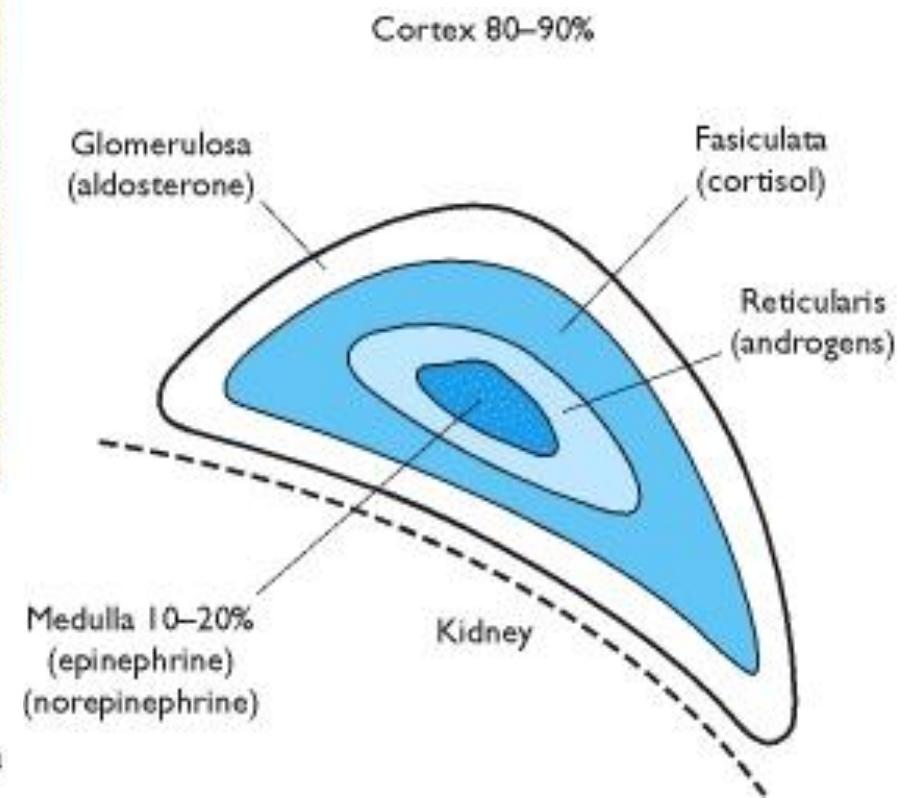
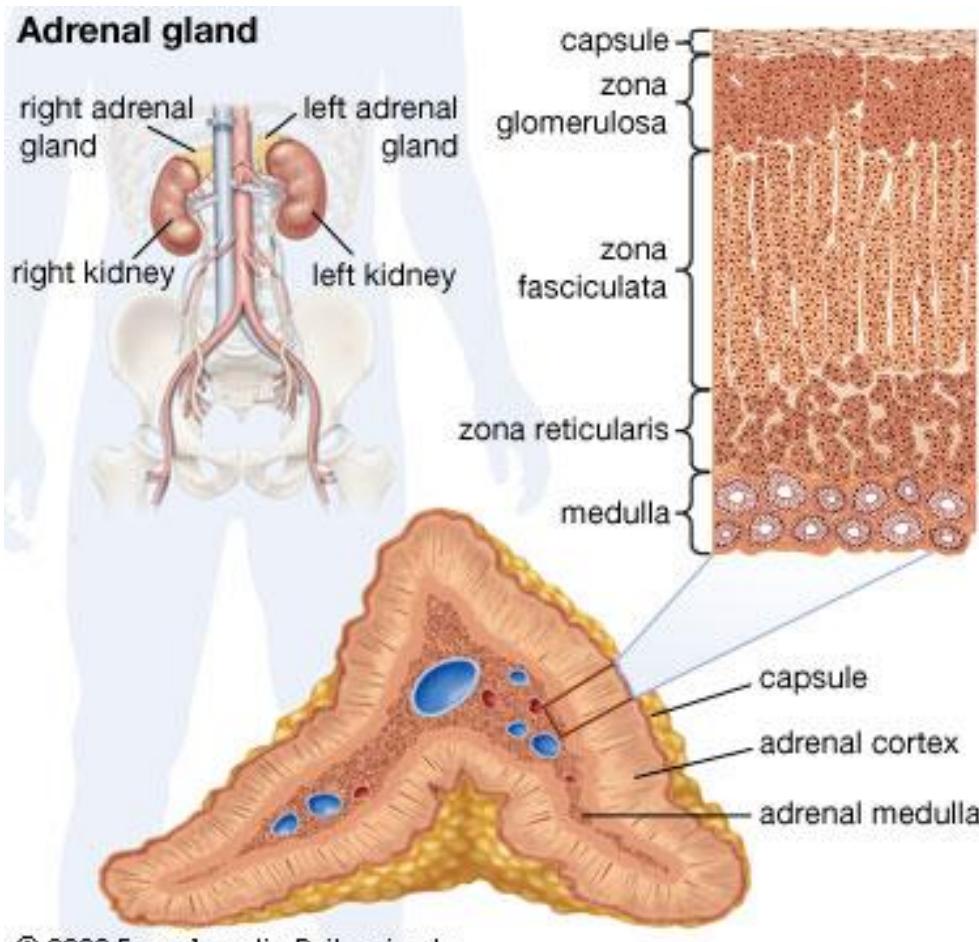


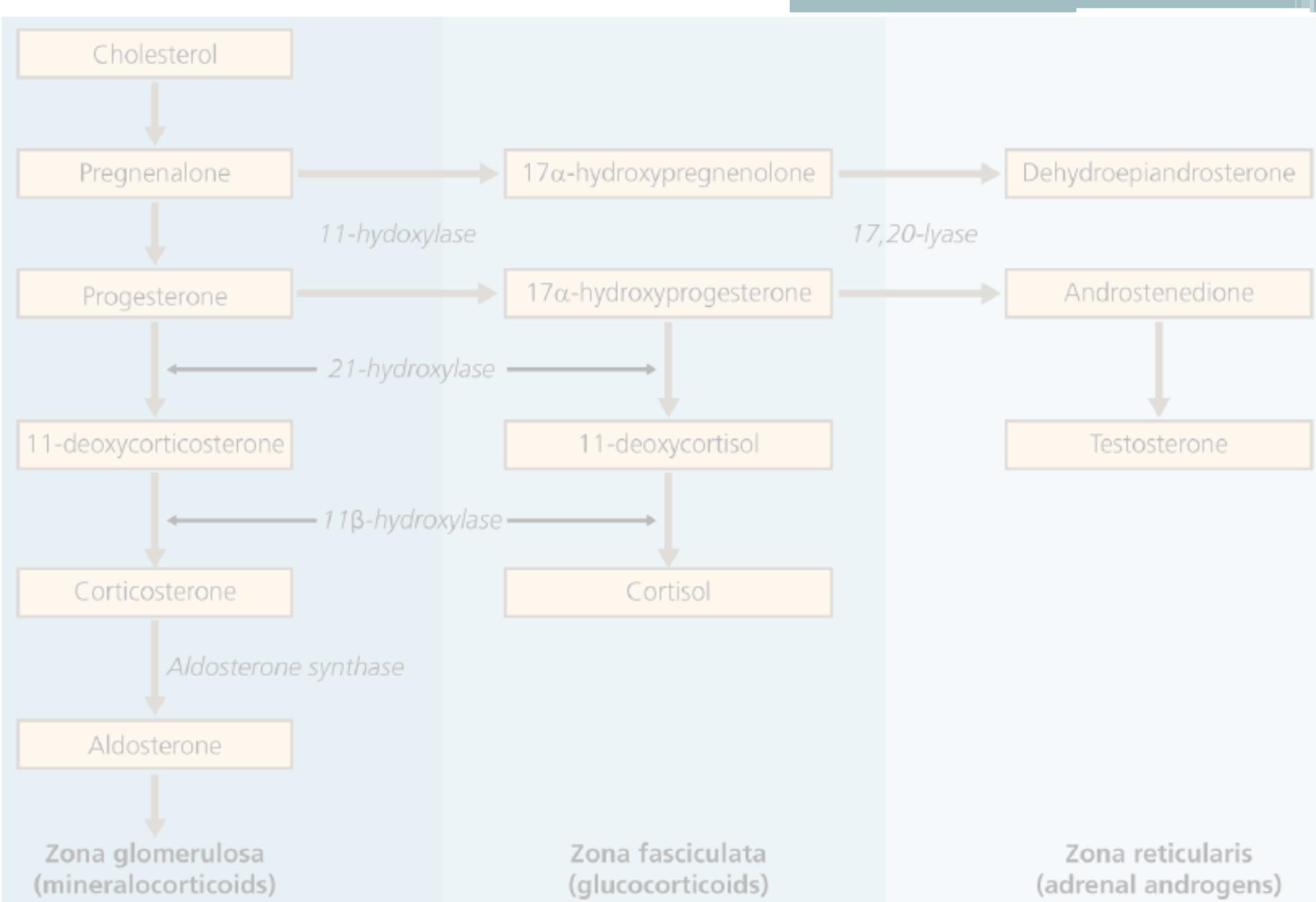
# Adrenal gland

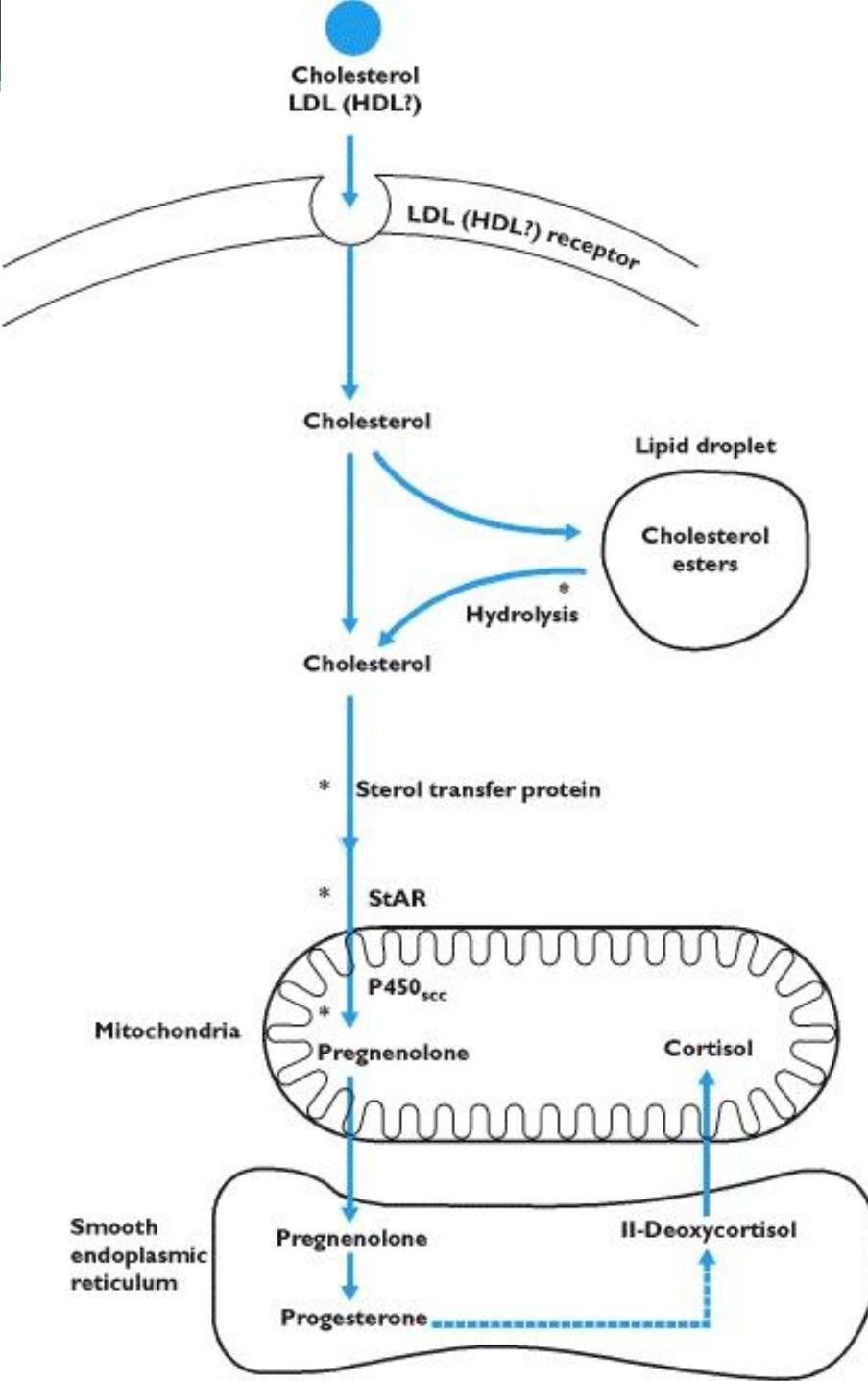
Mgr. Emese Renczés, PhD.

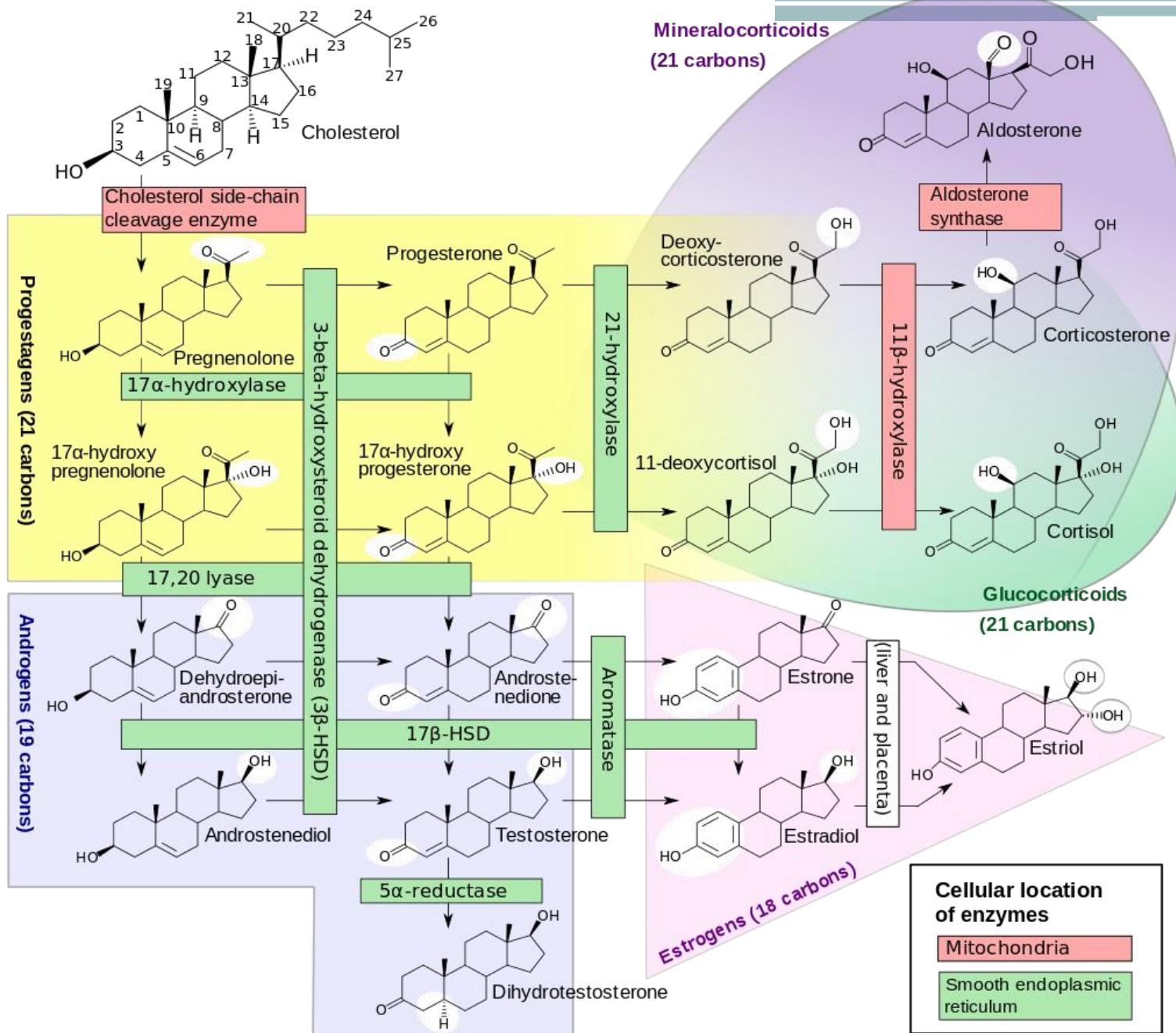
[renczes.emese@gmail.com](mailto:renczes.emese@gmail.com)

# Adrenal glands - anatomy

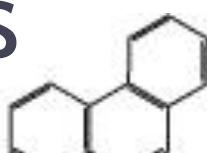




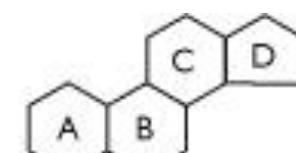




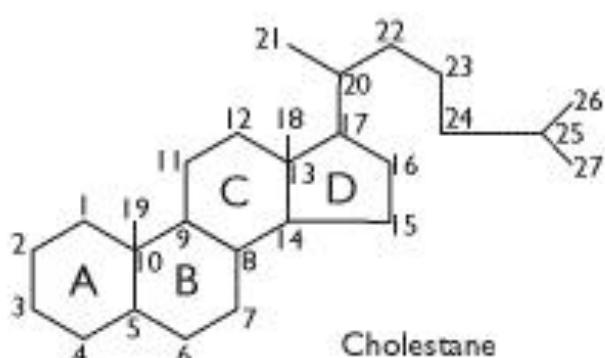
# Sterodiogenesis



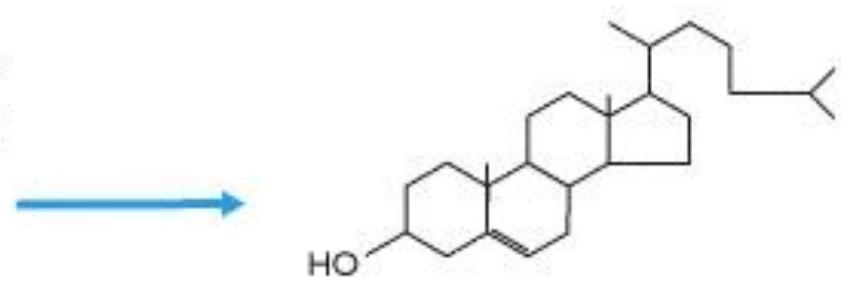
Phenanthrene



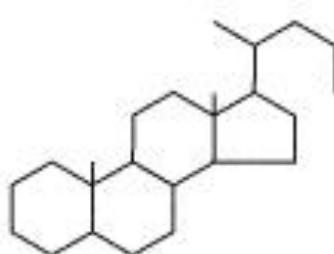
Cyclopentanoperhydrophenanthrene



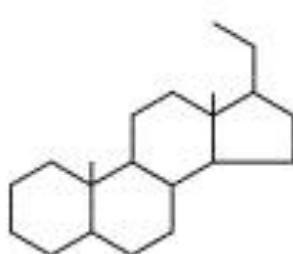
Cholestane



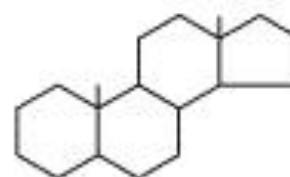
Cholesterol



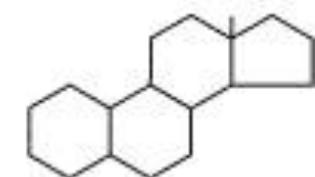
Cholane



Pregnane



Androstane



Estrane

C-24

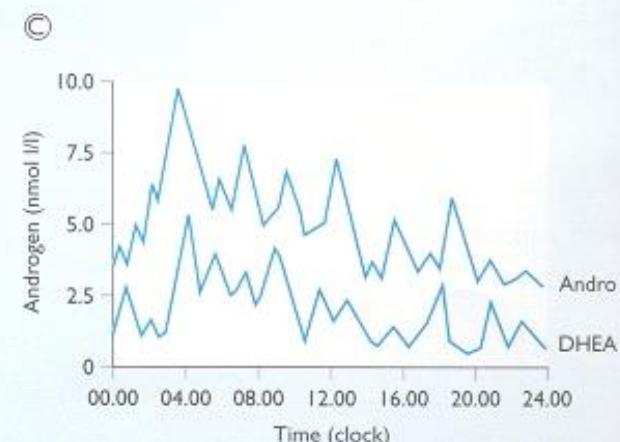
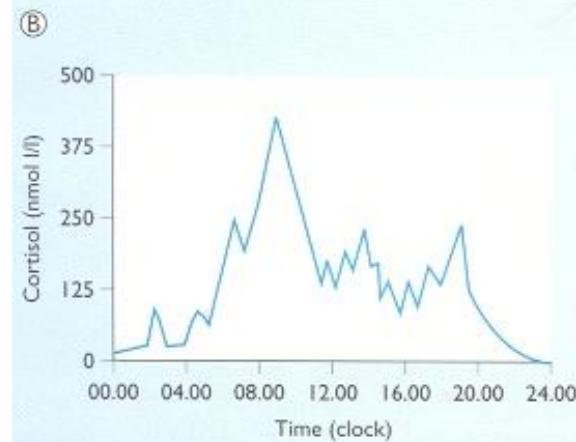
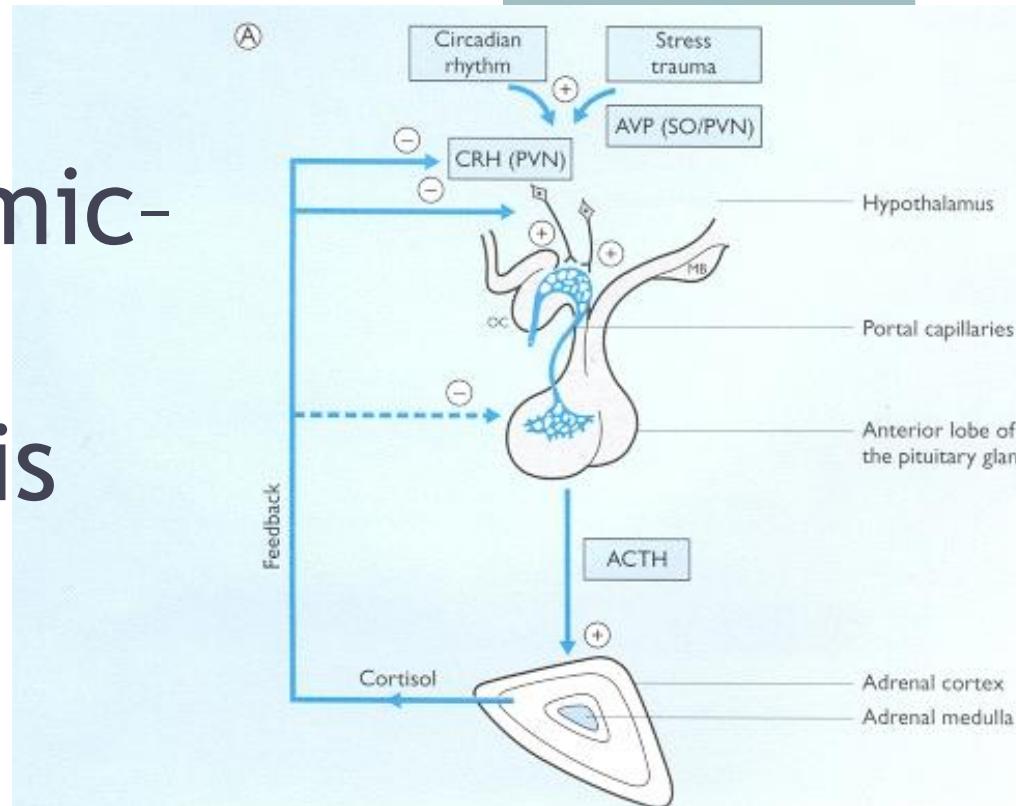
C-21

C-19

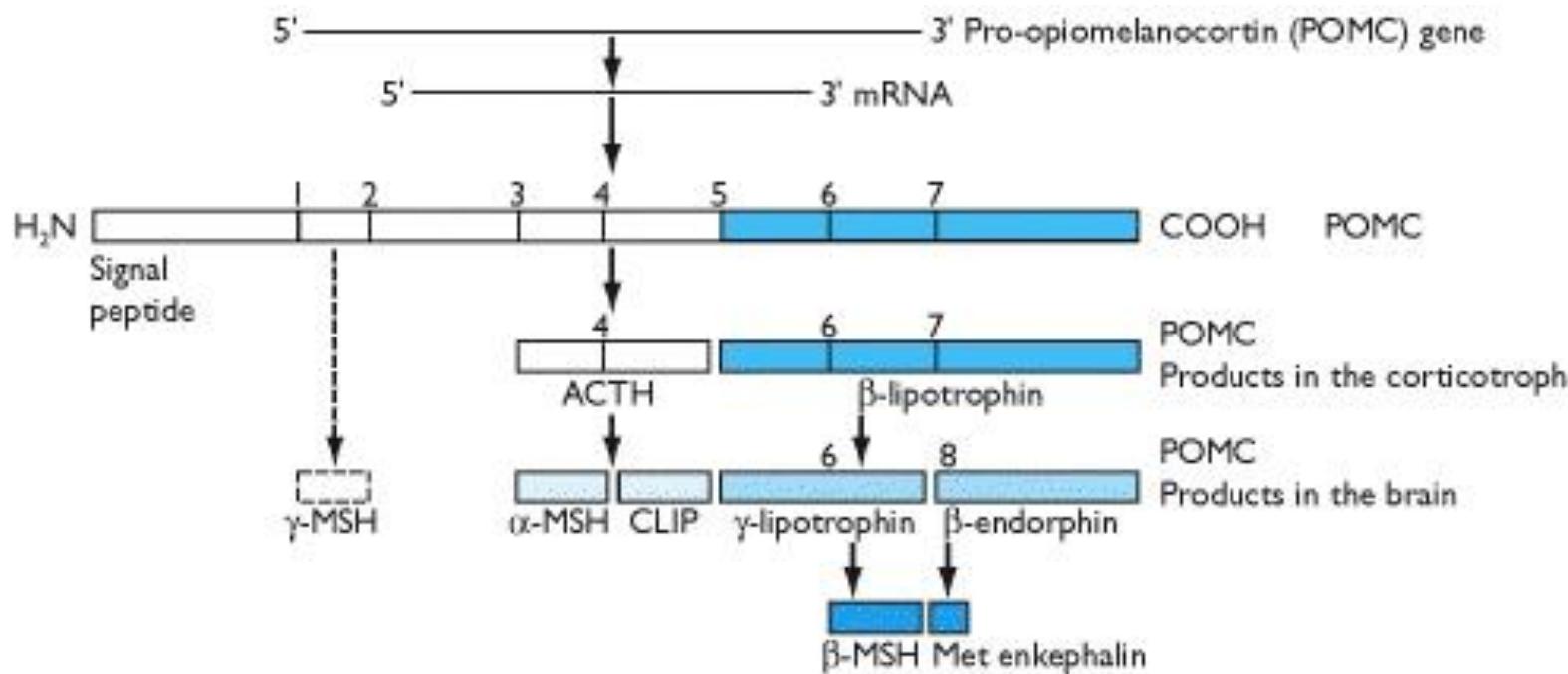
C-18

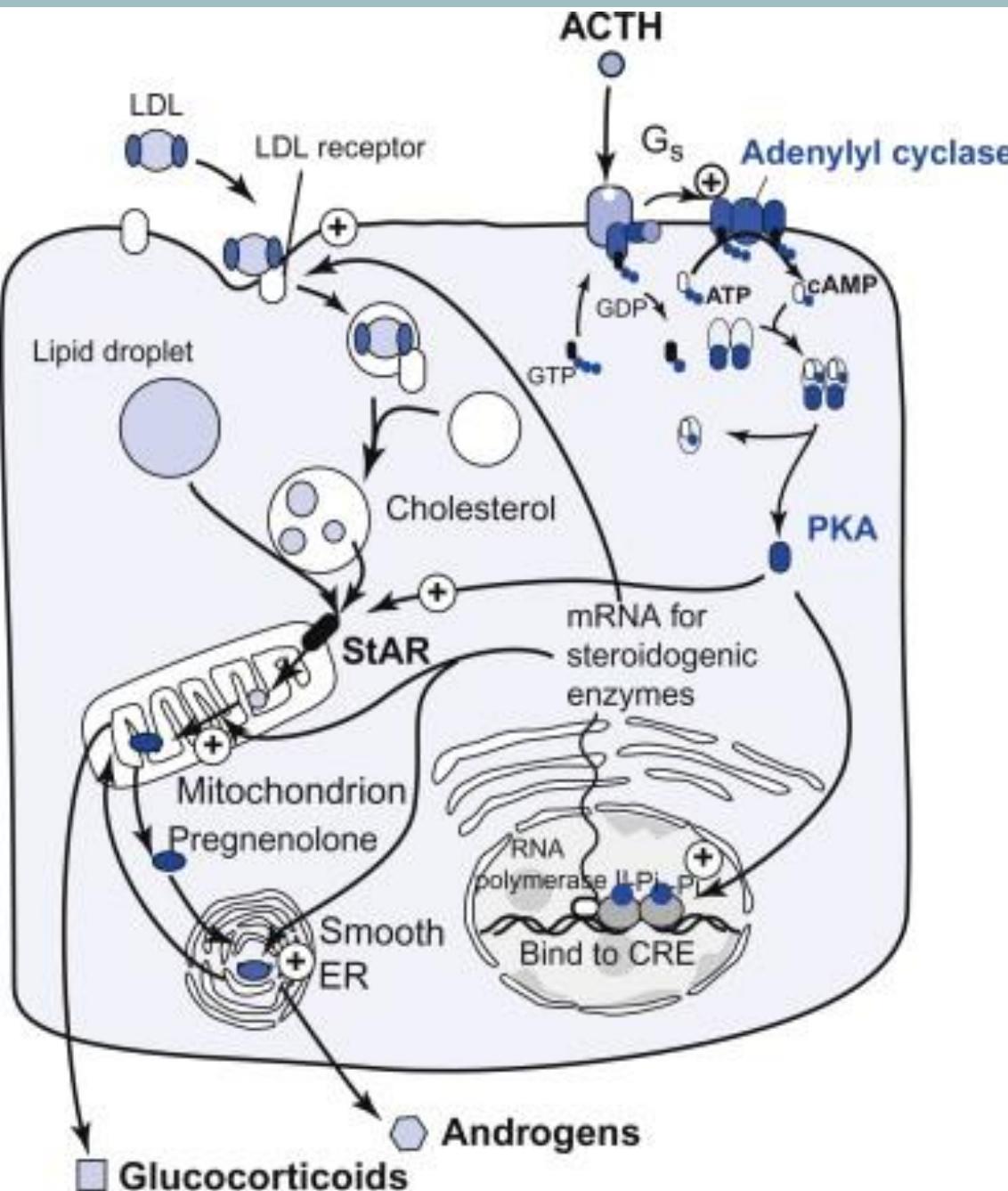
- Transcortin (CBG – corticosteroid-binding globulin)
  - Albumin
  - SHBG – sex hormone-binding globulin
- 
- Metabolism – liver
  - Excretion - kidney

# Hypothalamic-pituitary-adrenal axis



# ACTH



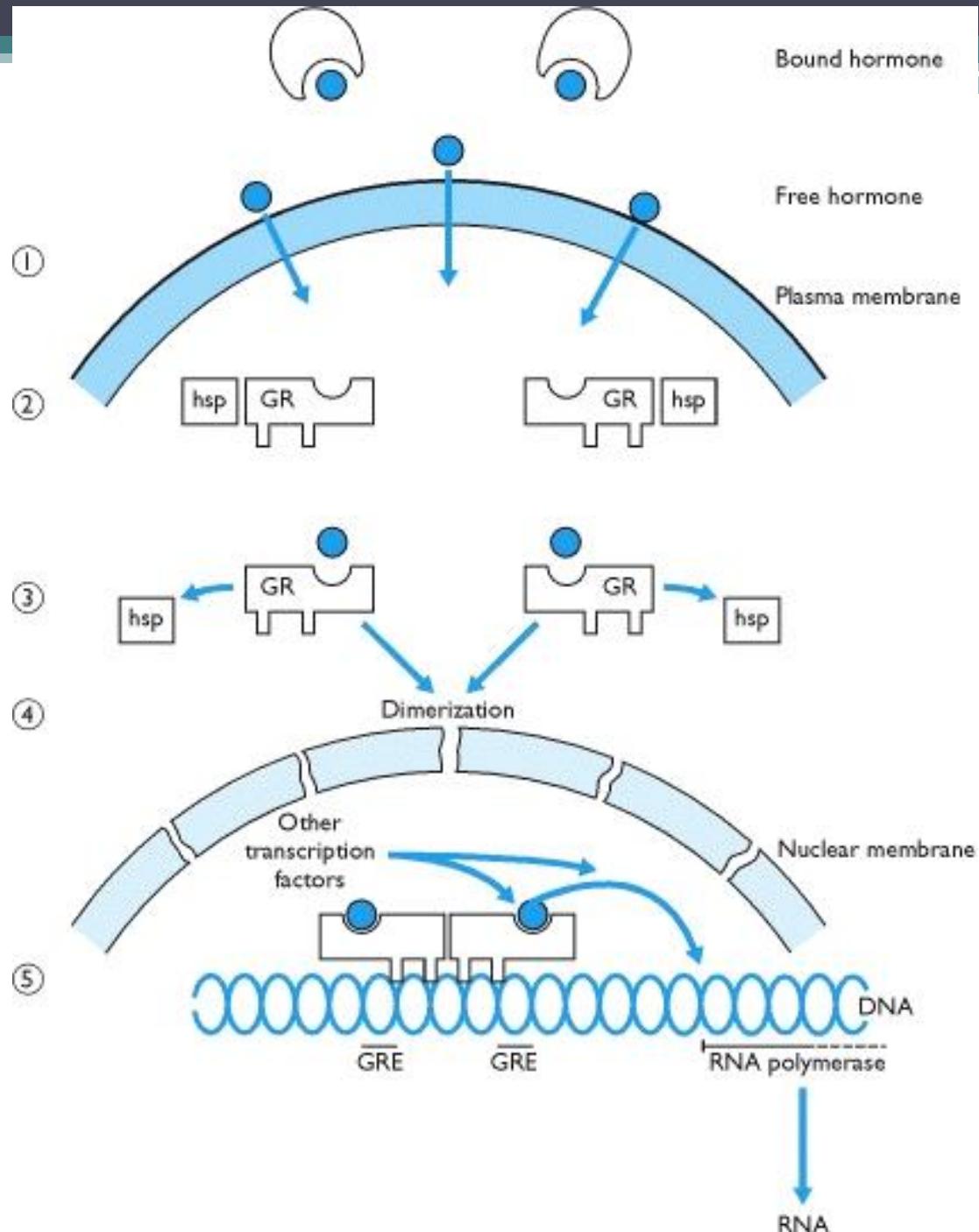


## ACTH action:

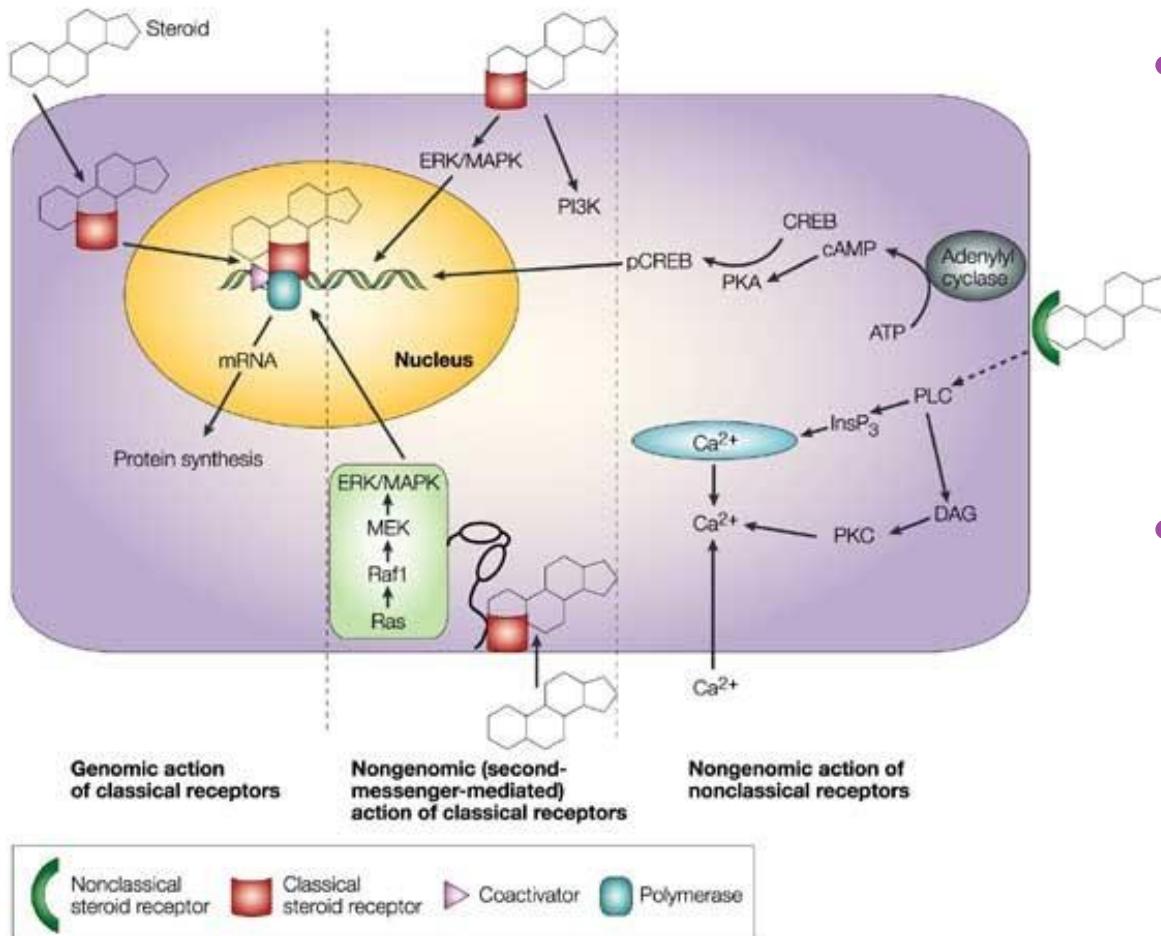
- ↑ LDL receptors on the cell surface
- ↑ transport proteins into the inner mitochondria
- ↑ steroidogenic enzymes
- ↑ growth and division of adrenocortical cells

# Adrenocortical hormones

- Glucocorticoids – metabolism of carbohydrates and proteins
- Mineralocorticoids – homeostasis of Na and K
- Androgens – anabolic and androgenic effect

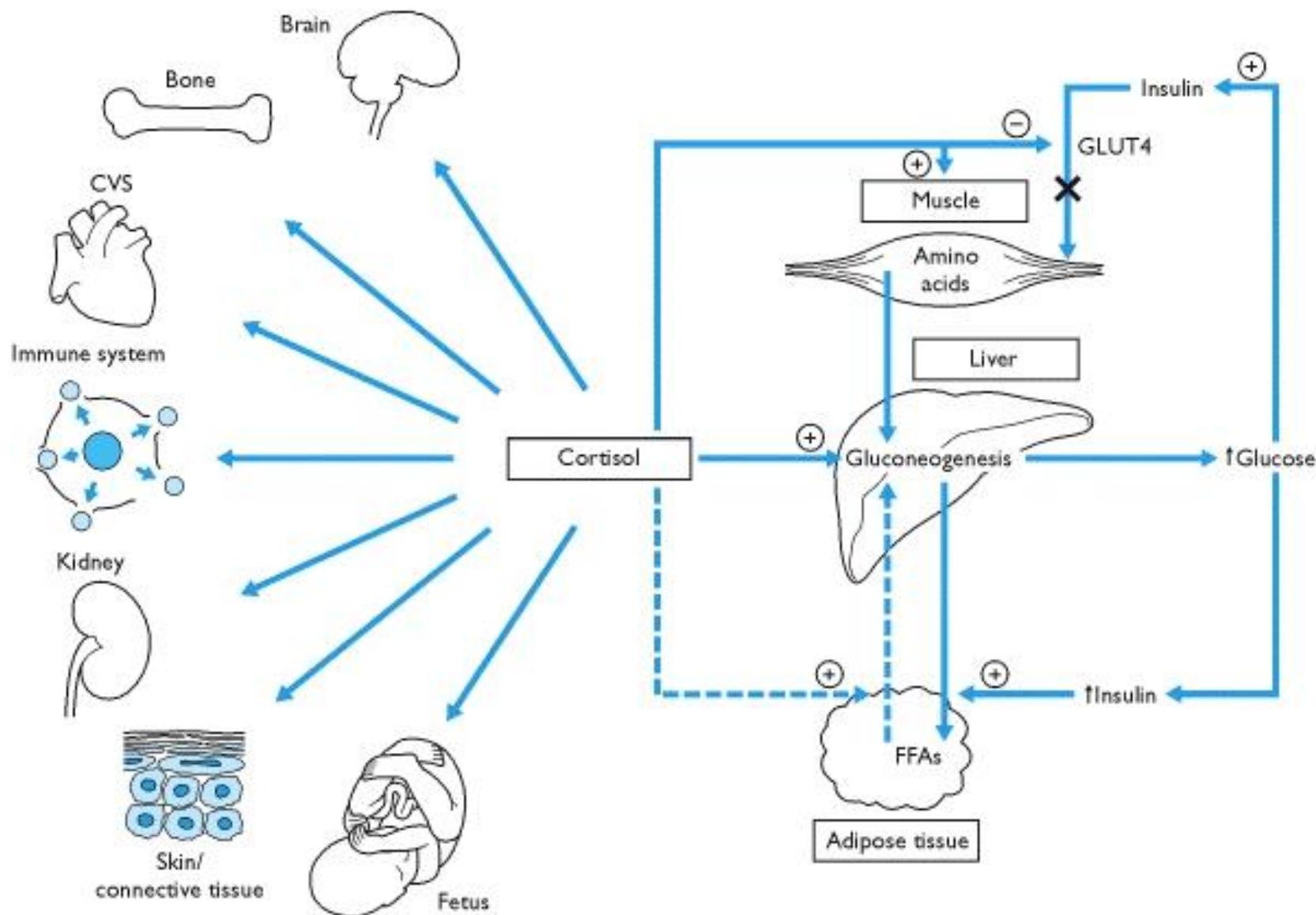


# Non-genomic mechanisms of action

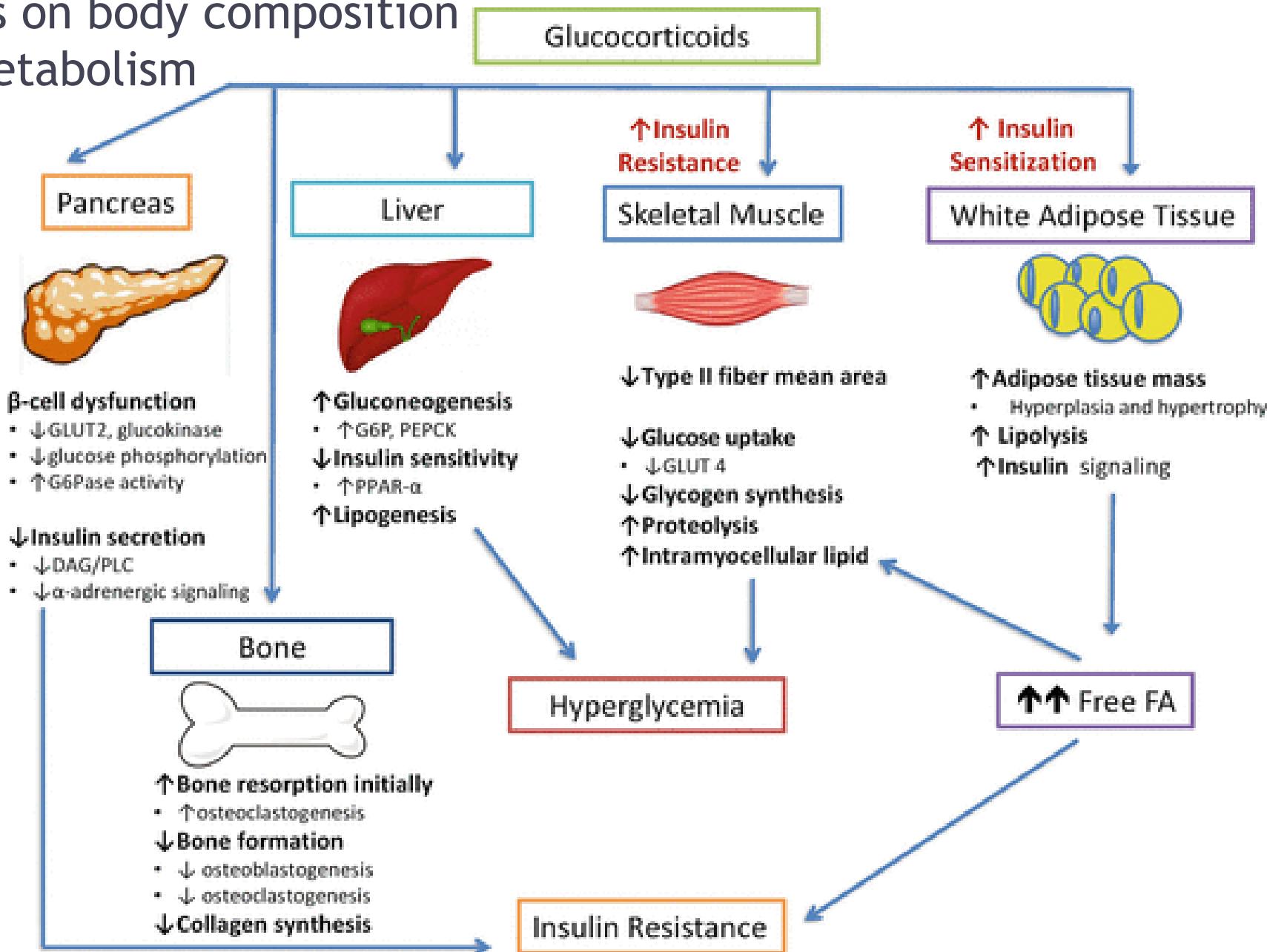


- **Genomic** = slow, intracellular receptors, gene transcription
- **Non-genomic** = rapid, membrane-bound, second-massangers, kinases, ion fluxes

# Cortisol

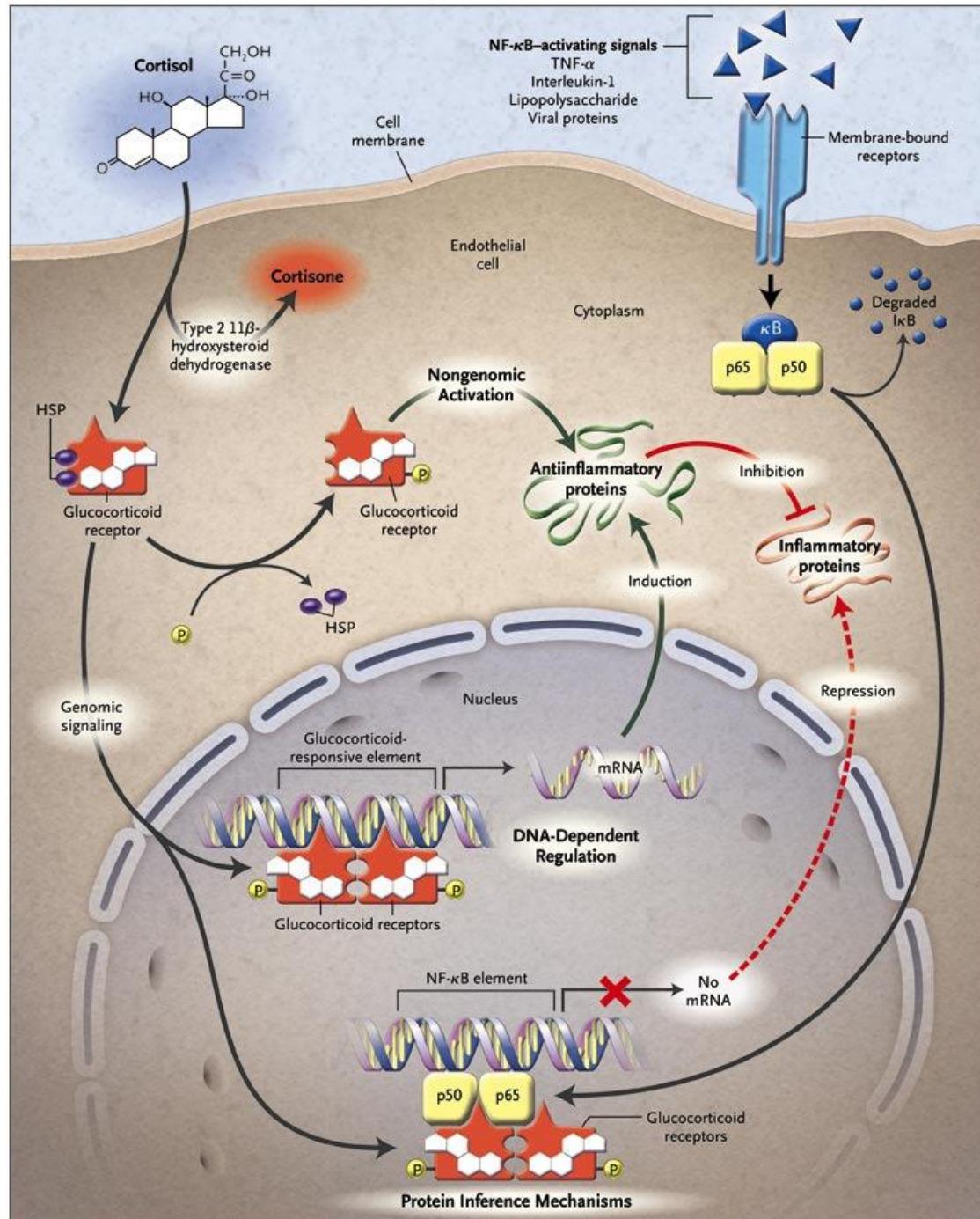


# Effects on body composition and metabolism



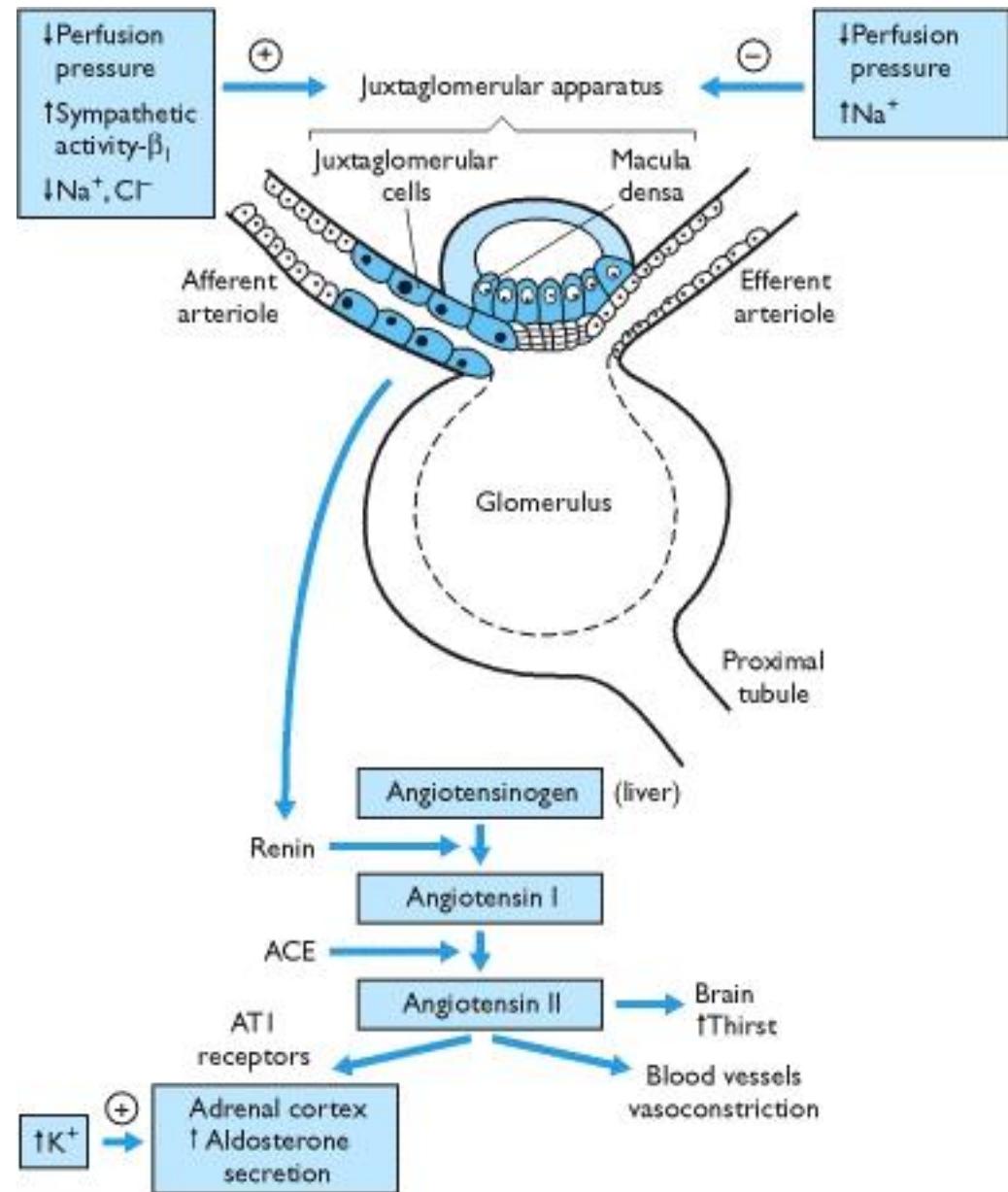
# Anti-inflammatory action of glucocorticoids

- suppression of inflammation in chronic inflammatory diseases
- ↑ expression of anti-inflammatory proteins
- ↓ expression of inflammatory proteins

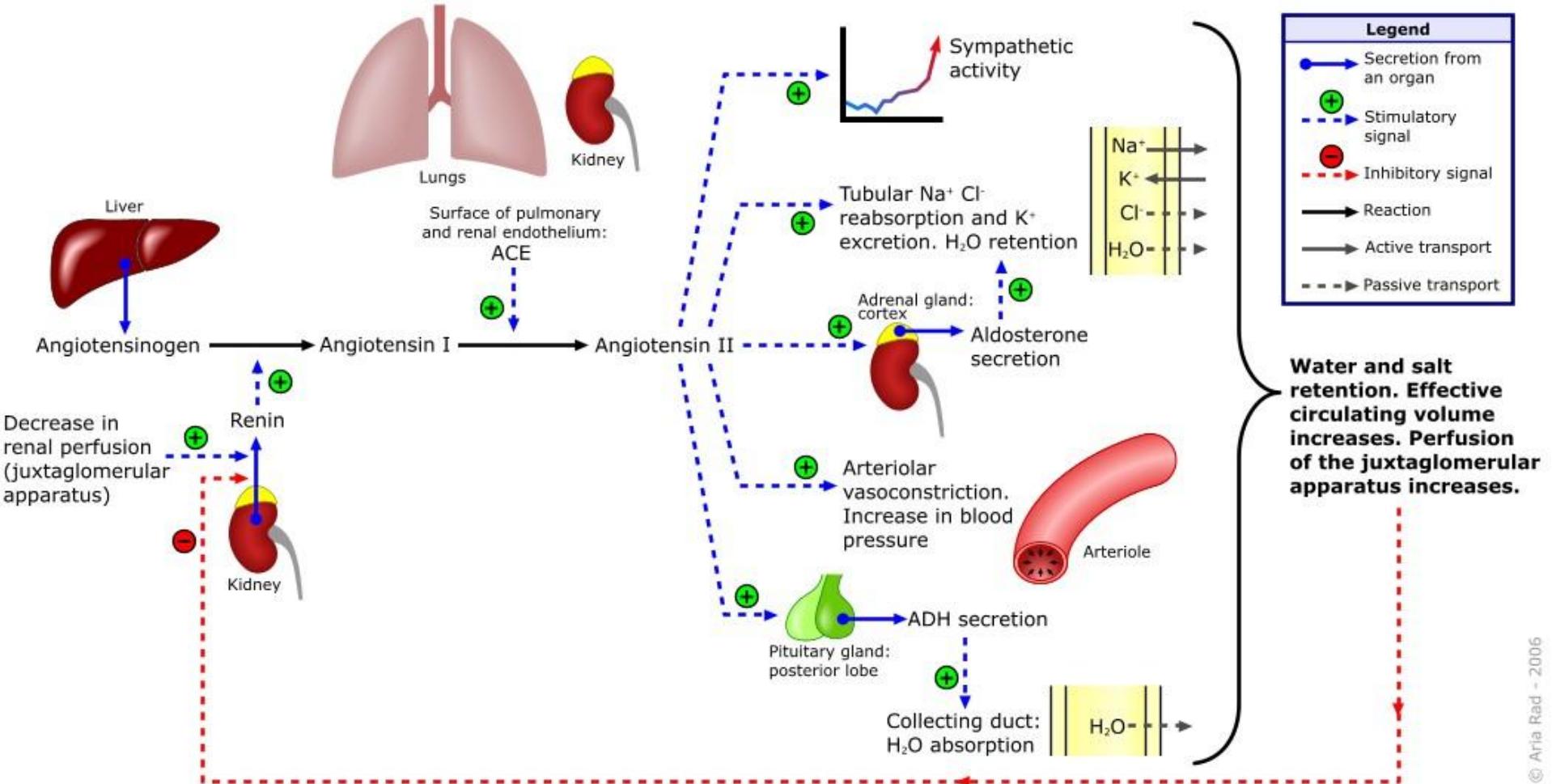


# Aldosterone

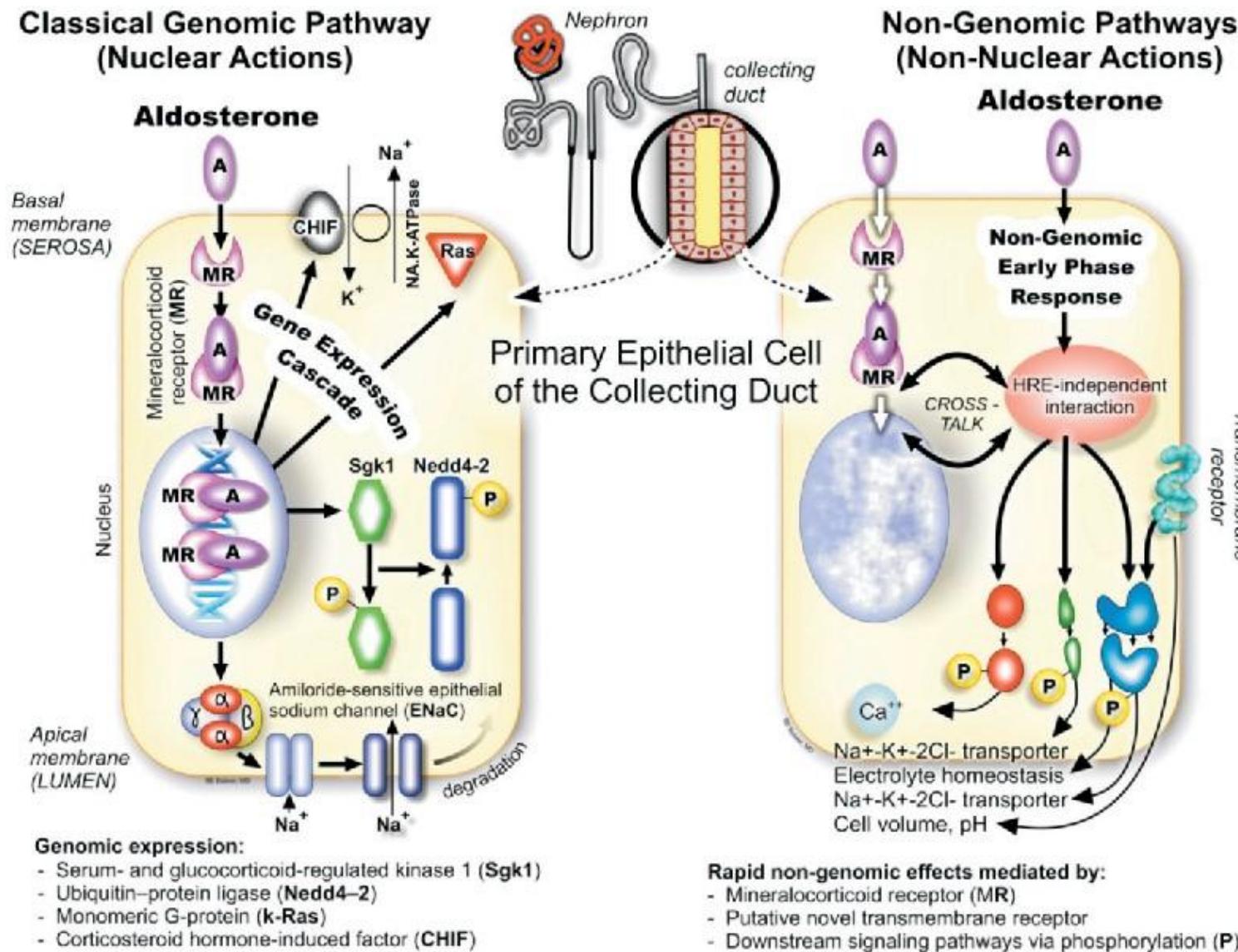
- Renin-angiotensin-aldosterone system
- ↓ blood pressure in renal artery activates juxtaglomerular cells
- Pro-renin cleaved into renin



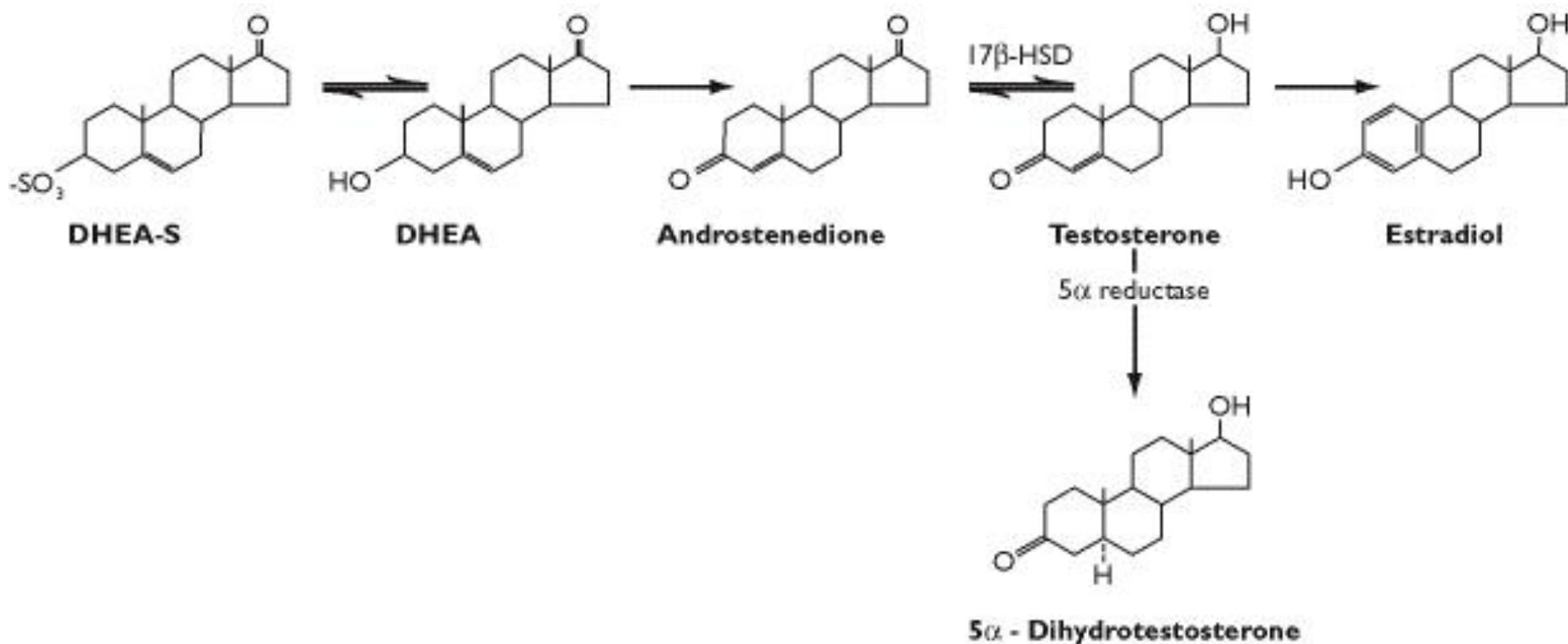
# Renin-angiotensin-aldosterone system



# Mechanisms of action of aldosterone



# Sex hormones

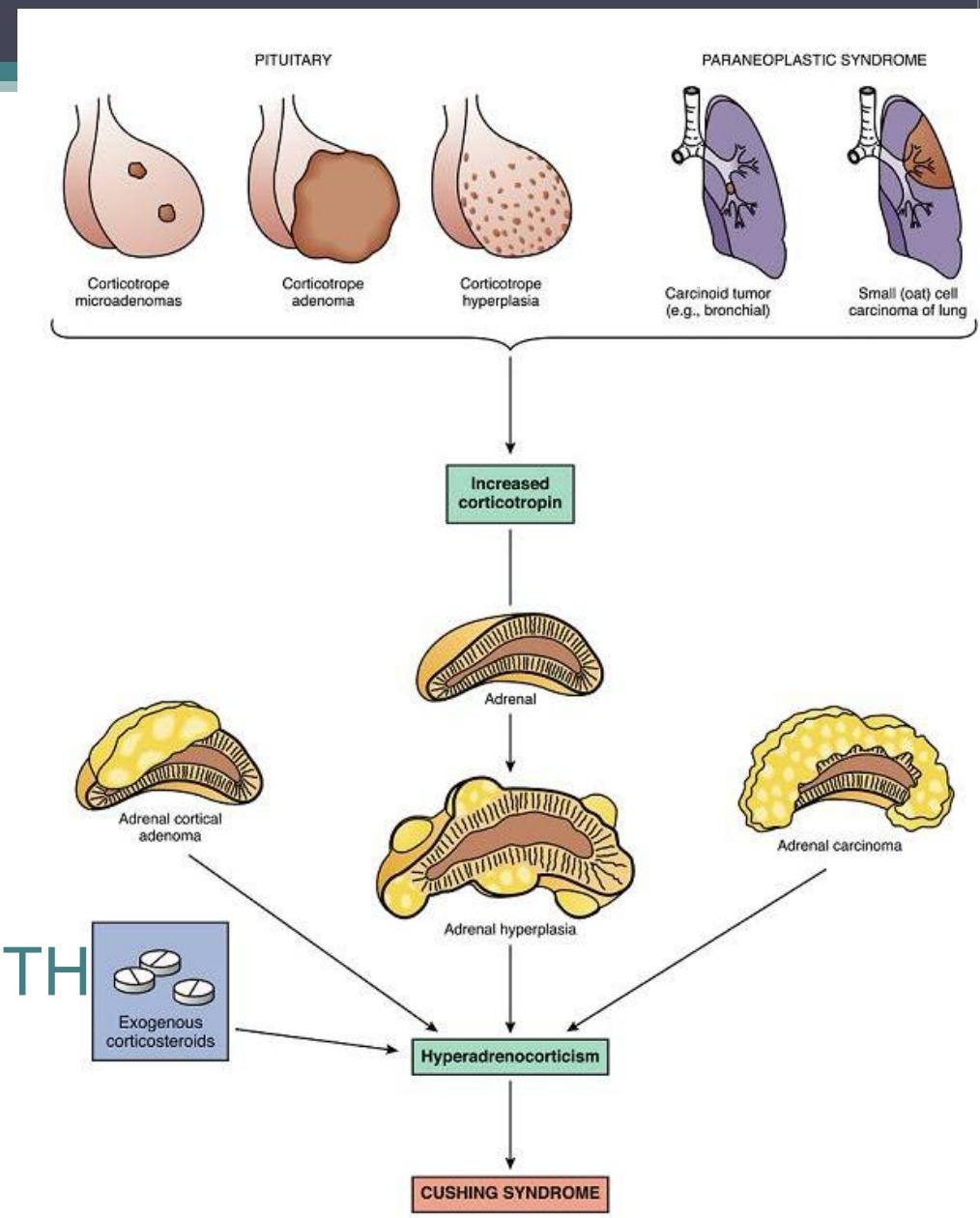


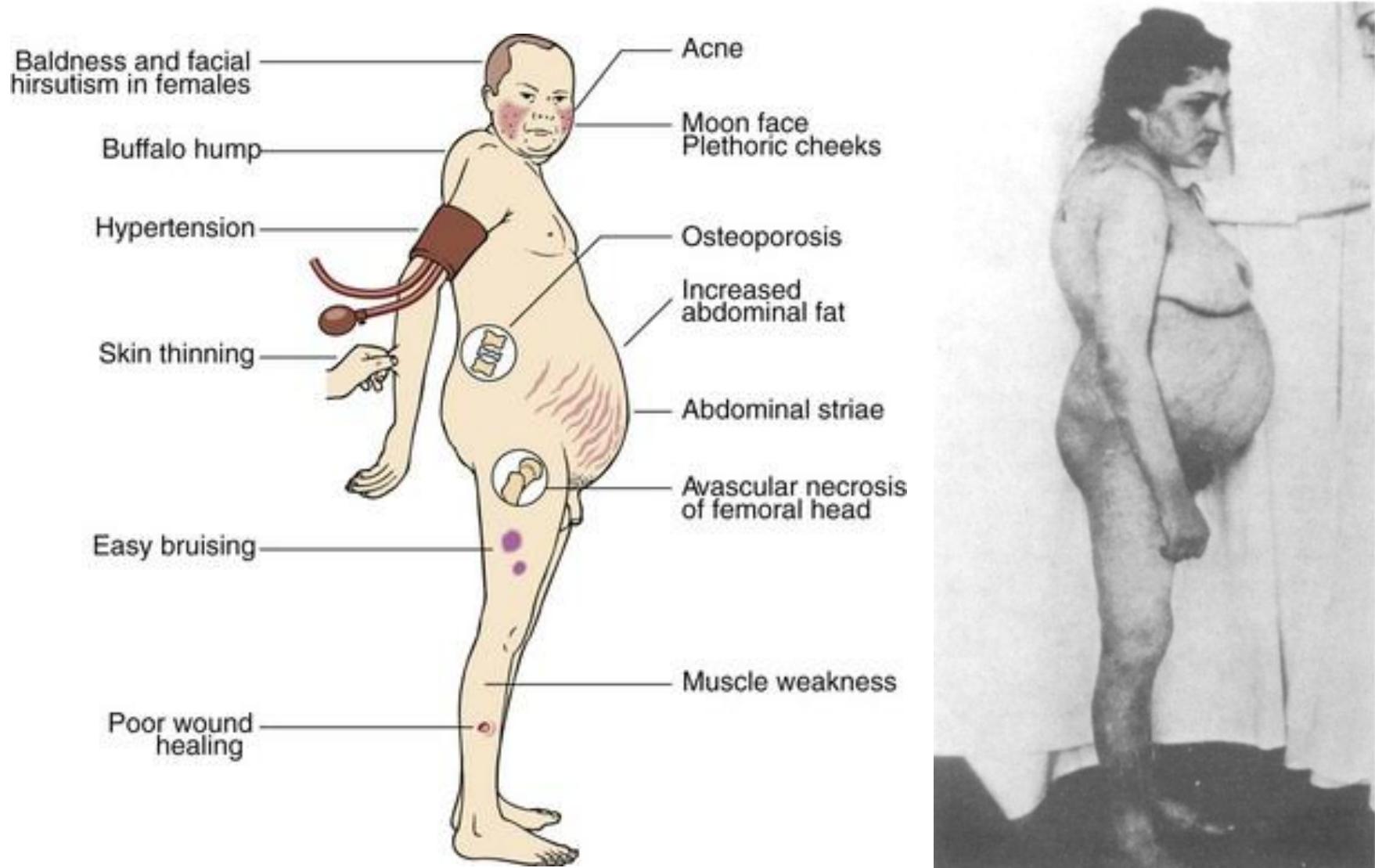
# Pathology

- Hyperadrenocorticism
  - Hypercortisolism (Cushing's syndrome)
  - Hyperaldosteronism (Conn's disease)
  - Adrenal hyperandrogenism
- Hypoadrenocorticism (Addison's disease)

# Hypercortisolism (Cushing's syndrome)

- ACTH dependent
- ACTH independent
- Endogenous
  - Central  $\rightarrow$   $\uparrow$  ACTH
  - Paraneoplastic  $\rightarrow$   $\uparrow$  ACTH
  - Peripheral  $\rightarrow$   $\downarrow$  ACTH
- Iatrogenic





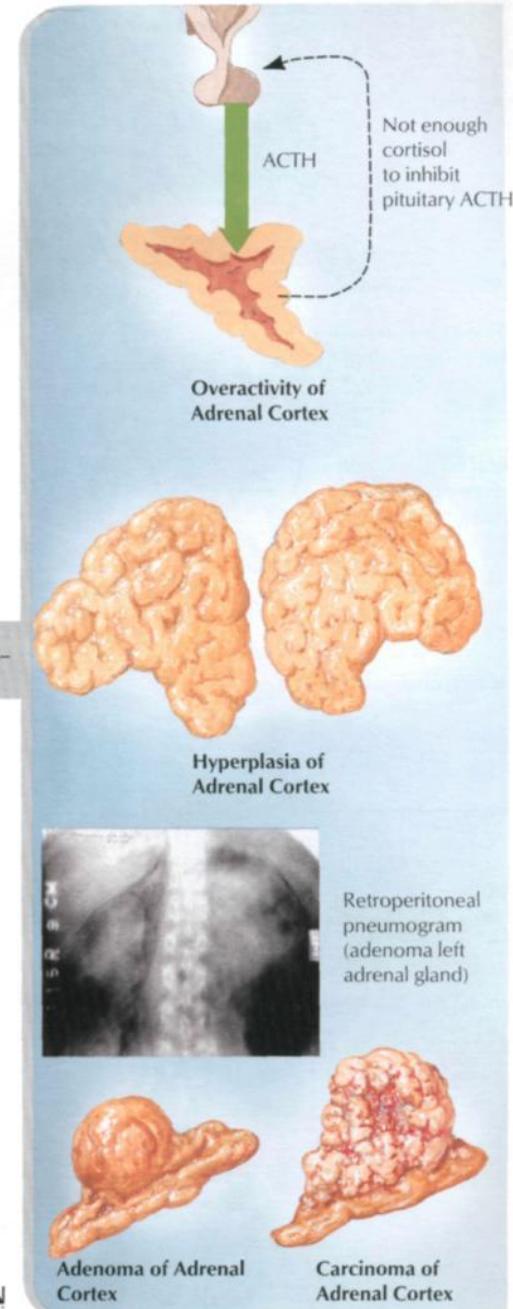
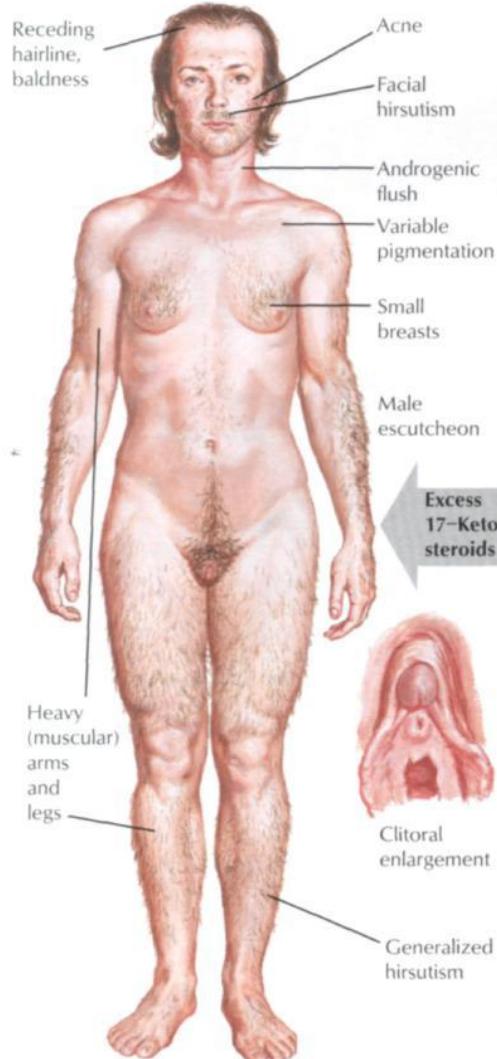
# Hyperaldosteronism

- Primary (Conn's disease) - ↓ RAAS
  - Adenoma (aldosteronoma), carcinoma
- Secondary - ↑ RAAS
  - cardiac failure, renal failure, liver cirrhosis, portal hypertension, ascites, edema
- Signs and symptoms:
  - Hypertension
  - Weakness
  - Frequent urination
  - Heart palpitations, arrhythmia

# Adrenal hyperandrogenism

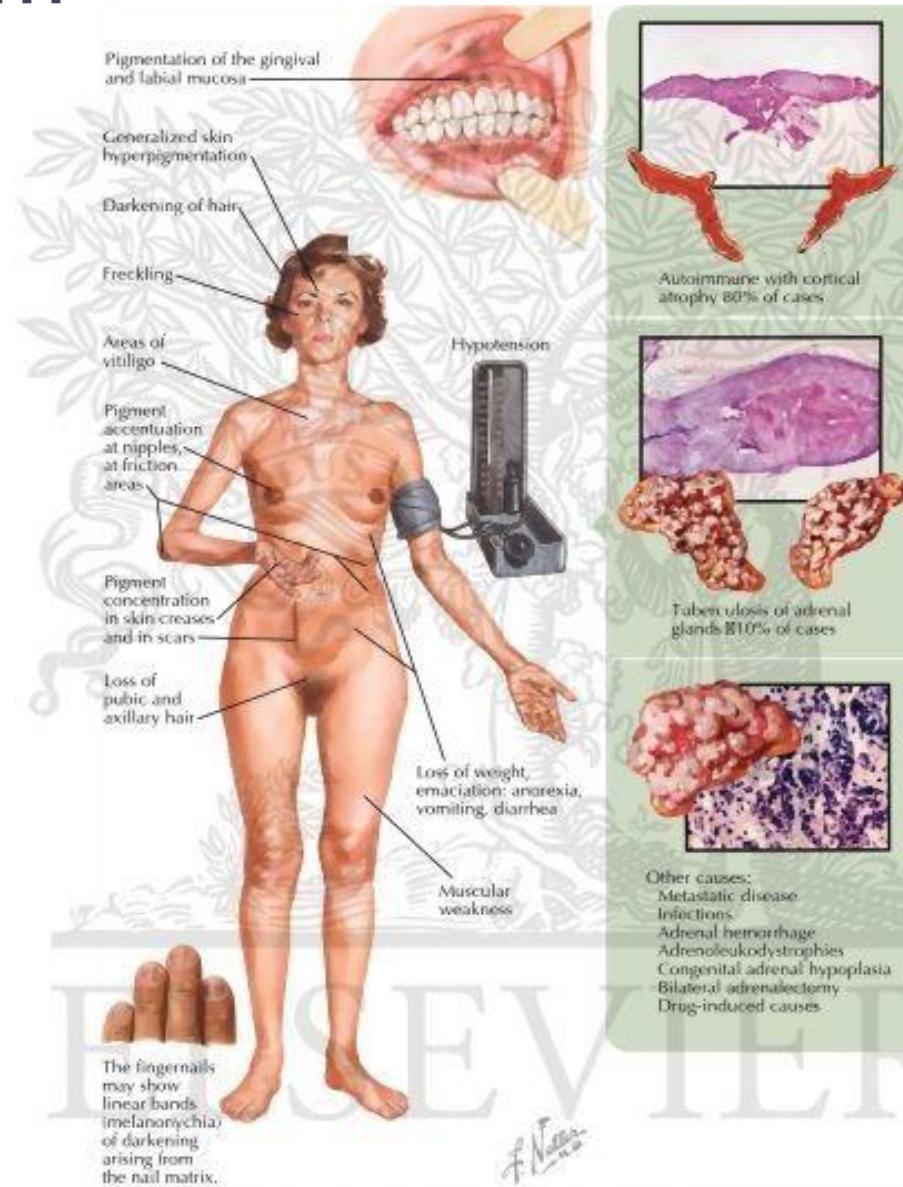
- Prenatal (congenital adrenal hyperplasia)
  - Enzymopathy → ↓ cortisol → ↑ ACTH → hyperplasia
- Postnatal
  - Hyperplasia, adenoma, carcinoma

Clinical manifestations of hyperandrogenism in adrenogenital syndrome



# Hypoadrenocorticism (Addison's disease)

- Primary → ↑ ACTH
  - Chronic (Addison's disease)
  - Acute (Addisonian crisis)
- Secondary (↓ HPA axis) → ↓ ACTH
- hypoglycemia
- hyponatremia
- hyperkalemia
- hypovolemia
- hypotension
- hyperpigmentation

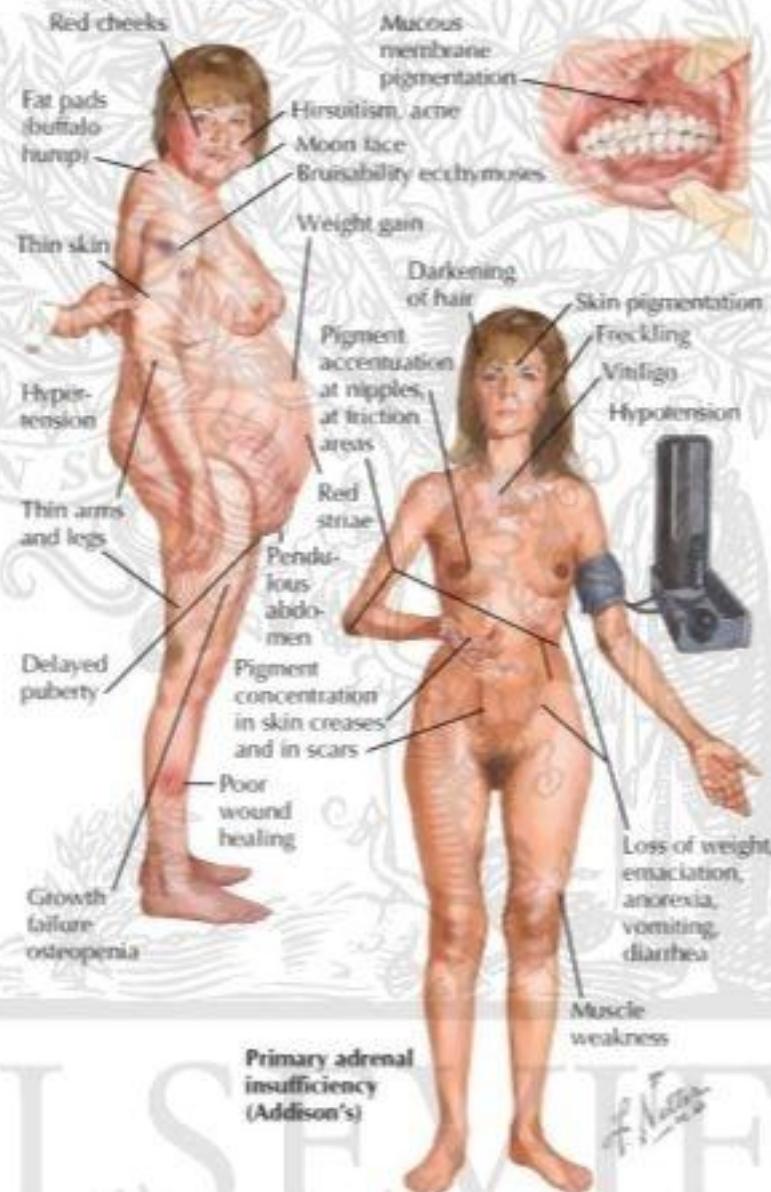


# Adrenal dysfunction

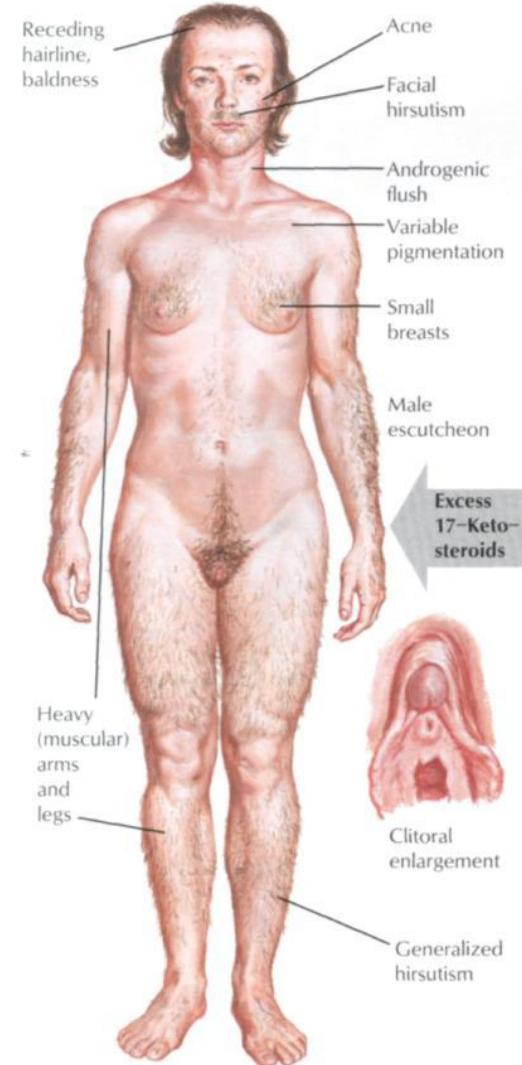
Adrenal hyperfunction – Cushing, Conn	Adrenal hypofunction – Addison
Na+ and water retention	Na+ and water losses
Hypokalemia	Hyperkalemia
Hyperglycemia	Hypoglycemia
Hypertension	Hypotension
Hirsutism	Axillary and pubic hair loss
Obesity	Weight loss

Clinical manifestations of hyperandrogenism  
in adrenogenital syndrome

**Cushing's cortisol excess**

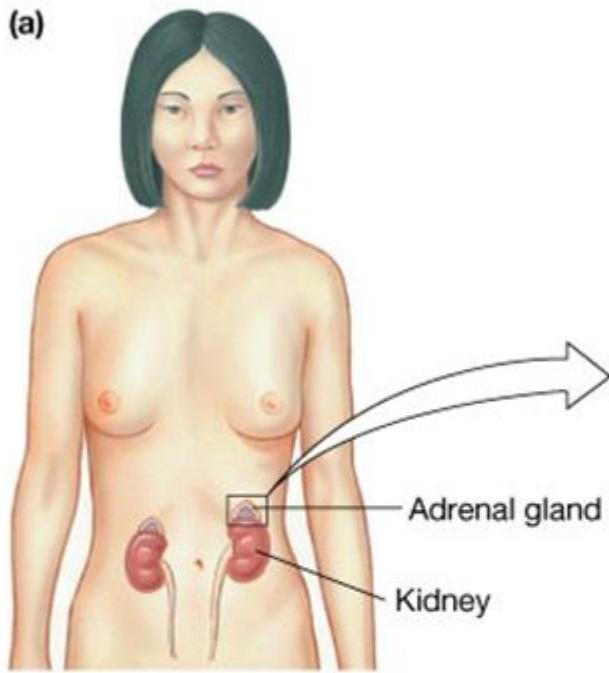


Primary adrenal insufficiency  
(Addison's)

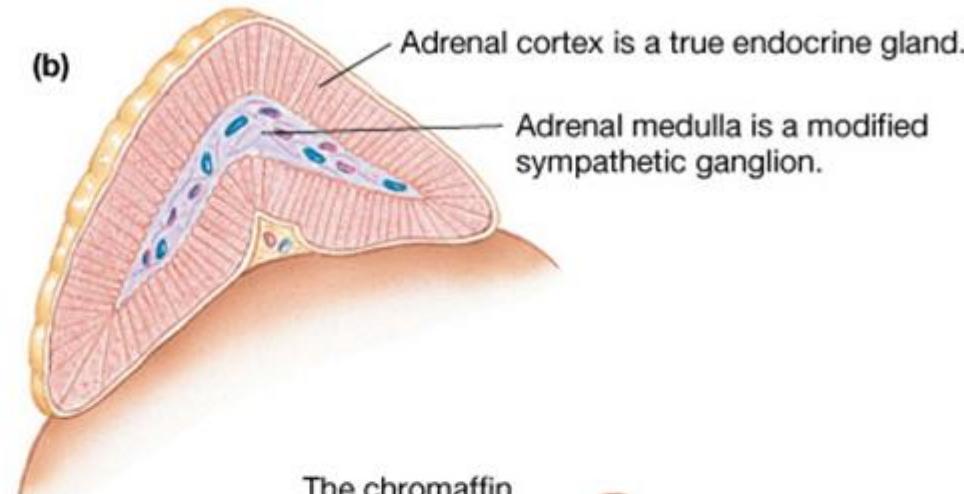


# Sympathetic adrenomedullary system

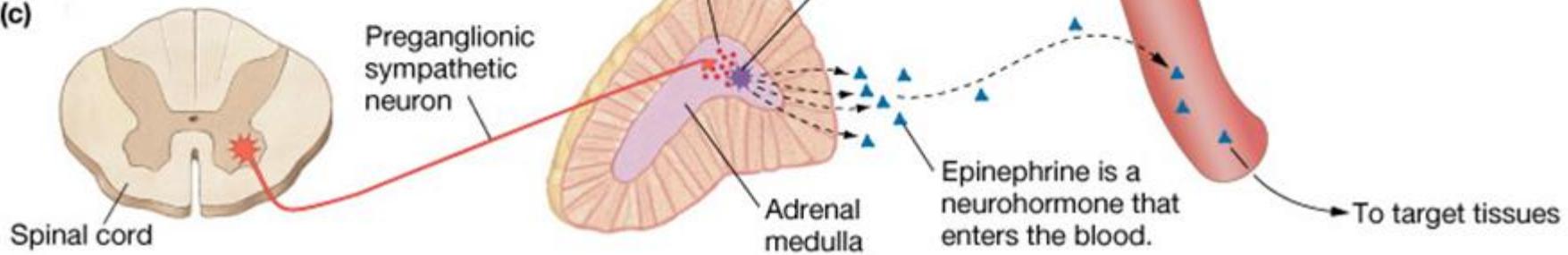
(a)



(b)



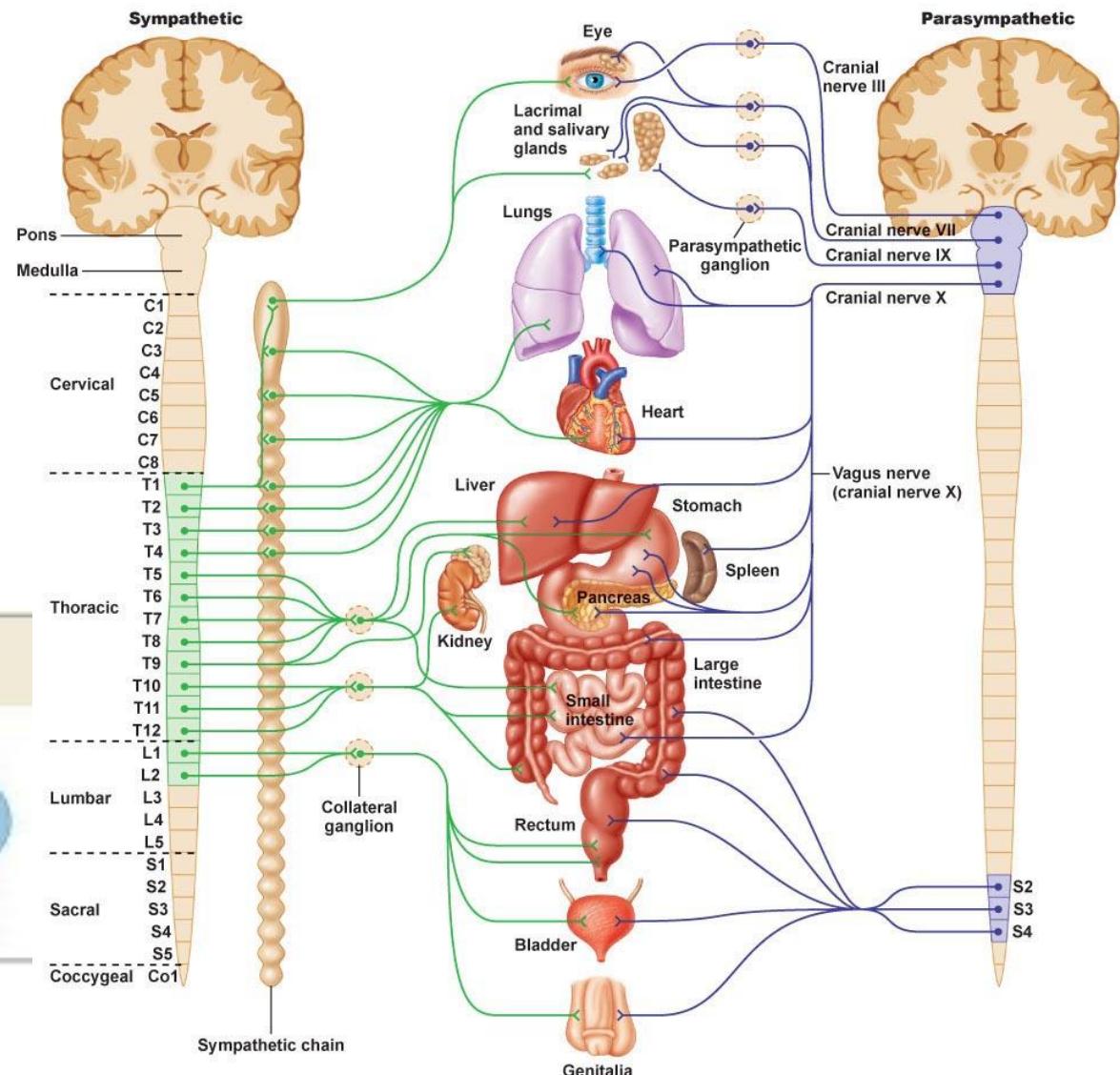
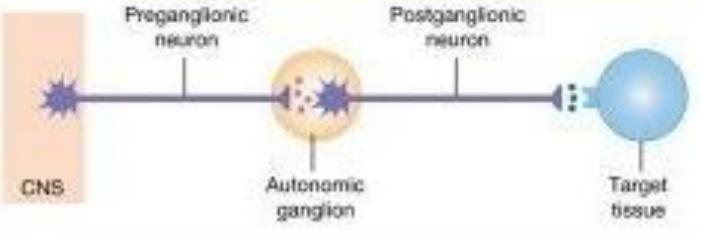
(c)

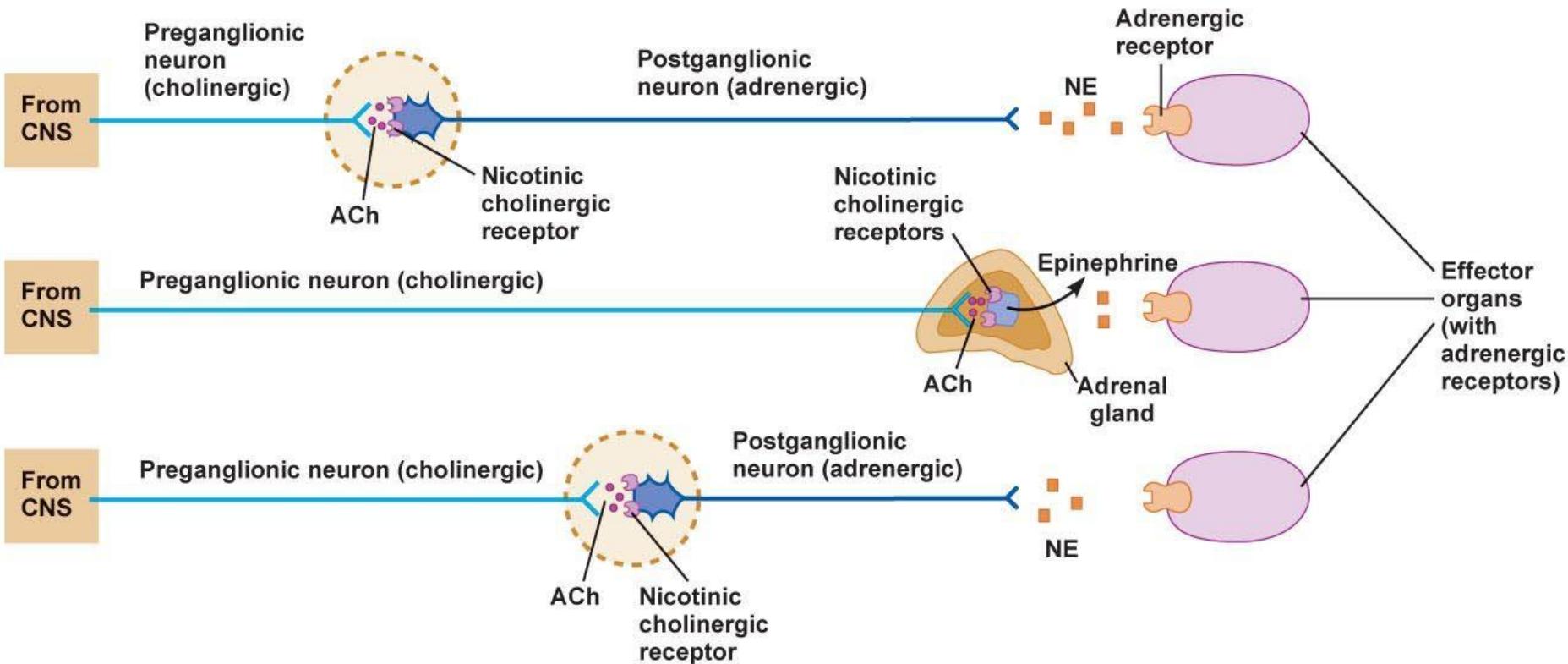


# Autonomic nervous system

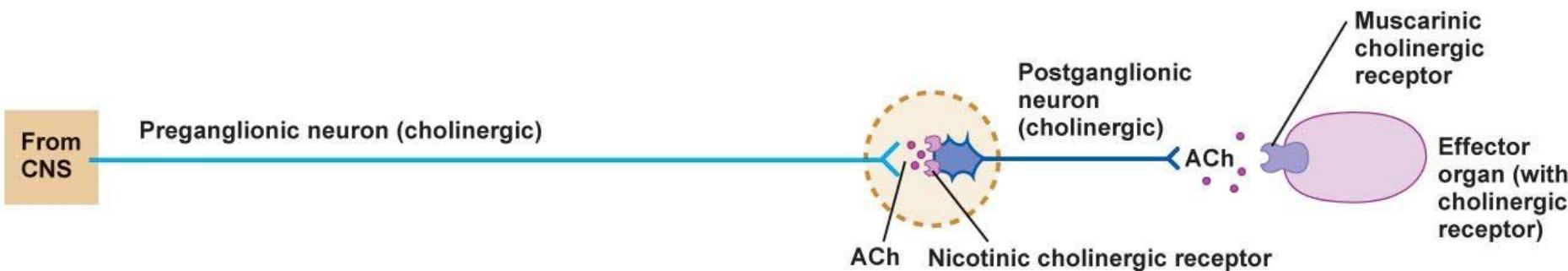
- Afferent
- Central
- Efferent

Autonomic pathways consist of two neurons that synapse in an autonomic ganglion.



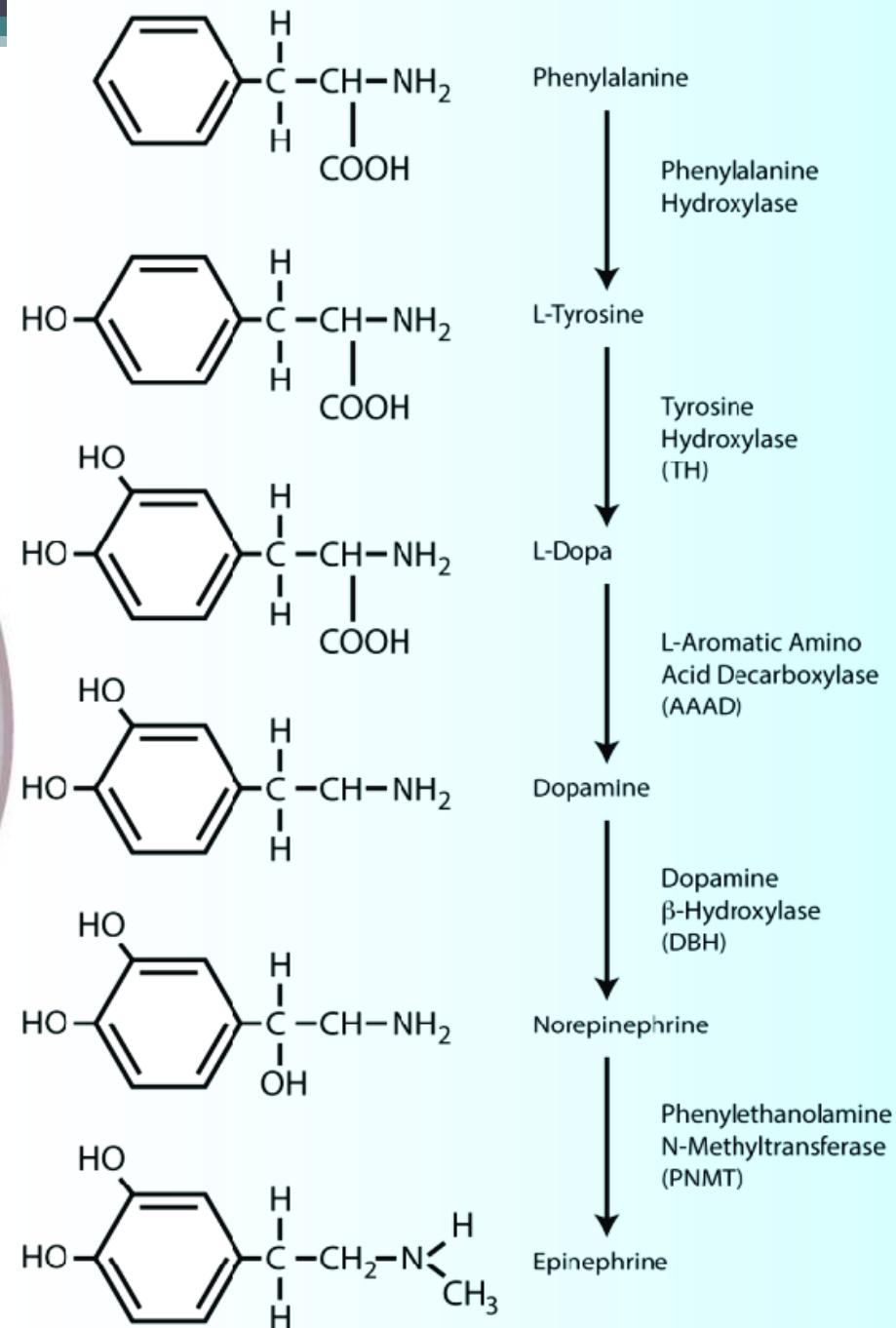
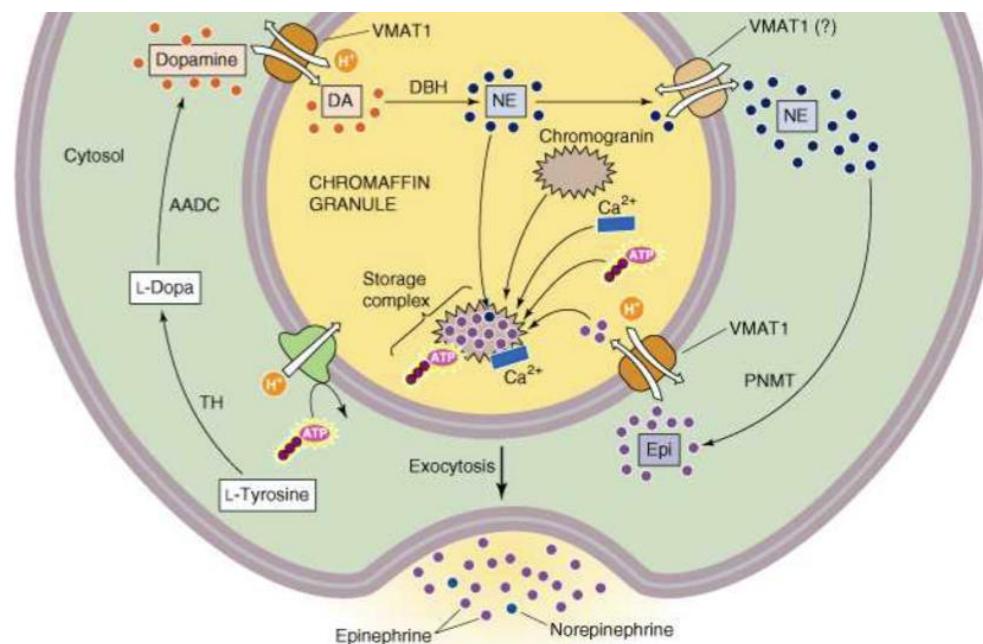


**(a) Sympathetic nervous system**



**(b) Parasympathetic nervous system**

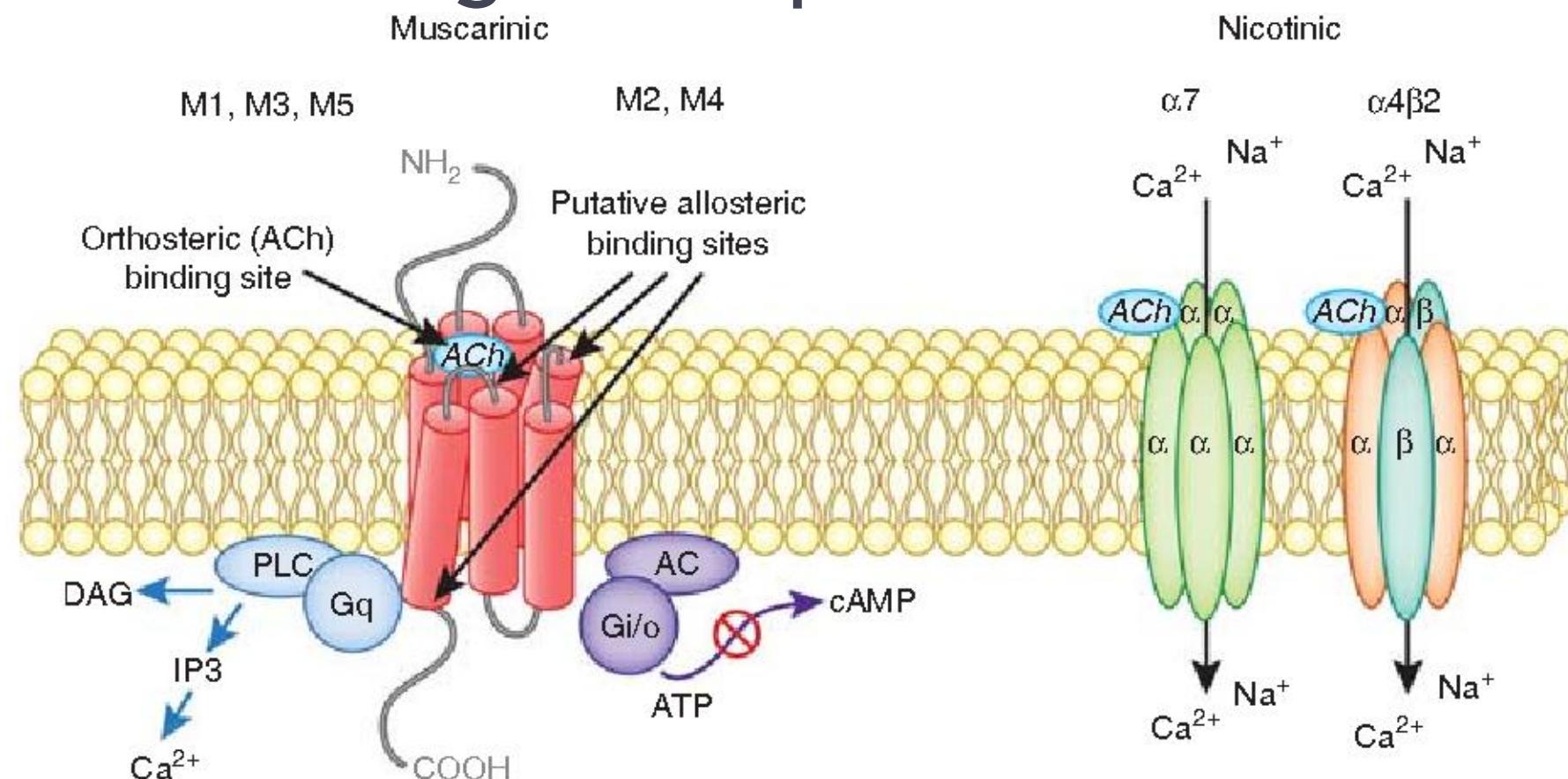
# Biosynthesis of catecholamines



# Secretion and metabolism

- Fight or flight response
- Depolarization of membranes
- Increase of intracellular  $\text{Ca}^{2+}$
- physical activity, stress stimuli, hemorrhage, hypoglycemia, hypoxia
- Metabolism: monoamine oxidase, catechol-O-methyltransferase

# Cholinergic receptors

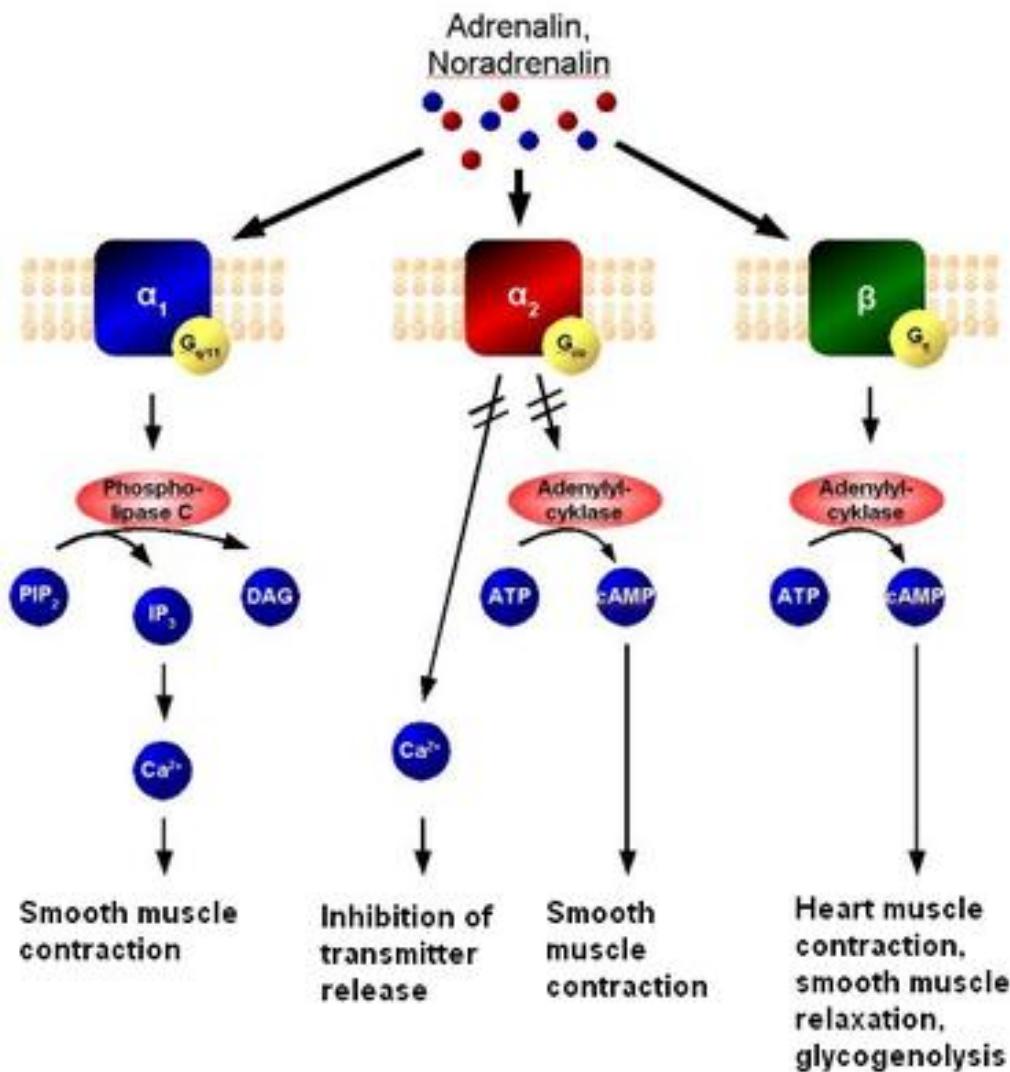


<https://www.youtube.com/watch?v=EChrlp4a-f4>

# Biological effects

- Liver – glycogenolysis, gluconeogenesis ( $\alpha$ )
- Muscle – glycogenolysis, glycolysis ( $\beta_2$ )
- Adipose – lipolysis ( $\beta_1$ )
- Pancreas – inhibited secretion of insulin ( $\alpha_2$ )
- Vasoconstriction – skin, mucous membranes, splanchnic organs, kidney
- Vasodilatation – skeletal muscles
- Inotropic, chronotropic, dromotropic, bathmotropic ( $\beta_1$ )
- Increase blood pressure
- Bronchodilatation ( $\beta_2$ )
- Mydriasis ( $\alpha_1$ )
- Inhibit the motility of GIT

# Mechanism of action



<https://www.youtube.com/watch?v=ejq99wLEMTw>

<https://www.youtube.com/watch?v=VrwpCitPRbE>

<https://www.youtube.com/watch?v=5zzE35tzRyQ>

<https://www.youtube.com/watch?v=moY8UefNlAw>

**Alpha Receptors**

1. Vasoconstriction of
  - a. Coronary arteries
  - b. Veins
2. ↓motility of GIT smooth muscle cells

**Beta Receptors****α1  
(postsynaptic)**

**Gq protein** coupled  
Activates **Phospholipase C**  
**PIP2 → IP3 + DAG**

1. Vasoconstriction of blood vessels of
  - a. Skin
  - b. GIT
  - c. Kidney
  - d. Brain
2. Contraction of smooth muscles of
  - a. Ureter
  - b. Vas deferens
  - c. Urethral sphincter
  - d. Uterus
  - e. Ciliary body (mydriasis)
3. Glucose metabolism
  - a. Glucconeogenesis
  - b. Glcolysis

**α2  
(presynaptic)**

**Gi protein** coupled  
Inhibits **Adenyl Cyclase**  
**ATP → X → cAMP**

1. Glucose metabolism
  - a. Inhibits insulin release
  - b. Stimulates glucagon release
2. Contraction of anal sphincter
3. Inhibits release of Norepinephrine

**β1  
(postsynaptic)**

**Gs protein** coupled  
Activates **Adenyl Cyclase**  
**ATP → cAMP**

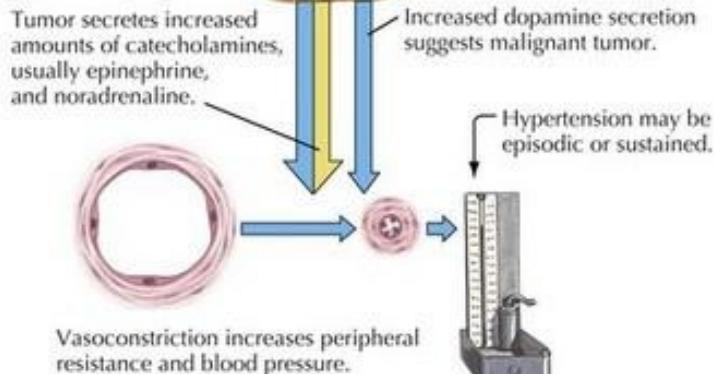
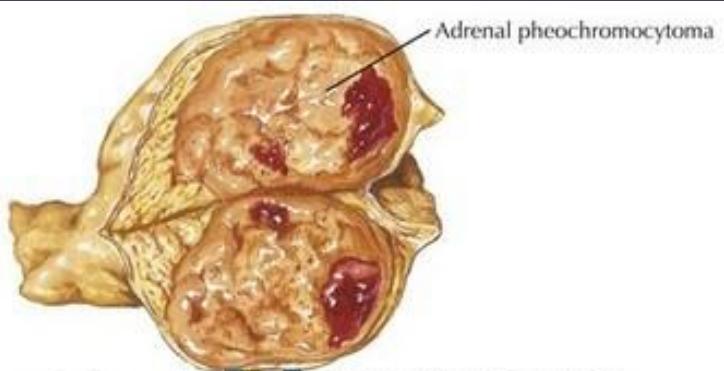
1. The heart
  - a. ↑heart rate (+ chronotropic)
  - b. ↑impulse conduction (+dromotropic)
  - c. ↑contraction (+ inotropic)
  - d. ↑ejection fraction
2. ↑renin release by Juxtaglomerular cells
3. ↑hunger
  - a. ↑ghrelin release by stomach

**β2  
(postsynaptic)**

1. Smooth muscle relaxation of
  - a. Bronchus
  - b. Bronchioles
  - c. Detrusor muscle
  - d. Uterine muscle
2. Contraction of urethral sphincter
3. ↑renin release by Juxtaglomerular cells
4. Glucose metabolism
  - a. Inhibits insulin release
  - b. Stimulate
    - i. Gluconeogenesis
    - ii. Glcolysis
5. Lipolysis
6. Thickened salivary secretion

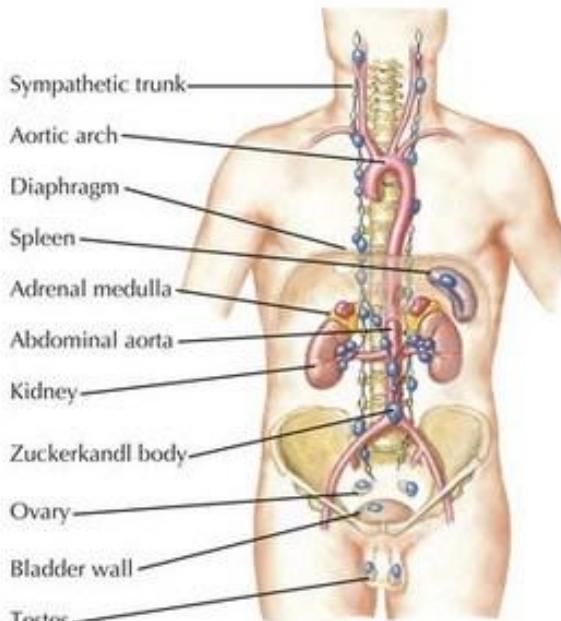
# Pheochromocytoma

- 90% - adenoma
- Intra- or extra-adrenal paraganglioma
- Excess of adrenalin and noradrenalin
- Hypertension (paroxysmal, persistent)
- Palpitations, tachycardia, hyperglycemia
- Sweating
- Complications
  - Stroke, nephropathy, retinopathy, ischemic heart disease



Pheochromocytoma is a chromaffin cell tumor secreting excessive catecholamines resulting in increased peripheral vascular resistance and hypertension.

Potential sites of pheochromocytoma

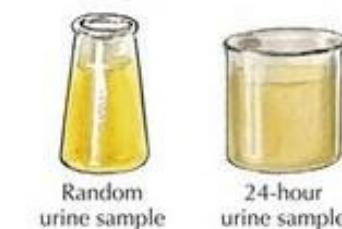


Most pheochromocytomas are adrenal in origin, but can occur in various sites in sympathetic ganglia and may be associated with multiple endocrine neoplasia syndromes. Most are sporadic, but some are hereditary.

### Clinical features of pheochromocytoma



Blood pressure  
Palpitations/  
chest pains  
Weakness  
Epigastric pain  
Tremor



Abnormal random urine assay for creatine and metanephrine or 24-hour urine assay of metanephrine and free catecholamines used in diagnosis



CT scan or MRI may reveal presence of tumor.

*J. Nettler, M.D.*  
JOHN A. CRAIG, M.D.  
*C. Machado, M.D.*

Symptoms are secondary to excessive catecholamine secretion and are usually paroxysmal. More than 90% of patients with pheochromocytoma have headaches, palpitations, and sweating alone or in combination.

Hypertenzia, nefrolitiáza a  
osteopénia sú následkami

A. Hypokalciémie

B. Hyperkalciémie

# Kalcitonín sa produkuje

A. v štítnej žľaze

B. v prištítňých telieskach

# Parathormón stimuluje

- A. aktivitu osteoklastov
- B. aktivitu osteoblastov
- C. renálnu exkréciu vápnika

Následkom jódového deficitu je

- A. hypertyreóza
- B. ↑ koncentrácia TSH
- C. deštrukcia štítnej žľazy

Antidiuretický hormón sa produkuje v

A. adenohypofýze

B. neurohypofýze

C. obličkách

D. hypotalame

Mechanizmus stimulácie produkcie ACTH následkom nízkej koncentrácie kortizolu je

- A. negatívna spätná väzba
- B. pozitívna spätná väzba

Prekurzorom steroidných  
hormónov je

A. tyrozín

B. cholesterol

# Glukokortikoidy

- A. ↑ inzulínovú senzitivitu
- B. spôsobujú hypoglykémiu
- C. majú protizápalový účinok