical correlation

- **Hyposecretion** of prolactin results in the failure to lactate.
- **Hypersecretion** (hyperprolactintemia):

- prolactinoma is the most common pituitary tumor;
- causes secondary amenorrhea, galactorrhea, infertility in women; infertility and impotence in men;
- treated with dopamine agonists (e.g. bromocriptine);
- primary hypothyroidism (↓ secretion of thyroid hormone) also causes hyperprolactinemia due to increased TRH, a prolactin stimulator.

Hypothalamic-pituitary-GH axis



- ***GH is released in a pulsatile fashion.***
- ***Secretion is increased by hypoglycaemia, ↓free fatty acids, starvation, arginine, hormones of puberty, stress, exercise, slow wave sleep, α-adrenergic agonists.***
- ***Secretion is decreased: hyperglycaemia, obesity, pregnancy, senescence, somatostatin, somatomedins, GH, β-adrenergic agonists.***
- ***Synthesis of GH in somatotrophs is regulated by GHRH and somatostatin of hypothalamus.***

Action of Growth hormone

- **Direct actions of GH:**

a. ↓ glucose uptake and glucose production;

b. ↑ protein synthesis in muscle;

c. ↑lipolysis, ketogenic effect;

d. ↑ insulin secretion and insulin resistance (diabetogenic effect).

e. stimulates production of IGF by liver:

- somatomedin B (insulin-like growth factor 2) plays an important role in the growth of fetus.
- somatomedin C (insulin-like growth factor 1) occurs growth-promoting effects.

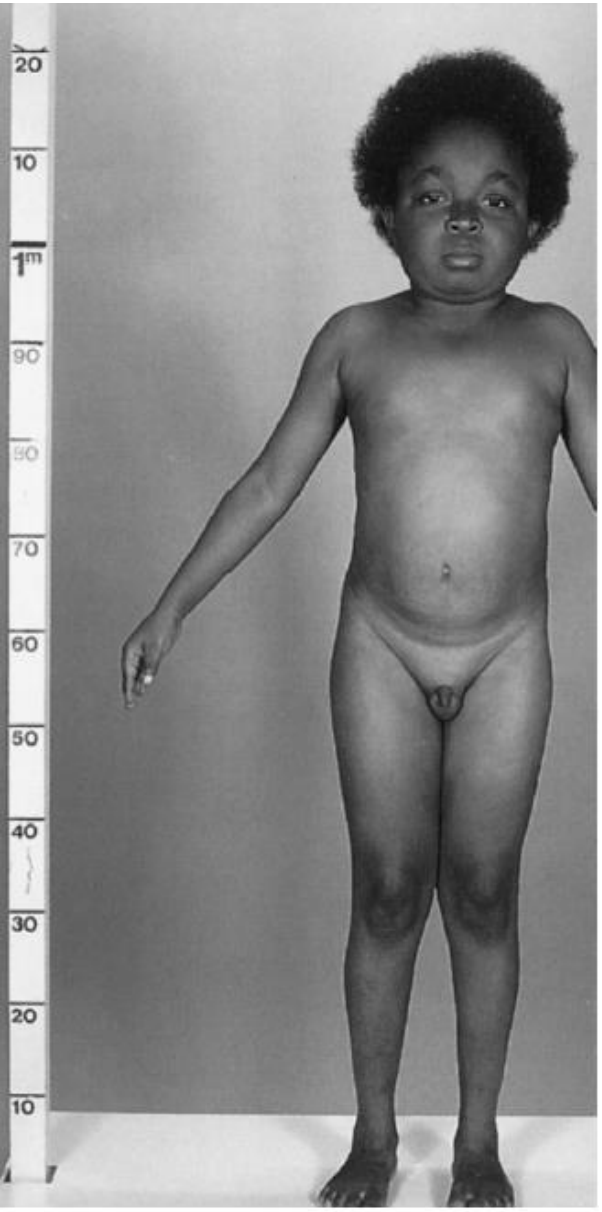
- **Action of GH via IGF:**

a. ↑ protein synthesis in chondrocytes and linear growth;

b. ↑ protein synthesis in muscle (anabolic effect);

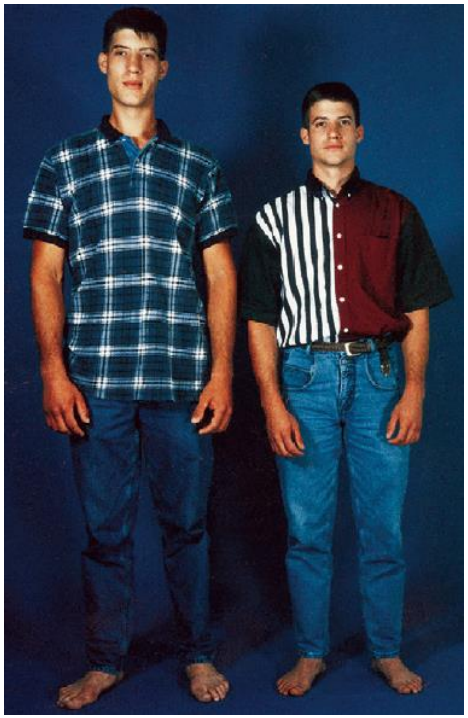
d. ↑ amino acids uptake and protein synthesis in most organs.

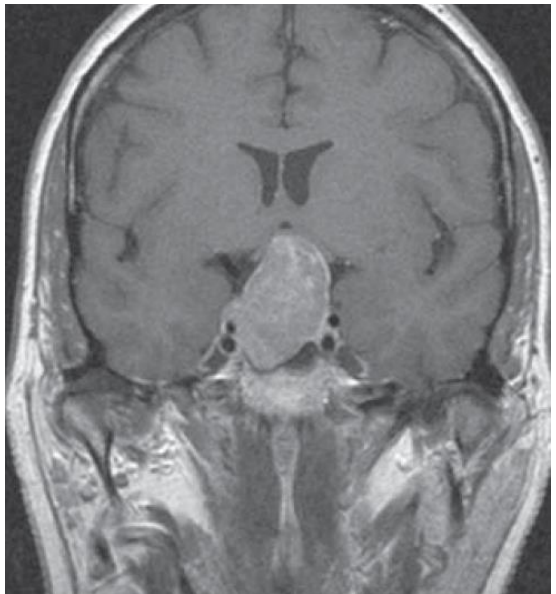
Pituitary dwarfism



- GH deficiency causes failure to grow, short stature, mild obesity, and delayed puberty.
- Can be caused by lack of GH, GHRH;
- Laron dwarfism is caused by deficiency of GH receptors and associated with high plasma levels of GH and low plasma level of IGF-1;
- In pygmies, GH receptor are present, but lack of IGF receptors.

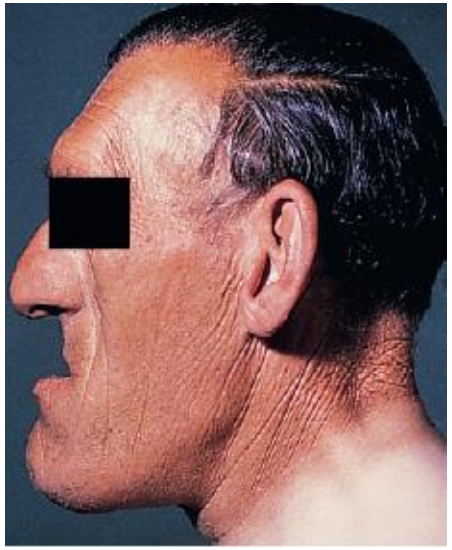
Pituitary gigantism





- Hypersecretion of GH during childhood causes **pituitary gigantism** (result of growth hormone-secreting adenoma). Pituitary giants are taller than 210 cm.
- **Diagnosis**: GH level is not suppressed after oral glucose load, increased level of IGF-1, MRI.
- **Treatment**: surgery (adenectomy), targeted irradiation, pharmacotherapy (somatostatin analogues -octreotide).

Acromegaly



- Chronic excess of GH (from tumor) in an adult causes **acromegaly**. It is associated with increased hands, foot, and organ size, change of facial features, arthritis, low-pitched voice, prognatism, and insulin resistance.
- **Diagnosis and treatment** as for pituitary gigantism.

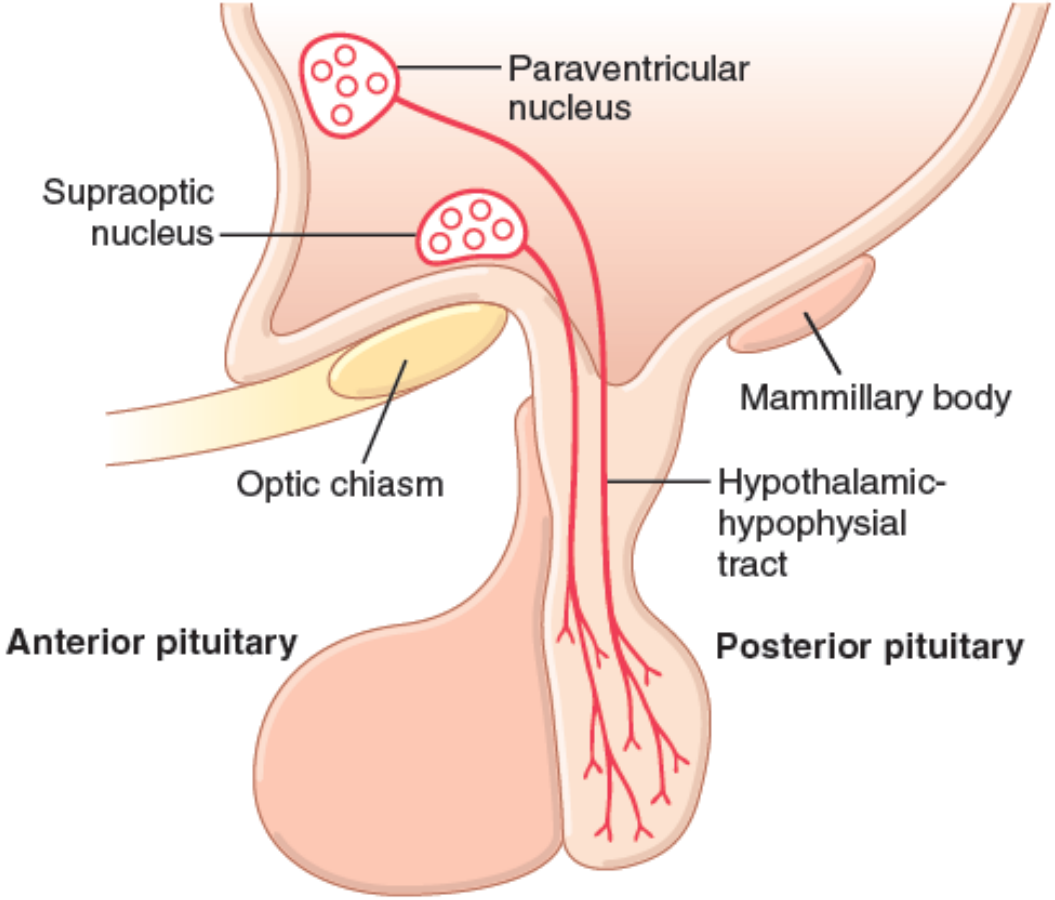
Age 9

Age 16

Age 33

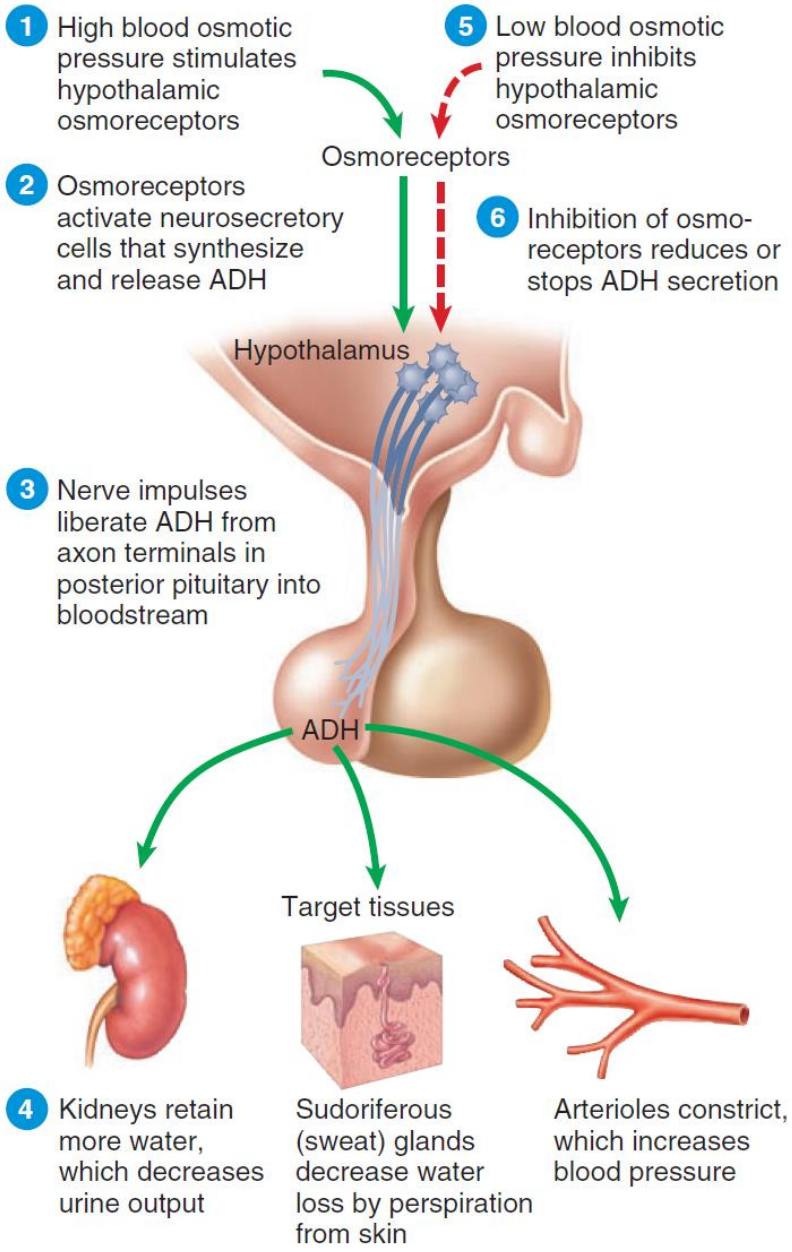
Age 52

Posterior pituitary gland



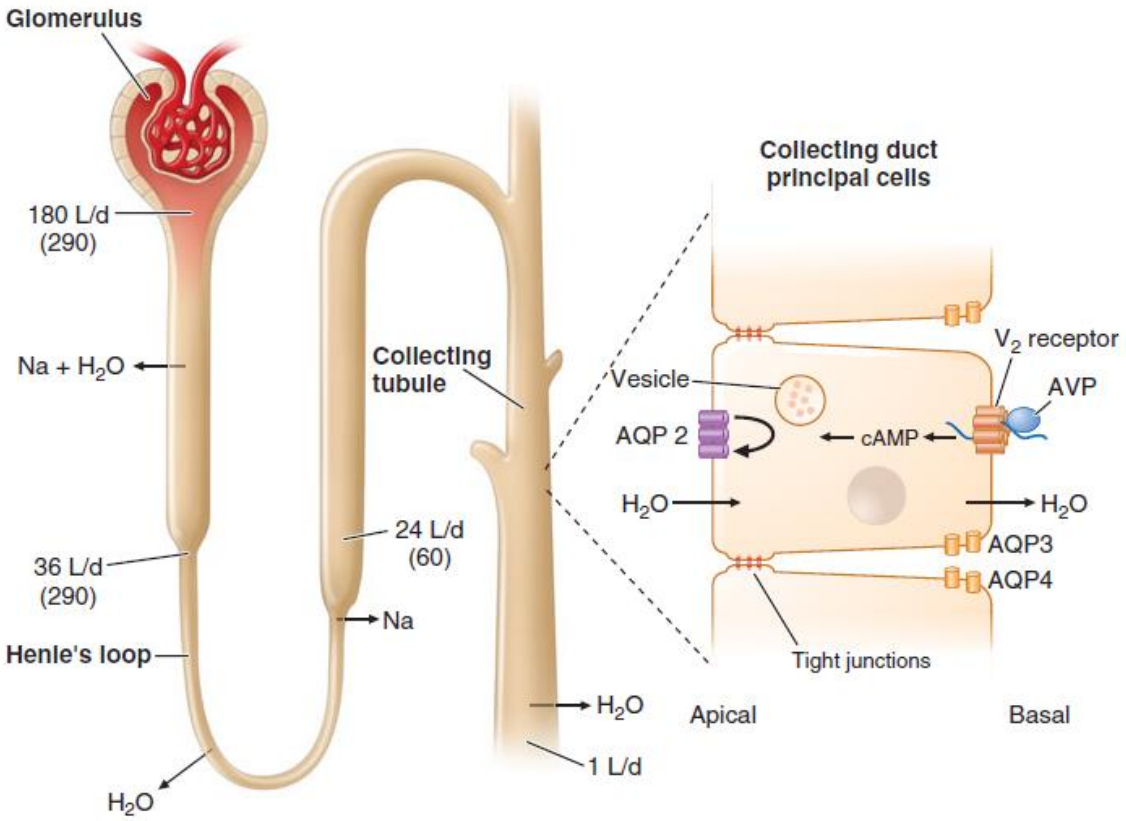
- ADH is formed primarily in the supraoptic nuclei;
- Oxytocin is formed primarily in the paraventricular nuclei.

Antidiuretic hormone (ADH) or vasopressin



- ***ADH secretion is stimulated by a high osmolarity of the blood (detected by osmoreceptors of hypothalamus), hypovolemia and a decrease in blood pressure. Also, pain, hypoglycaemia, nausea, drugs (nicotine, opiates).***
- ***ADH secretion is inhibited by low osmolarity, hypervolemia, high blood pressure, atrial natriuretic peptide (ANP), ethanol, α-adrenergic agonists, and cold inhibit ADH secretion.***

Actions of ADH

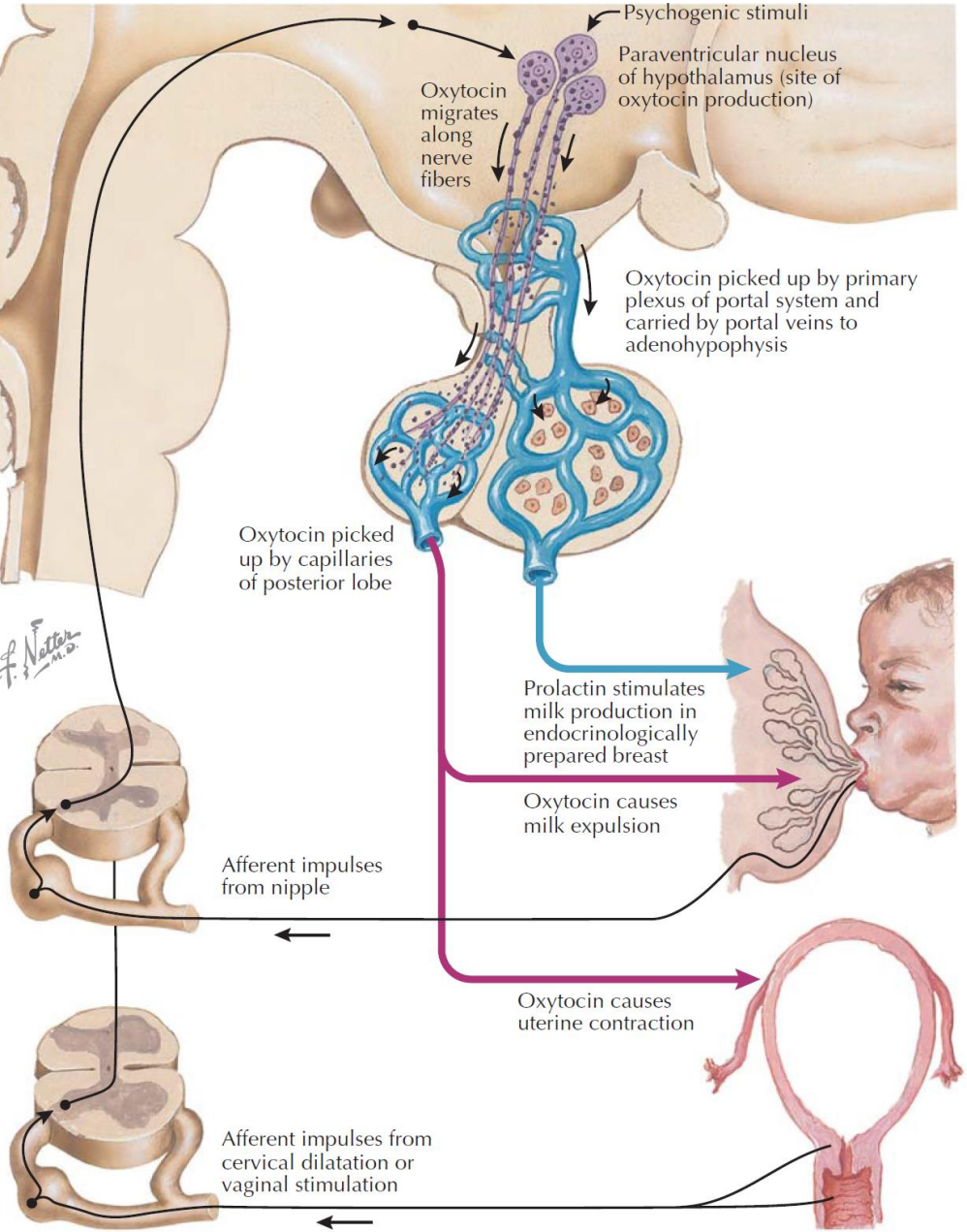


- a. causes vasoconstriction through V1 receptors and increases peripheral vascular resistance and blood pressure;
- b. increases of water reabsorption in the kidneys (distal tubules and collecting ducts) by regulating the water channel – aquaporins (AQP2) through binding to V2 receptors.

Clinical correlation

- **Hyposecretion** of ADH causes *neurogenic (central) diabetes insipidus* It is associated with polyuria (5-15 L/day), polydipsia and hypernatraemia. It is treated with ADH analogue. Defect in V2 receptors causes *nephrogenic diabetes insipidus.*
- **Hypersecretion** of ADH causes *SIADH (syndrome of inappropriate antidiuretic hormone secretion)* which is associated with hypervolemia, hyponatraemia, and high blood pressure.

Oxytocin



Oxytocin secretion is stimulated by suckling and dilation of the cervix.

Actions of oxytocin:

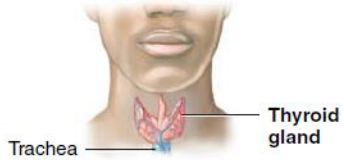
a. the milk-ejection reflex;

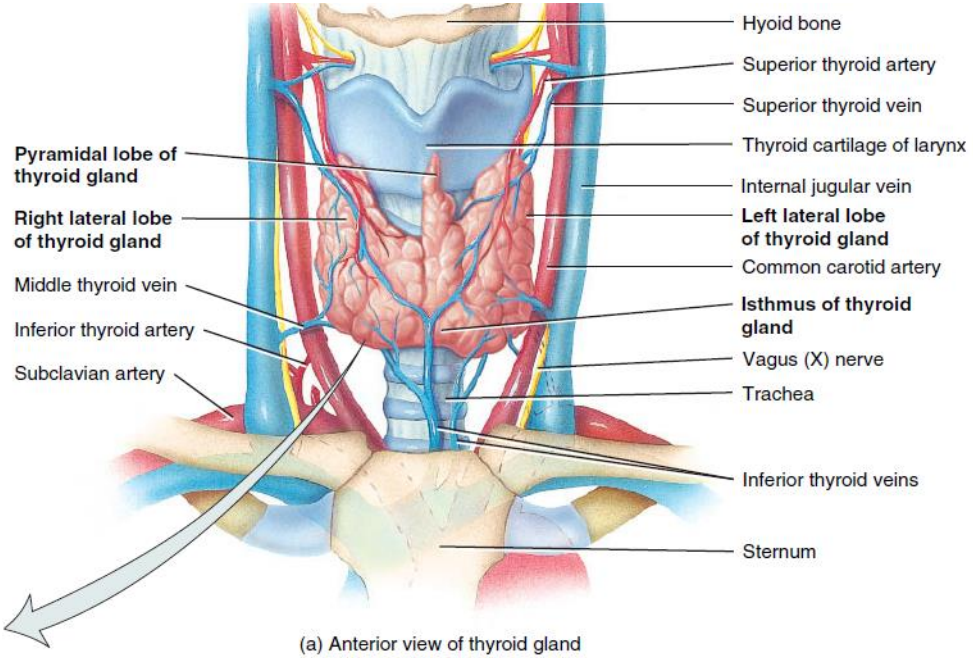
b. contractions of uterus during labour.

Clinical correlation:

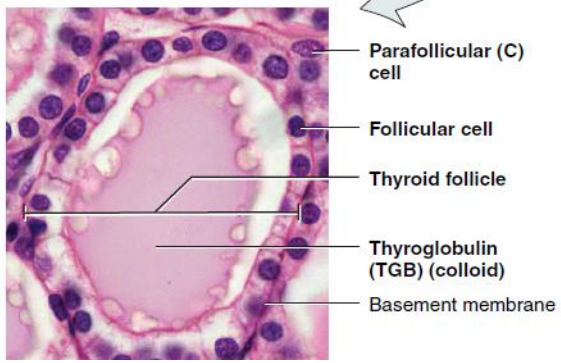
Injections of oxytocin may be given to a induce labour. Oxytocin administration during postpartum period decreases the danger of bleeding and promotes uterine involution.

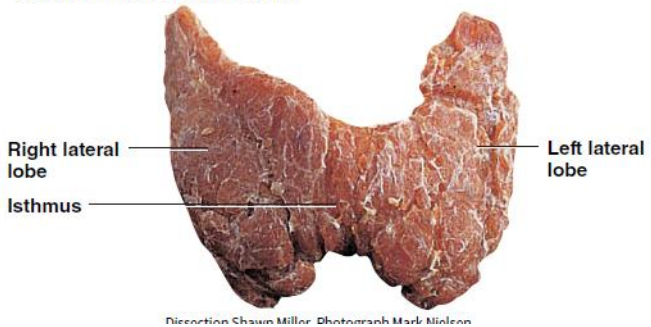
Thyroid gland





(a) Anterior view of thyroid gland



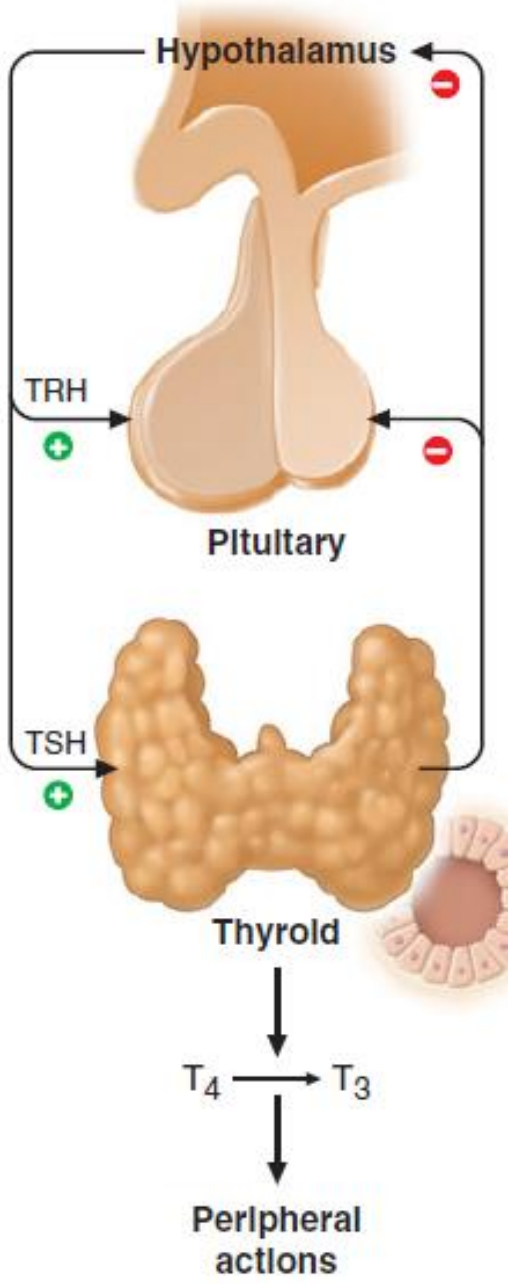


Dissection Shawn Miller, Photograph Mark Nielsen

Thyroid gland secretes thyroid hormones: thyroxine (T4), triiodothyronine (T3) in follicular cells;

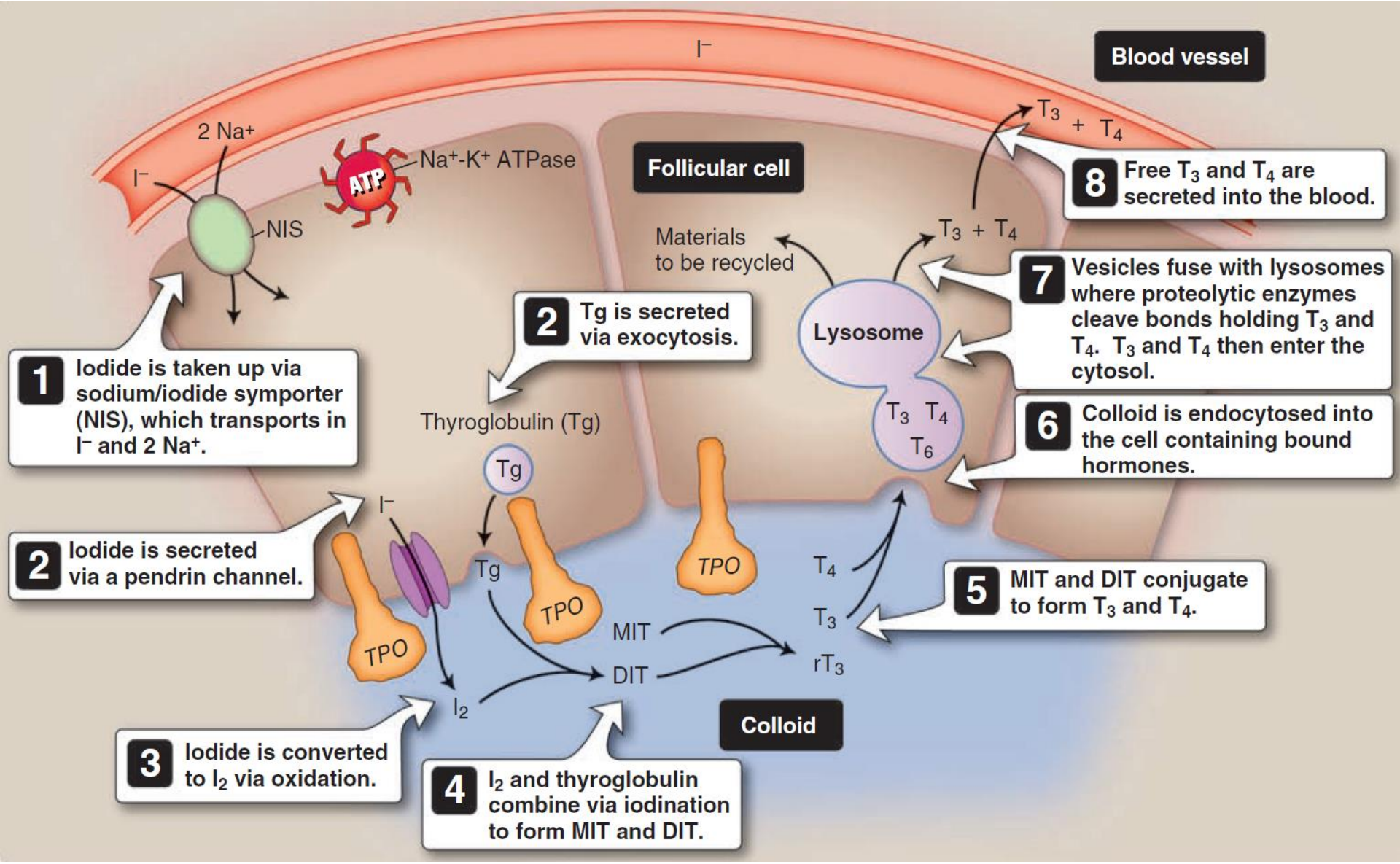
calcitonin in parafollicular or C cells.

Hypothalamic-pituitary-thyroid axis



- TRH stimulates the secretion of TSH by the anterior pituitary;
- TSH increases secretion of thyroid hormones by the follicular cells (cAMP);
- Chronic elevation of TSH causes hypertrophy of the thyroid gland (goiter);
- Thyroid-binding globulin and albumins transport thyroid hormones in plasma.

T_3 and T_4 formation



Actions of thyroid hormones

- **Growth**: promote bone formation;
- **CNS**: contribute to normal development in the perinatal period;
- **Cardiovascular and respiratory systems**: ↑ cardiac output and respiration due to **permissive effect** for catecholamines (induce β-adrenergic receptors);
- **Energy metabolism**:

a. ↑ basal metabolic rate (BMR) and oxygen consumption by increasing the activity of the Na+-K+ ATPase;

b. increase body heat production (**thermogenic action**) by synthesis of uncoupling proteins;

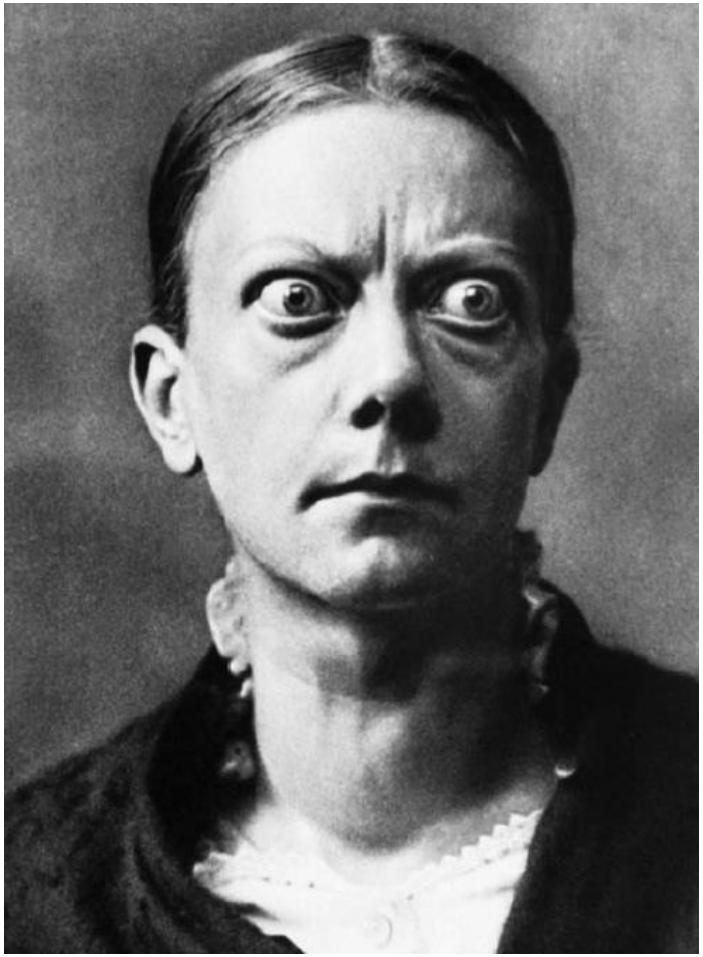
- **Metabolic effects**:

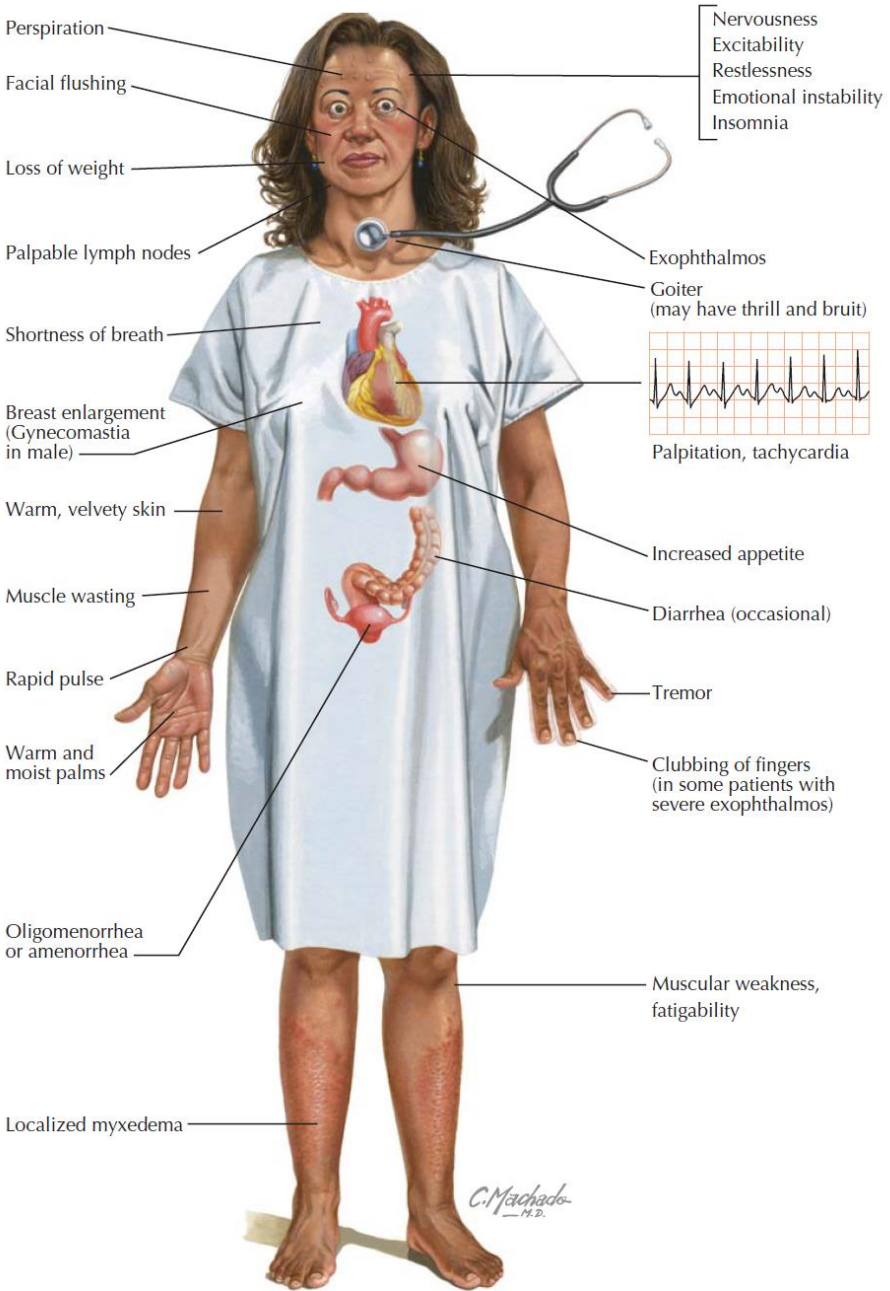
a. stimulate synthesis of many enzymatic and structural protein, but also activate proteolysis, net effect is **catabolic**;

b. stimulate lipolysis, glycogenolysis, gluconeogenesis;

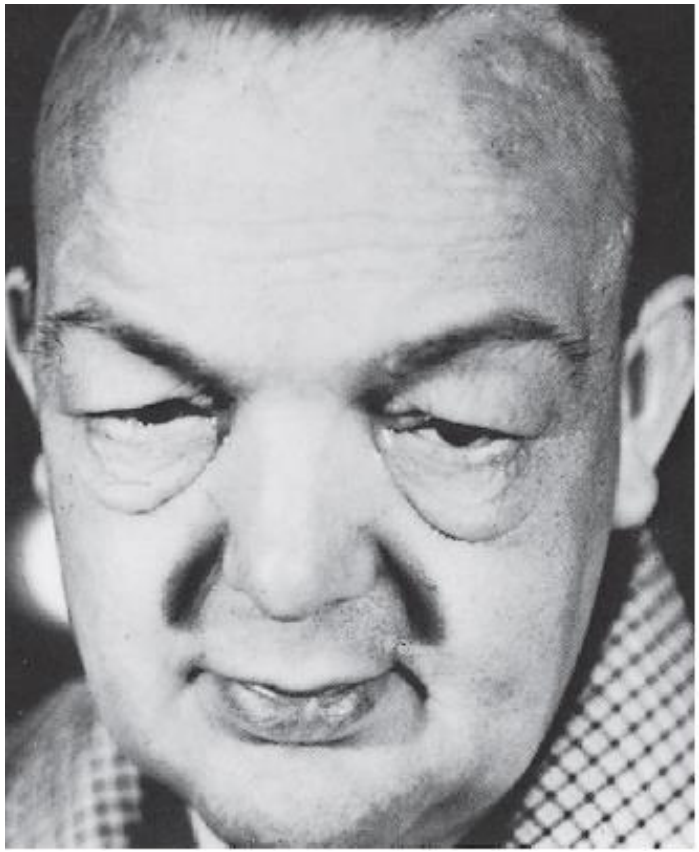
Hyperthyroidism	Hypothyroidism
↑ BMR Weight loss Negative nitrogen balance ↑ heat production (sweating) ↑ cardiac output Dyspnea Tremor, weakness Exophtalmos Goiter	↓ BMR Weight gain Positive nitrogen balance ↓ heat production (cold sensitivity) ↓ cardiac output Hypoventilation Lethargy, mental slowness Drooping eyelids Goiter Growth and mental retardation Myxedema
Graves' disease (diffusive toxic goiter) Thyroid neoplasm ↑ TSH secretion	Thyroiditis Surgical removal of thyroid Iodide deficiency Cretinism (congenital) ↓TSH or TRH
Thyroidectomy Propylthiouracis (↓ synthesis of thyroid) I131 (destroys thyroid) β-blockers (adjunct therapy)	Thyroid hormone replacement

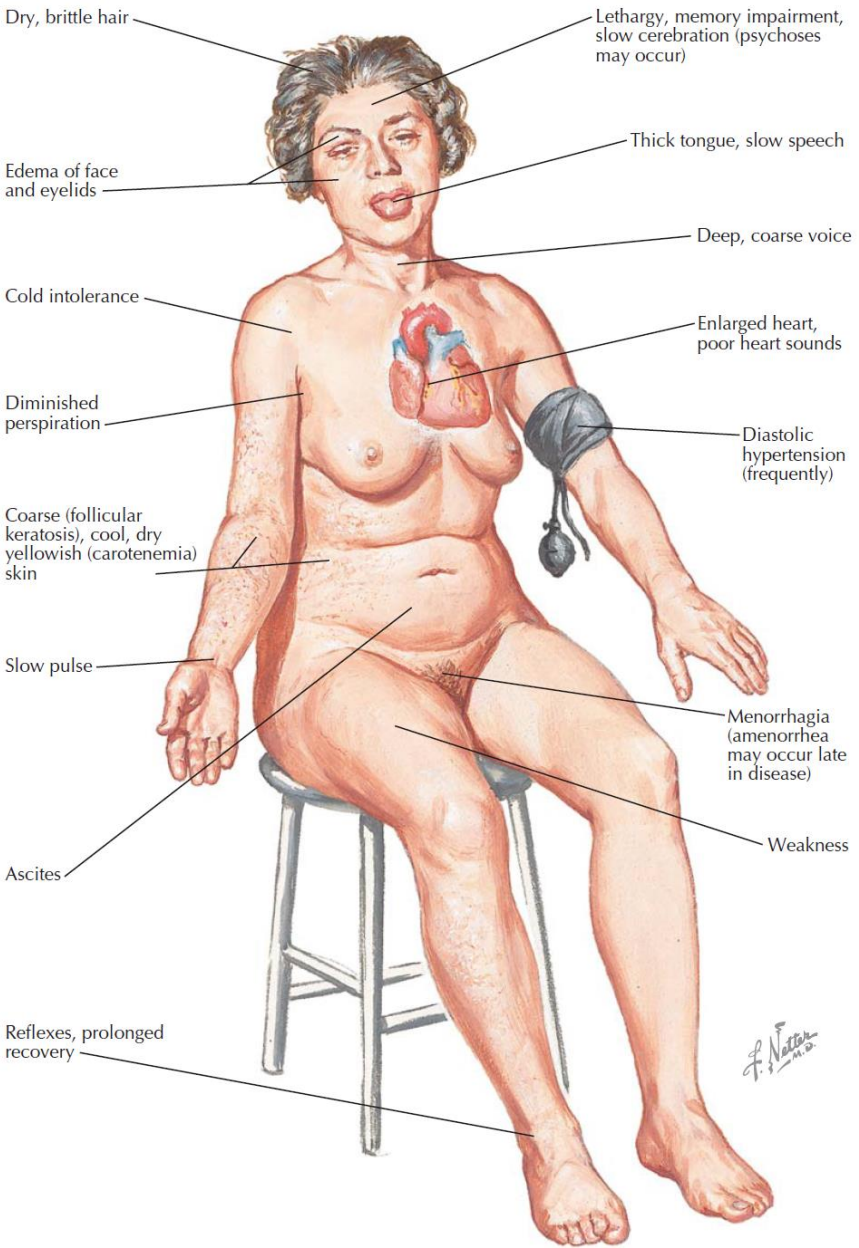
Graves' disease





Myxedema

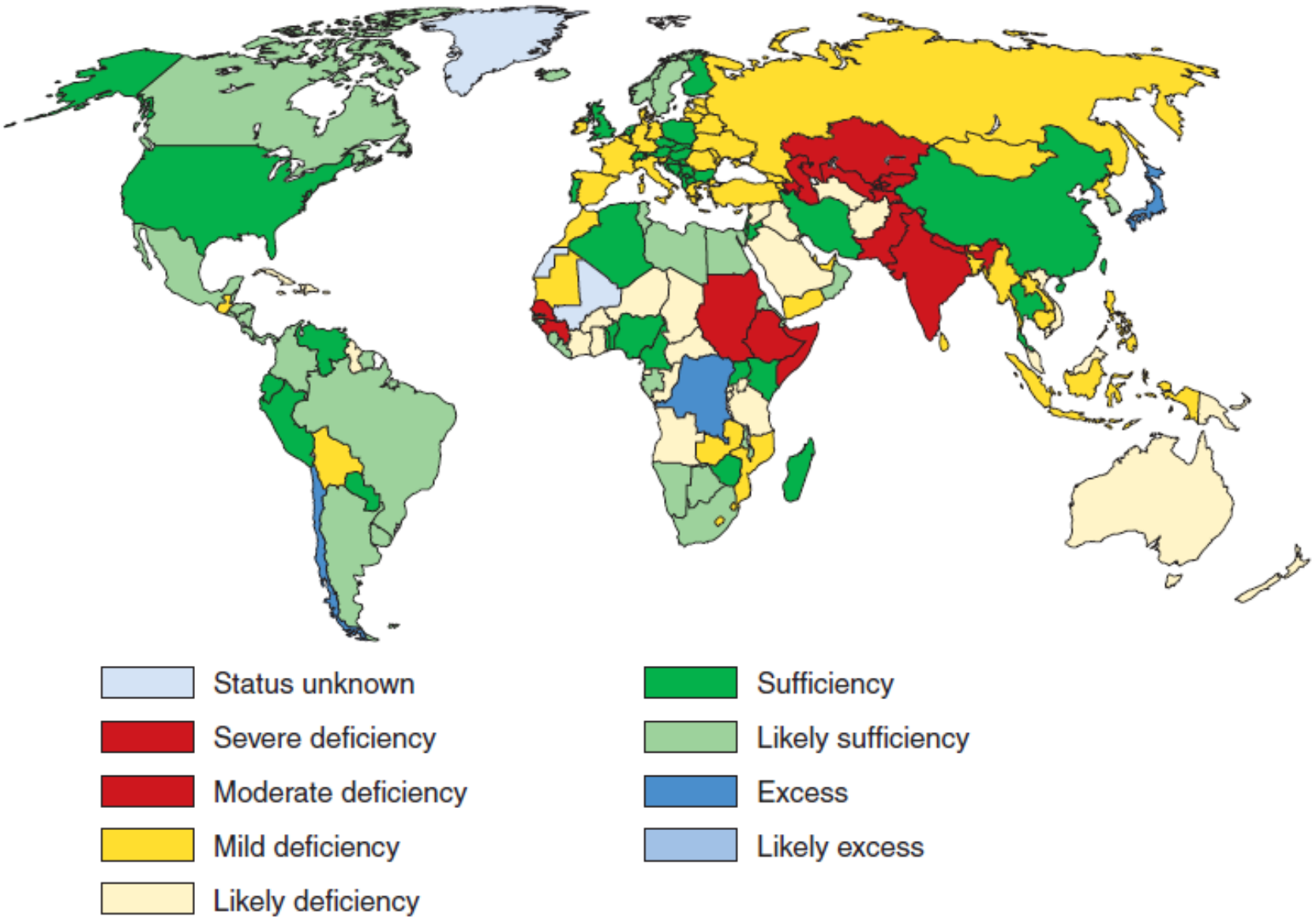



Dry, brittle hair
Lethargy, memory impairment, slow cerebration (psychoses may occur)
Thick tongue, slow speech
Edema of face and eyelids
Deep, coarse voice
Cold intolerance
Enlarged heart, poor heart sounds
Diminished perspiration
Diastolic hypertension (frequently)
Coarse (follicular keratosis), cool, dry yellowish (carotenemia) skin
Slow pulse
Menorrhagia (amenorrhea may occur late in disease)
Weakness
Ascites
Reflexes, prolonged recovery

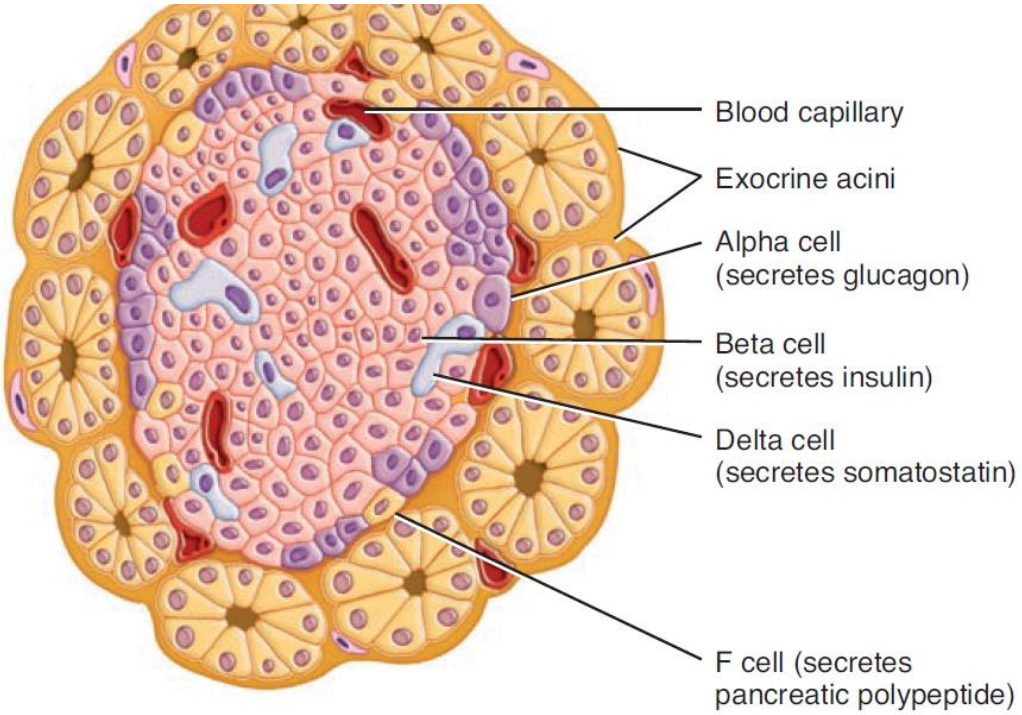
Cretinism

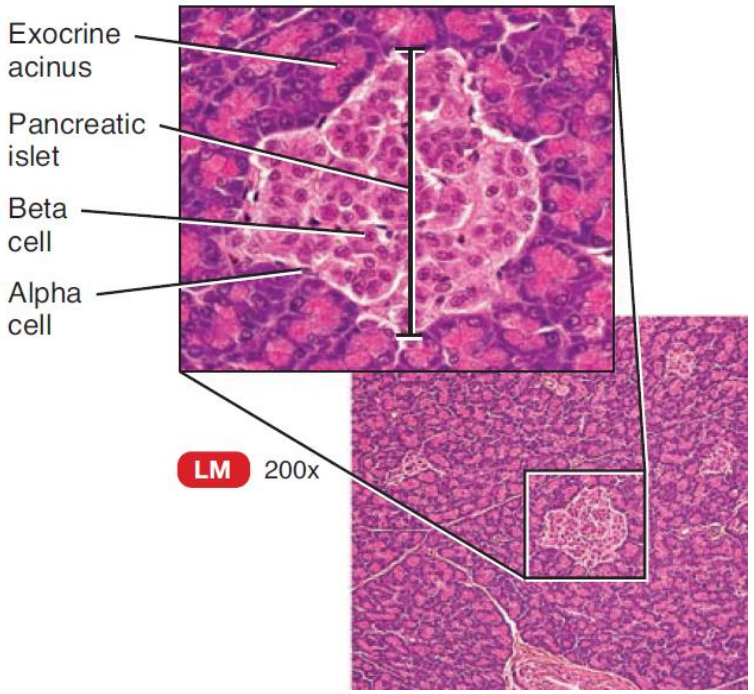
- Individuals who are hypothyroid from the birth are dwarfed and mentally retarded.

Worldwide iodine nutrition



Islets of Langerhans



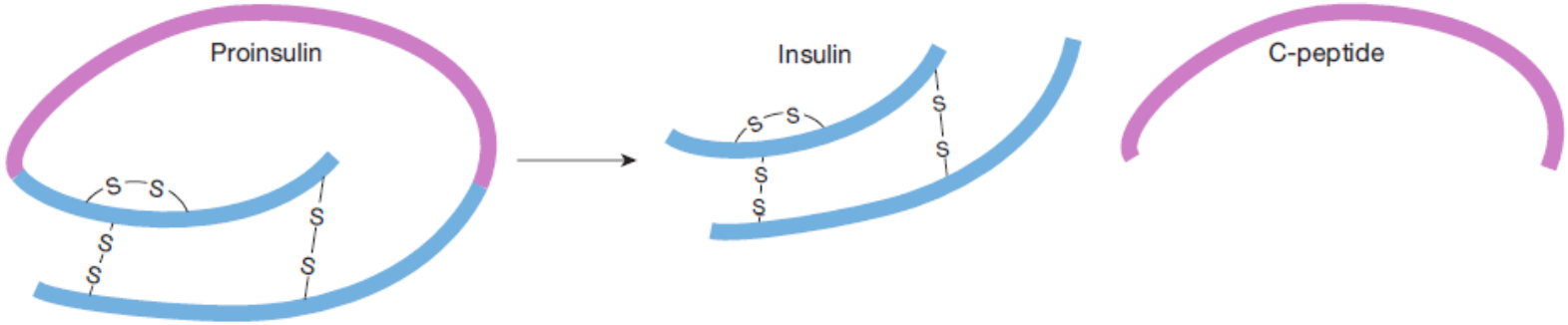


- *1. A cells (α-cells) secrete glucagon (20%);*
- *2. B cells (β-cells) secrete insulin (65%);*
- *3. D cells (δ-cells) secrete somatostatin (10%);*
- *4. F cells or PP cells secrete pancreatic polypeptide (5%).*

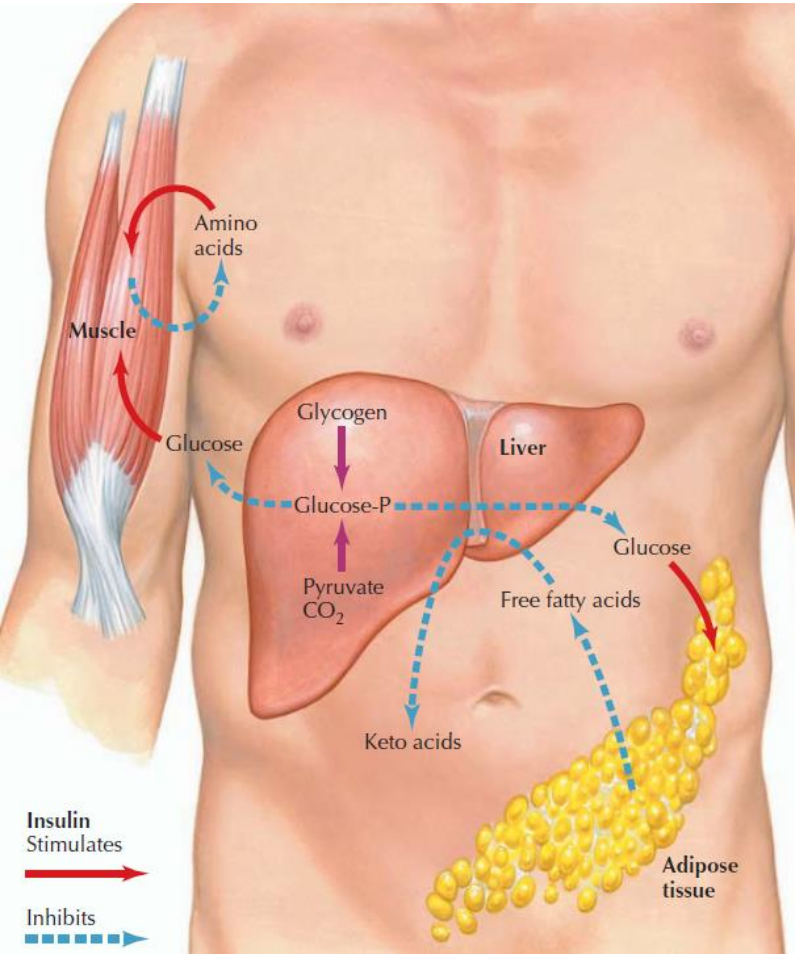
Insulin secretion

- Insulin is a peptide consisting of A chain and B chain.
- The β-cells firstly produce preproinsulin, after removal of signal peptide it converts to proinsulin and then proteases cleave the connecting peptide (C peptide), yielding insulin. Determination of C peptide is an important diagnostic test for insulin secretion level.

1. **Stimuli of insulin secretion**: hyperglycaemia, ↑ free fatty acids and amino acids; gastrointestinal hormones (gastrin, secretin, CCK, GIP); glucagon, GH, cortisol; potassium; β-adrenergic stimulation; parasympathetic stimulation, acetylcholine; insulin resistance; obesity.
2. **Inhibitors of insulin secretion**: hypoglycaemia; fasting; exercise; somatostatin; α-adrenergic activity; leptin.

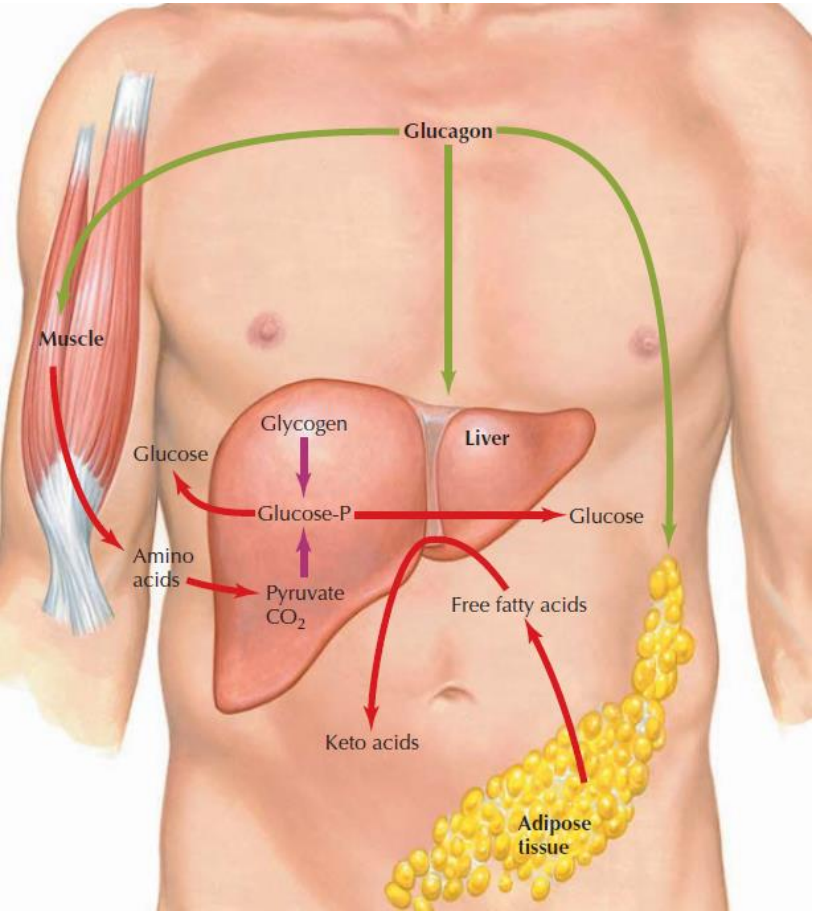


Actions of insulin



1. **On carbohydrate metabolism (↓blood glucose):**
   - a. increases glucose uptake by ↑ of permeability (GLUT 4) in muscle and adipose;
   - b. promotes peripheral utilization of glucose and inhibits gluconeogenesis;
   - c. stimulates glycogenesis and inhibits glycogenolysis.
2. **On protein metabolism (anabolic effect):**
   - a. increases amino acids uptake;
   - b. increases protein synthesis.
3. **On fat metabolism:**
   - a. promotes synthesis of fatty acids and triglycerides;
   - b. inhibits lipolysis and oxidation of fatty acids.
   - c. stimulates cholesterol synthesis in the liver.

Glucagon

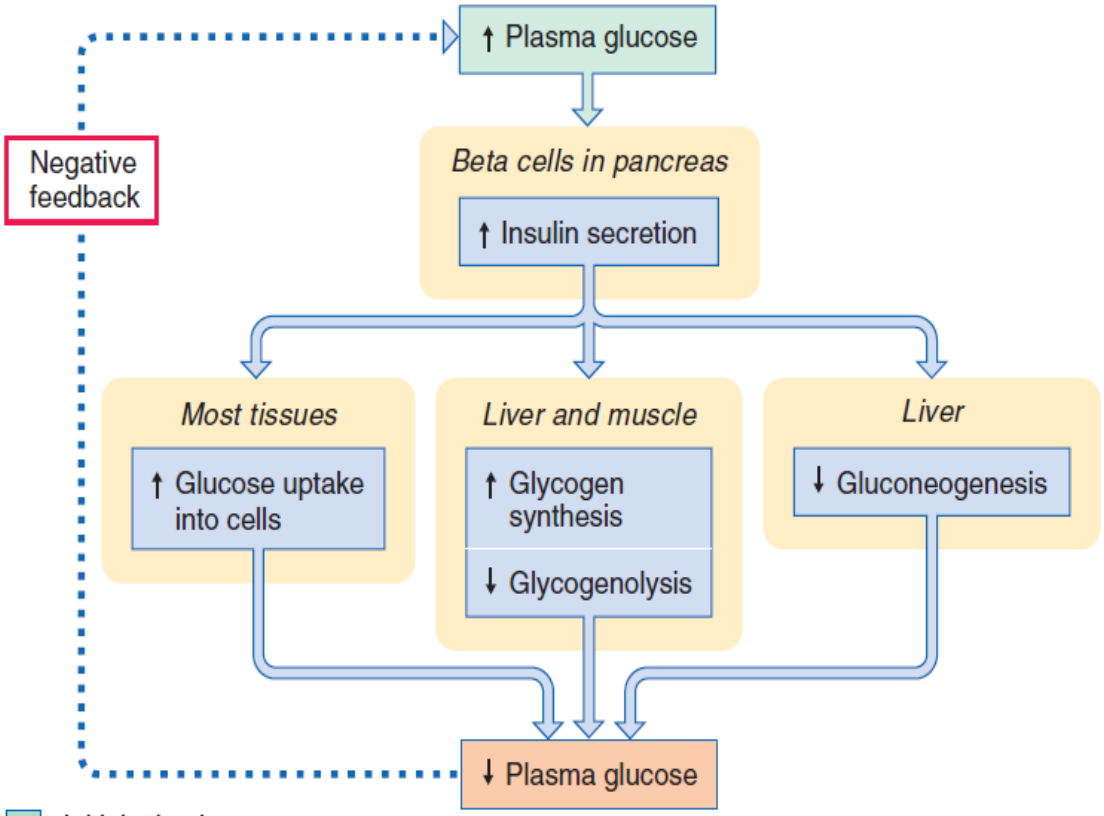


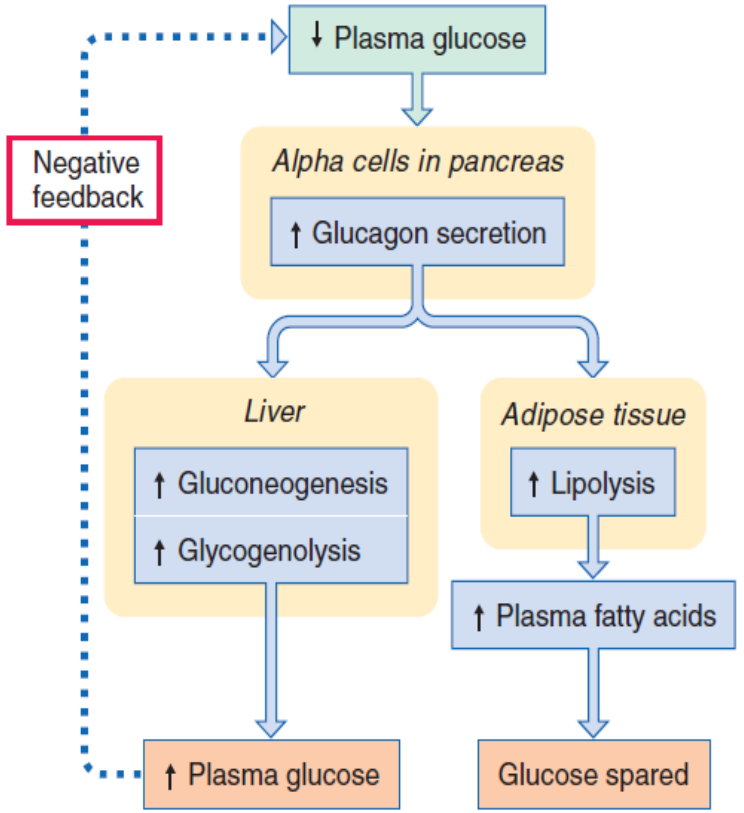
- Glucagon secretion is stimulated by hypoglycaemia, fasting, increased blood amino acids, and cholecystokinin. Glucagon secretion is inhibited by insulin, increased blood fatty acids, somatostatin.

Action of glucagon:

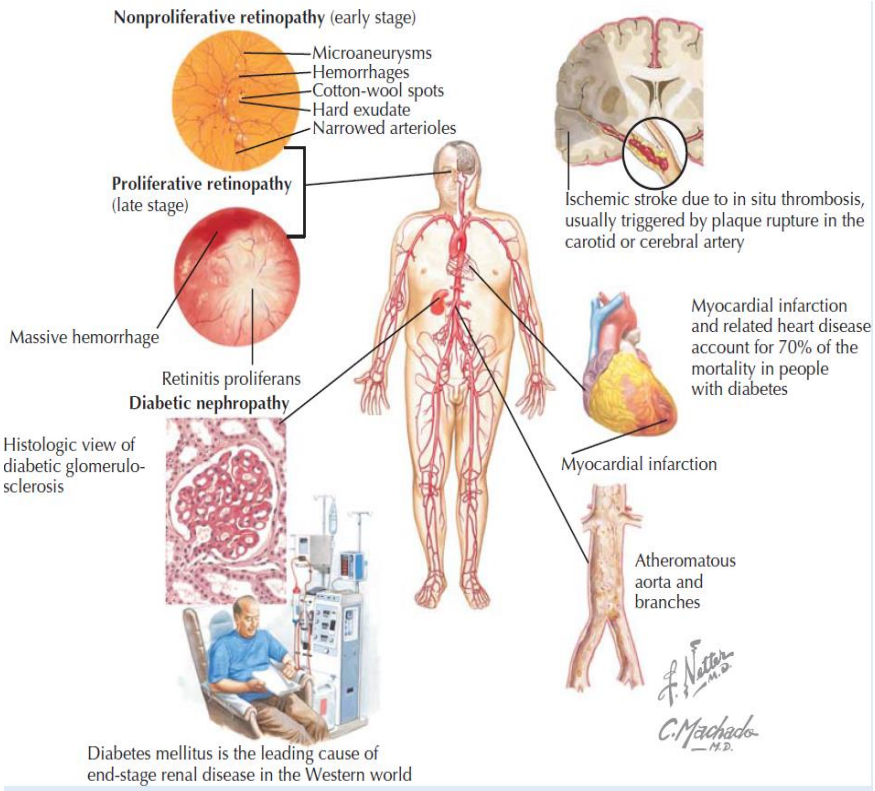
- a. stimulates glycogenolysis;
- b. stimulates gluconeogenesis (increases blood glucose);
- c. inhibits glycogenesis and glycolysis;
- d. stimulates lipolysis and ketoacid formation.
- e. increases urea production.

Regulation of plasma glucose





Diabetes mellitus



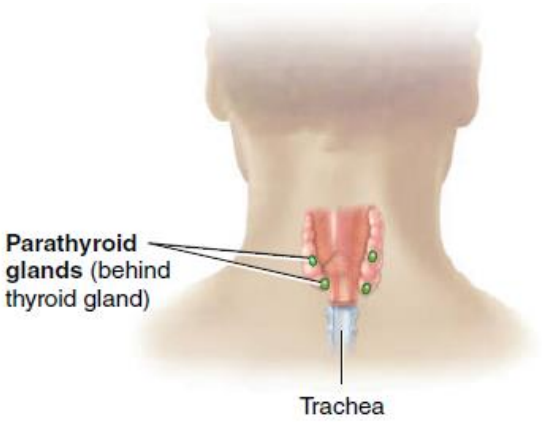
- ***Type 1 diabetes (insulin-dependent diabetes mellitus)*** *is caused by destruction of β-cells by autoimmune attack. It is characterized by hyperglycaemia, loss of weight, metabolic acidosis (diabetic ketoacidosis), hyperkalemia, polyuria (osmotic diuresis), polydipsia (thirst), and polyphagia. It is treated with insulin replacement therapy.*

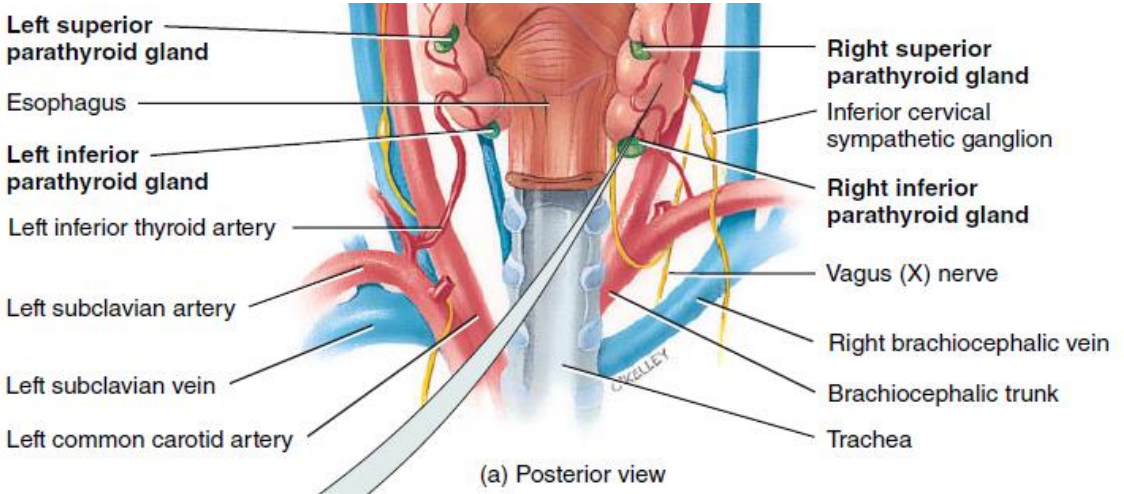
Type 2 diabetes (non-insulin-dependent diabetes mellitus) *is caused by insulin resistance, resulting from reduction in the insulin receptors. It is characterized by hyperglycaemia, obesity, hyperosmolarity, polyuria, and polydipsia. It is treated with weight reduction, sulfonylurea drugs (glyburide), which stimulate insulin secretion, and biguanide drugs (metformin), which activate insulin receptors.*

Comparison of IDDM and NIDDM

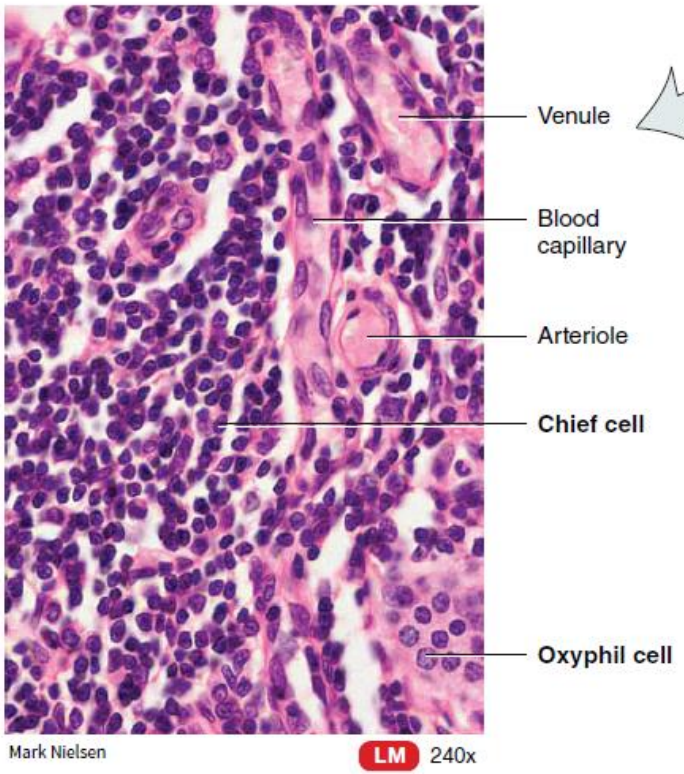
Characteristic	Type I (IDDM)	Type II (NIDDM)
Age of onset	Before 40 year (juvenile-onset diabetes)	After 40 year (adult-onset diabetes)
Mode of onset	Rapid	Gradual
Main cause	Absolute insulin deficiency	Insulin resistance or relative insulin deficiency
B cells of pancreas	Destroyed	Normal
Insulin level	Low to absent	Normal or elevated
Body weight	Not obese	Obese
Incidence of ketoacidosis	High	Low
Genetic predisposition	Moderate: concordance rate is < 50%	Strong: concordance rate is > 50%
Usual complication	Ketoacidotic coma	Hyperosmolar coma
Treatment with insulin	Essential	Usually not required
Treatment with oral hypoglycaemic drugs	Unresponsive	Responsive

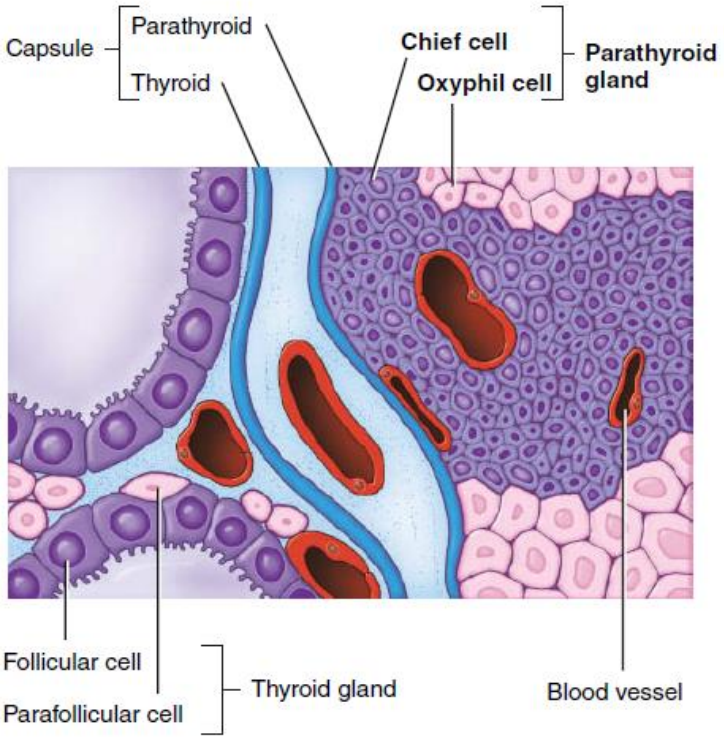
Parathyroid glands



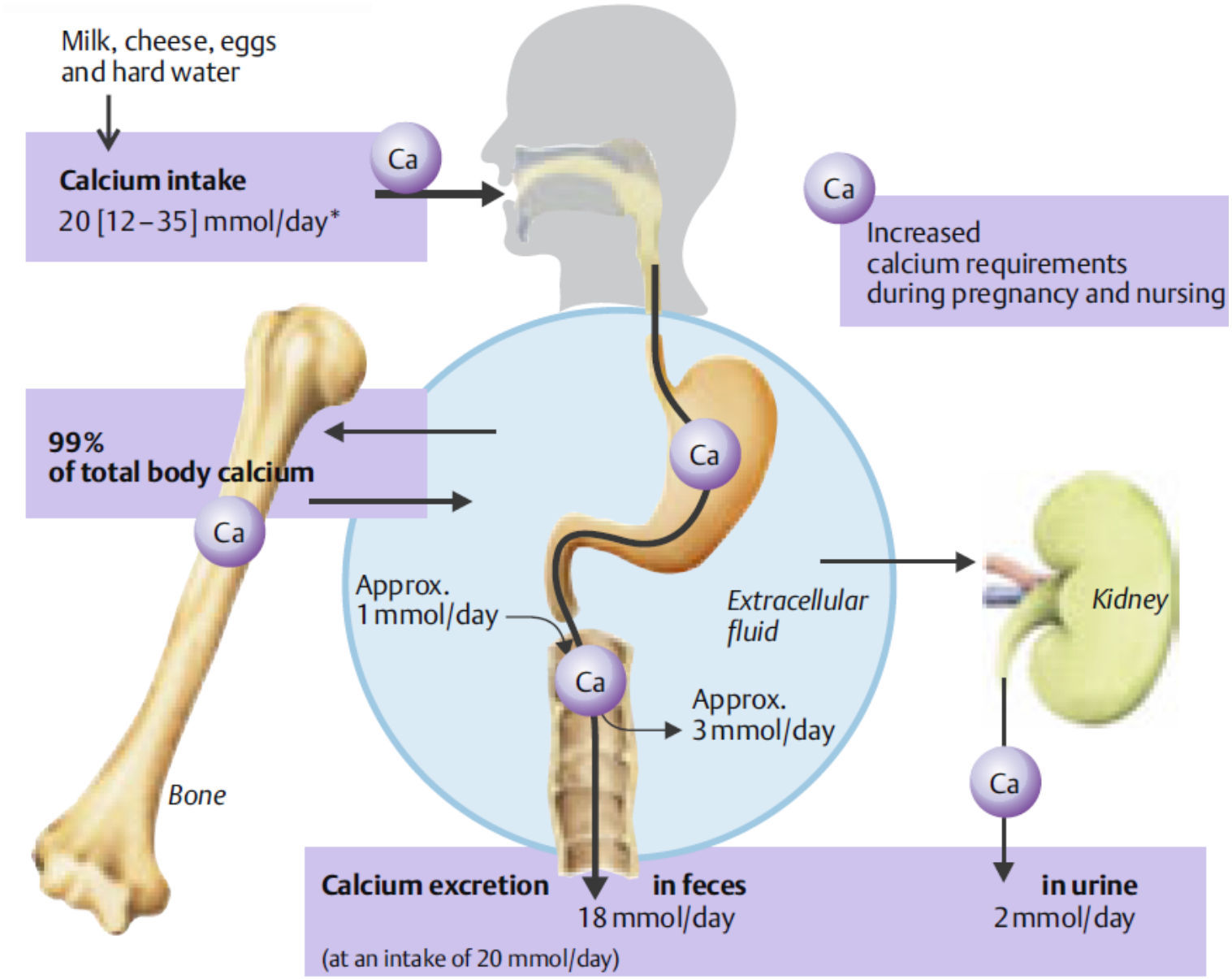


(a) Posterior view



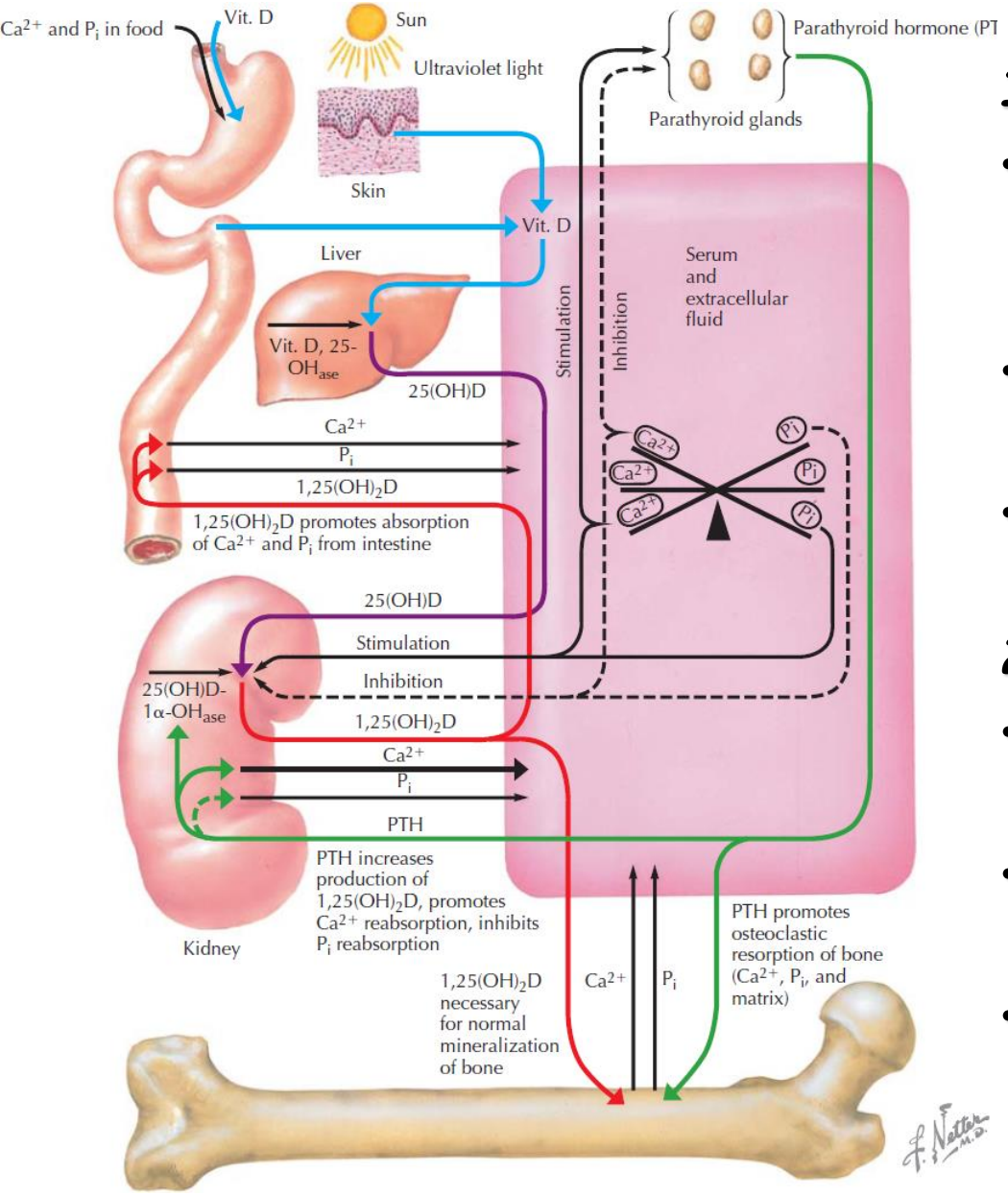


Calcium metabolism



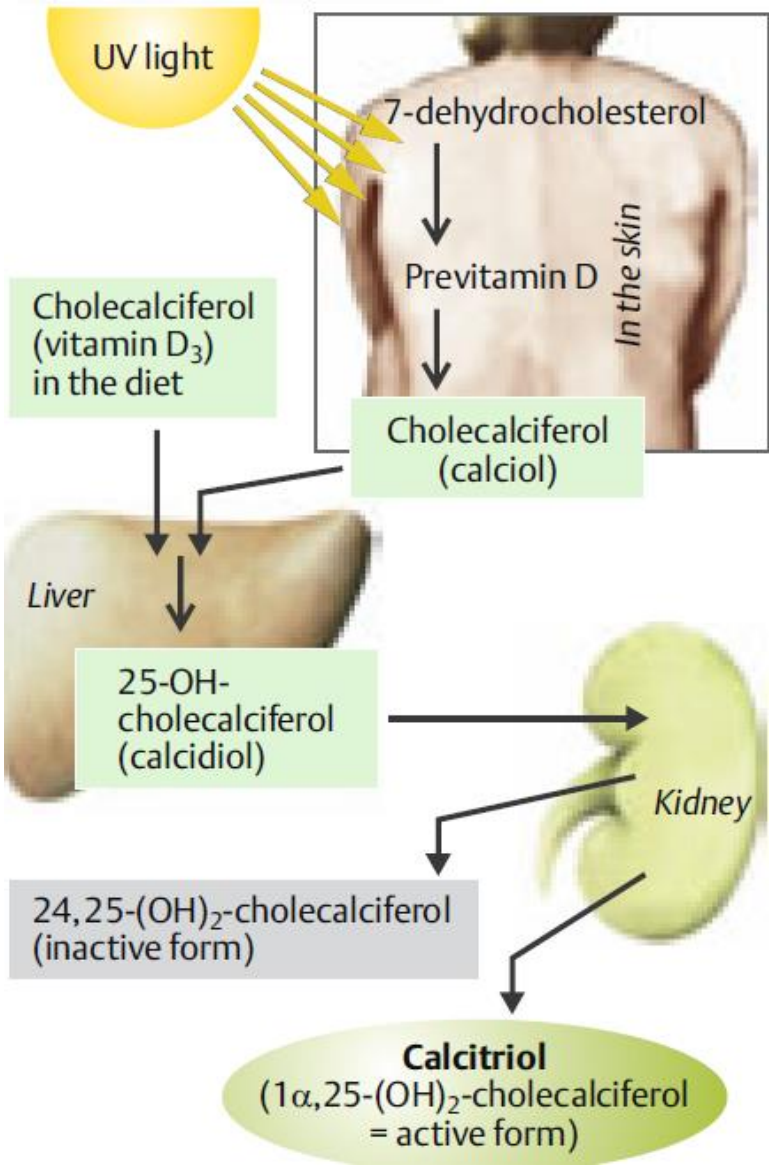
* 1 mmol Ca^{2+} = 2 mEq Ca^{2+} = 40 mg Ca^{2+}

Actions of PTH



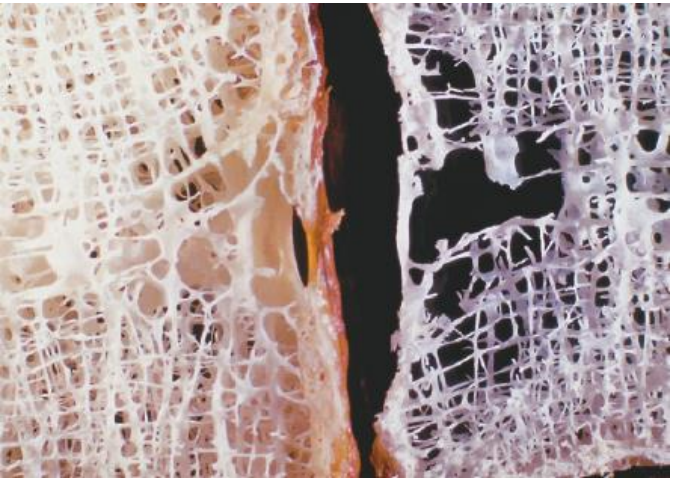
1. **At the bones:**
   - a. activates bone resorption and calcium and phosphate mobilization from bones;
   - b. simulates maturation of osteoclasts;
   - c. inhibits collagen synthesis by osteoblasts.
2. **At the kidneys:**
   - a. increases renal tubular reabsorption of calcium;
   - b. decreases renal tubular reabsorption of phosphate;
   - c. increases the formation of 1,25-dihydroxycholecalciferol

Actions of vitamin D



1. **At the small intestine:**
   - a. increases calcium absorption (stimulates production of calcium binding proteins);
   - b. increases phosphate absorption.
2. **At the bones:**
   - a. increases bone remodelling and mineralization;
   - b. promotes actions of PTH on osteoclasts, increasing bone resorption.
3. **At the kidneys:**
   - a. increases renal tubular reabsorption of calcium;
   - b. increases renal tubular reabsorption of phosphate.

Actions of Calcitonin

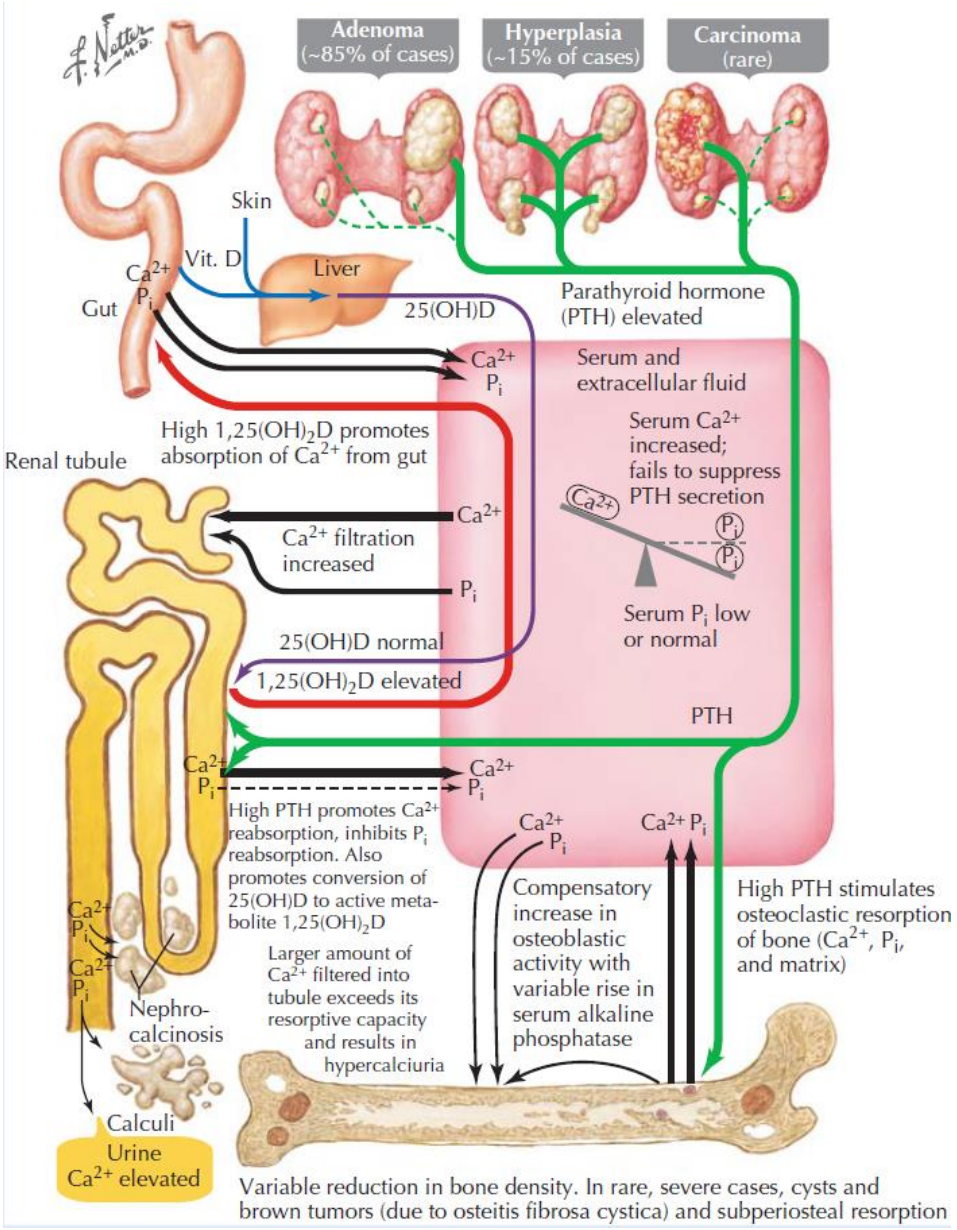


1. At the kidneys:

- a. decreases renal tubular reabsorption of calcium;
- b. decreases renal tubular reabsorption of phosphate.
- 2. At the bones:
- a. decreases bone resorption;
- b. inhibits osteoclasts.

CT deficiency or CT hypersecretion does not lead to clinical abnormalities of calcium concentrations. However, calcitonin is used for treatment of malignancy-related hypercalcaemia and osteoporosis.

Hyperparathyroidism

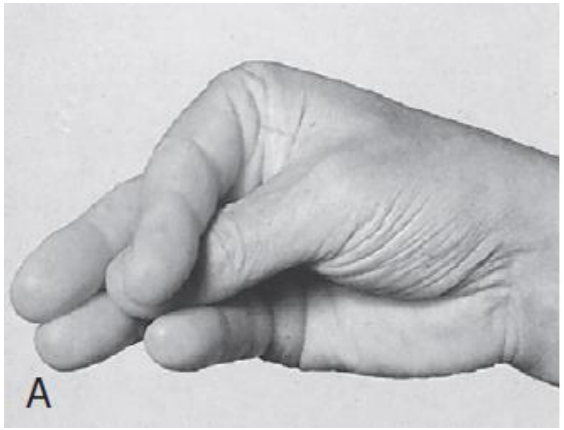


Hyperparathyroidism leads to hypercalcaemia and hypophosphatemia.

It is associated with extensive decalcification and multiple fractures (osteitis fibrosa cystica), kidney stone formation (urolithiasis), depression of CNS, muscle weakness, constipation, abdominal pain.

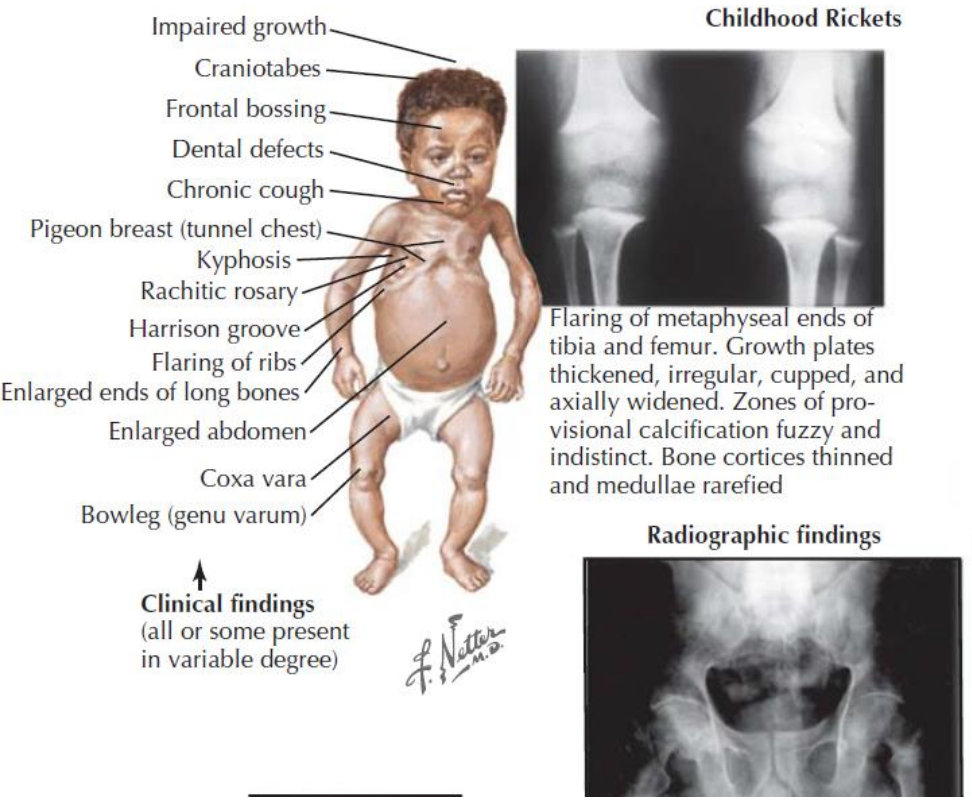
It is treated with surgical removal of glands.

Hypoparathyroidism



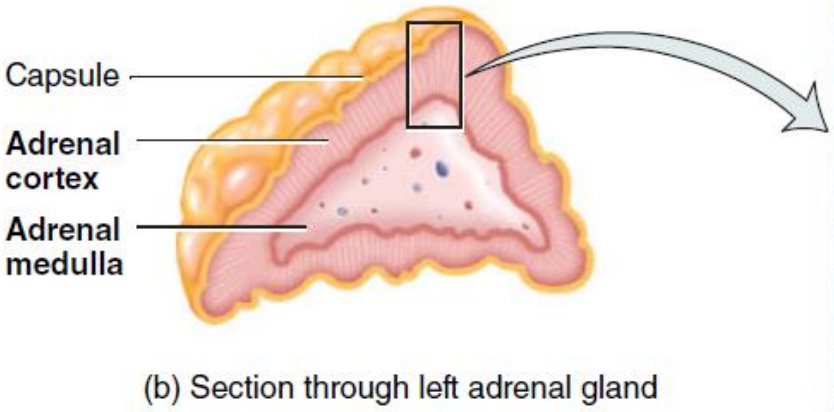
- The absence or decreased function of the parathyroid glands results in hypocalcemia and hyperphosphatemia.
- Hypocalcaemia increases the excitability of sensory and motor neurons and muscle cells (tingling or numbness, cramping, seizures, tetanic muscle spasms).
- It is treated with oral calcium supplement and active form of vitamin D. The complete absence of PTH (e.g. after removing of parathyroid glands) leads to death from hypocalcemic tetany.

Clinical correlation

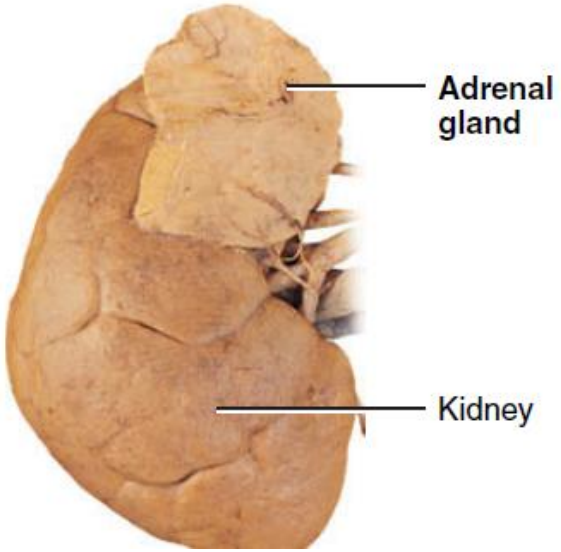


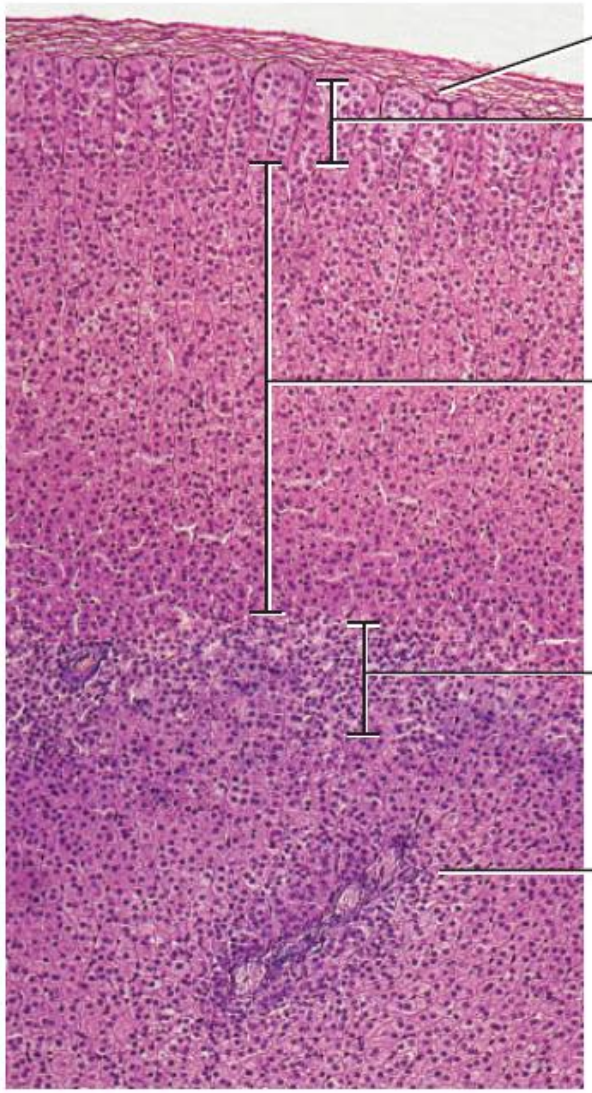
- *Vitamin D deficiency during childhood causes rickets (skeletal deformities and growth failure). It is treated with vitamin D supplement.*
- *Vitamin D deficiency in an adult causes osteomalacia (impairment of bone mineralization leads to the softening of bones).*
- *Excess of vitamin D (vitamin D toxicity) leads to calcinosis (calcification of soft tissues), kidney stone formation, hypercalcaemia, and cardiac arrhythmia.*

Adrenal cortex



(b) Section through left adrenal gland





Capsule

Adrenal cortex:

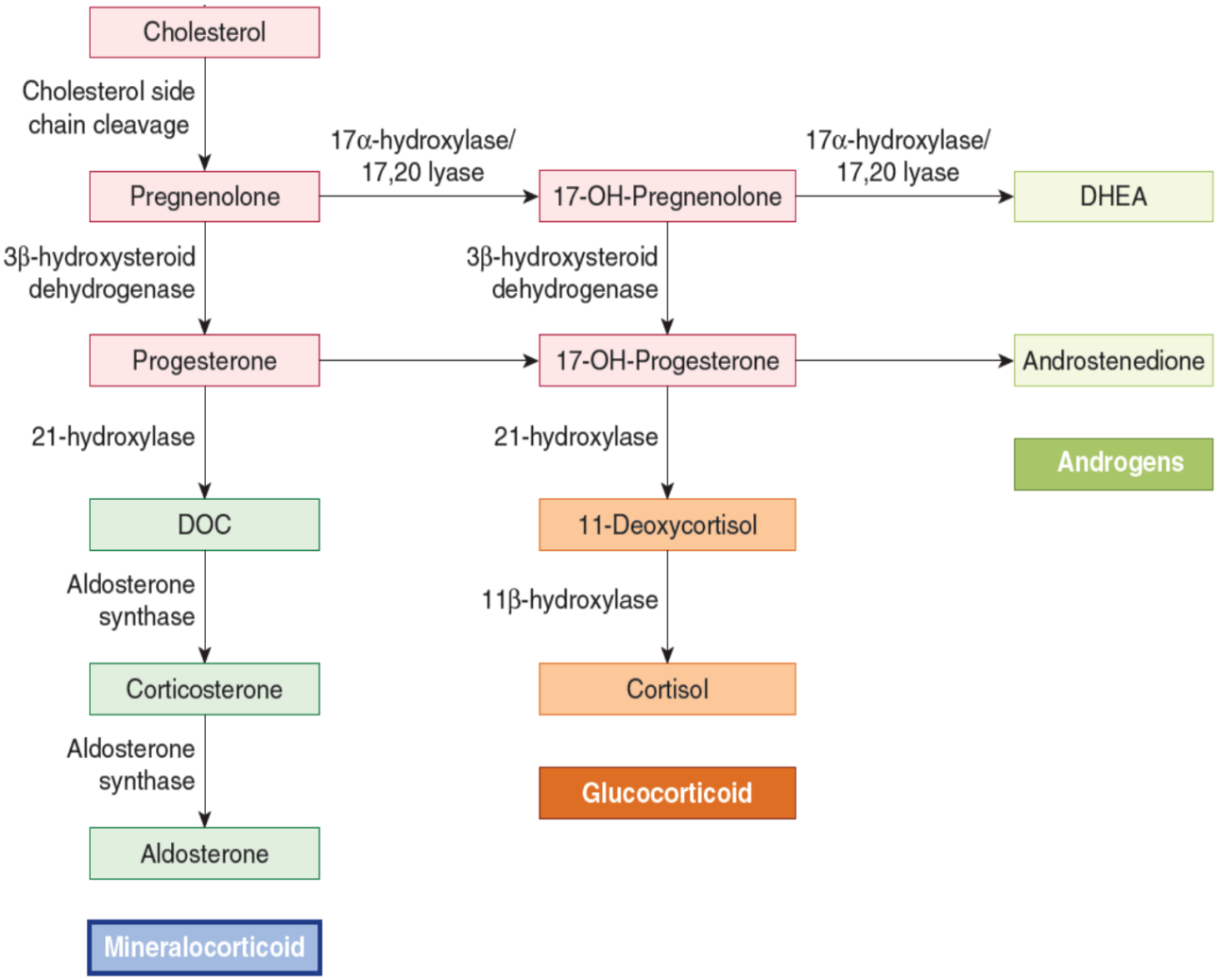
Zona glomerulosa
secretes mineralocorticoids, mainly aldosterone

Zona fasciculata
secretes glucocorticoids, mainly cortisol

Zona reticularis
secretes androgens

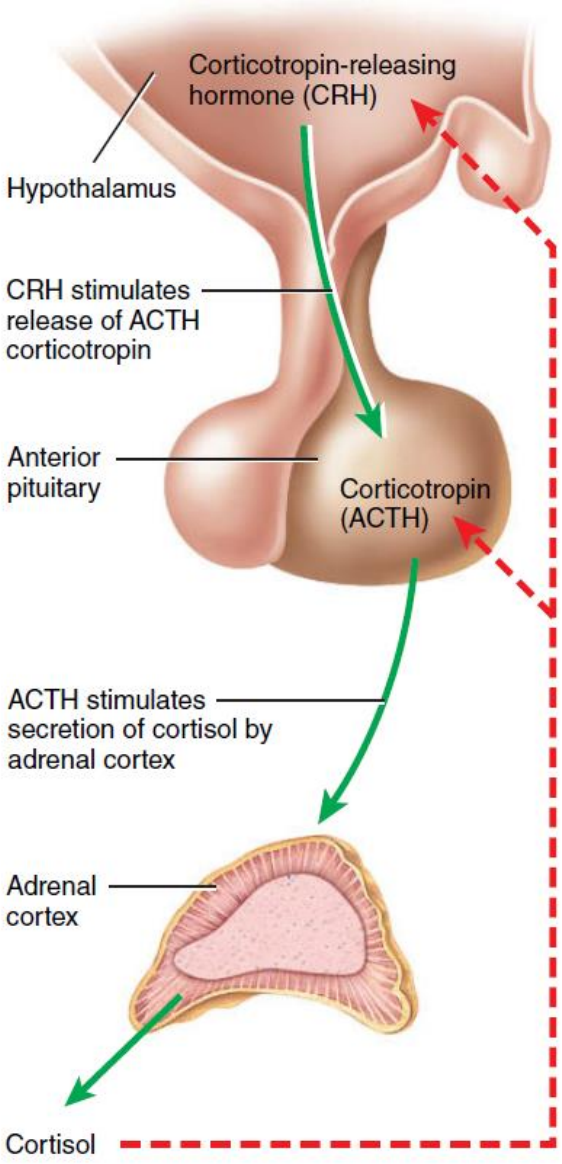
Adrenal medulla
chromaffin cells secrete epinephrine and norepinephrine (NE)

Synthesis of steroid hormones



- *21-carbon steroids*: progesterone, deoxycorticosterone, aldosterone, and cortisol.
- *19-carbon steroids*: dehydroepiandrosterone androstenedione, testosterone in the testes;
- *18-carbon steroids*: estrogens in the ovaries and placenta.

Hypothalamic-pituitary-adrenal axis



- Glucocorticoids secretion oscillates with circadian rhythm.
- Hypothalamus releases CRH that stimulates secretion of ACTH.
- Pro-opiomelanocortin (POMC) is a precursor of ACTH, β-lipotropin, α-melanocyte-stimulating hormone (MSH), β-endorphin.
- ACTH increases steroid hormone synthesis by stimulating cholesterol desmolase.
- Chronically increased levels of ACTH cause hypertrophy of the adrenal cortex (Cushing's disease).

Actions of glucocorticoids

1. On carbohydrate metabolism (increase blood glucose):
- a. stimulate of gluconeogenesis;
- b. decrease uptake and utilization of glucose;
- c. ↑ secretion of glucagon and epinephrine that cause glycogenolysis, but also promotes hepatic glycogenesis.

2. On protein metabolism:
- a. ↑ proteolysis, especially in skeletal muscle, skin, bone, and connective tissue;
- b. inhibits synthesis of proteins (antianabolic effect),
- c. ↑ synthesis of many plasma and liver proteins.

3. On fat metabolism:
- a. promote lipolysis, ketogenesis and mobilization of fatty acids;
- b. have lipogenic effect (due to compensatory hyperinsulinemia) and cause centripetal redistribution of fat;
- c. stimulate leptin synthesis in adipose tissue.

Actions of glucocorticoids

4. Anti-inflammatory effects:

- a. induce synthesis of lipocortins (inhibitors of phospholipase A2), decreasing amount of arachidonic acid available for conversion to prostaglandins and leukotrienes that mediate inflammatory response;
- b. decrease capillary permeability and reduce inflammatory exudations;
- c. stabilize lysosomal membrane and inhibit release of proteolytic enzymes;
- d. inhibit the release of histamine and serotonin from mast cells.

5. Immunosuppressive effects:

- a. involution of the lymph nodes, thymus and spleen;
- b. inhibit T-cells proliferation and release of interleukins;
- c. reduce B-cells and decrease antibody production.

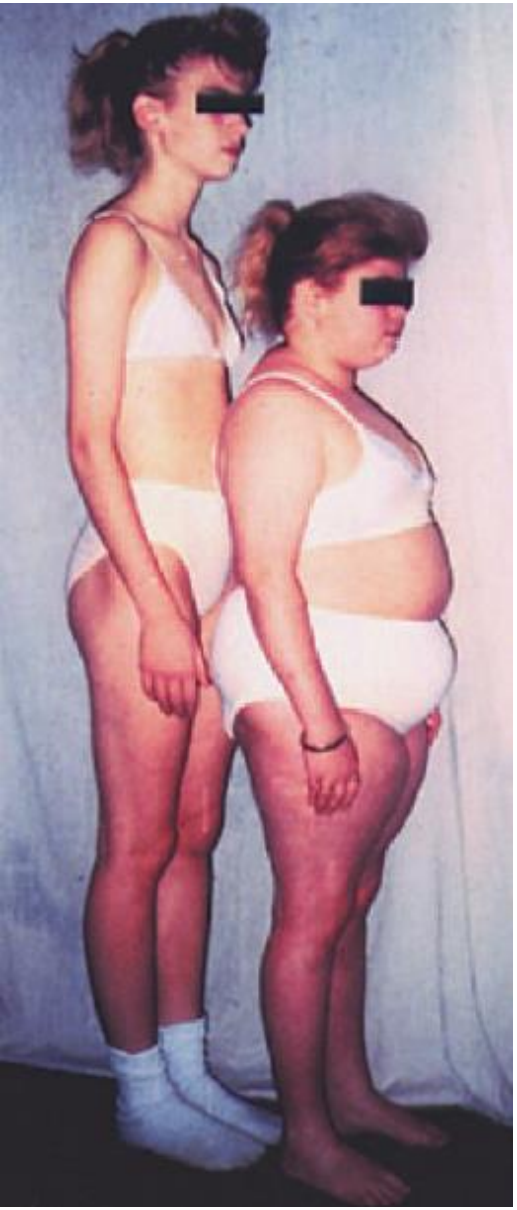
Actions of glucocorticoids

6. Permissive effects:
- a. increase catecholamine synthesis and vascular responsiveness to them;
- b. increase metabolic effects of glucagon and catecholamines.

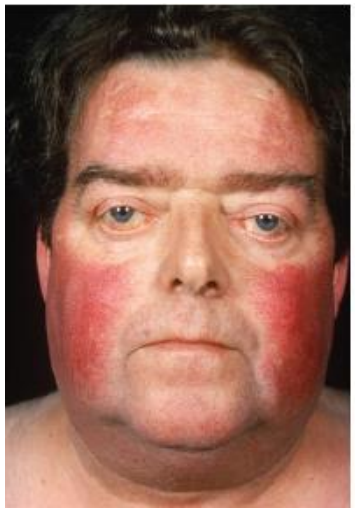
7. Psychoneural effects:
- a. decrease REM sleep and increase slow-wave sleep, high levels can cause insomnia;
- b. influence the mood and behaviour, high levels can cause depression and irritability.

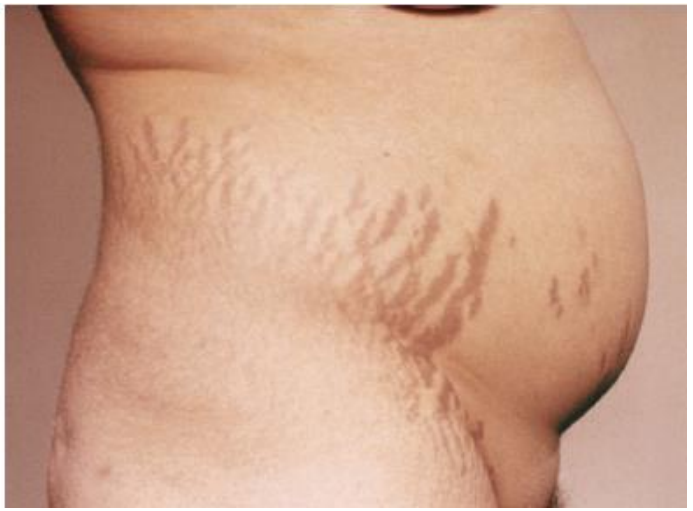
8. Other effects:
- a. stimulate surfactant synthesis in the fetal lungs;
- b. increase glomerular filtration rate, causing vasodilation of afferent arterioles;
- c. increase red blood cell, platelet, and neutrophil counts and decrease eosinophil, basophil, and lymphocyte counts.

Hypersecretion of cortisol

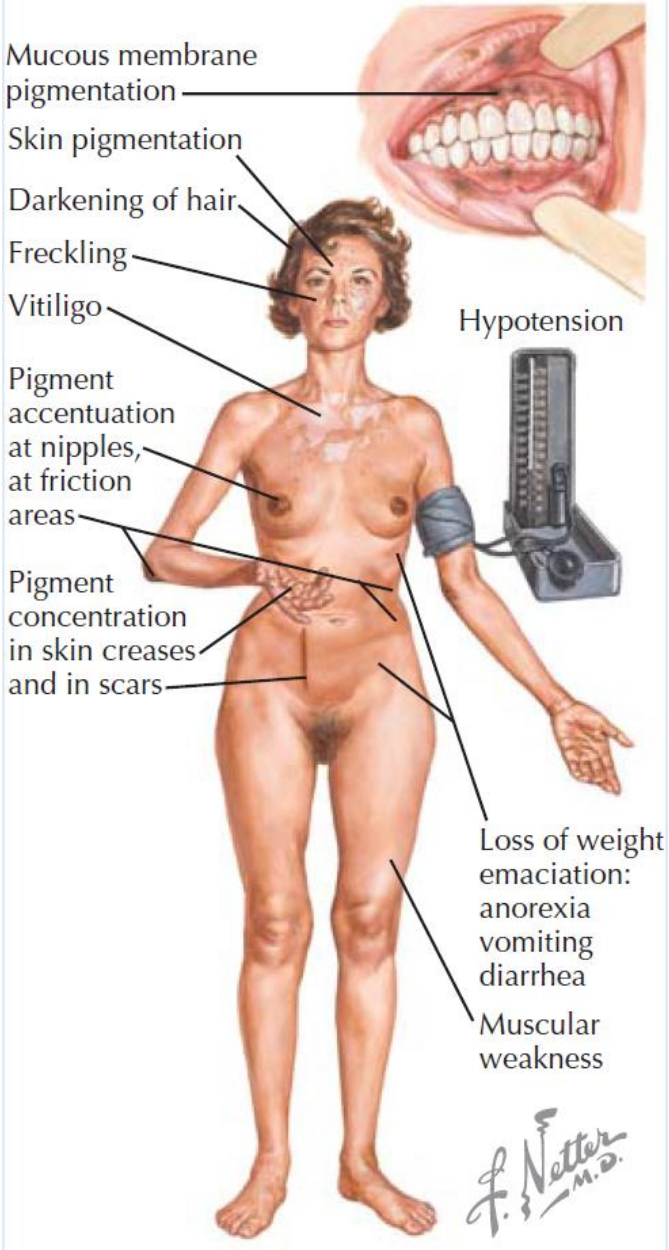


- *Cushing's syndrome* (primary hyperplasia of adrenal cortex) or *Cushing's disease* (excess of ACTH).
- It is associated with centripetal obesity (moon face, buffalo hump), hypertension, hyperglycaemia and insulin resistance (steroid diabetes), osteoporosis, muscle wasting, striae, poor wound healing, immunosuppression, virilisation and menstrual disorders in females.



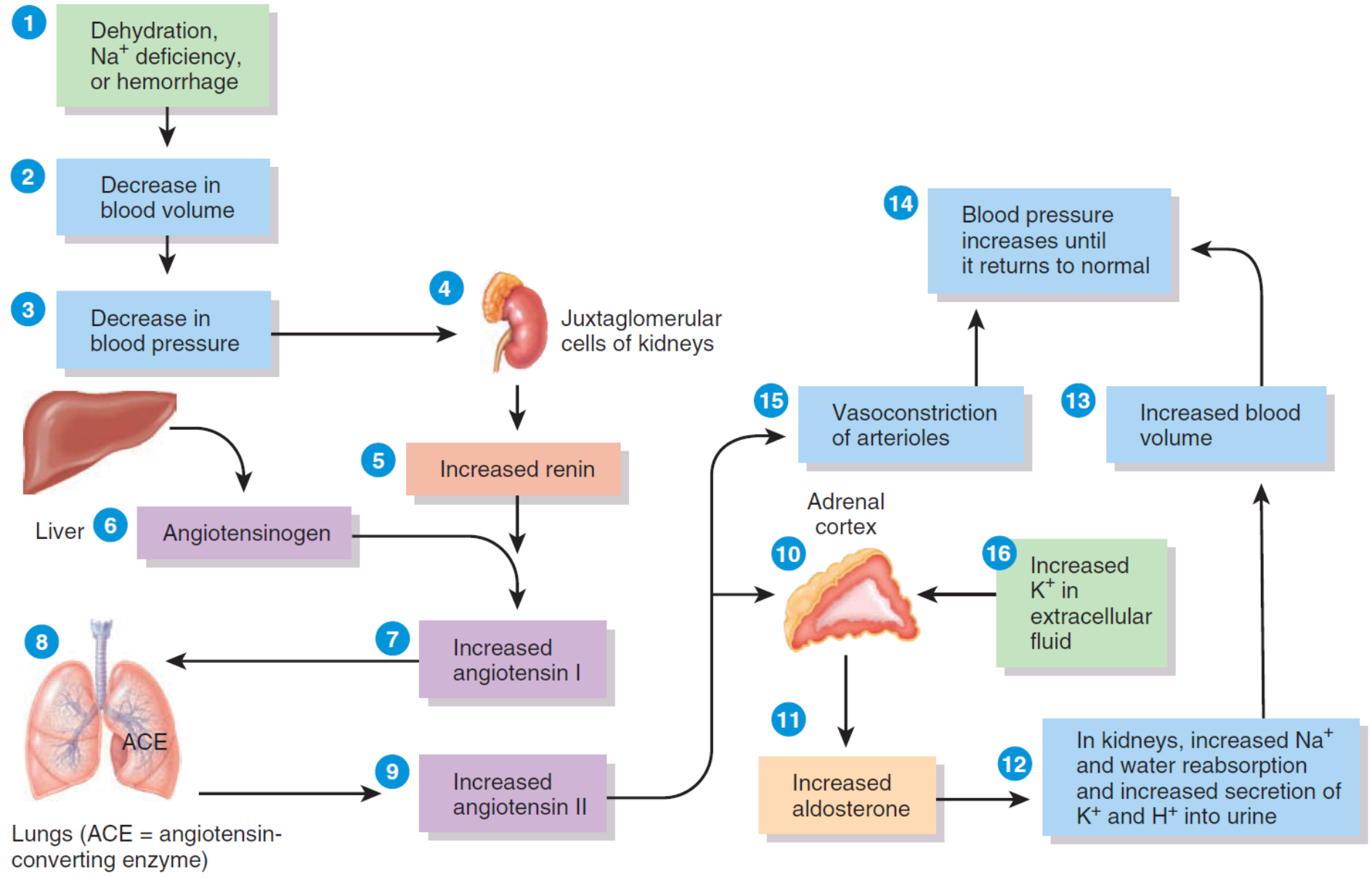


Addison's disease



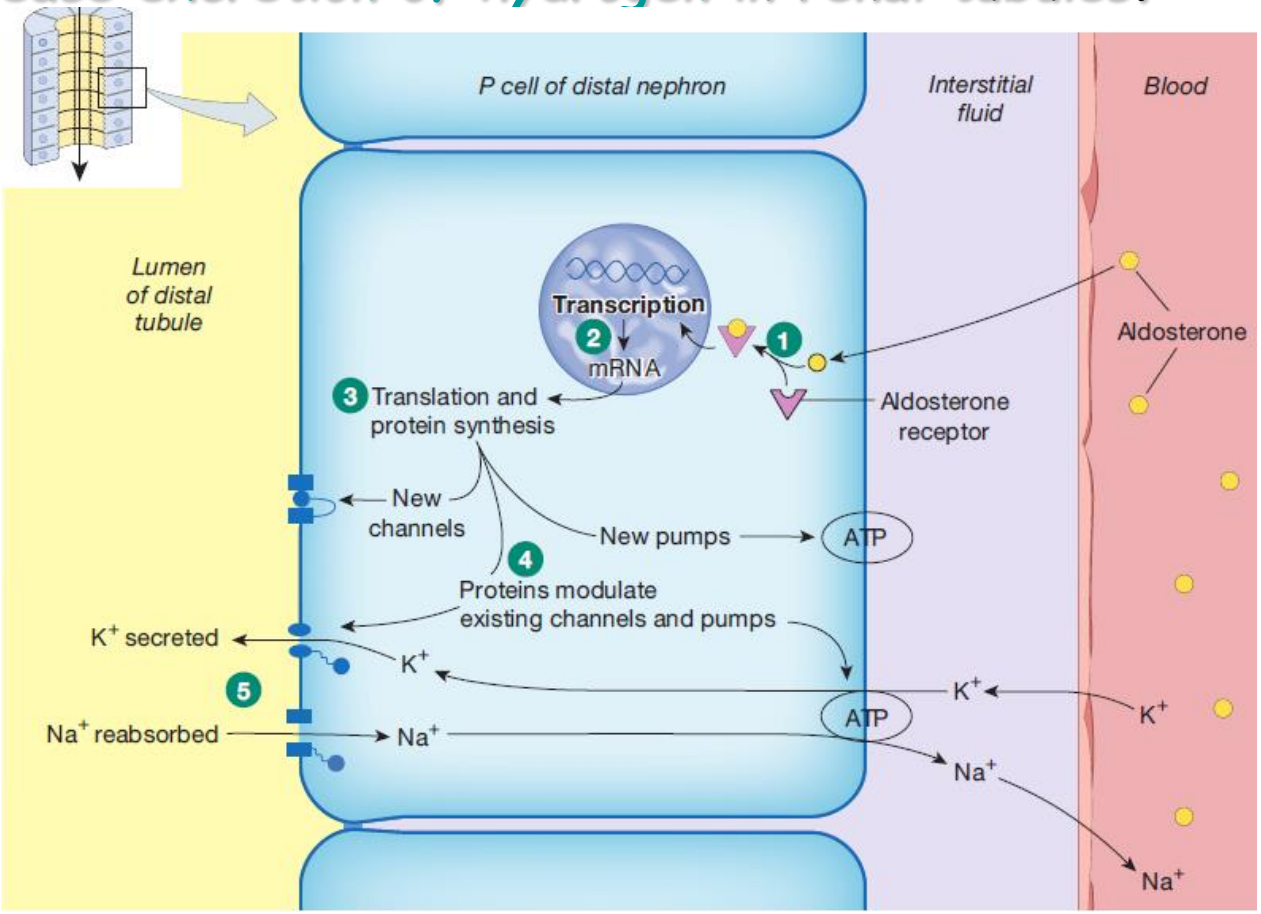
- Autoimmune destruction of the adrenal glands.
- It is associated with hypoglycaemia, rapid weight loss,anorexia, nausea. weakness, dehydration,hypotension, metabolic acidosis, hyponatremia, hyperkalemia, and diffusive hyperpigmentation (increased ACTH and MSH level).
- Treatment involves replacement of glucocorticoids and mineralcorticoids.

Regulation of aldosterone secretion



Actions of aldosterone

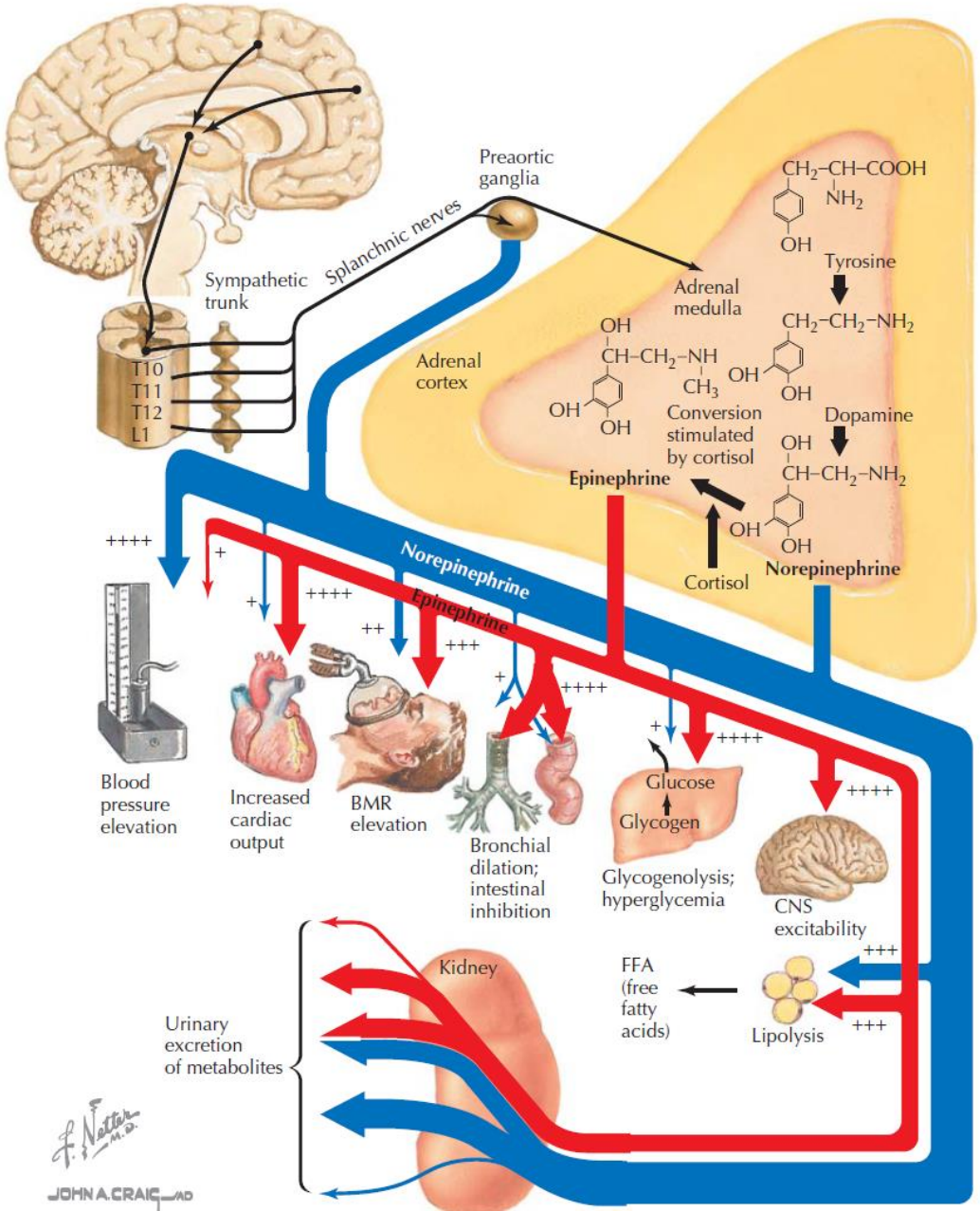
- a. increase reabsorption of sodium in renal tubules, and as a result, water retention and increasing of extracellular fluid volume, in excess, hypertension results;
- b. increase excretion of potassium in renal tubules;
- c. increase excretion of hydrogen in renal tubules.



Conn's syndrome

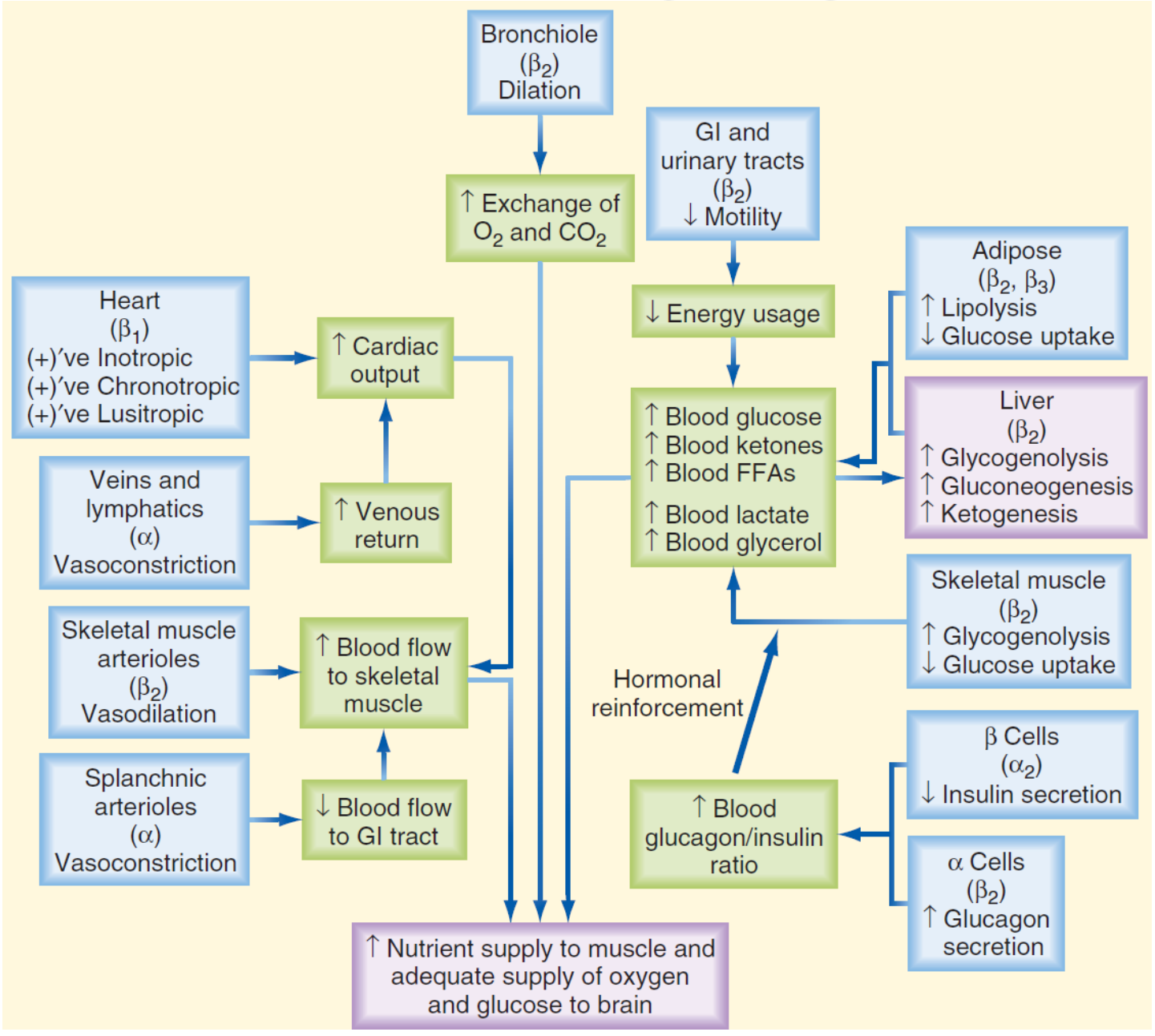
- Primary aldosteronism is caused by aldosterone-secreting tumour.
- It leads to hypernatraemia, hypokalemia, metabolic alkalosis, and hypertension.
- It is treated with surgery and aldosterone antagonist (spironolactone).
- In patients with renal artery stenosis, edema, and secondary aldosteronism, similar symptoms are noted, along with increased renin and angiotensin II levels.

Adrenal medulla

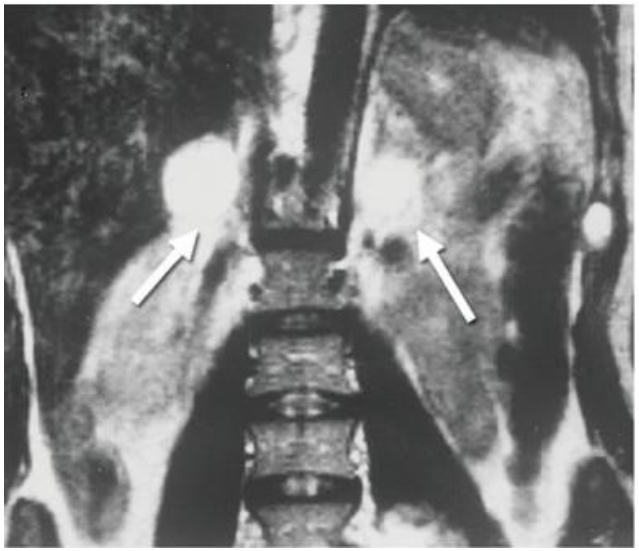


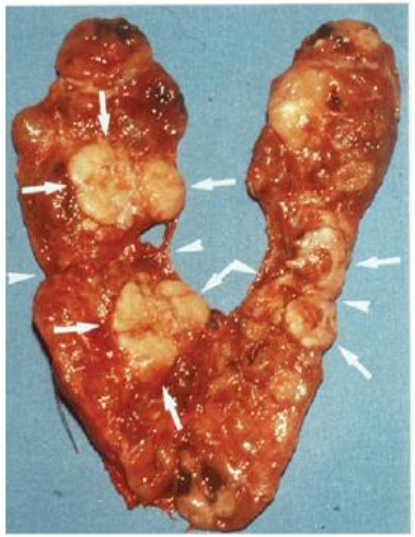
- The adrenal medulla is innervated by sympathetic nervous system, and secretion of its hormones is activated during "fight or flight" reaction (injury, pain, hypoglycaemia, anxiety, anger, cold).
- The chromaffin cells of adrenal medulla produce about 80% of epinephrine (adrenaline) and 20% of norepinephrine (noradrenaline).

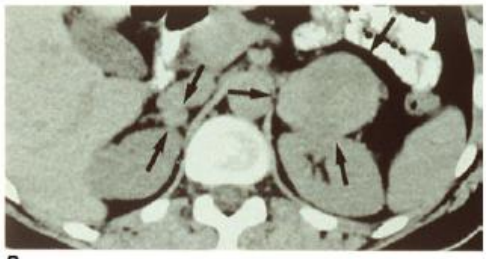
Actions of epinephrine



Pheohromocytoma







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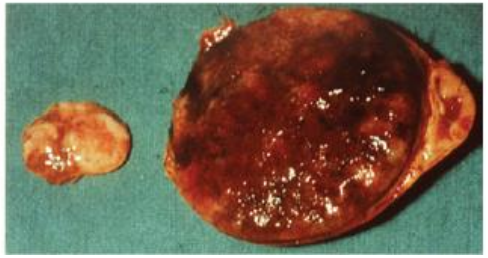
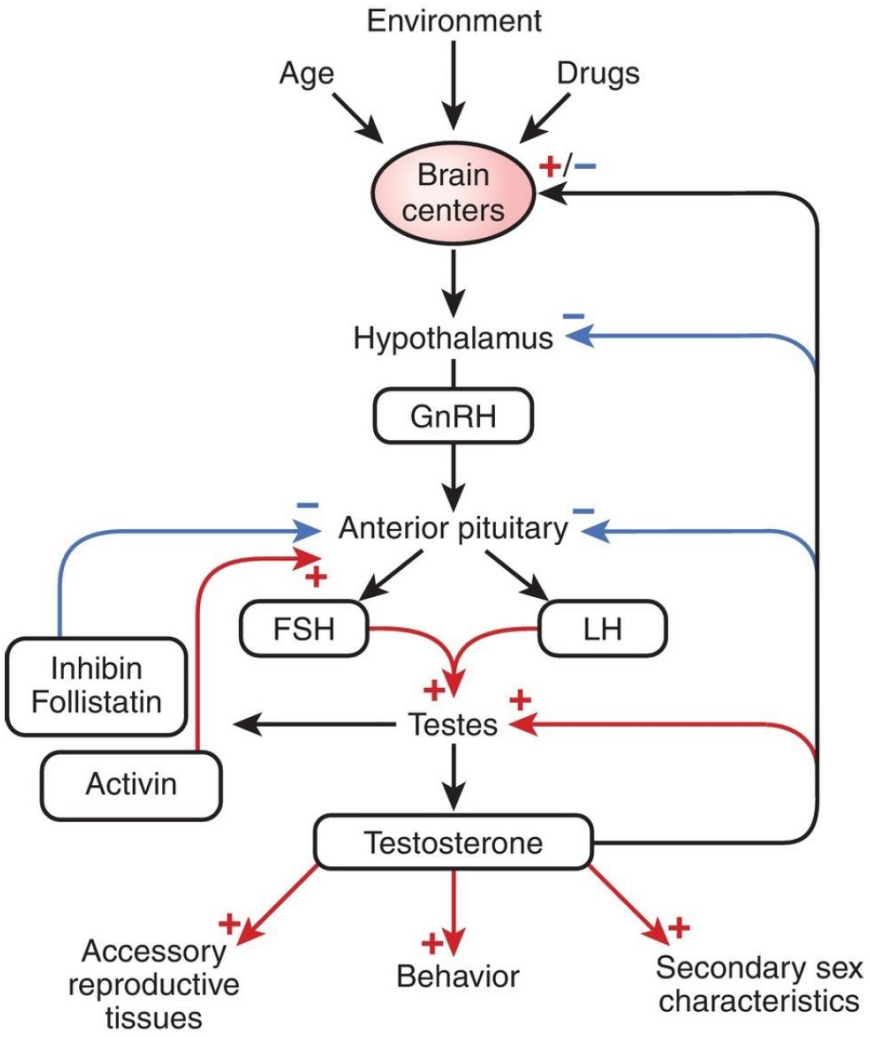


- Hypersecretion of epinephrine (e.g. tumour of the adrenal medulla) is pheohromocytoma (associated with hypertension, tachycardia, palpitations, hyperglycaemia, headache, nervousness, profuse sweating). Treatment: tumor removal, α-blockers (phenoxybenzamine).
- Hyposecretion causes no clinical symptoms.

Hypothalamic-pituitary-gonad axis



- LH stimulates testosterone production.
- FSH stimulates spermatogenesis and function of Sertoli cells in testes.
- Sertoli cells produce inhibin, inhibitor of FSH secretion.

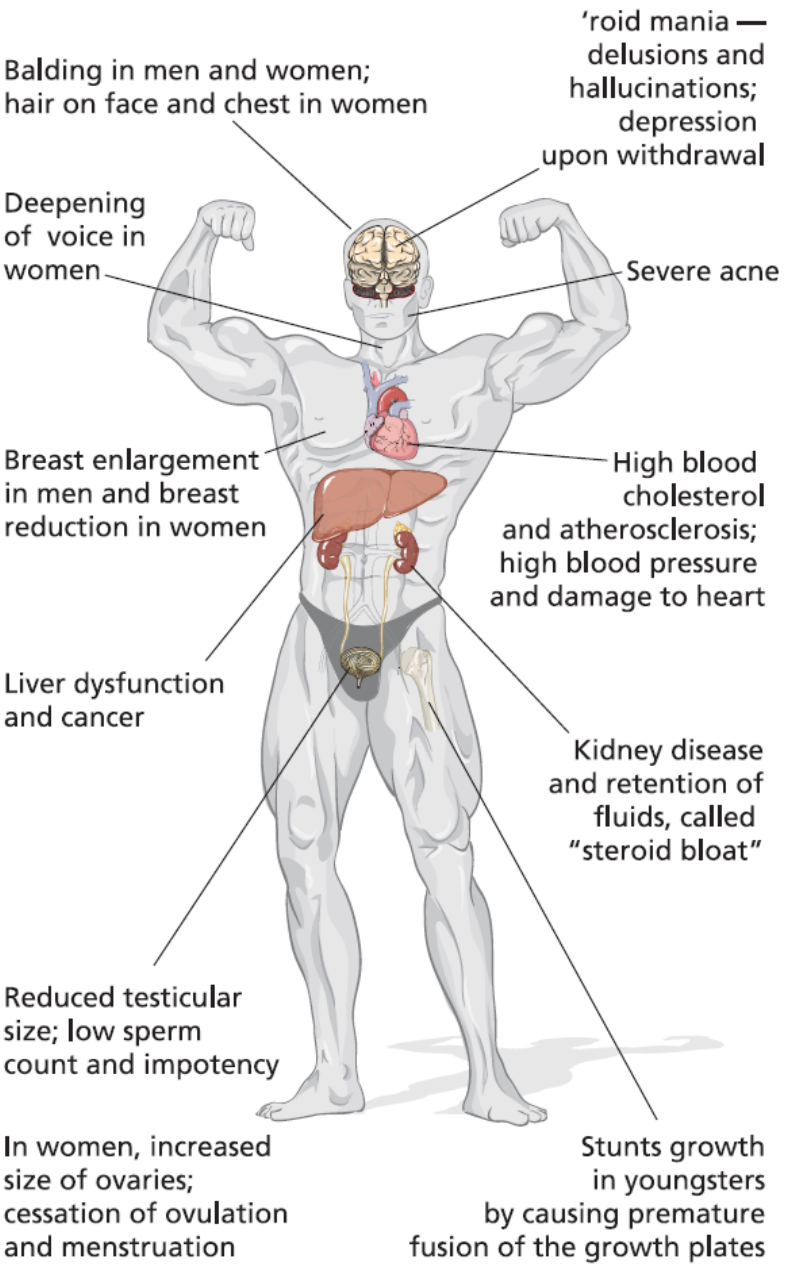
Actions of testosterone

- a. differentiation and growth of the male genitalia during fetal life;
- b. development of the secondary sex characteristics (hair distribution, bone growth, deepening of voice) at puberty;
- c. stimulate spermatogenesis; libido;
- d. anabolic effect (increase in muscle size);
- e. stimulate erythropoiesis in the bone marrow.

Actions of DHT:

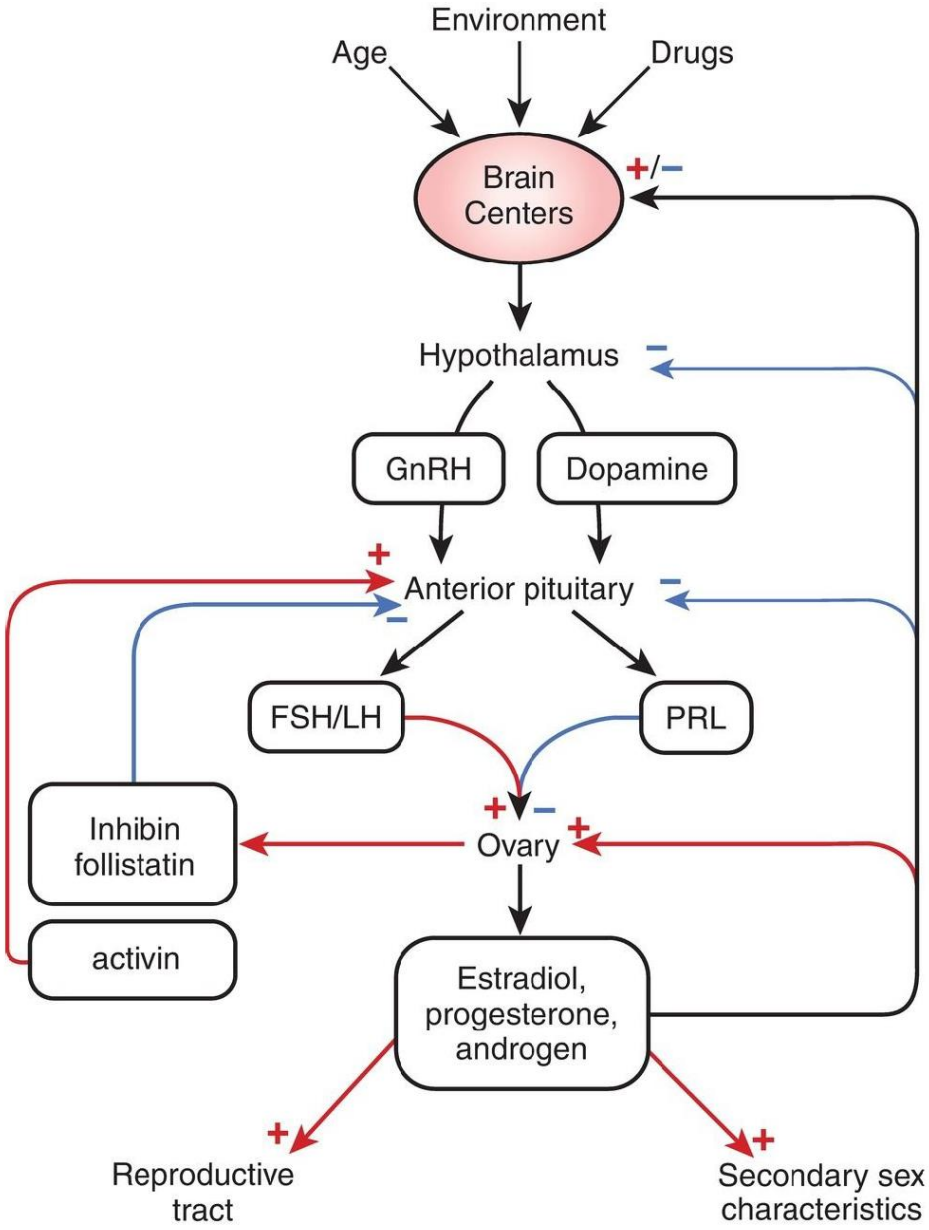
- a. embryonic development of prostate;
- b. descent of testes and phallic growth;
- c. growth of axillary and pubic hair; male pattern balding;
- d. activity of sebaceous glands.

Anabolic steroids



- Exogenous testosterone cannot achieve the local high concentration in the testis. It inhibits LH release and lead to suppression of endogenous testosterone production. Testosterone has an anabolic effect and causes an increase in muscle mass and strength (bodybuilders and athletes). Also androgen abuse is associated with aggressive behaviour and increased risk of liver tumours.

Hypothalamic-pituitary-gonad axis



- **Actions of FSH:**

a. the development of follicles in the ovaries;

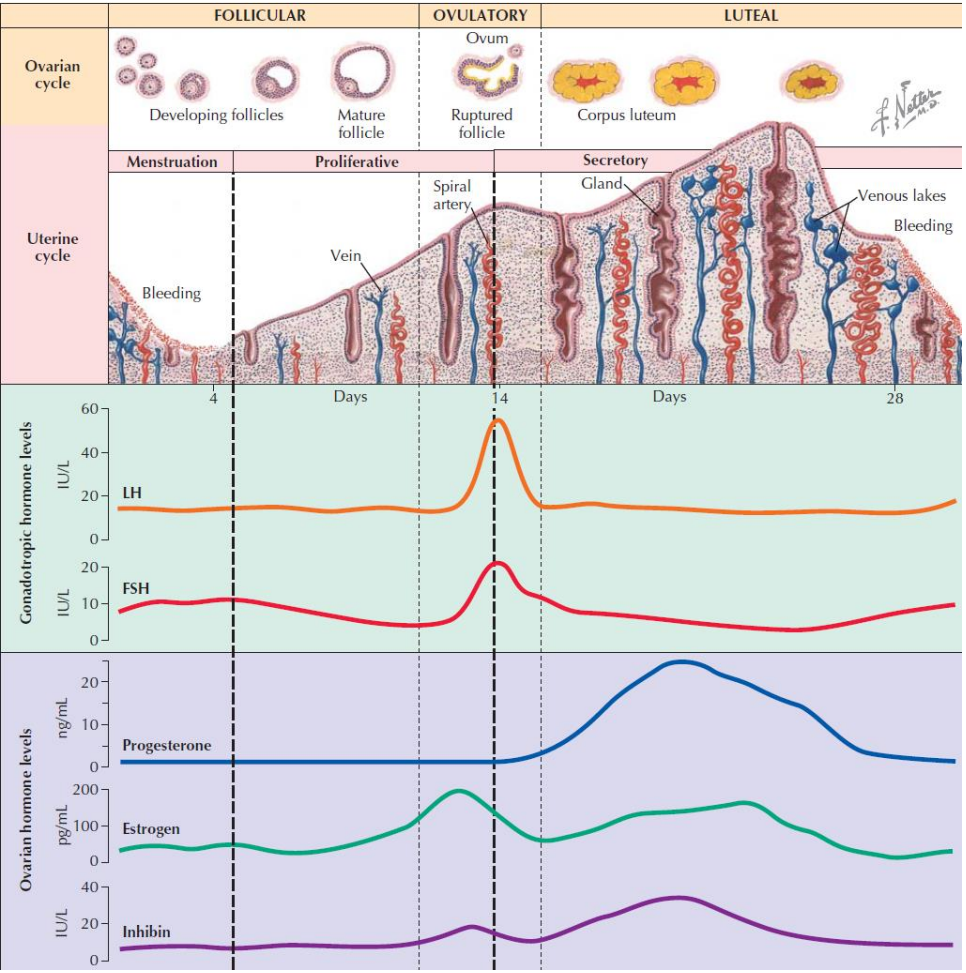
b. secretion of estrogens by the ovary;

- **Actions of LH:**

a. ovulation and luteinization of the ovulated follicle;

b. secretion of estrogens and progesterone by the ovary.

Menstrual cycle



- ***In the follicular phase*: FSH and LH stimulate estrogen secretion and follicular development. Estradiol has negative feedback on secretion of GnRH, FSH, and LH.**
- ***At midcycle*: elevated estradiol levels has positive feedback on secretion of GnRH, FSH, and LH. The LH level rises sharply and induces ovulation of the mature oocyte.**
- ***In the luteal phase*: corpus luteum produces progesterone, which has negative feedback on secretion of GnRH, FSH, and LH.**

Actions of estrogens

- a. development and maintenance of female reproductive organs:
- - in the ovaries cause proliferation of granulosa cells and enhance action of FSH; responsible for follicular development;
- - in the uterus cause proliferation of endometrium and myometrium, increase uterine contractility;
- - in the fallopian tubes stimulate ciliary activity and contractility;
- - in the cervix make cervical mucus watery and elastic;
- - in the vagina stimulate proliferation of epithelium;
- b. development of the female secondary sexual characteristics at puberty;
- c. promotes growth of mammary glands;
- d. maintenance of pregnancy;
- e. other effects:

- increase osteoblastic activity and promote deposition of bone matrix (anti-osteoporosis effect), stimulate bone maturation and epiphyseal closure;
- protein anabolic effect;
- neuroprotective and cardioprotective effects;
- increase synthesis coagulation factors, angiotensinogen, and transport globulin in the liver;
- decrease LDL (low-density lipoprotein) cholesterol.

Actions of progesterone:

- a. arrests endometrial proliferation and induces secretory activity of uterus;
- b. inhibits uterine motility;
- c. promotes growth of mammary glands but suppresses milk production before parturition;
- d. promotes implantation and maintains pregnancy;
- e. other effects:
- - modulates sexual behaviour;
- - antagonizes the action of aldosterone;
- - increase basal body temperature;
- - stimulates of the respiratory centre.

Placenta

- ***human chorionic gonadotropin*** *(maintains the corpus luteum, stimulates the corpus luteum to produce progesterone, stimulates secretion of testosterone in the male fetus. It is produced by the trophoblast. HCG is detectable in urine in 14 days after fertilization and it is used for pregnancy diagnostic tests);*
- ***human chorionic somatomammotropin*** *(stimulates breast development and activates lipolysis and increases maternal blood glucose levels);*
- ***relaxin*** *(inhibits uterine motility);*
- ***estrogens*** *(maintain pregnancy);*
- ***progesterone*** *(maintains pregnancy).*