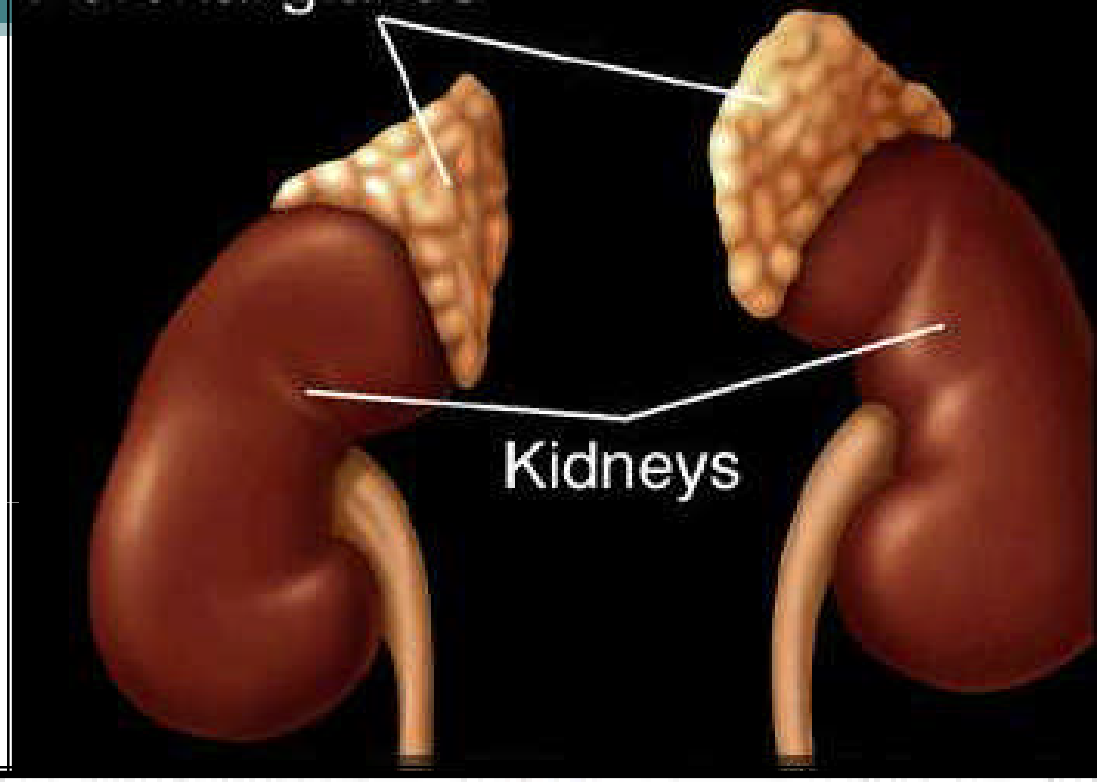
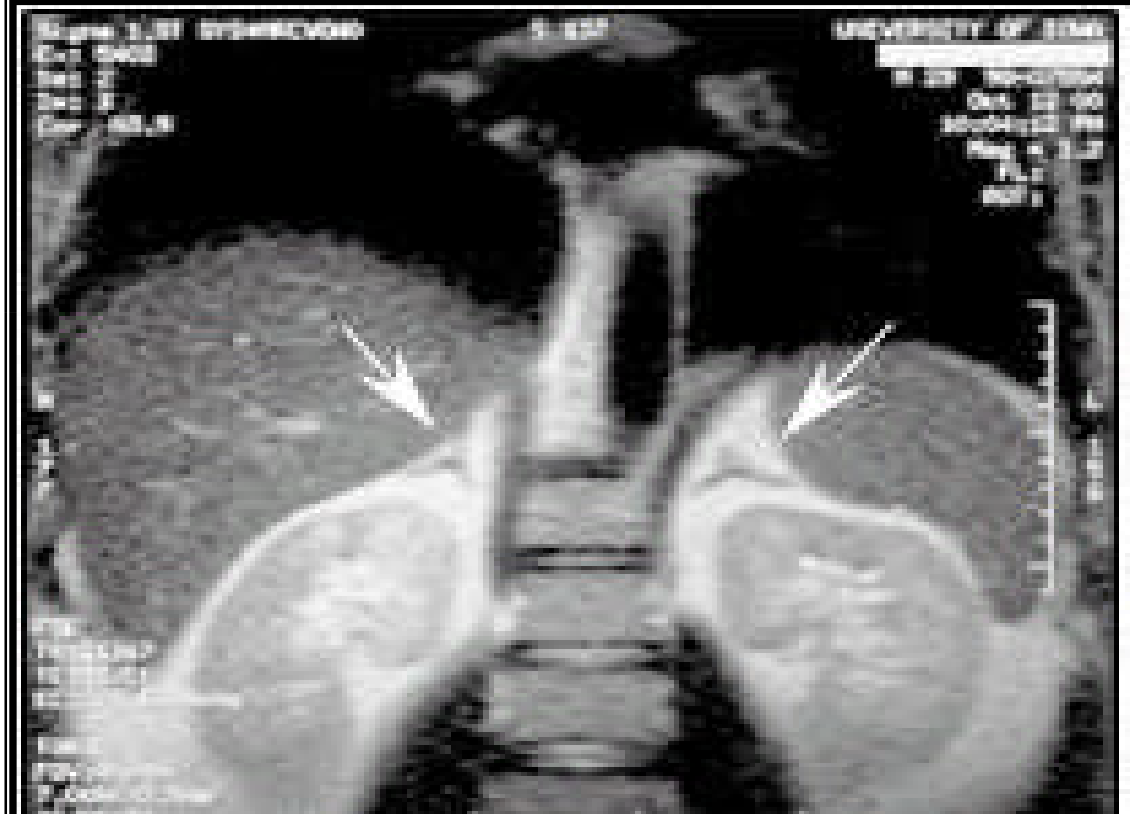
D.Hammoudi.MD

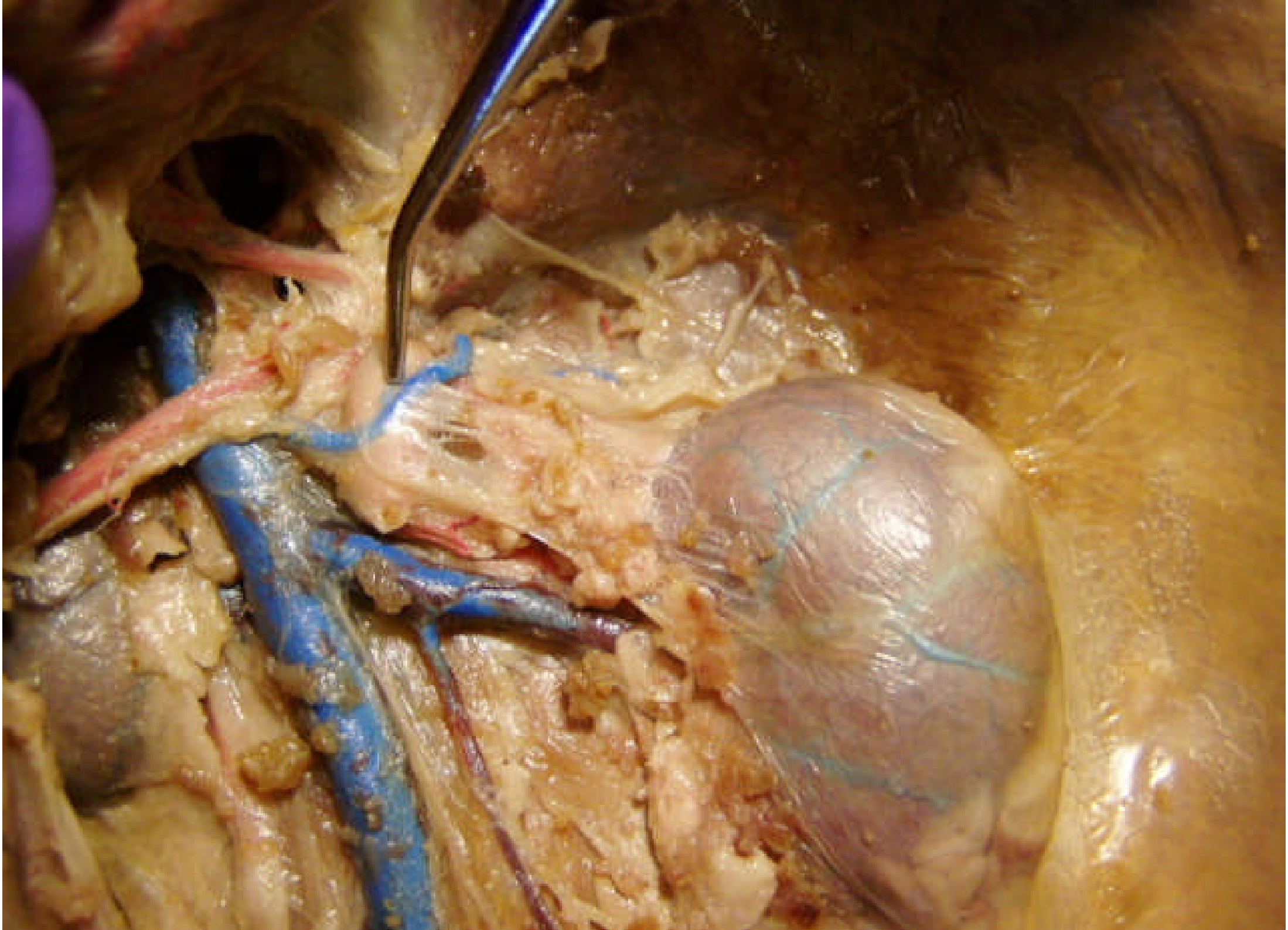
ADRENAL GLAND

Introduction

- Among most important and vital endocrine organ
- Small bilateral yellowish retroperitoneal organ
- Lies just above kidney in gerota's fascia







The Adrenal Gland

Anatomy was first described in 1563.

Is located above (or attached to) the upper pole of the kidney.

Is pyramidal in structure and weights about 4-5 grams.

Consists of the adrenal cortex and adrenal medulla

Activities are regulation of fluid volume and stress response

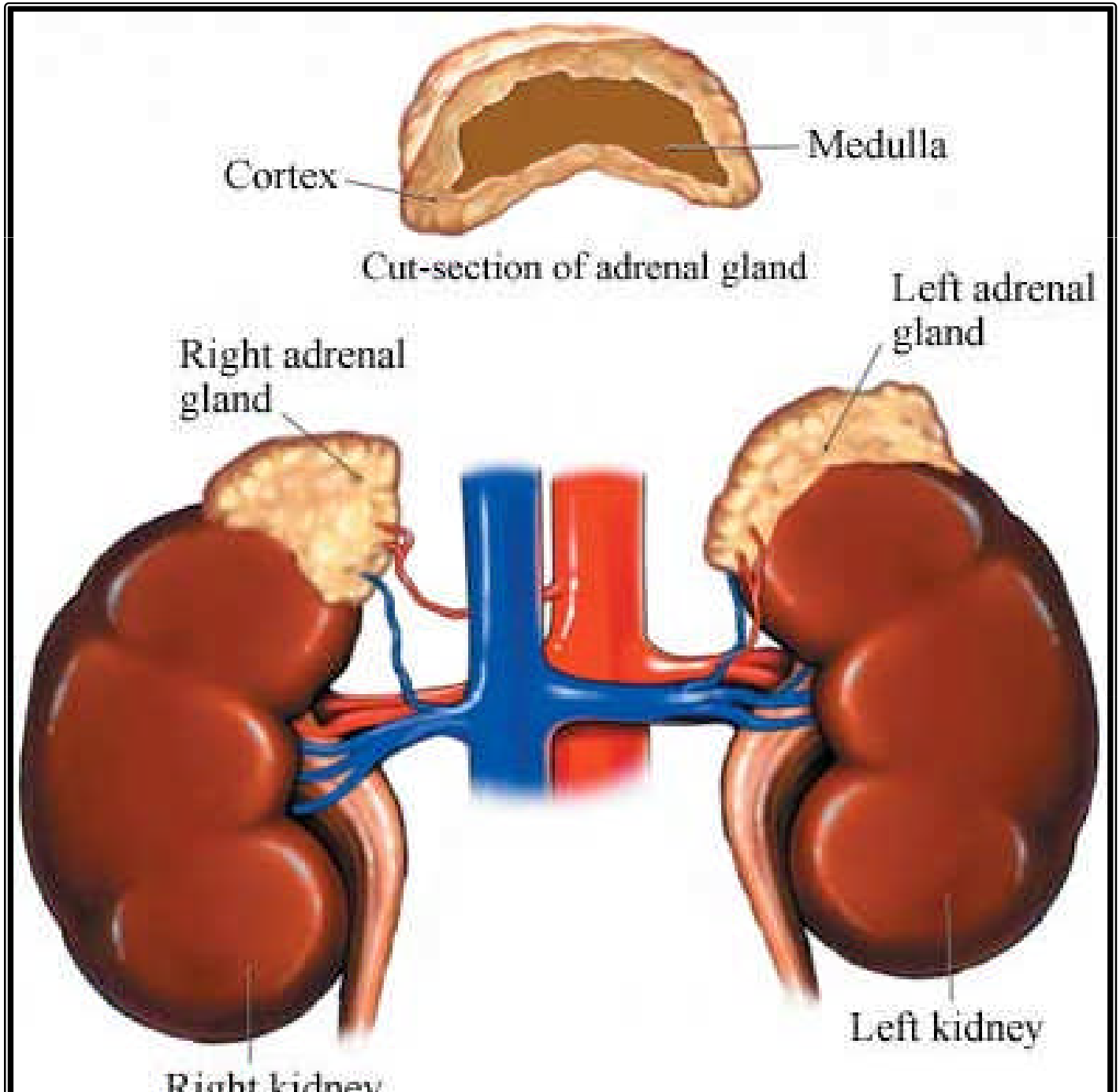
Anatomy

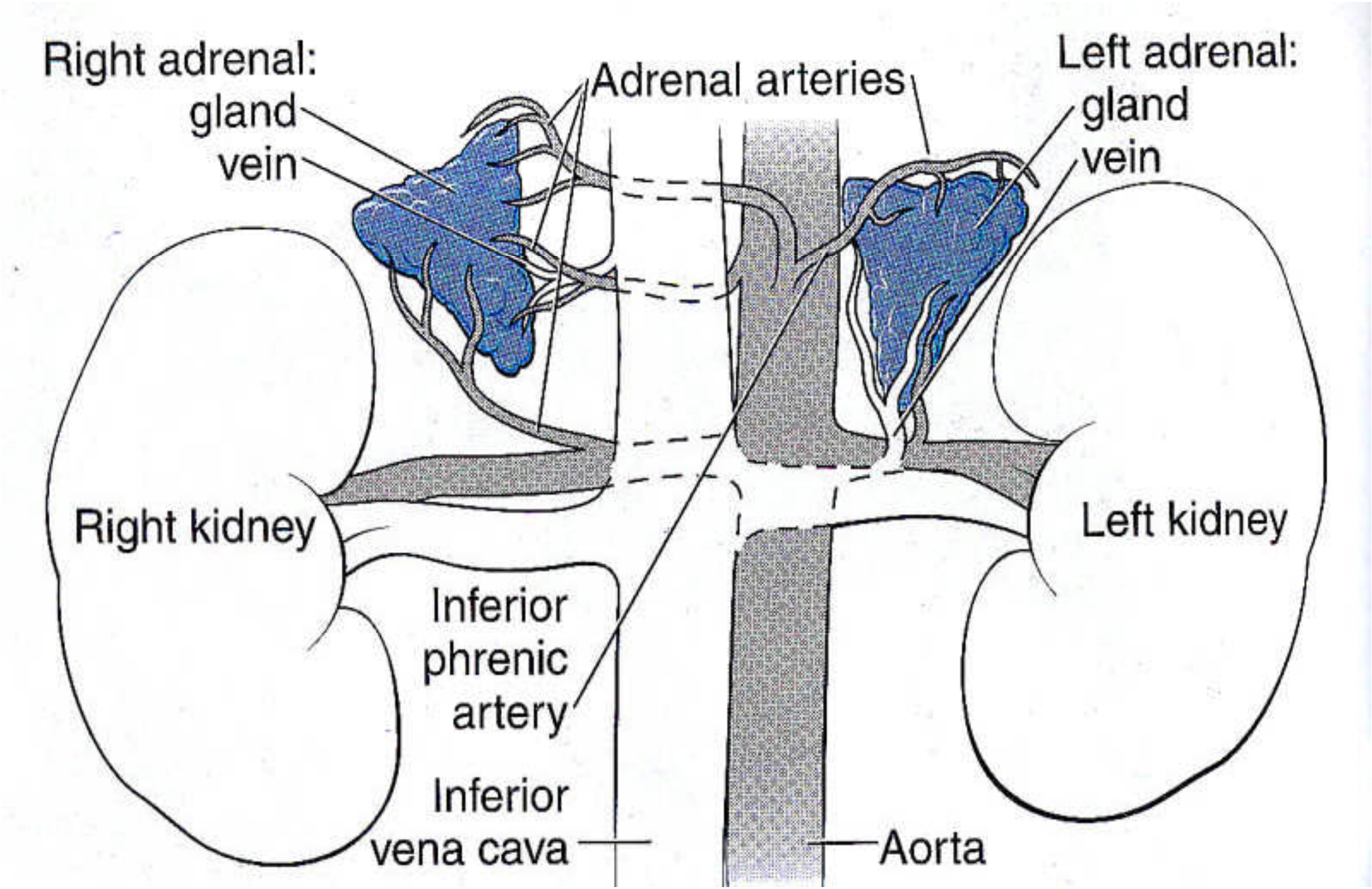
- Right adrenal is triangular, related to upper pole Right kidney

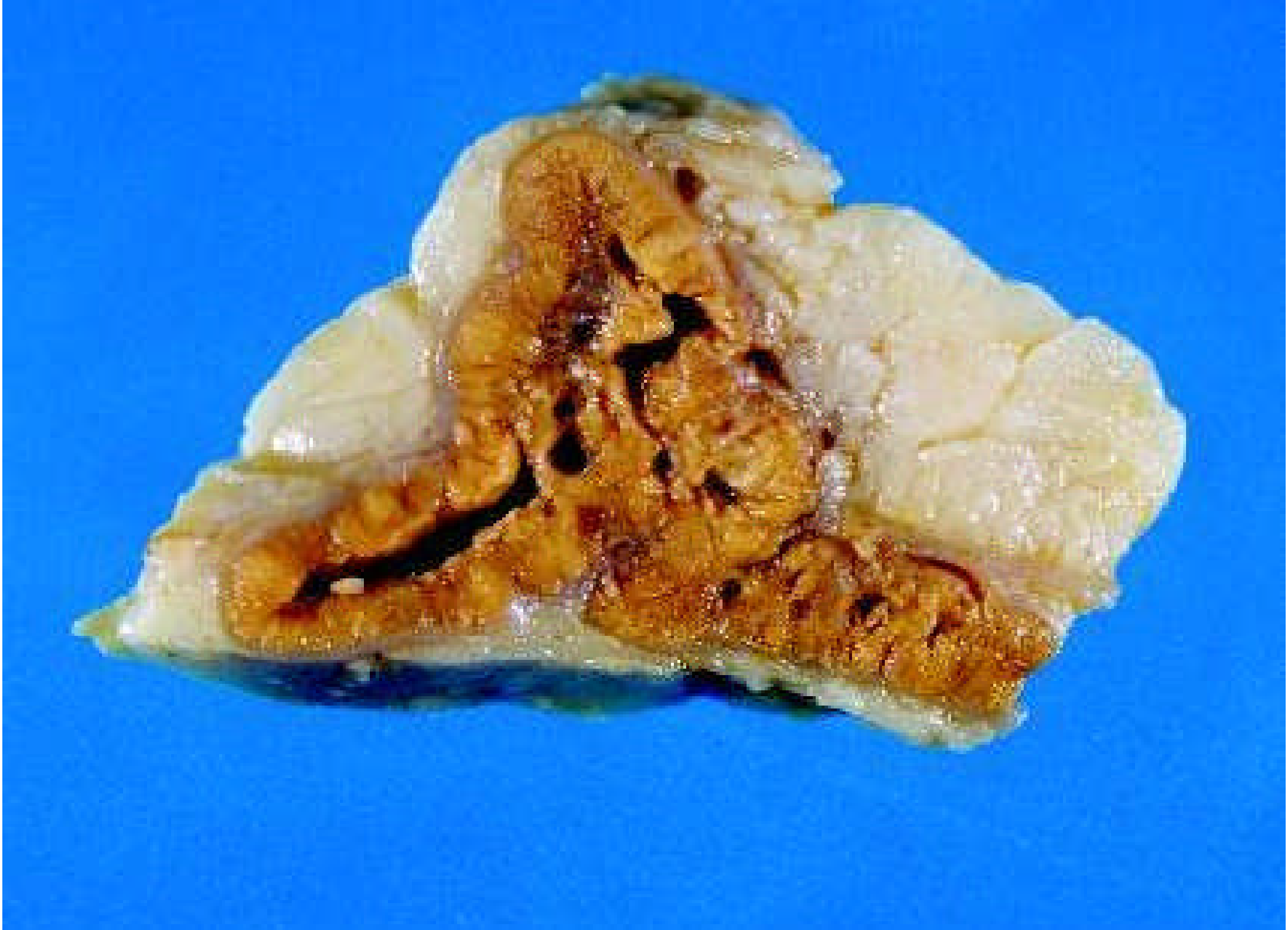
- Left adrenal is crescent shaped, related to upper and medial part Left kidney

- Size : 3 - 6cm long, 0.9 – 3.6cm
- Weight : 3-5 gm app
- Width : 2-3 cm

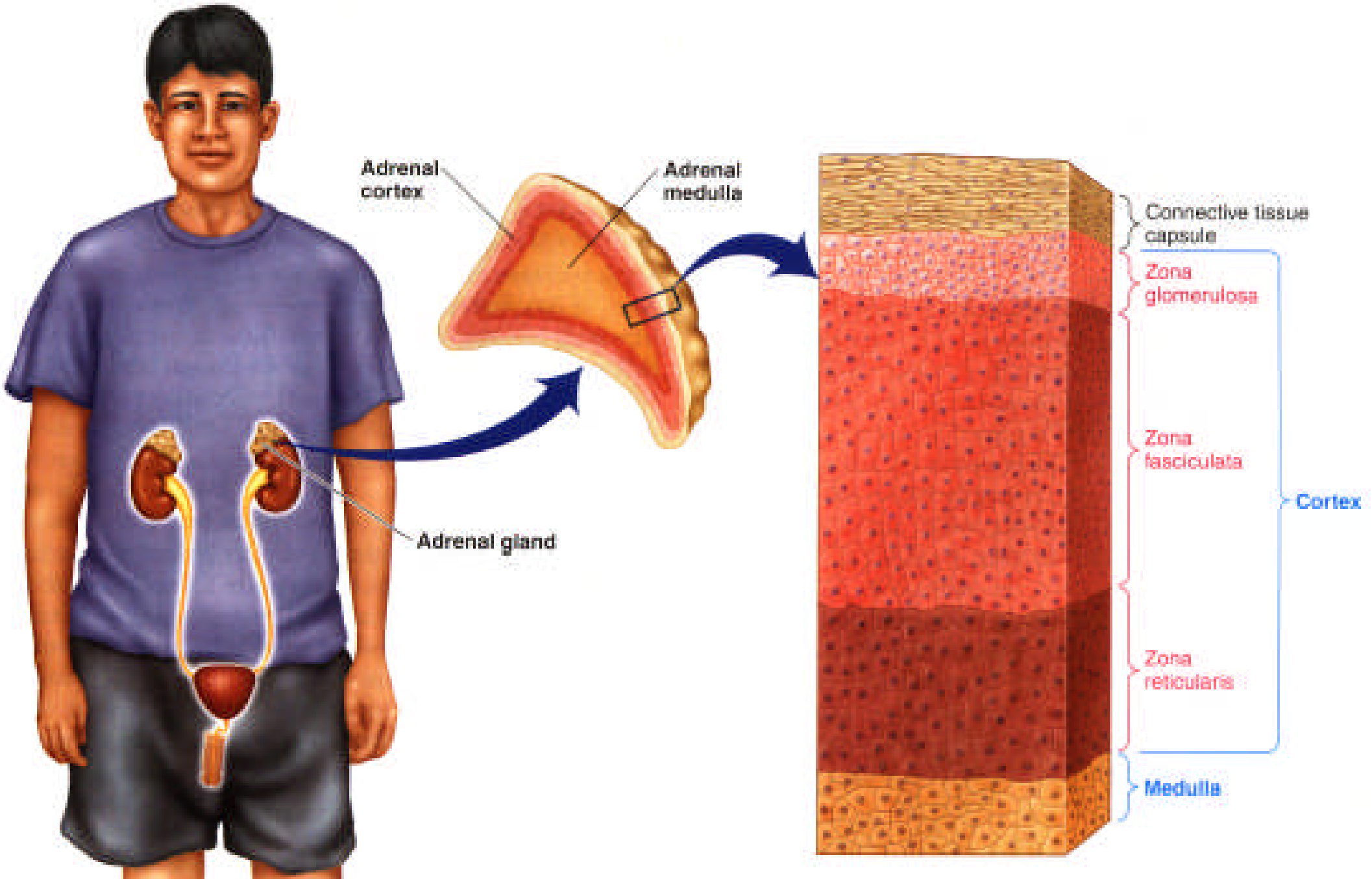
Anatomy

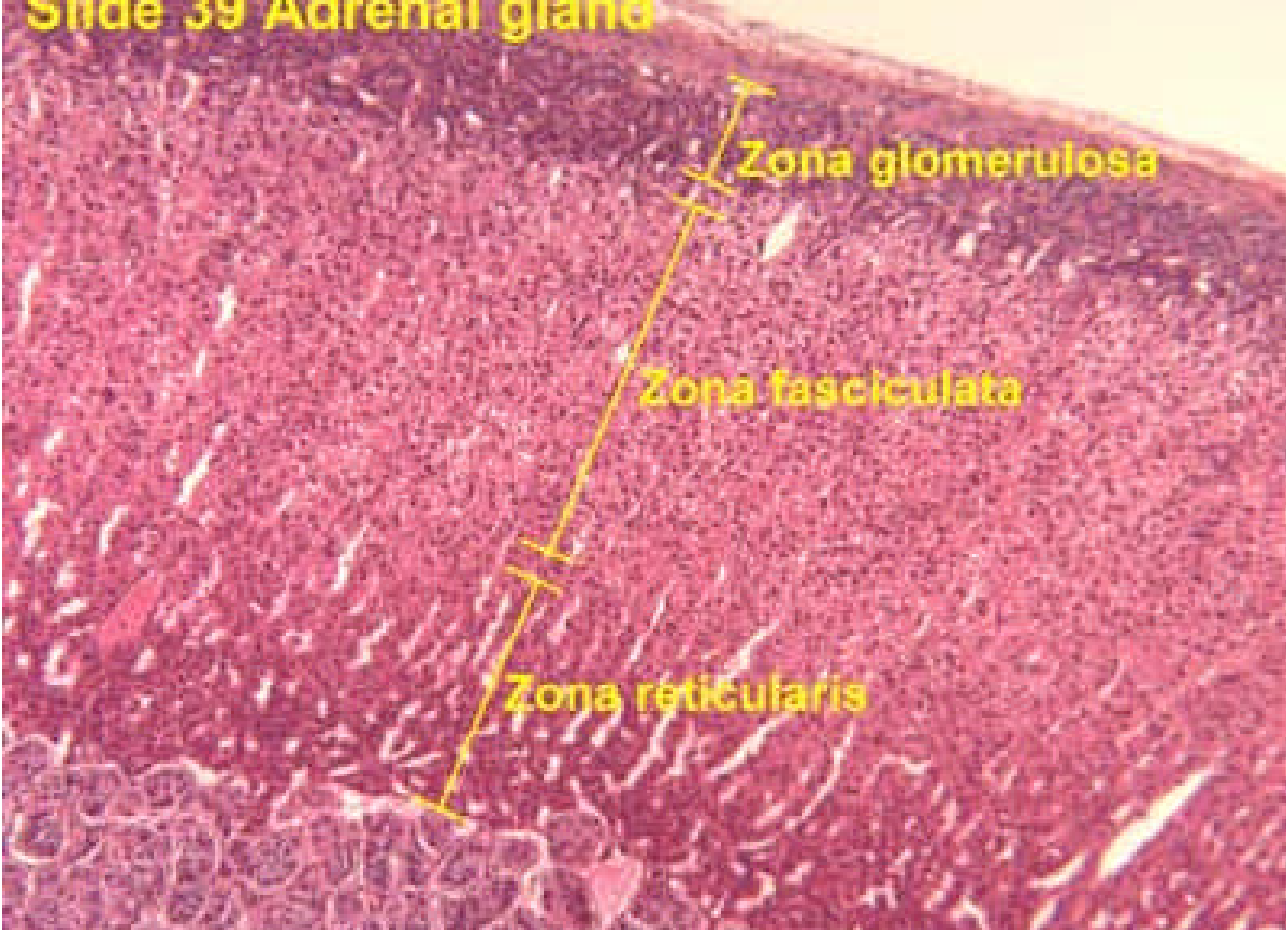

Cortex
Medulla
Cut-section of adrenal gland
Left adrenal gland
Right adrenal gland
Left kidney
Right kidney

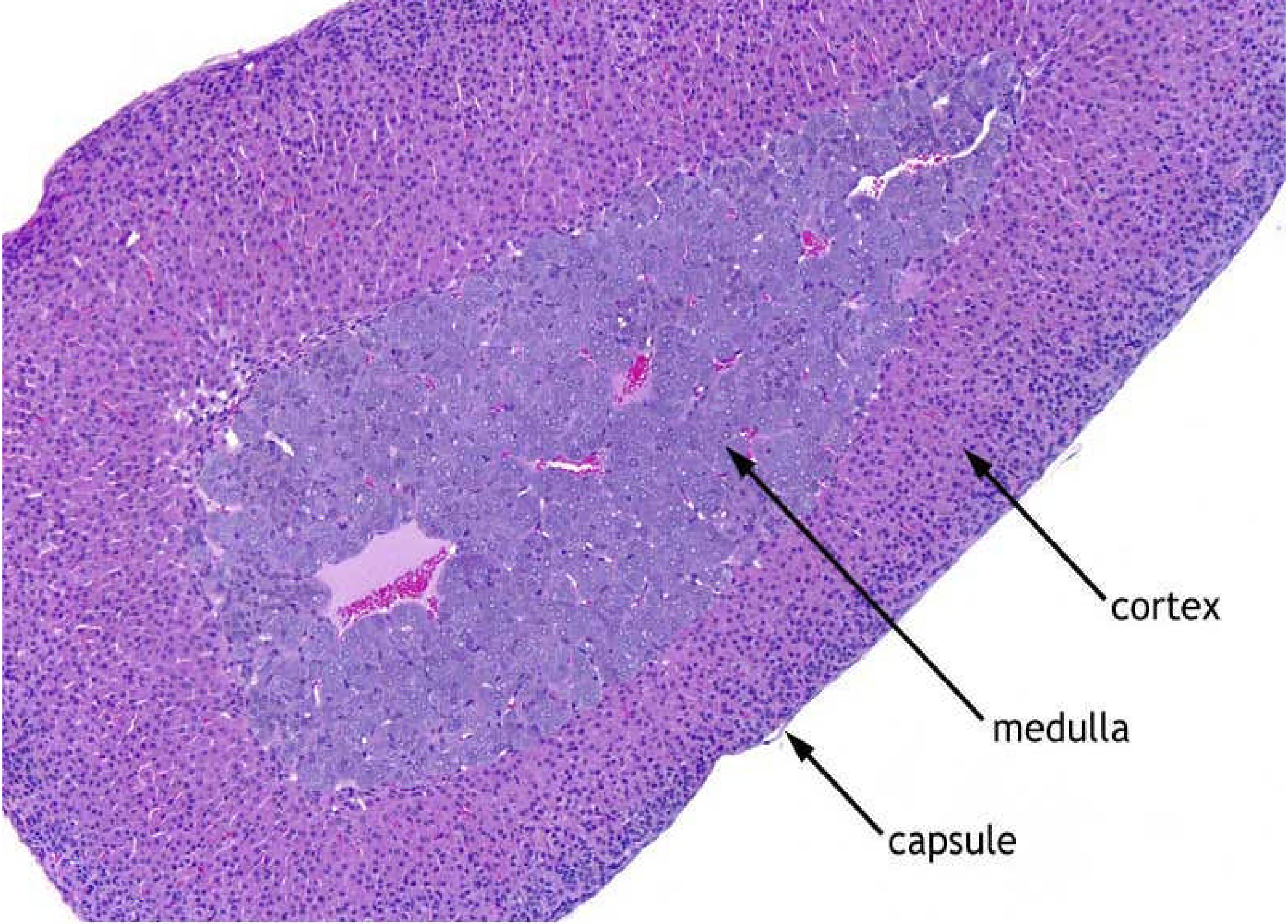

Right adrenal:
gland
vein
Adrenal arteries
Left adrenal:
gland
vein
Right kidney
Left kidney
Inferior
phrenic
artery
Inferior
vena cava
Aorta

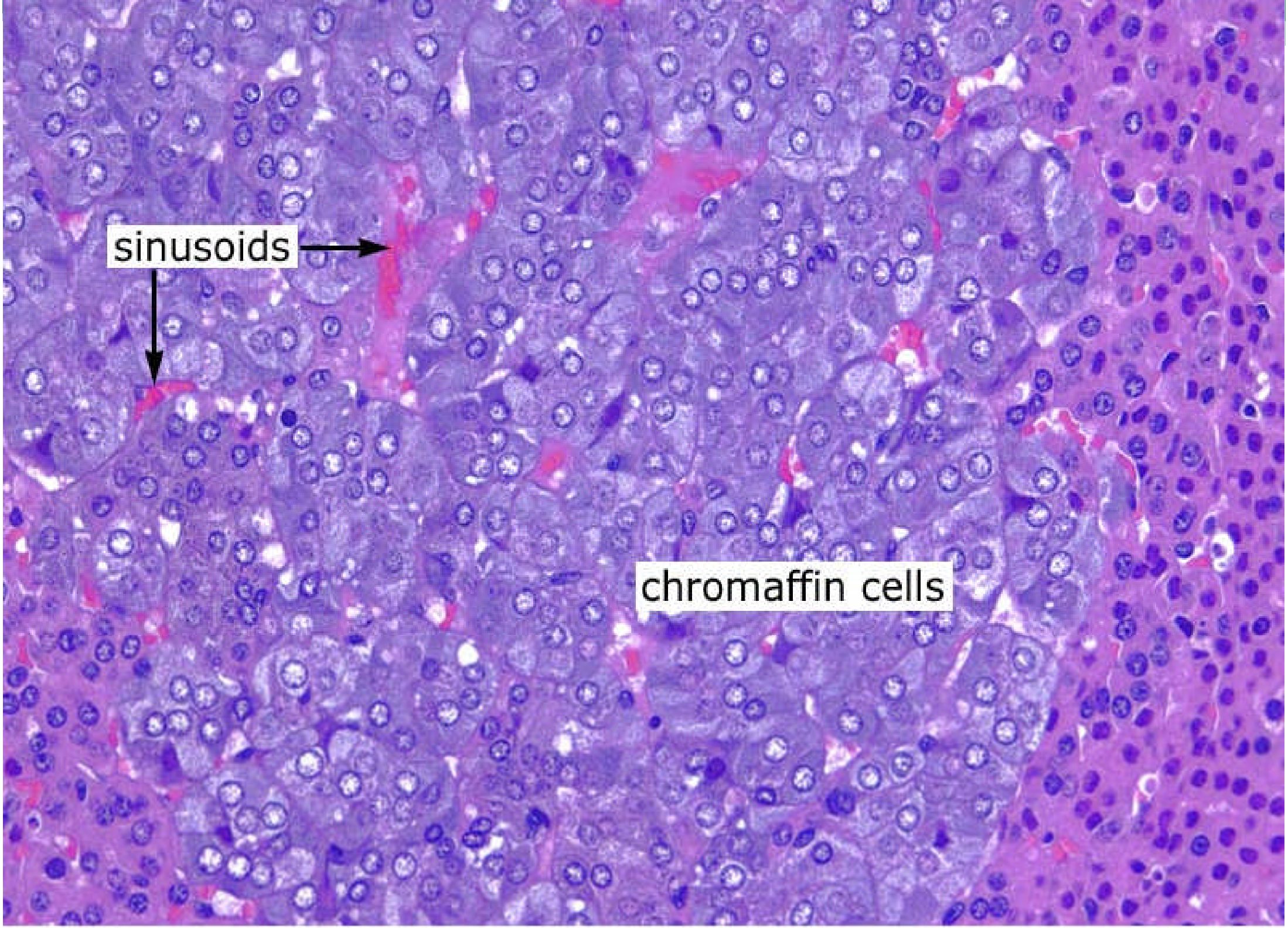


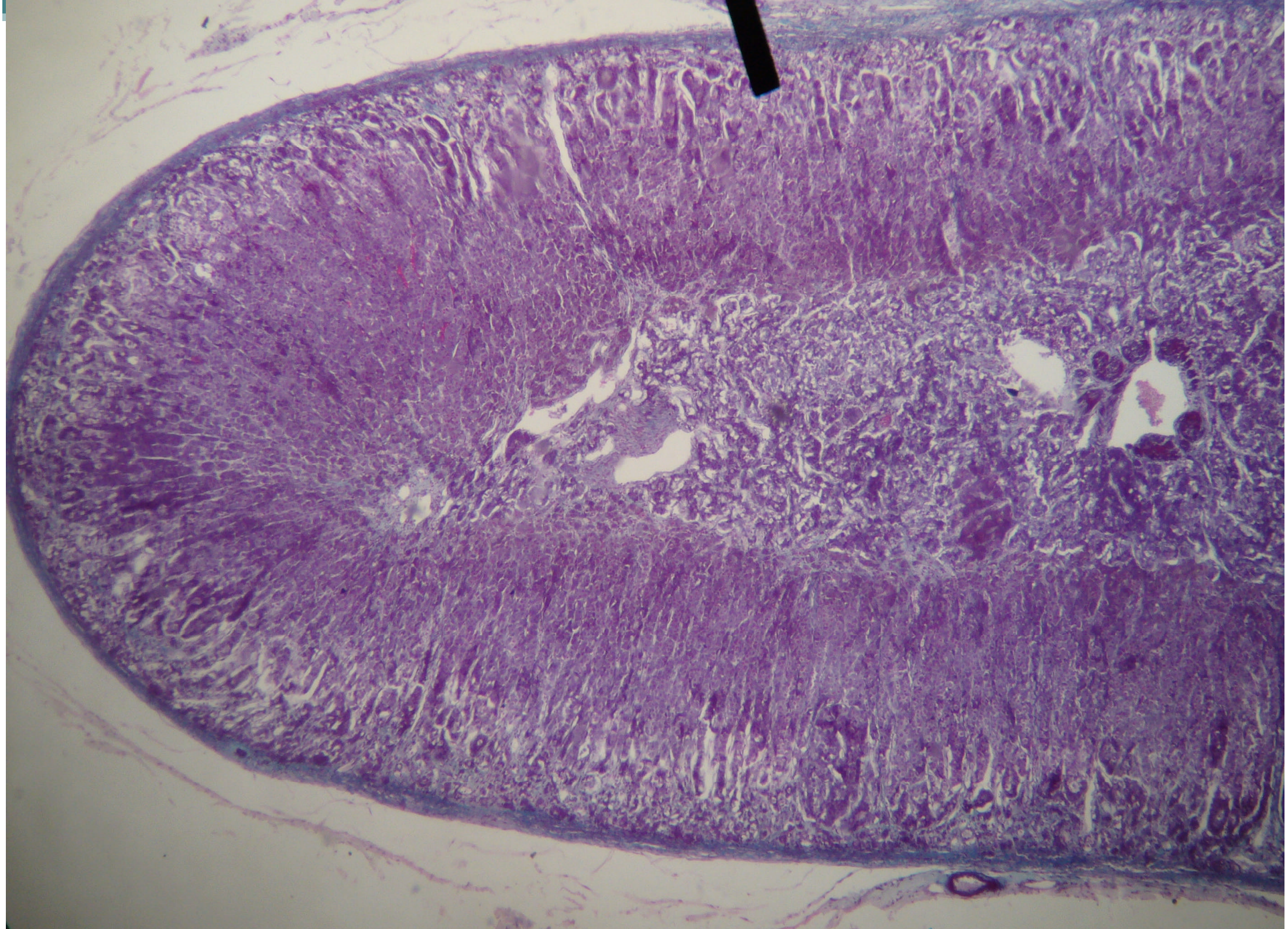
Adrenal Histology

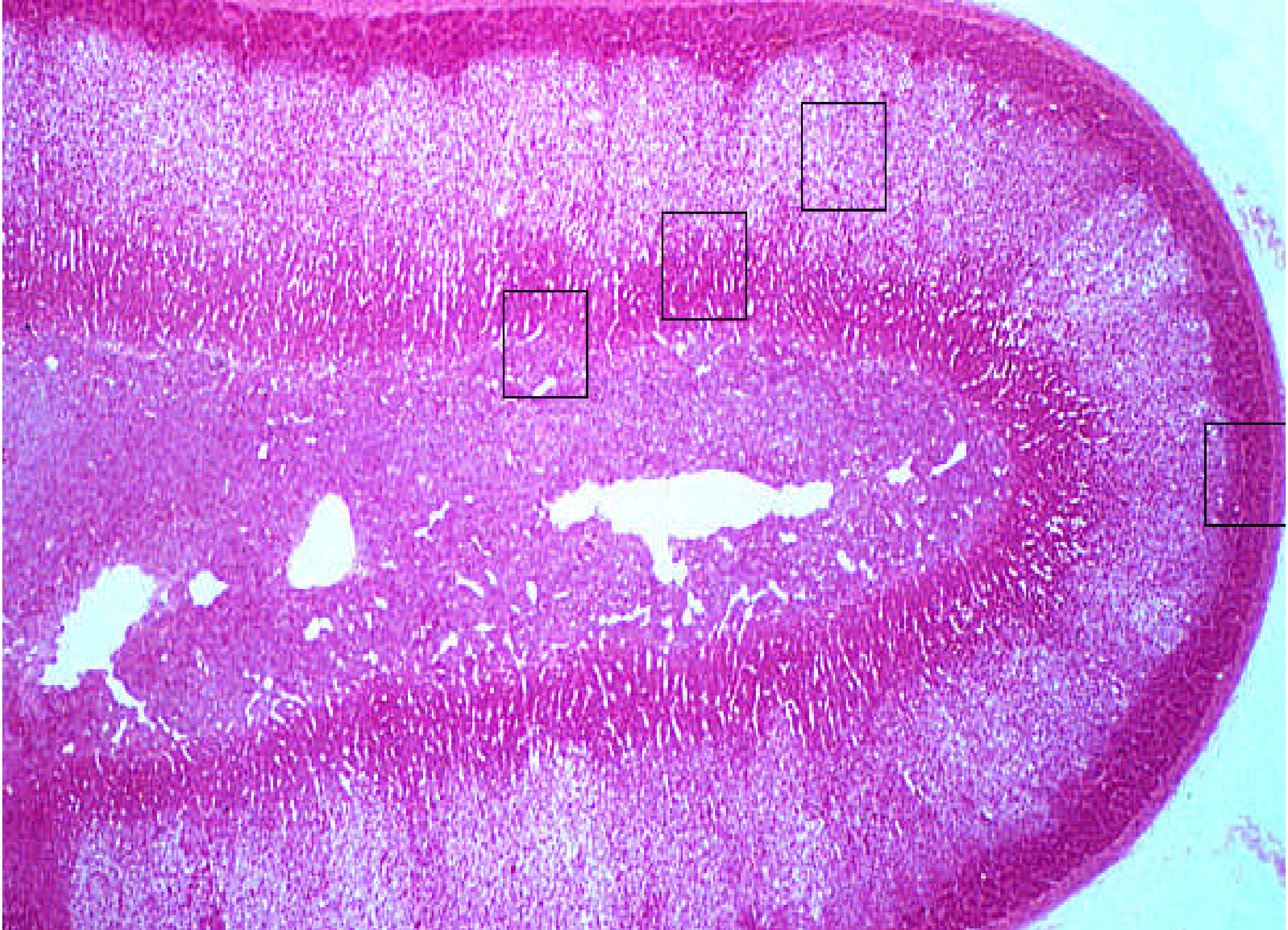


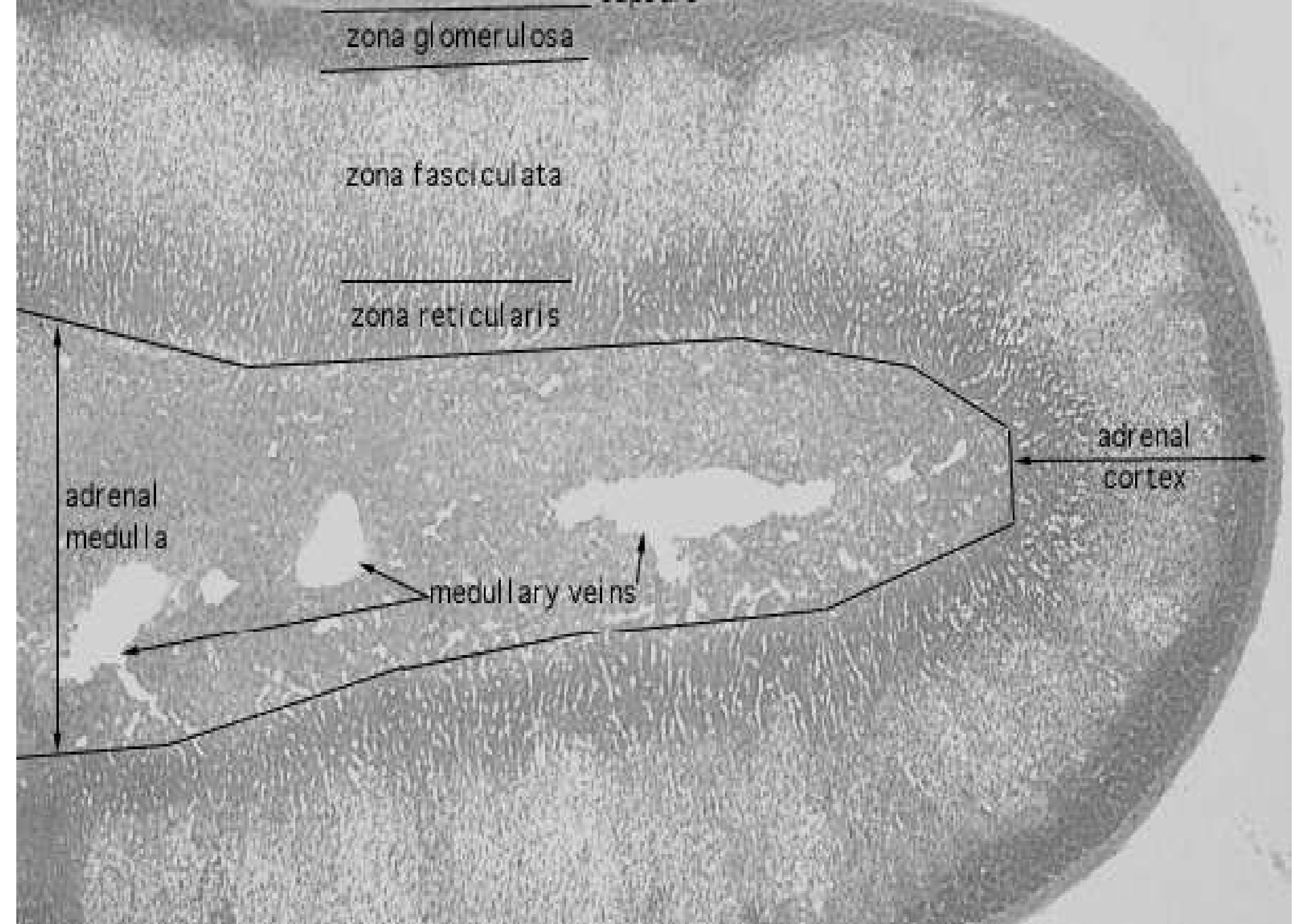

Slide 39 Adrenal gland
Zona glomerulosa
Zona fasciculata
Zona reticularis

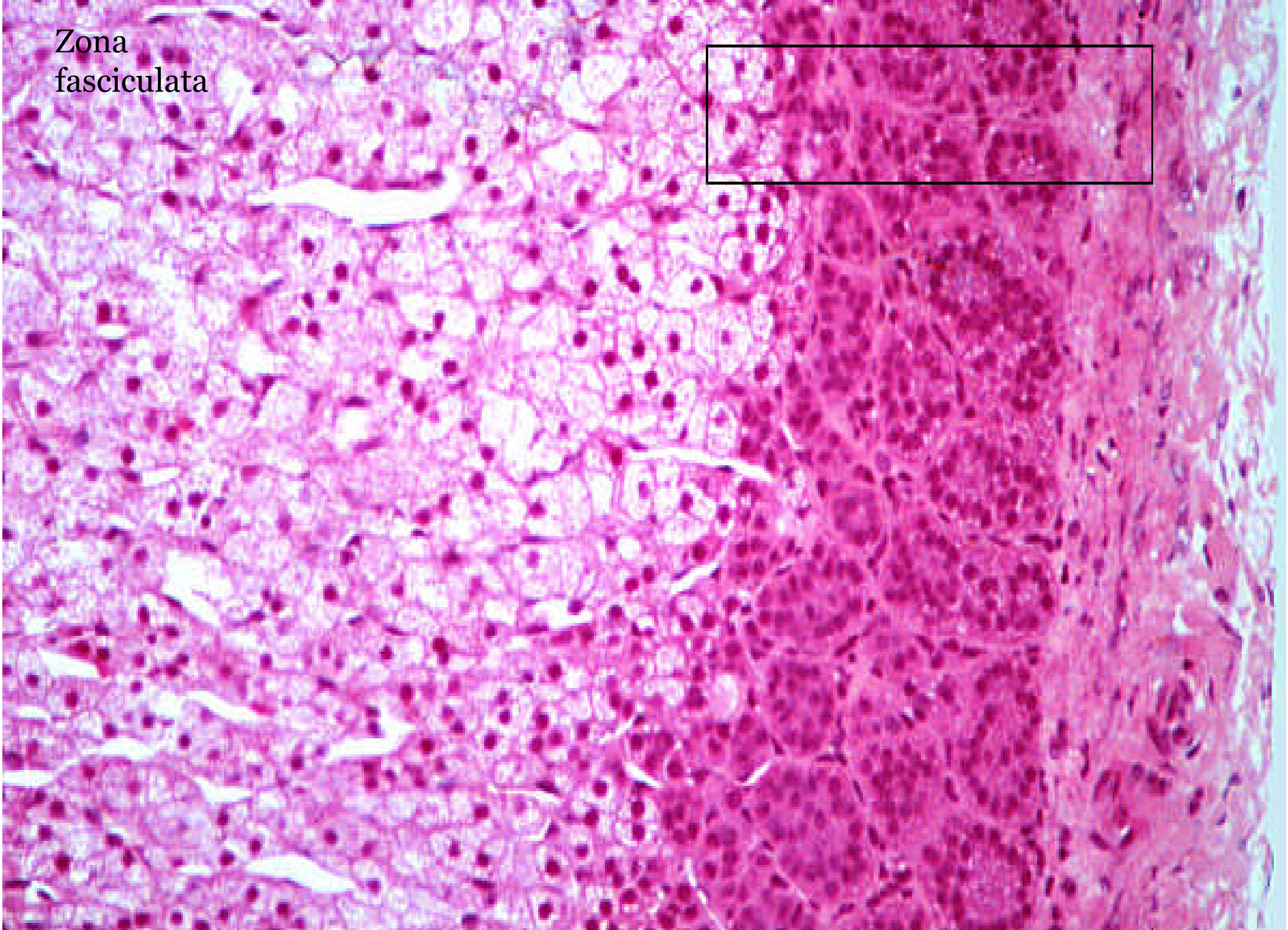

cortex
medulla
capsule

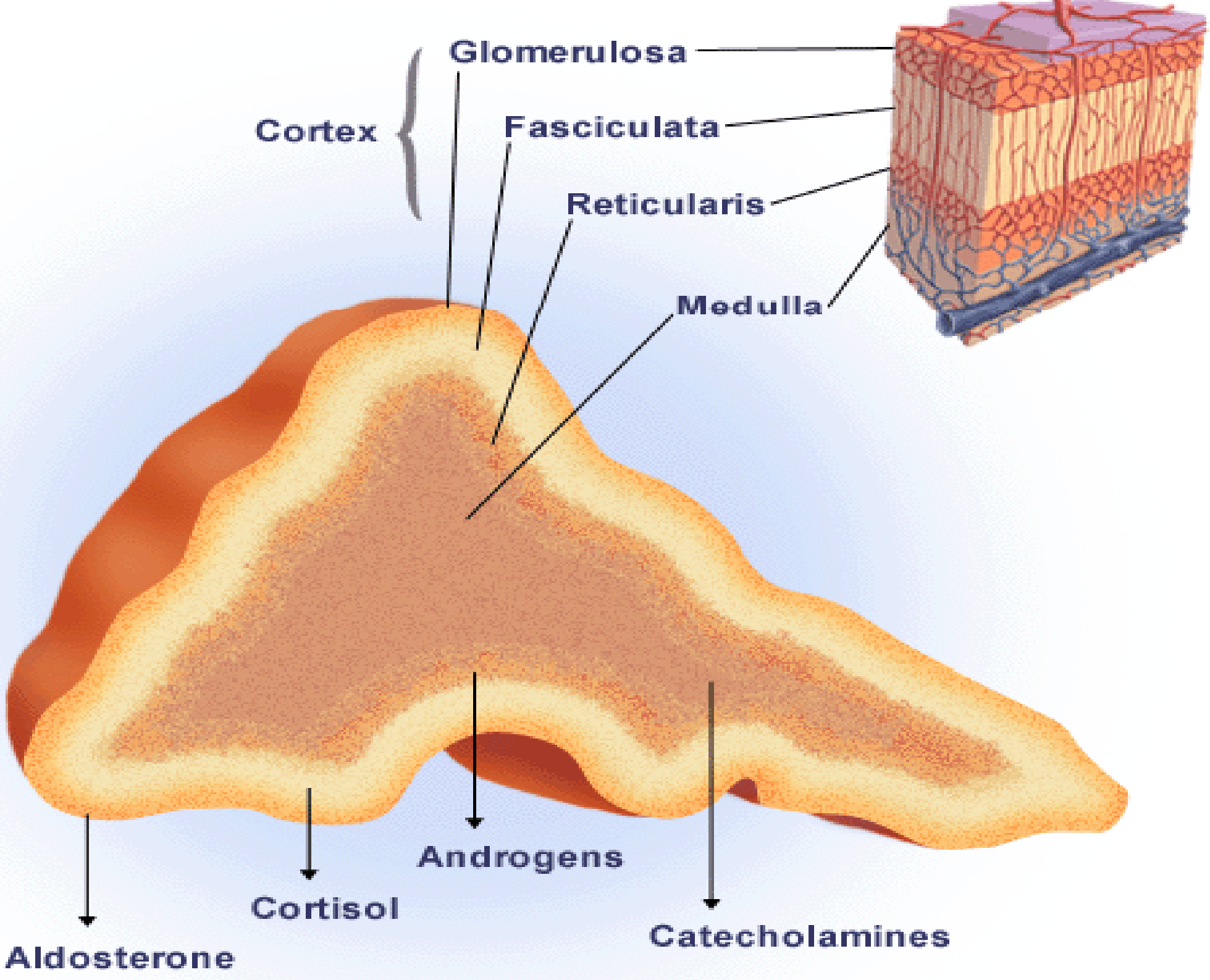

sinusoids
chromaffin cells






zona glomerulosa
zona fasciculata
zona reticularis
adrenal
medulla
adrenal
cortex
medullary veins


Zona
fasciculata


Glomerulosa
Cortex
Fasciculata
Reticularis
Medulla
Androgens
Cortisol
Aldosterone
Catecholamines

Adrenal Cortex

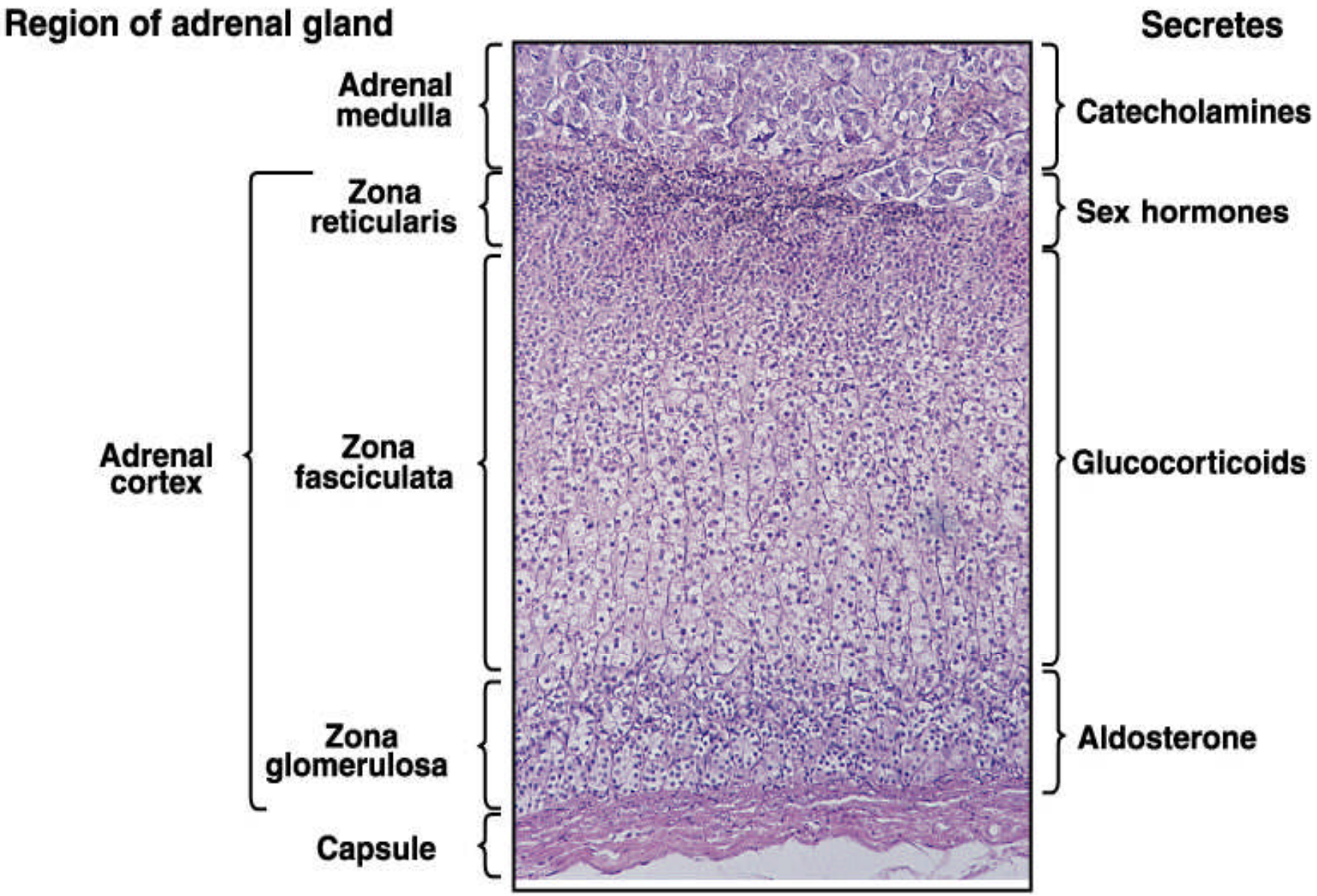
- Is divided into 3 zones in the adult gland:
  - Zona Glomerulosa,
  - Zona Fasciculata,
  - Zona Rericularis.

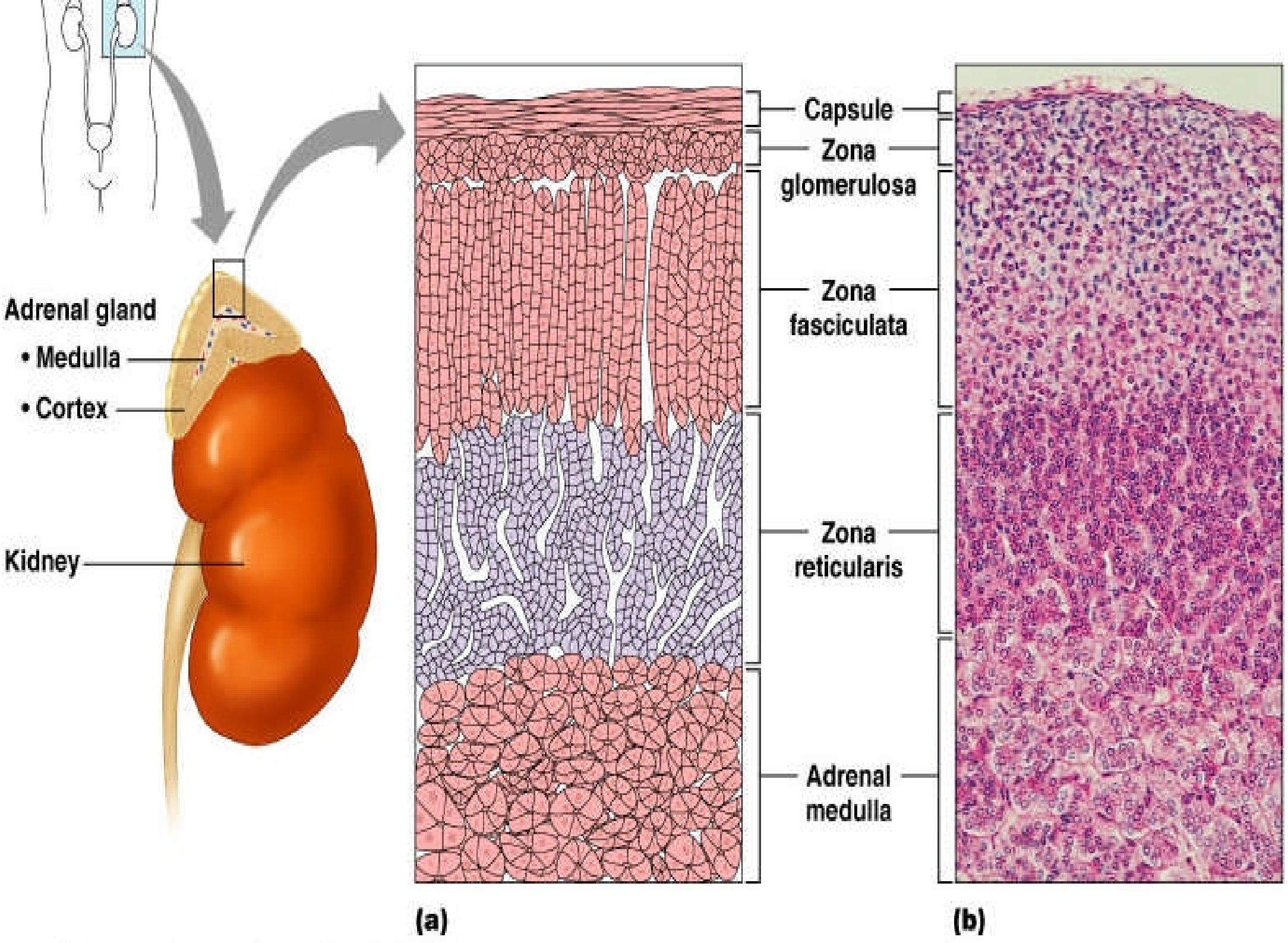
- Is divided onto 4 zones in the fetal gland.

- The three zones of the permanent cortex constitutes only 20% of the fetal gland's size.
- The remaining zone (fetal cortex) comprises up to 80% of gland's size during fetal life.

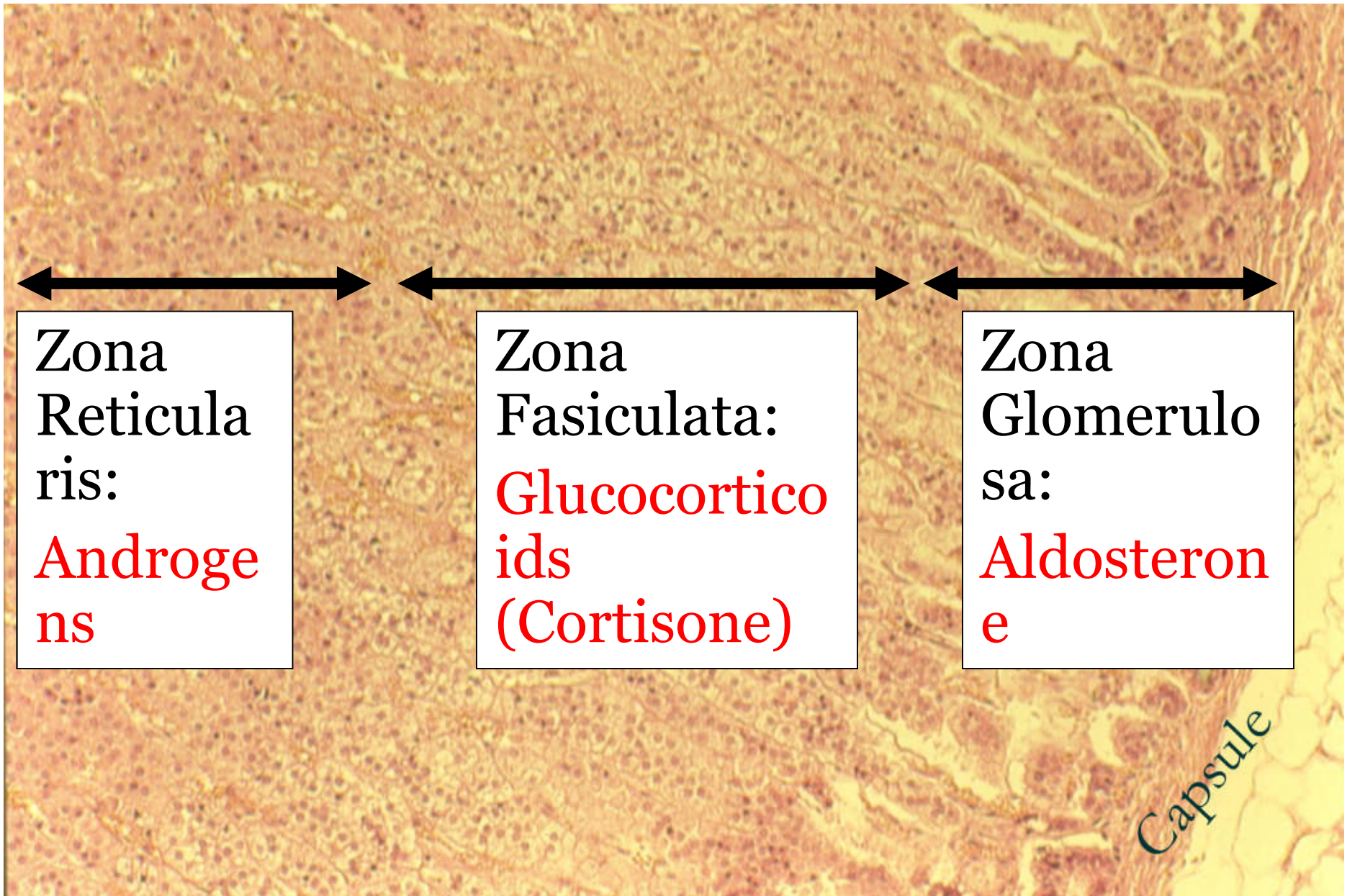
Adrenal Cortex: Steroid Hormone Production

- Aldosterone, sex hormones, cortisol
- Synthesized from cholesterol–steroid ring

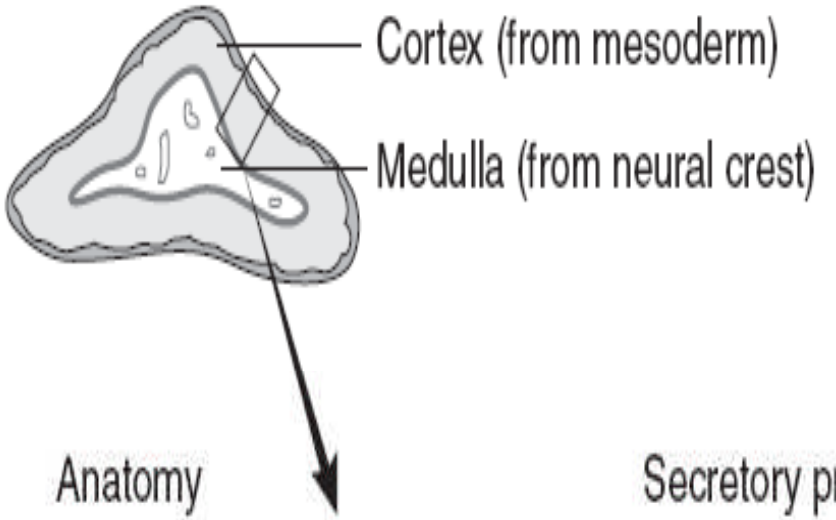

Region of adrenal gland
Secretes
Adrenal medulla
Zona reticularis
Adrenal cortex
Zona fasciculata
Zona glomerulosa
Capsule
Catecholamines
Sex hormones
Glucocorticoids
Aldosterone


Adrenal gland
• Medulla
• Cortex
Kidney
Capsule
Zona glomerulosa
Zona fasciculata
Zona reticularis
Adrenal medulla
(a)
(b)

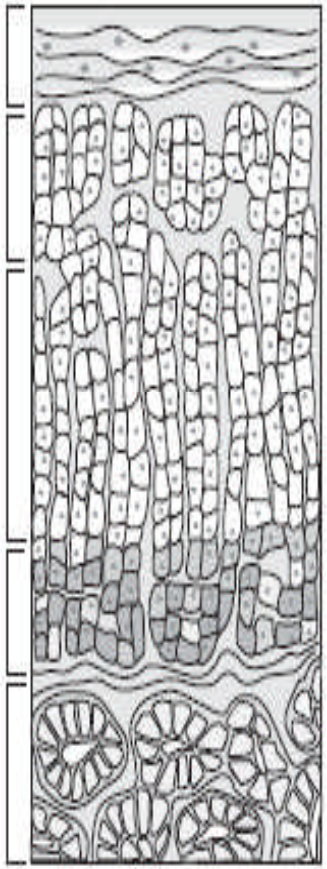
Adrenal Cortex



Adrenal cortex and medulla



Primary regulatory control	Anatomy	Secretory products
	Capsule	
Renin-angiotensin	→ Zona Glomerulosa	→ Aldosterone
ACTH, hypothalamic CRH	→ Zona Fasciculata	→ Cortisol, sex hormones
ACTH, hypothalamic CRH	→ Zona Reticularis	→ Sex hormones (e.g., androgens)
Preganglionic sympathetic fibers	→ Medulla	→ Catecholamines (epi, NE)



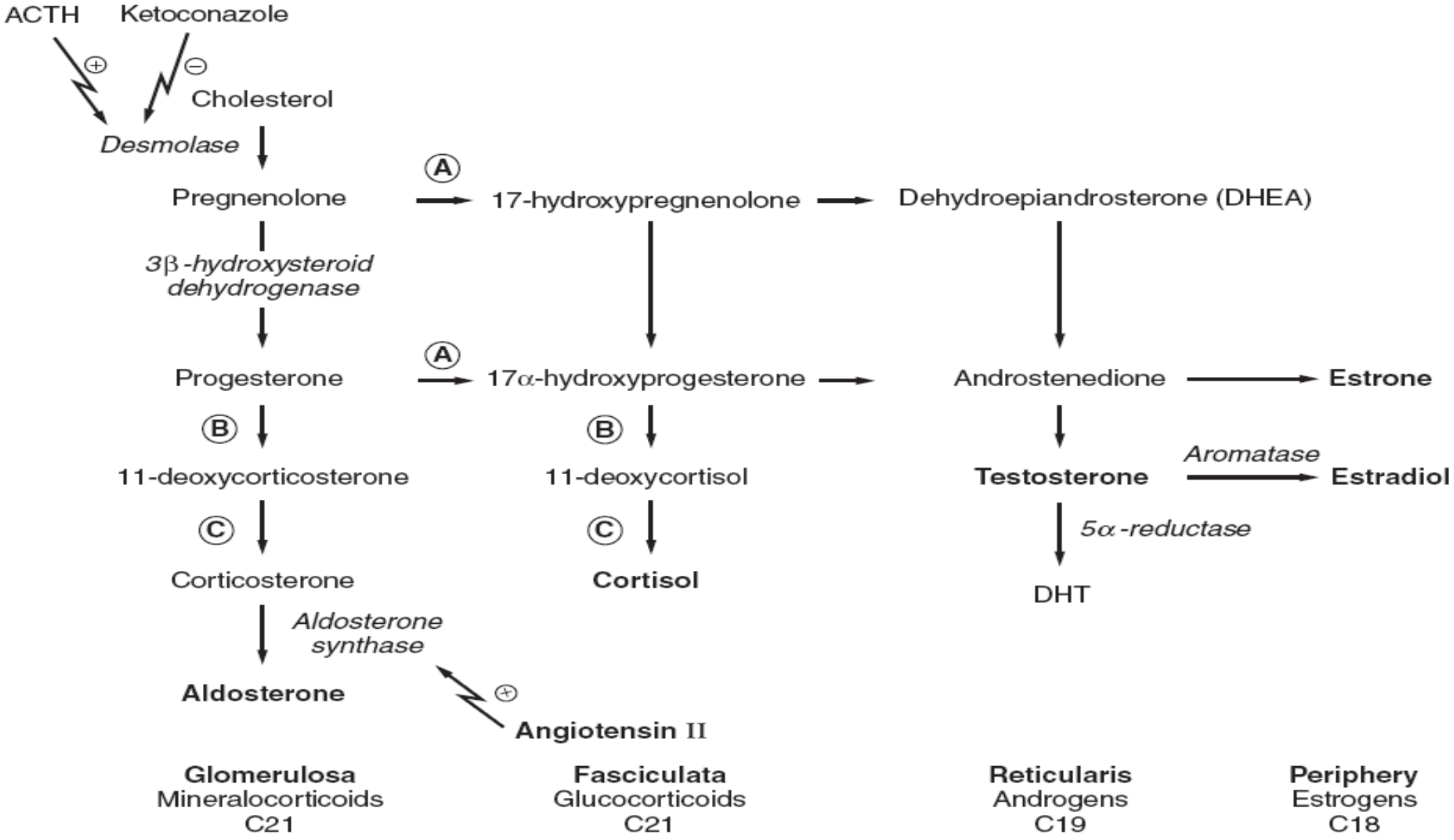
GFR corresponds with Salt (Na^+), Sugar (glucocorticoids), and Sex (androgens).

"The deeper you go, the sweeter it gets."

Pheochromocytoma—most common tumor of the adrenal medulla in adults.

Neuroblastoma—most common in children.

Pheochromocytoma causes episodic hypertension; neuroblastoma does not.



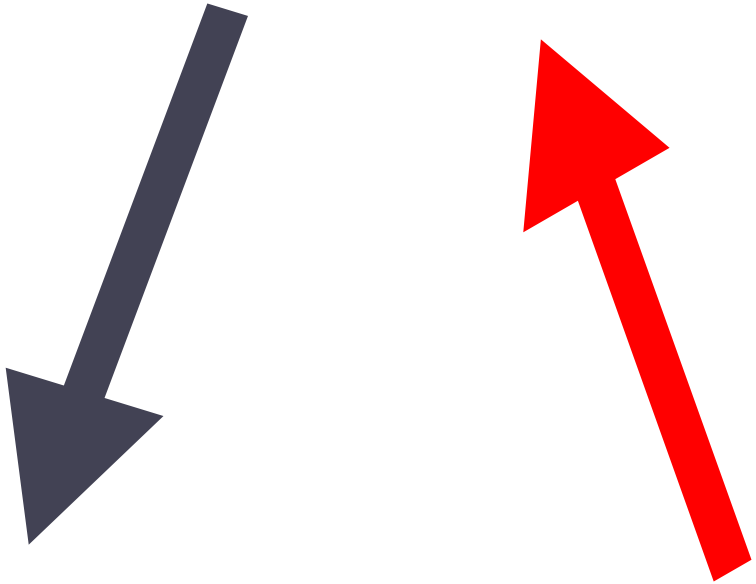
Congenital bilateral adrenal hyperplasias*

- **A = 17α-hydroxylase deficiency.** ↓ sex hormones, ↓ cortisol, ↑ mineralocorticoids. Cx = **HYPER**tension, hypokalemia; phenotypically female but no maturation.
- **B = 21α-hydroxylase deficiency.** Most common form. ↓ cortisol (increased ACTH), ↓ mineralocorticoids, ↑ sex hormones. Cx = masculinization, female pseudohermaphroditism, **HYPO**tension, hyperkalemia, ↑ plasma renin activity, and volume depletion. Salt wasting can lead to hypovolemic shock in the newborn.
- **C = 11ß-hydroxylase deficiency.** ↓ cortisol, ↓ aldosterone and corticosterone, ↑ sex hormones. Cx = masculinization, **HYPER**tension (11-deoxycorticosterone is a mineralocorticoid and is secreted in excess).

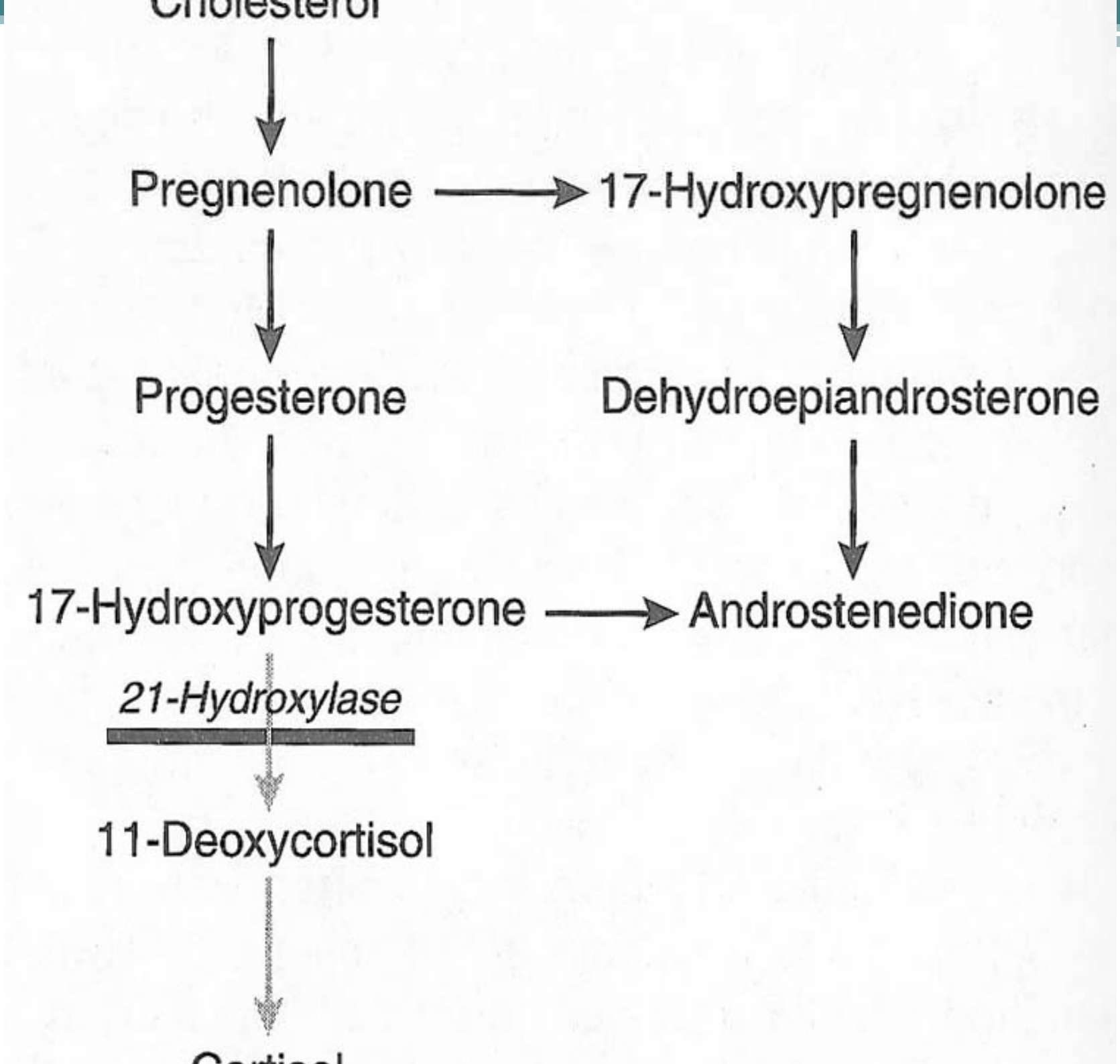
Hypothalamus:

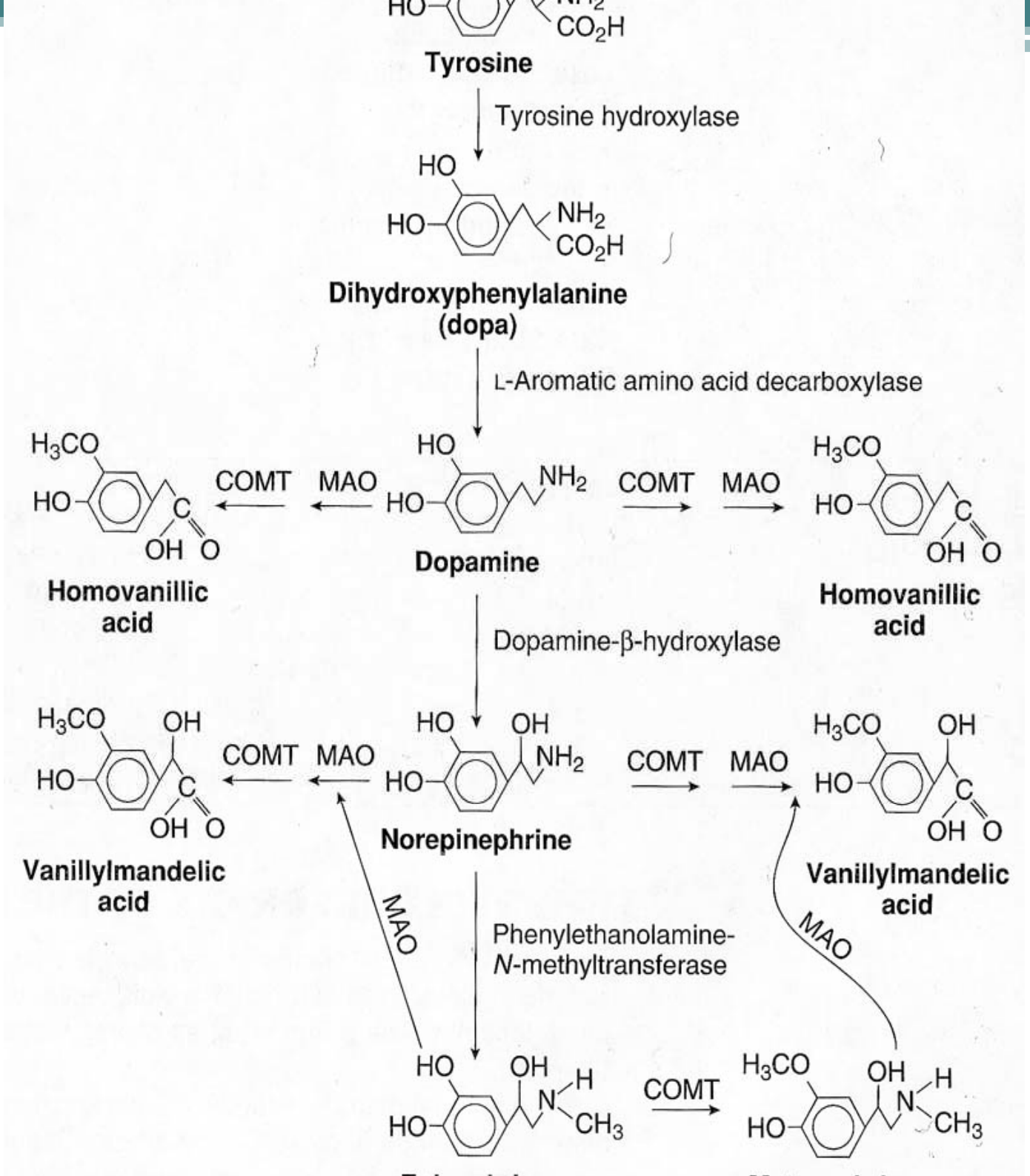
CRH

Pituitary: ACTH



Adrenal: **Cortisol**


Cholesterol
Pregnenolone
17-Hydroxypregnenolone
Progesterone
Dehydroepiandrosterone
17-Hydroxyprogesterone
Androstenedione
21-Hydroxylase
11-Deoxycortisol


Tyrosine
Tyrosine hydroxylase
Dihydroxyphenylalanine (dopa)
L-Aromatic amino acid decarboxylase
COMT
MAO
Homovanillic acid
Dopamine
Homovanillic acid
Dopamine-β-hydroxylase
Vanillylmandelic acid
Norepinephrine
Vanillylmandelic acid
Phenylethanolamine-N-methyltransferase

Adrenal Cortex: Steroid Hormone Production

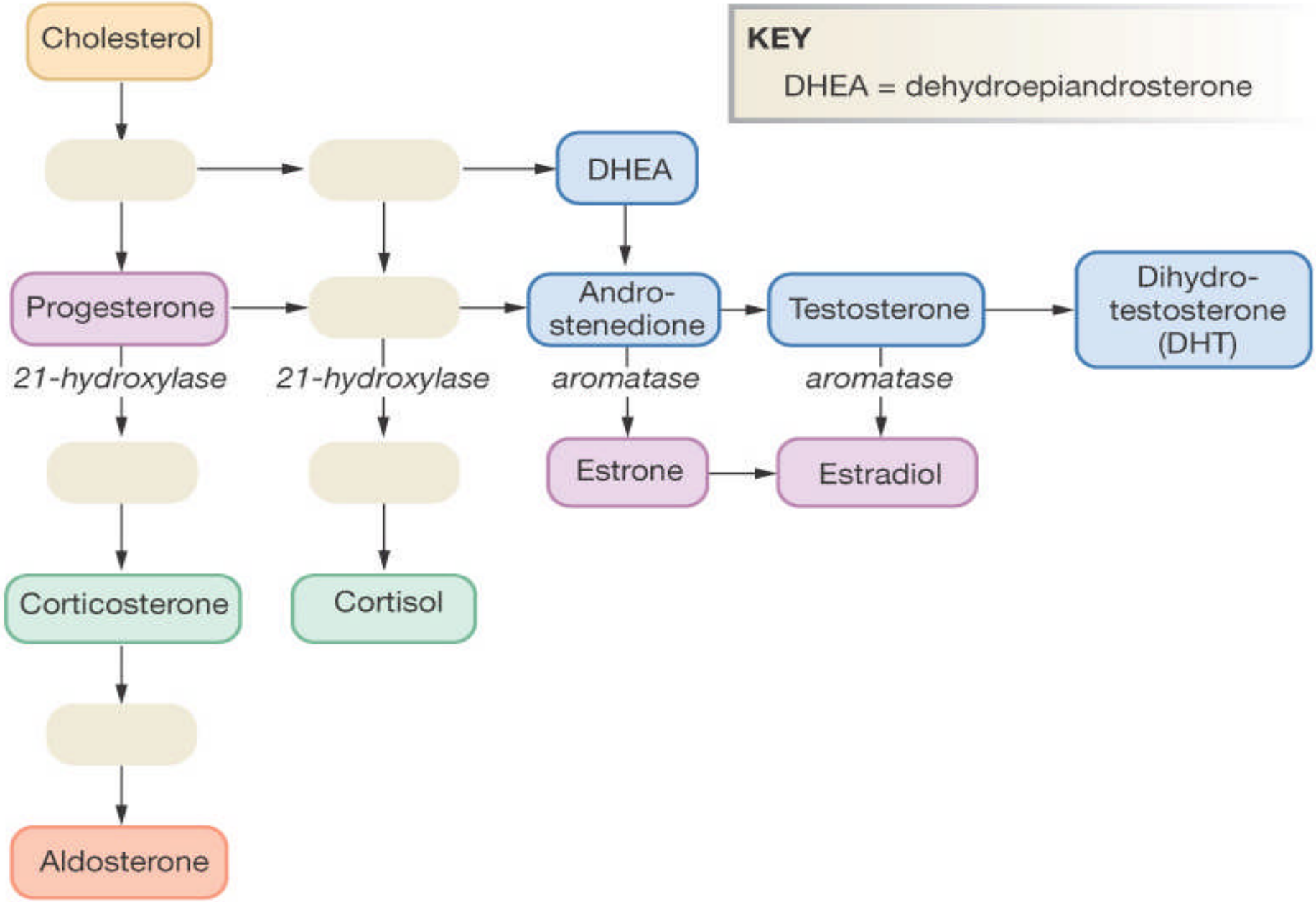
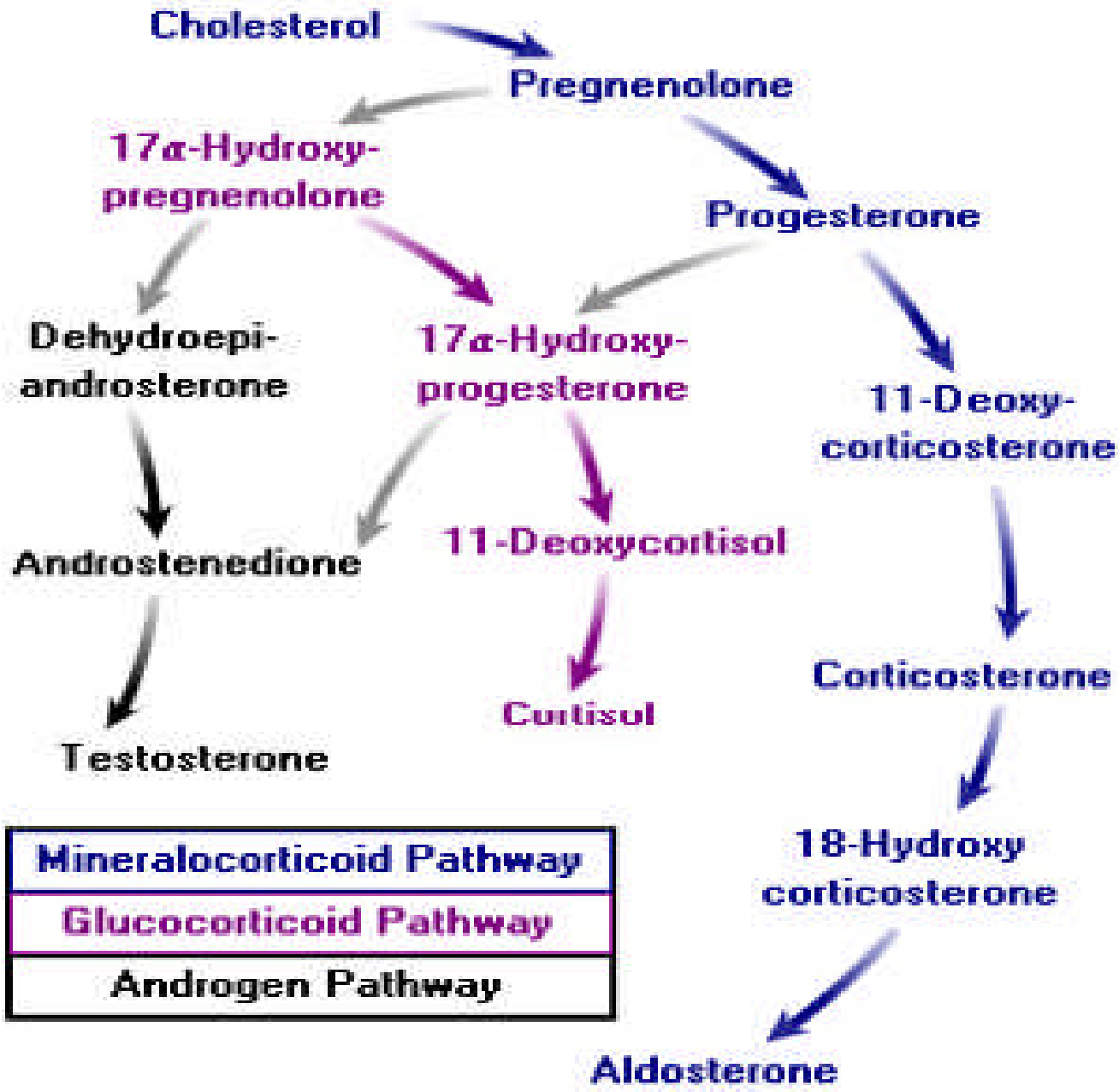


Figure 23-2: Synthesis pathways of steroid hormones

Adrenal Cortex



Adrenal Medulla

phenylethanolamine-N-methyltransferase

Norepinephrine

Epinephrine

Physiology

- Adrenal cortex produces

  -Glucocorticoids (Zona Fasciculata)

  -Mineralocorticoids (Zona Glomerulosa)

  -Adrenal androgens (Zona Reticularis)

Physiology

- Adrenal medulla produces
  -Epinephrine (adrenaline)
  -Norepinehrine (noradrenaline)

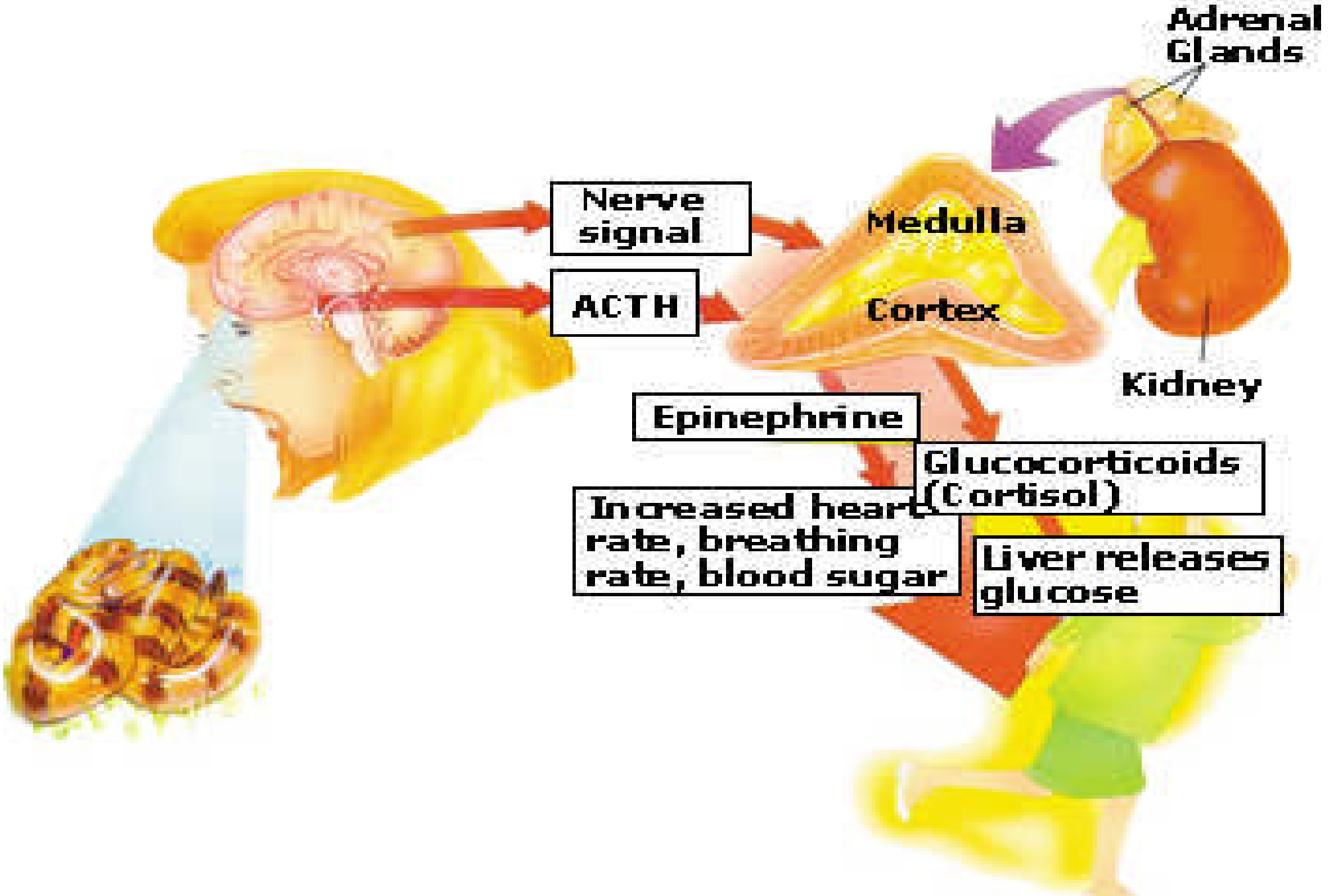
- Help inc in cardiac output, vascular resistance and mediate stress response

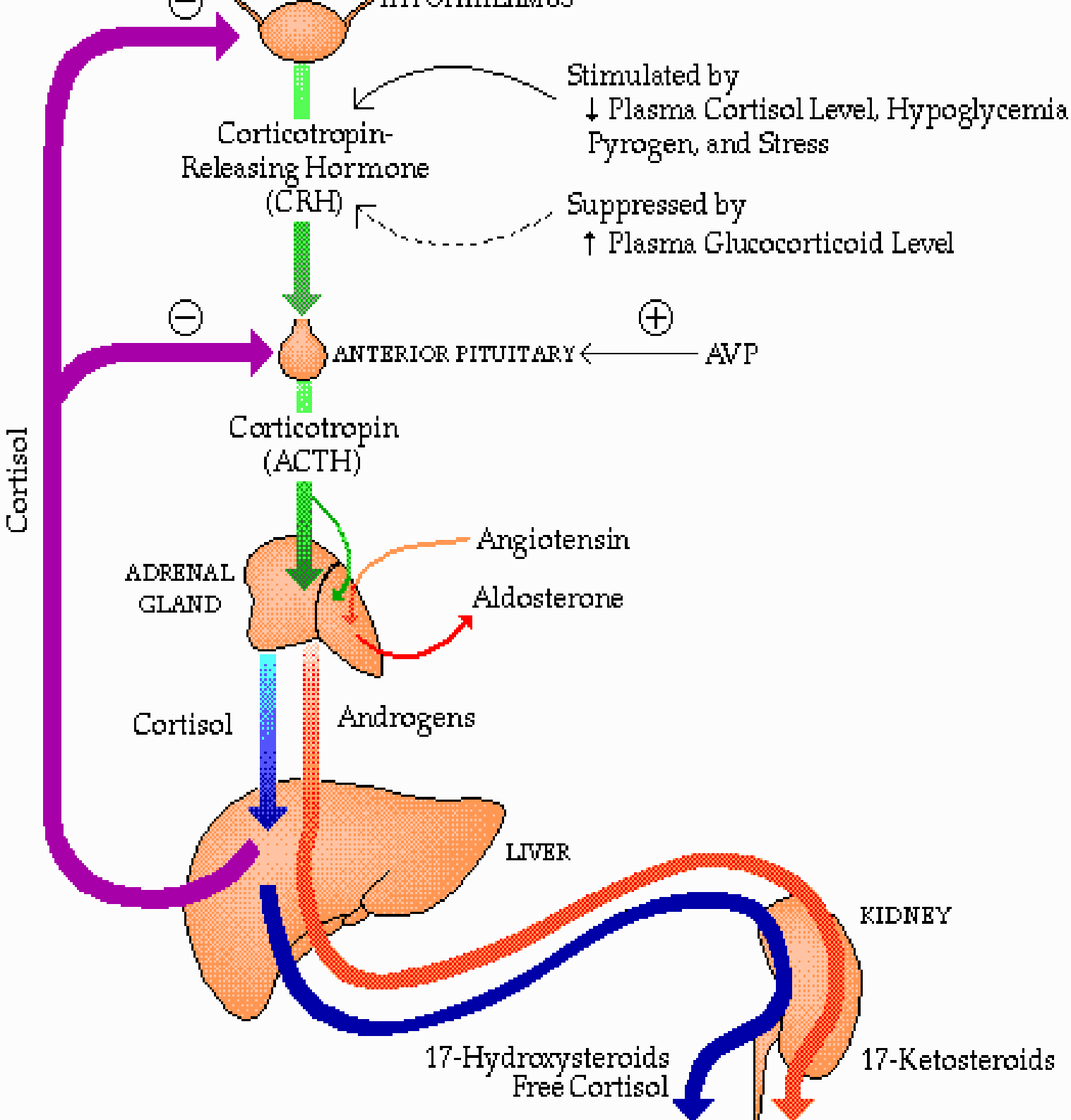
- All are absolutely required for life

Functions

- Aldosterone helps in Na reabsorption & potassium excretion & preventing dehydration
- Cortisol stimulate protein breakdown, inhibition of tissue response in injury & antagonism to action of insulin
- Androgens helps in early development of male sex organ in childhood

Functions


Adrenal Glands
Nerve signal
ACTH
Medulla
Cortex
Kidney
Epinephrine
Glucocorticoids (Cortisol)
Increased heart rate, breathing rate, blood sugar
Liver releases glucose


Stimulated by
↓ Plasma Cortisol Level, Hypoglycemia
Pyrogen, and Stress
Corticotropin-
Releasing Hormone
(CRH)
Suppressed by
↑ Plasma Glucocorticoid Level
ANTERIOR PITUITARY
AVP
Corticotropin
(ACTH)
Cortisol
ADRENAL
GLAND
Angiotensin
Aldosterone
Cortisol
Androgens
LIVER
KIDNEY
17-Hydroxysteroids
Free Cortisol
17-Ketosteroids

Cortisol Effects: Body Responses to Stress

- Permissive effect on glucagon
- Memory, learning & mood
- Gluconeogenesis
- Skeletal muscle breakdown
- Lipolysis, calcium balance
- Immune depression
- Circadian rhythms

Cortisol Effects: Body Responses to Stress

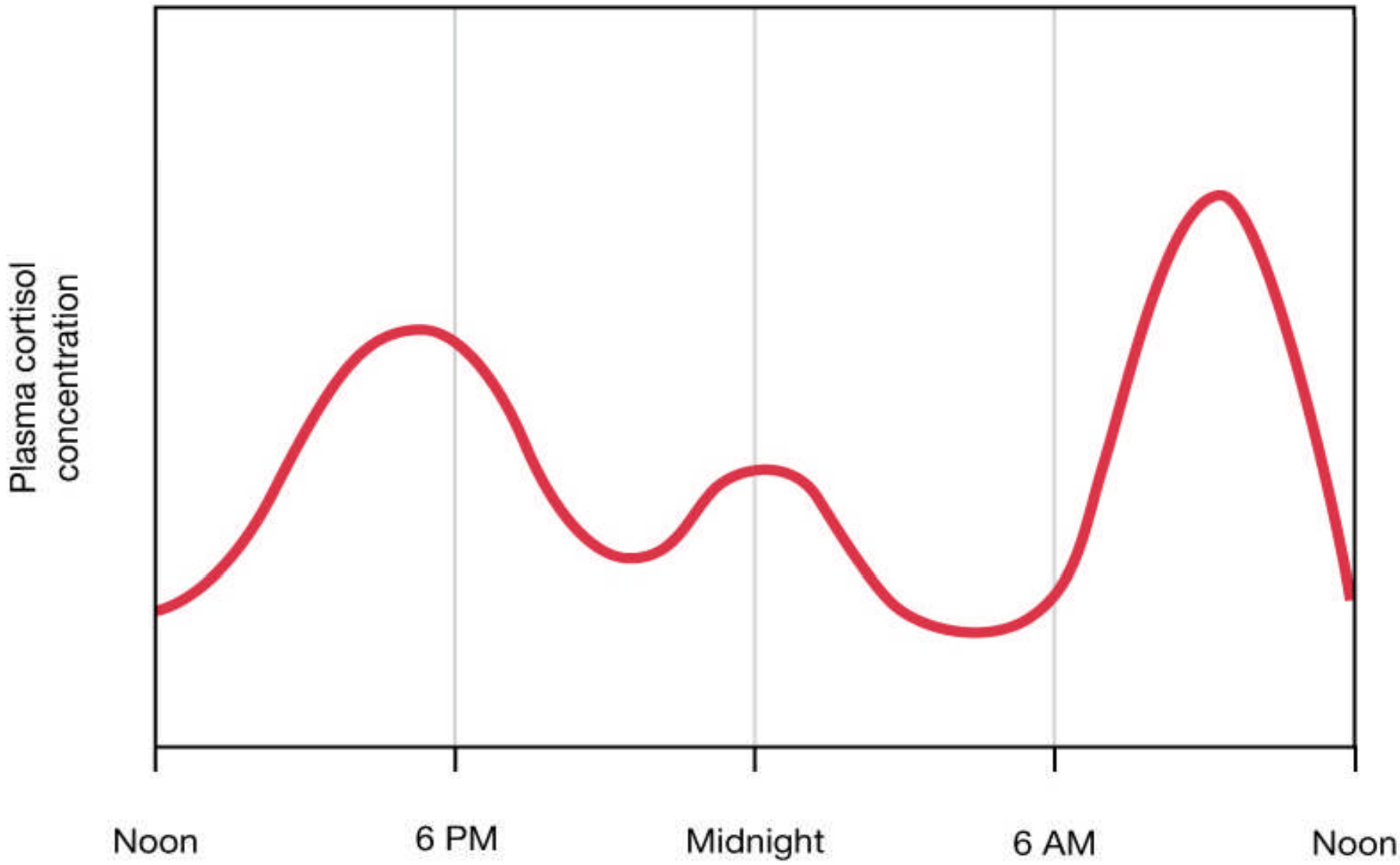
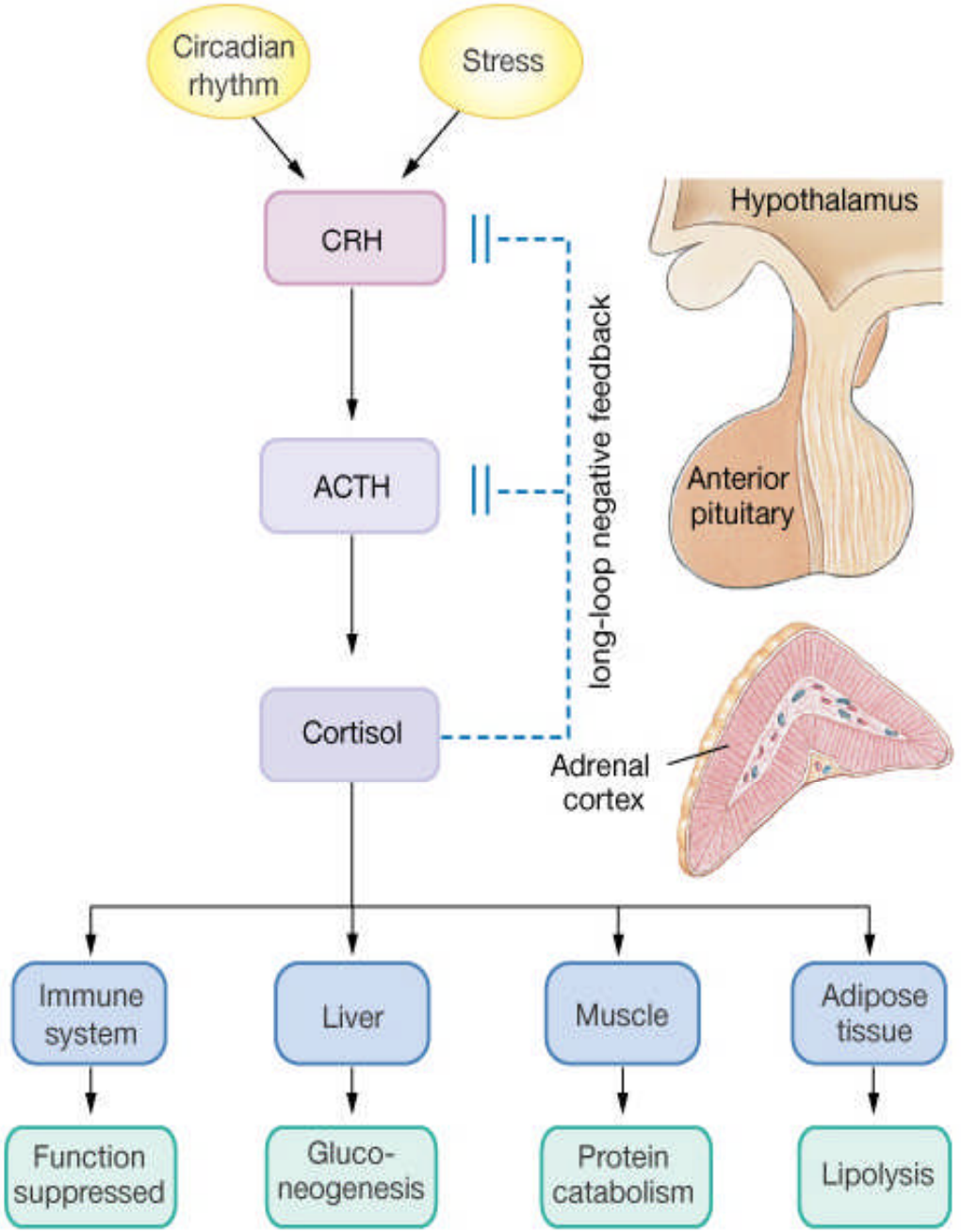


Figure 23-4: Circadian rhythm of cortisol secretion

Control of Cortisol Secretion: Feedback Loops

- External stimuli
- Hypothalamic
- Anterior Pituitary
- Adrenal cortex
- Tissues



Cortisol: Role in Diseases and Medication

- Use as immunosuppressant
  - Hyperimmune reactions (bee stings)
  - Serious side effects
- Hypercortisolism (Cushing's syndrome)
  - Tumors (pituitary or adrenal)
  - Iatrogenic (physician caused)
- Hypocortisolism (Addison's disease)

Aldosterone

- **Exclusively synthesized in Z. Glomerulosa**
- **Essential for life.**
- **Promotes sodium retention and Potassium elimination by the kidney.**
- **Expands ECF volume**

Aldosterone

acts mainly on the distal tubules and collecting ducts of the nephron, the functioning unit of the kidney,

cause the:

- **conservation of sodium,**
- **secretion of potassium,**
- **increased water retention,**
- **increased blood pressure.**

- **The overall effect of aldosterone is to**
  - **increase reabsorption of ions and water in the kidney –**
  - **increasing blood volume and, therefore, increasing blood pressure**

Aldosterone

Its activity is

•reduced in Addison's disease
•increased in Conn's syndrome.

Stimulation

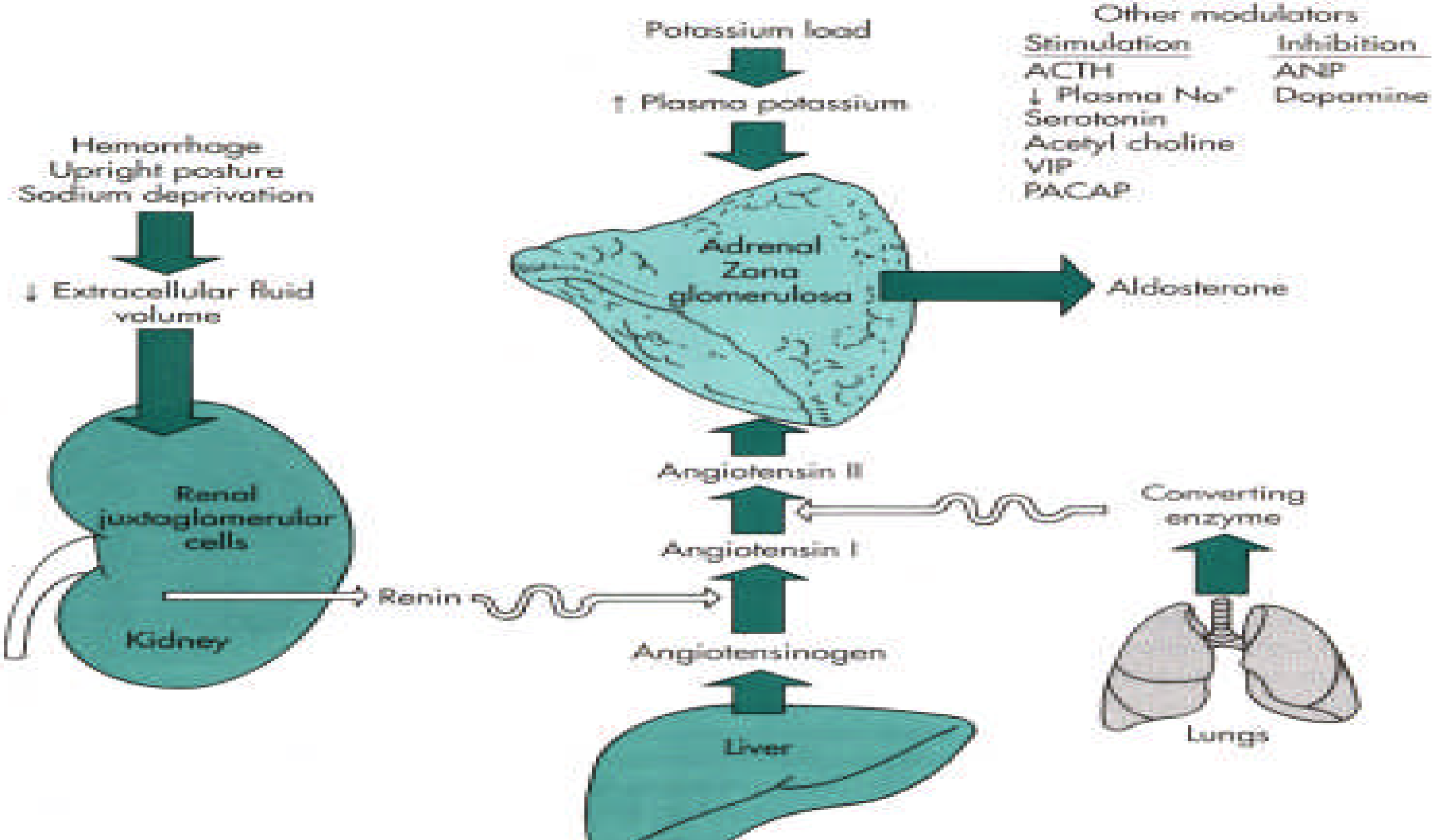
•increase in the plasma concentration of Angiotensin III, a metabolite of Angiotensin II increase in plasma angiotensin II,
•ACTH, or potassium levels, which are present in proportion to plasma sodium deficiencies. (The increased potassium level works to regulate aldosterone synthesis by depolarizing the cells in the zona glomerulosa, which opens the voltage-dependent calcium channels.)
•Potassium levels are the most sensitive stimulator of aldosterone.
plasma acidosis

•the stretch receptors located in the atria of the heart.

If decreased blood pressure is detected, the adrenal gland is stimulated by these stretch receptors to release aldosterone, which increases sodium reabsorption from the urine, sweat, and the gut.

The secretion of aldosterone has a diurnal rhythm

Regulation of Aldosterone Secretion



Aldosterone: Role in diseases

- Complete failure to secrete aldosterone leads to death (dehydration, low blood volume).

- Hyperalsdosterone states: Contribute to hypertension associated with increased blood volume.

Adrenal Medulla: A Modified Sympathetic Ganglion

- Sympathetic stimulation
  - Catecholamine release to blood
    - Epinephrine
    - Norepinephrine
  - Travel to:
    - Multiple targets
    - Distant targets

Adrenal Medulla: A Modified Sympathetic Ganglion

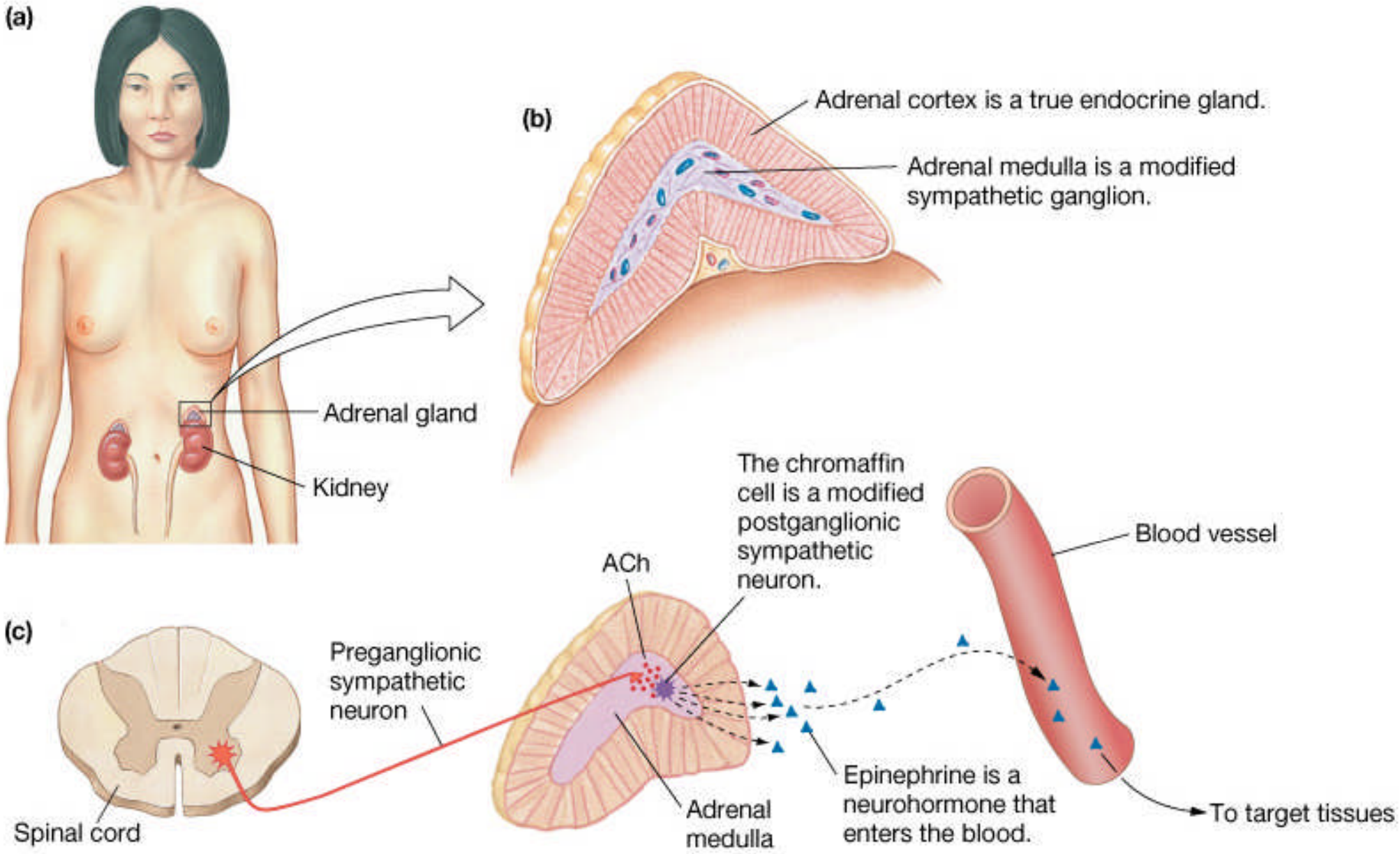


Figure 11-10: The adrenal medulla

Release and Recycling

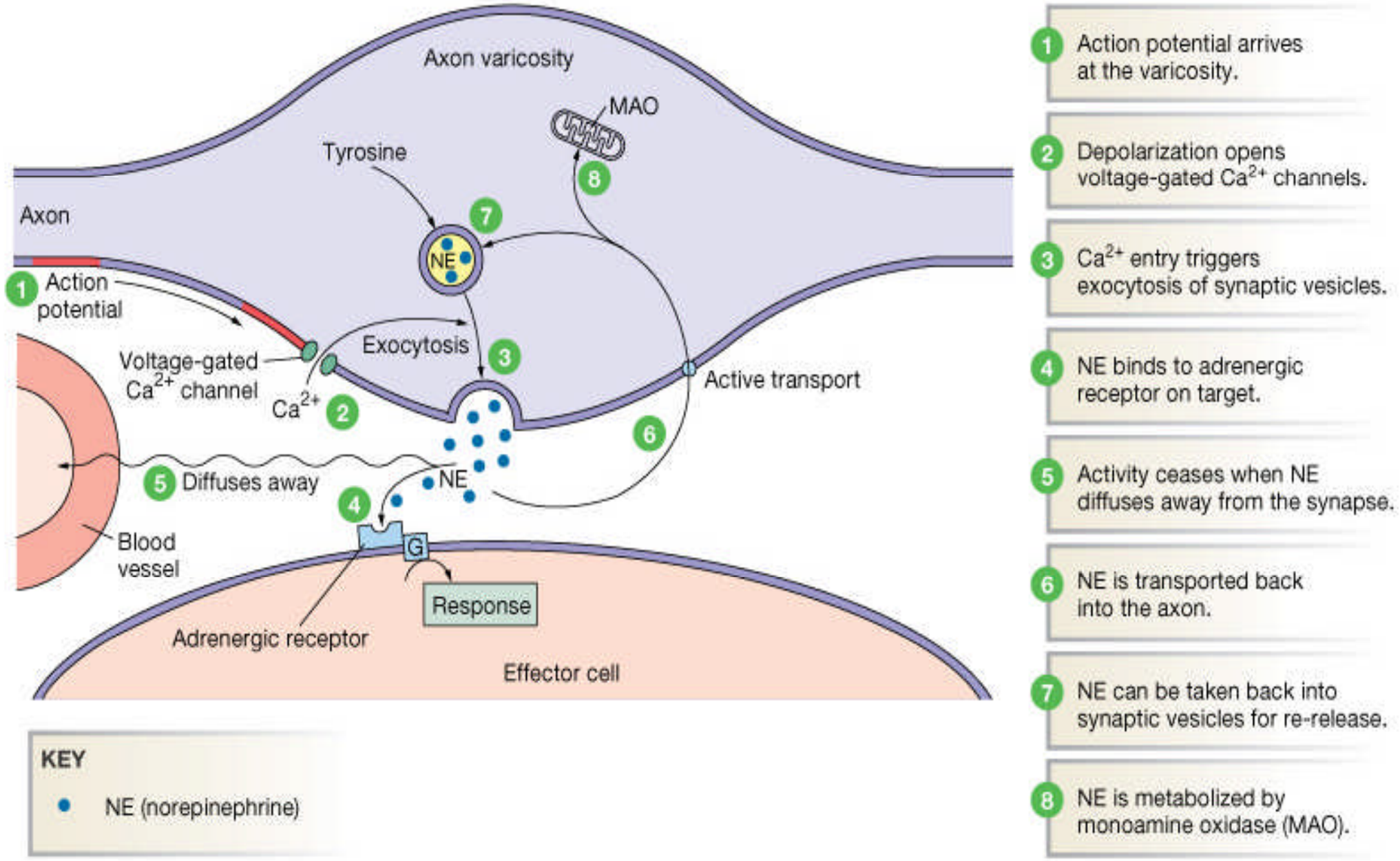


Figure 11-9: Norepinephrine release at a varicosity of a sympathetic neuron

Review of Efferent Pathways: Motor & Autonomic

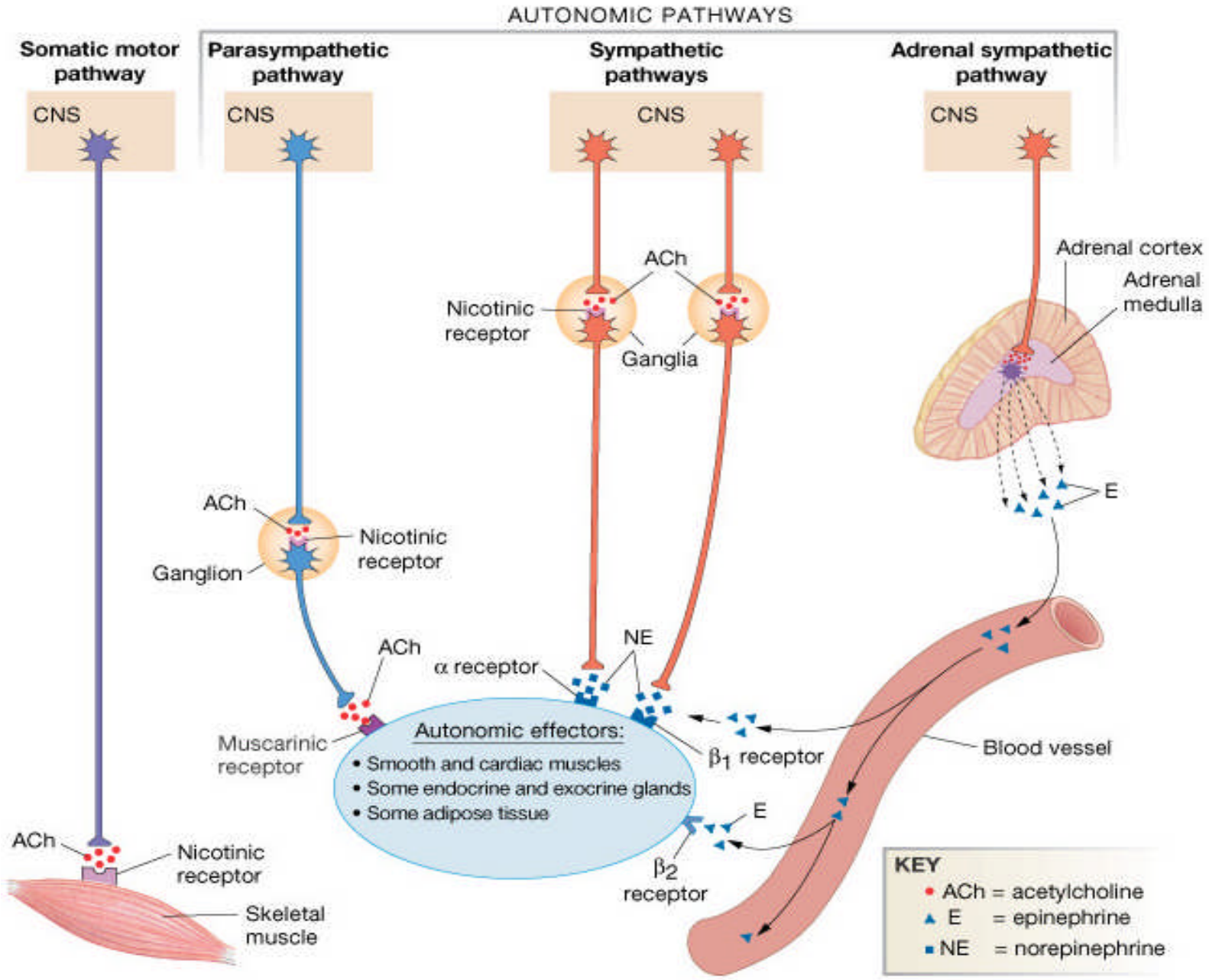
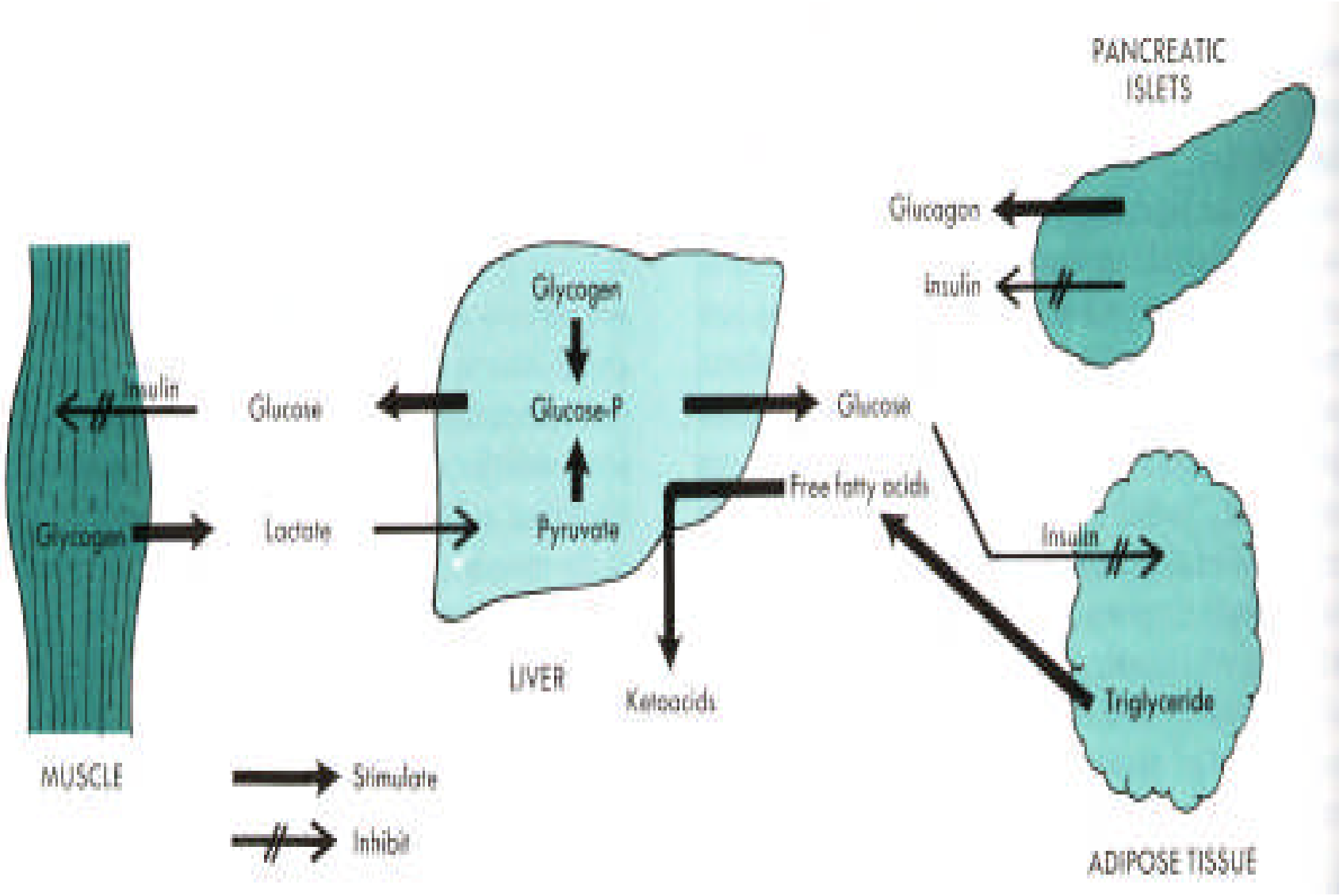


Figure 11-11: Summary of efferent pathways.

Catechalomines: Activity

- Stimulates the “fight or fight” reaction
- Increased plasma glucose levels
- Increased cardiovascular function
- Increased metabolic function
- Decreased gastrointestinal and genitourinary function

Activity of Epinephrine



Aldosterone

MOA: transcription of enzymes and proteins

Major actions: ⇧Na reabsorption in distal tubule

Extrarenal effects: Na reabsorption in saliva, sweat, stool

Hypersecretion of Aldosterone

1º aldosteronism – Conn's syndrome

2º aldosteronism – liver/kidney disease

SXS: hypertension

hypokalemia

metabolic alkalosis

Primary Hyperaldosteronism

↑Aldosterone ➔ ↑ Na retention ➔ [↑ ECF volume + ↑ Renal perfusion pressure] ➔
↓Renin

Secondary Hyperaldosteronism

retention ↓Renal perfusion ➔ ↑ Renin ➔ ↑ Aldosterone ➔ [↑ Na ➔ ↑ ECF]
+ pressure
volume

Hyposecretion of Aldosterone

1° hyposecretion – Addisons' dse

2° hyposecretion – kidney damage

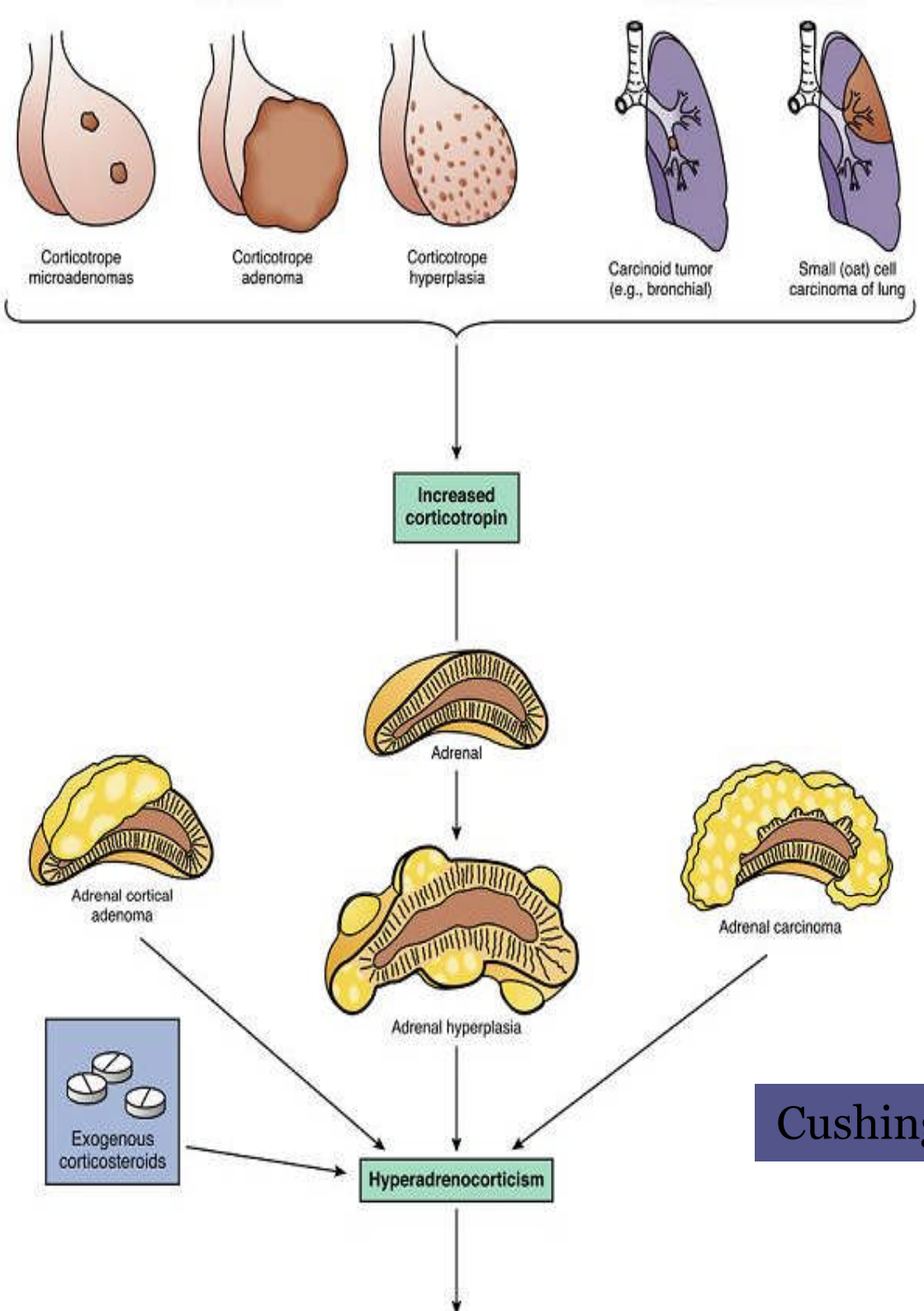
SXS: hypovolemia

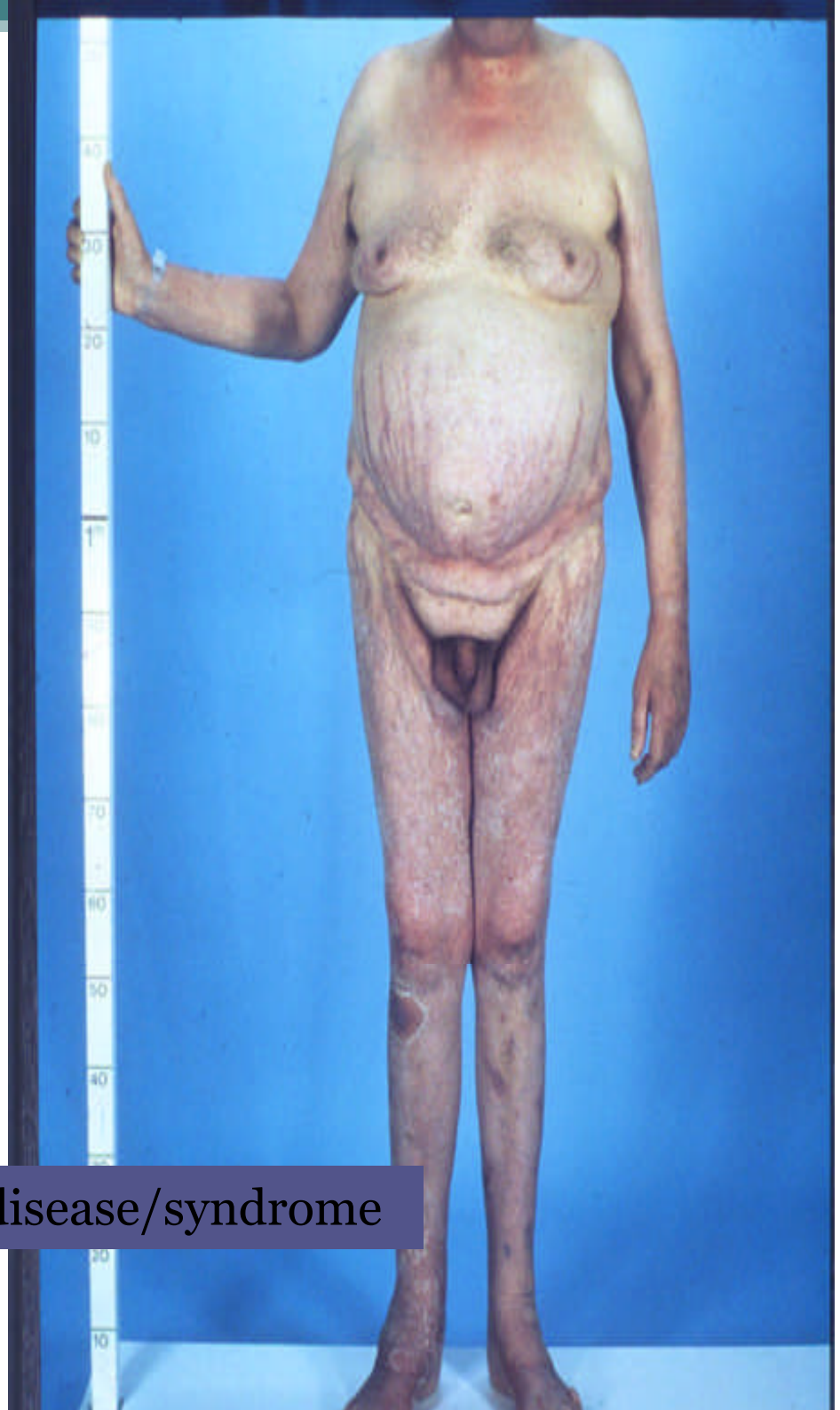
hyponatremia

hyperkalemia

Pathology

- pheochromocytoma
  - adrenal medulla tumor
  - increase BP due to release of catacholamines
- Addison's disease - decrease cortisol
  - hyponatremia, dehydration
  - hyperkalemia
- Cushing's disease - increase cortisol
  - moon face, hirsutism

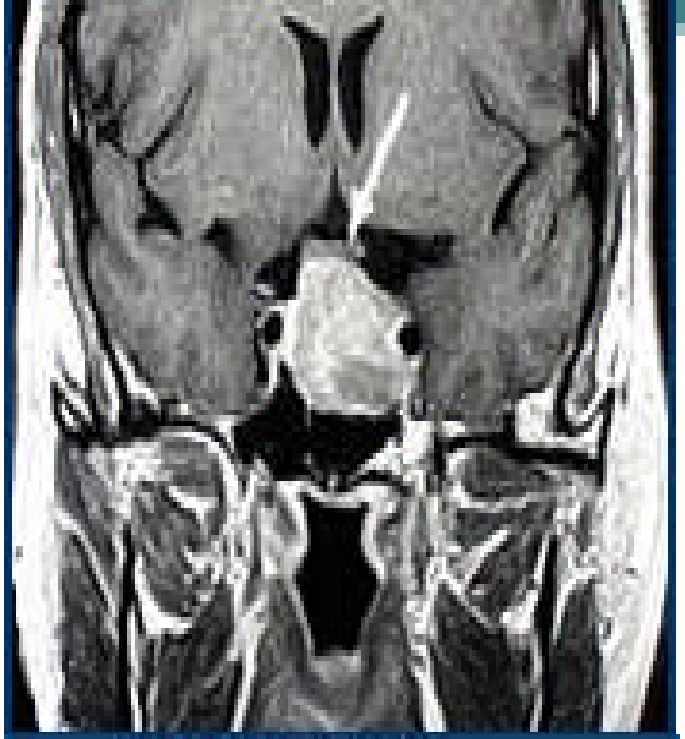


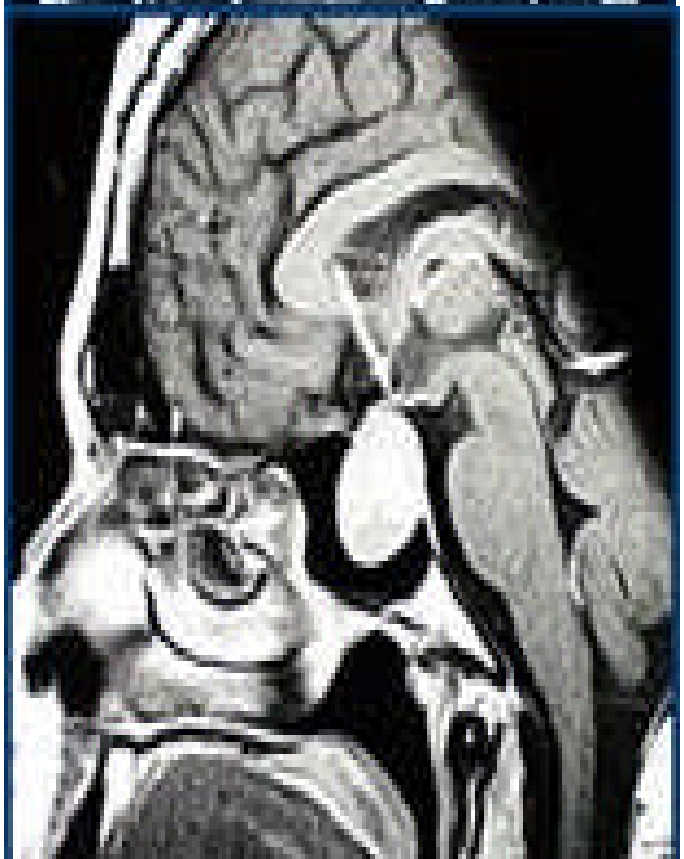


Cushing's disease/syndrome

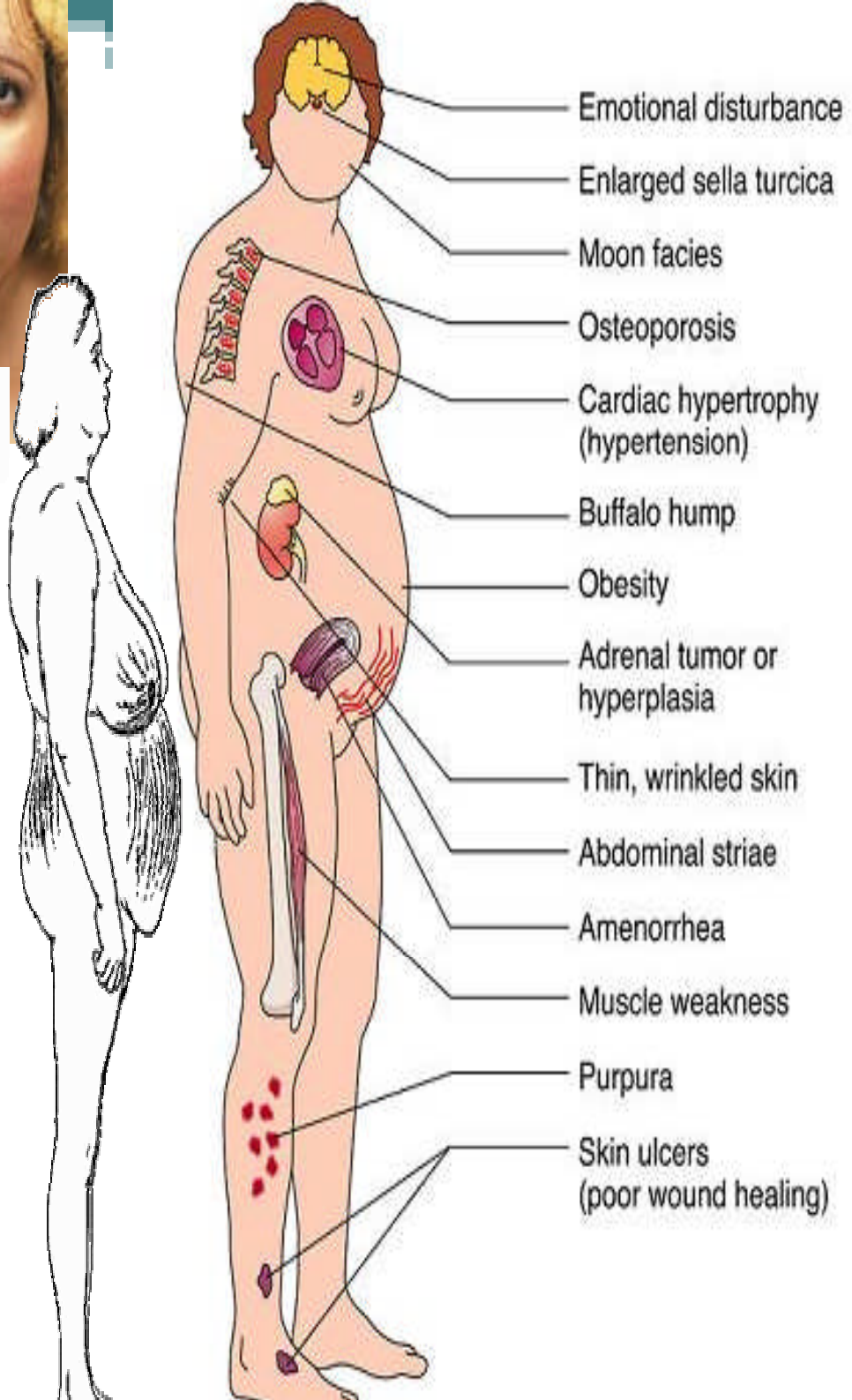
Clinical Features:

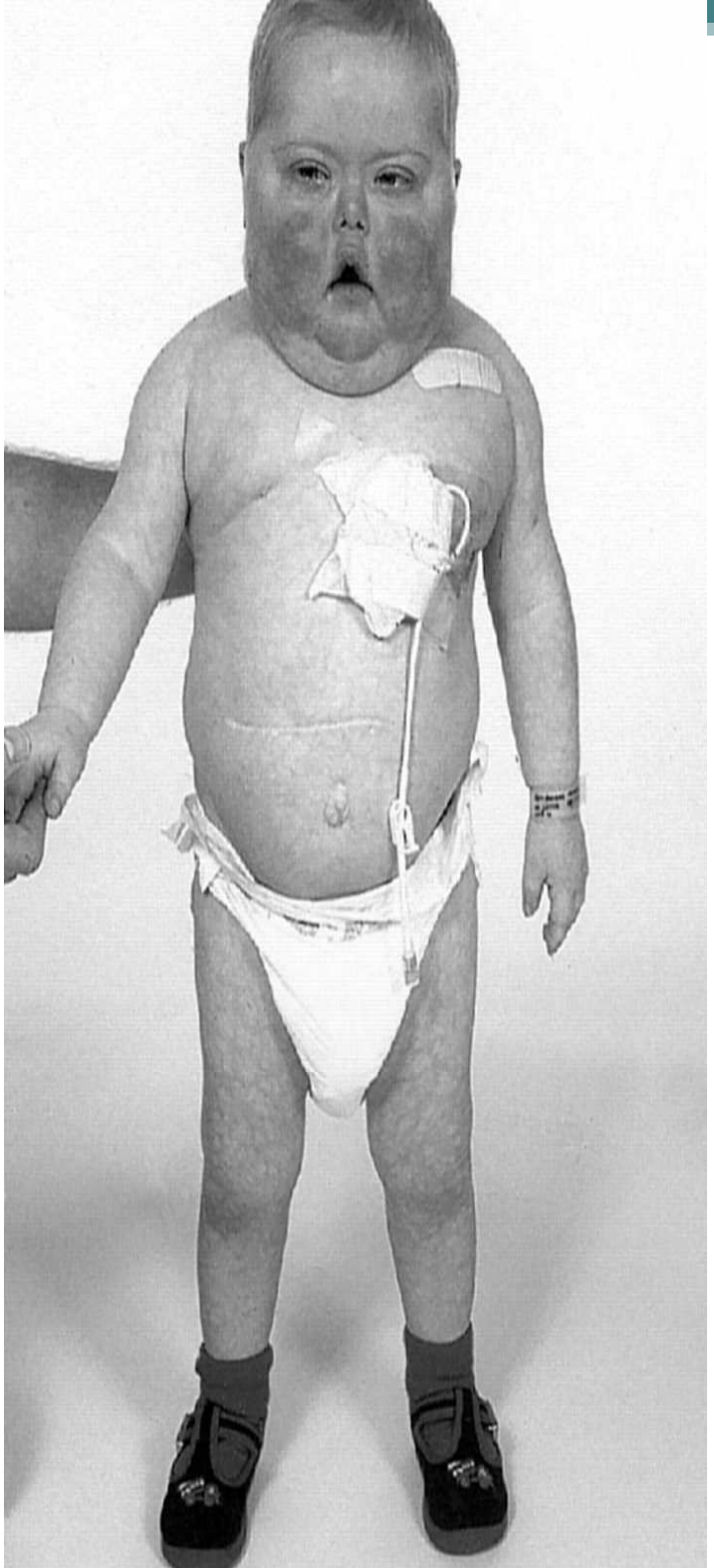
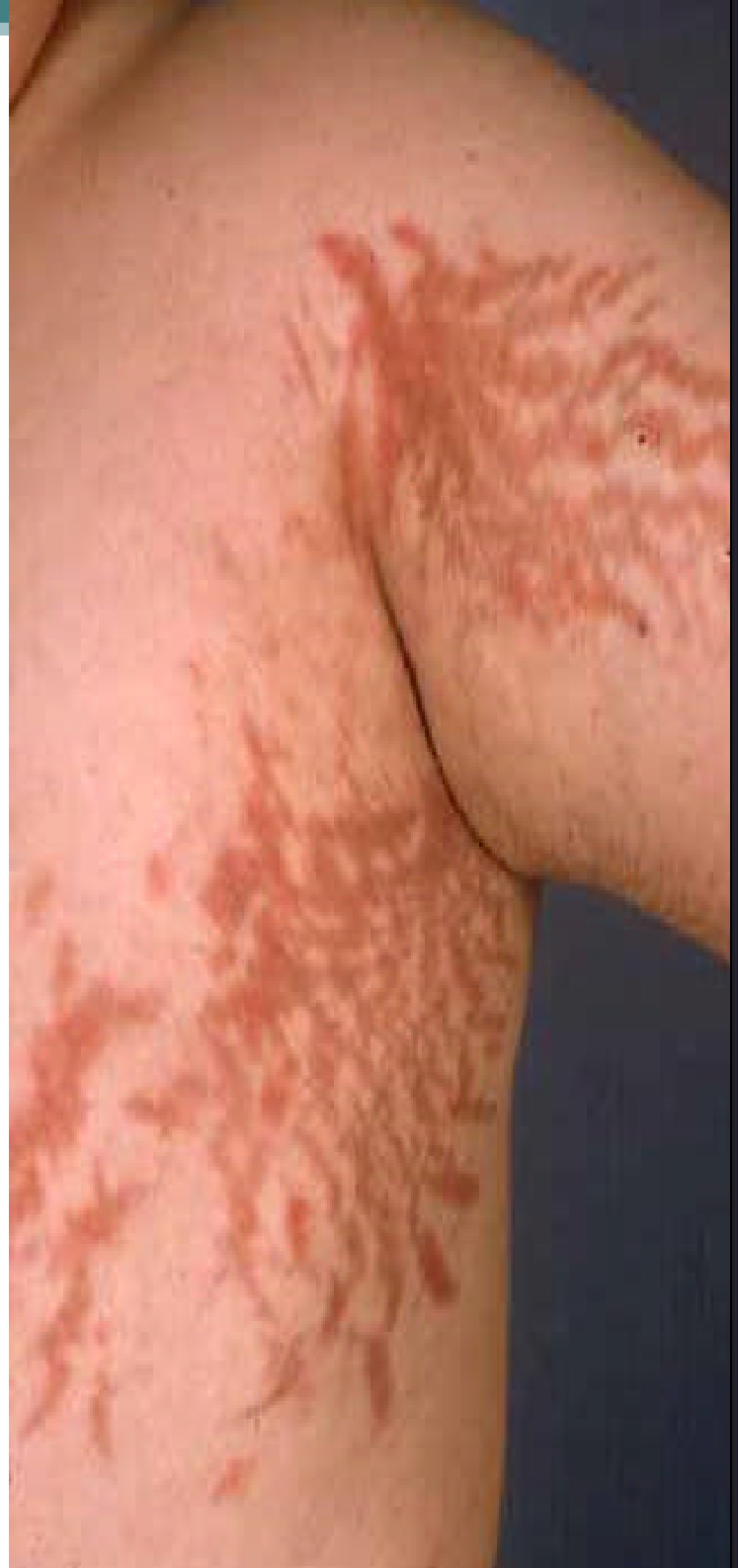
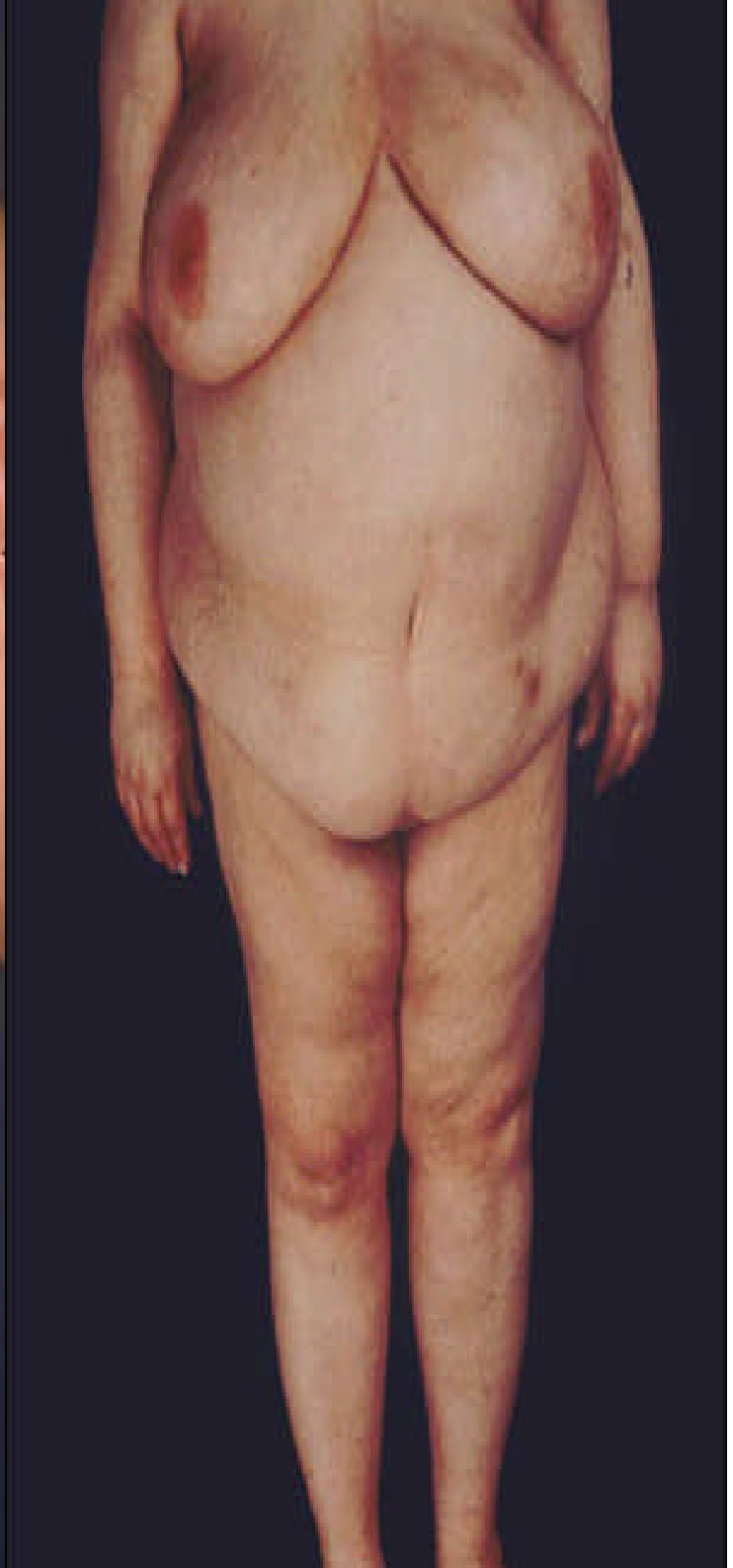
METABOLIC EFFECT	SYMPTOM	SIGN
Carbohydrate metabolism: •increased glycogenesis •increased glucogenesis	•polydypsia •polyuria	Diabetes Mellitus: •impaired glucose use •hyperglycaemia •insulin resistance
Increased protein catabolism	•muscle weakness •easily bruised thin skin* •growth retardation	•thin osteoporotic bone •pathological fractures* •poor wound healing •abdominal striae* •proximal muscle wasting and myopathy*
Increase and redistribution of body fat	•central obesity	•moon face •'buffalo hump' •*"lemon-on-sticks " appearance*
Reduced inflammatory response		•susceptibility to infection
Increased stomach acid production		•predisposition to gastric ulcer
Mineralcorticoid effects •sodium retention •redistribution of fluids		•hypertension* •oedema
Mood	•depression •psychosis	
Sex hormones	•acne •hirtuism •amenorrhoea/oligomenorrhoea	

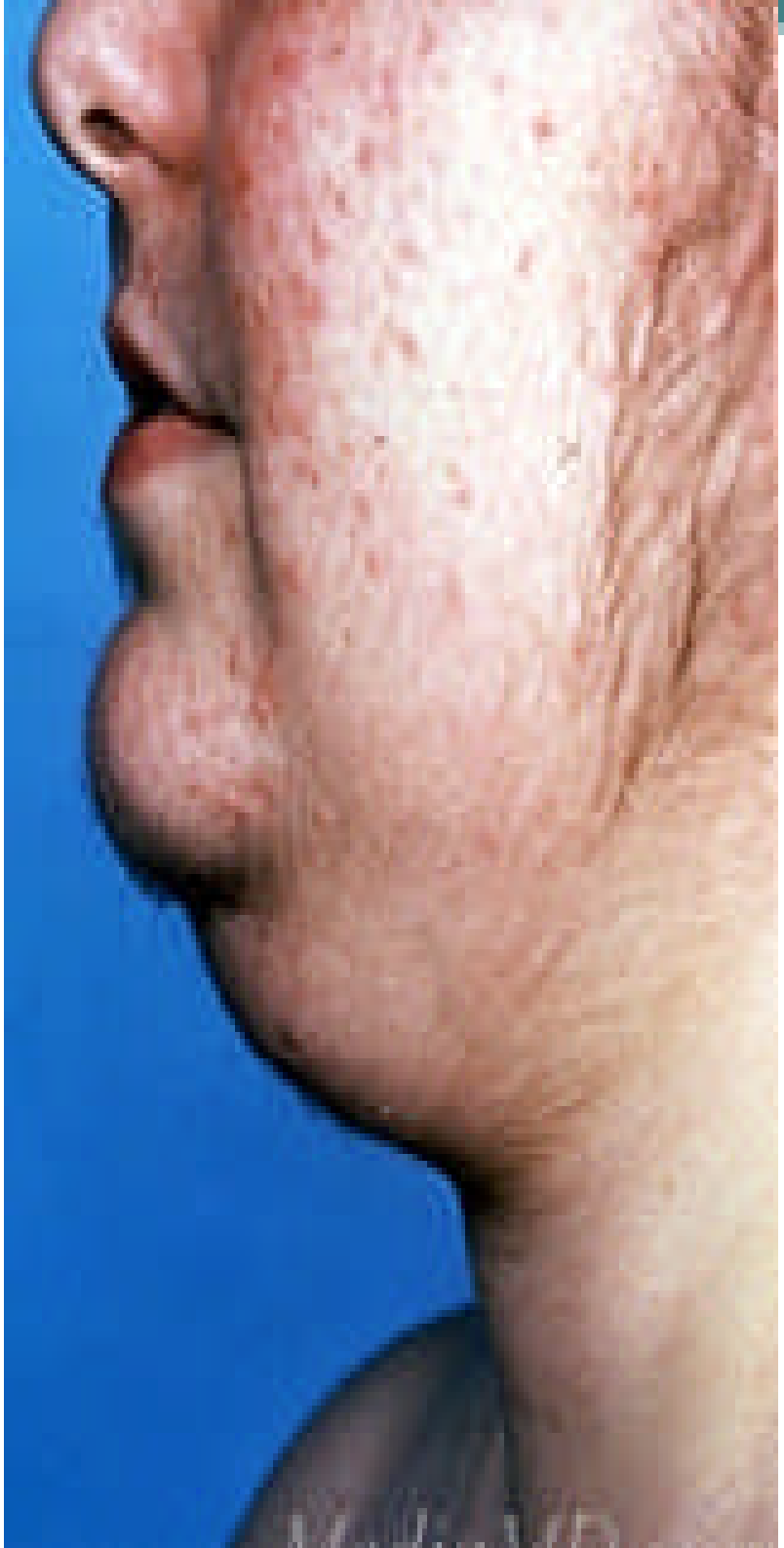


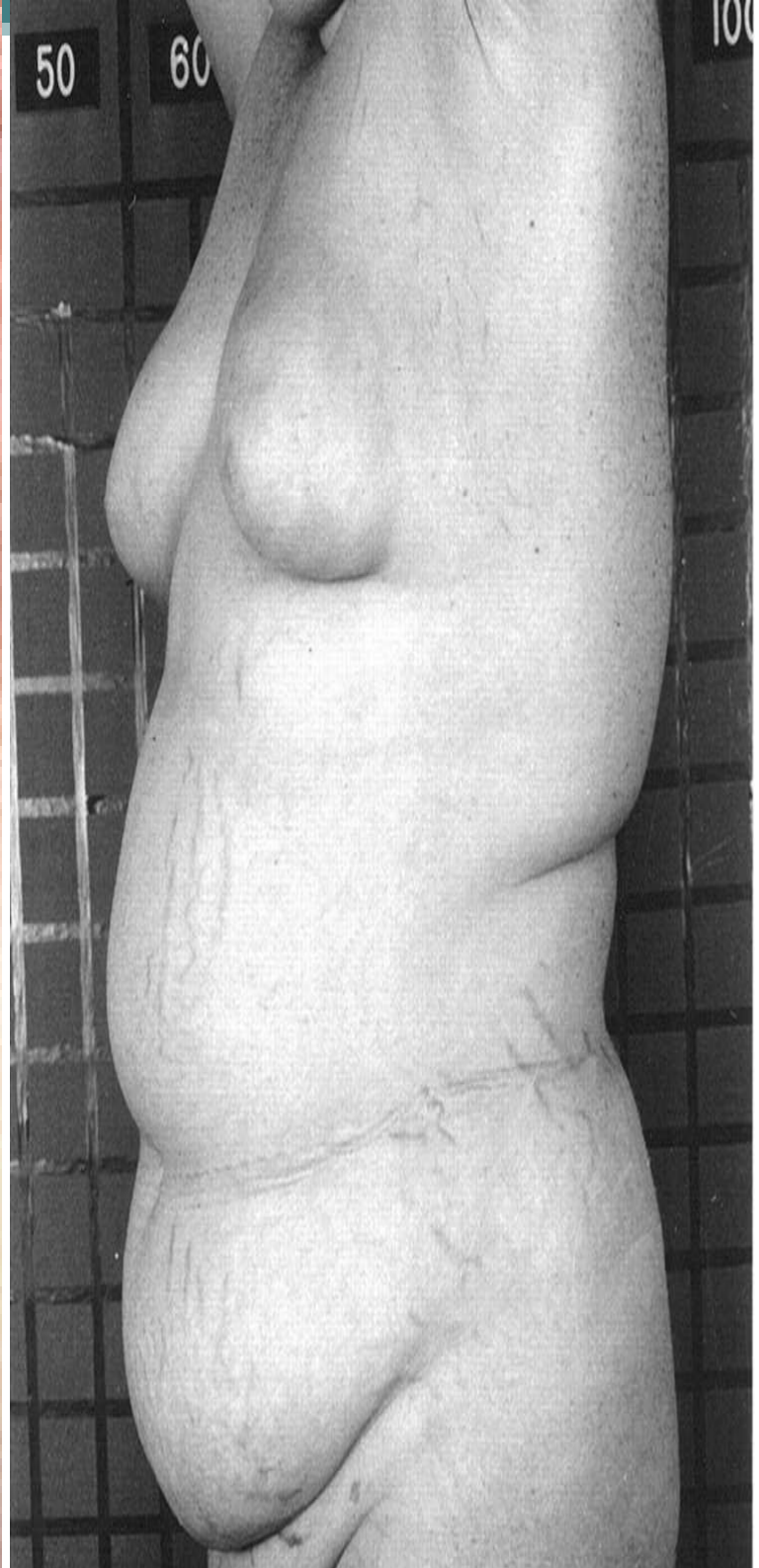


- Upper body obesity with thin arms and legs
- Buffalo Hump
- Red, Round Face
- High Blood Sugar
- High Blood Pressure
- Vertigo
- Blurry Vision
- Acne
- Female Balding
- Water Retention
- Menstrual Irregularities
- Thin Skin and Bruising
- Purple Striae
- Poor Wound Healing
- Hirsutism
- Severe Depression
- Cognitive Difficulties
- Emotional Instability
- Sleep Disorders
- Fatigue



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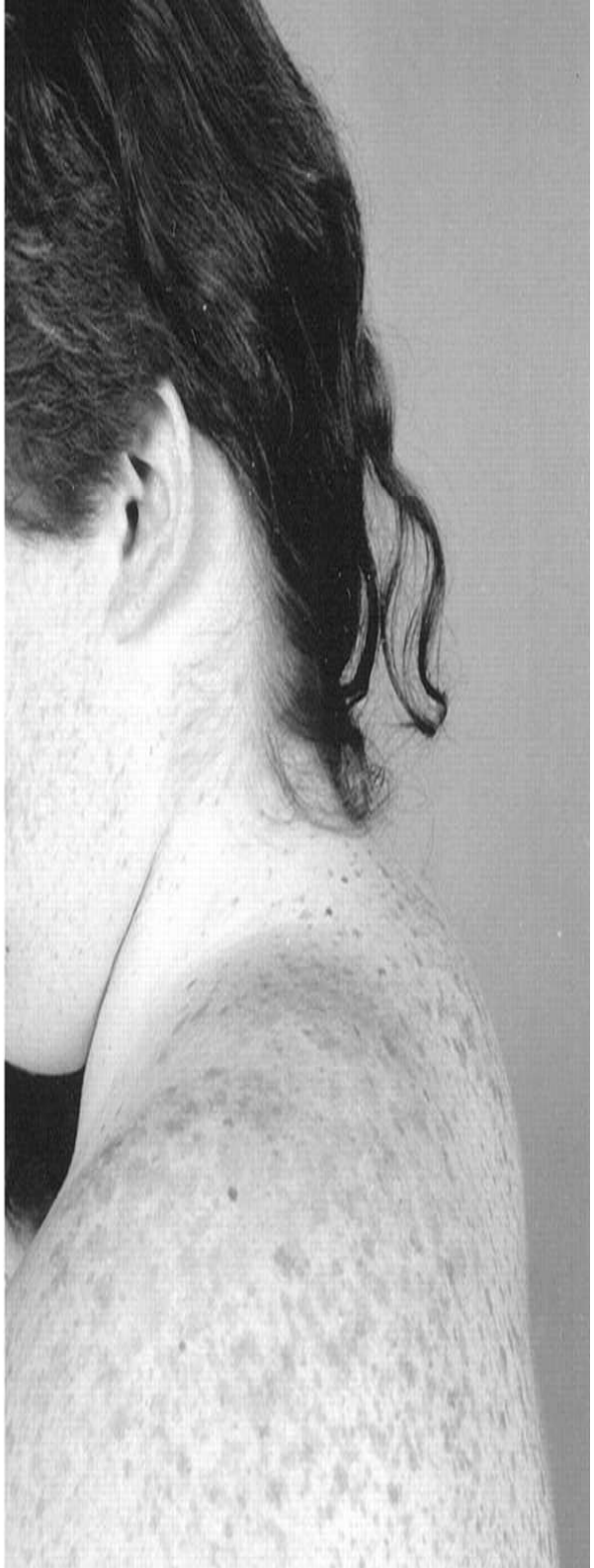
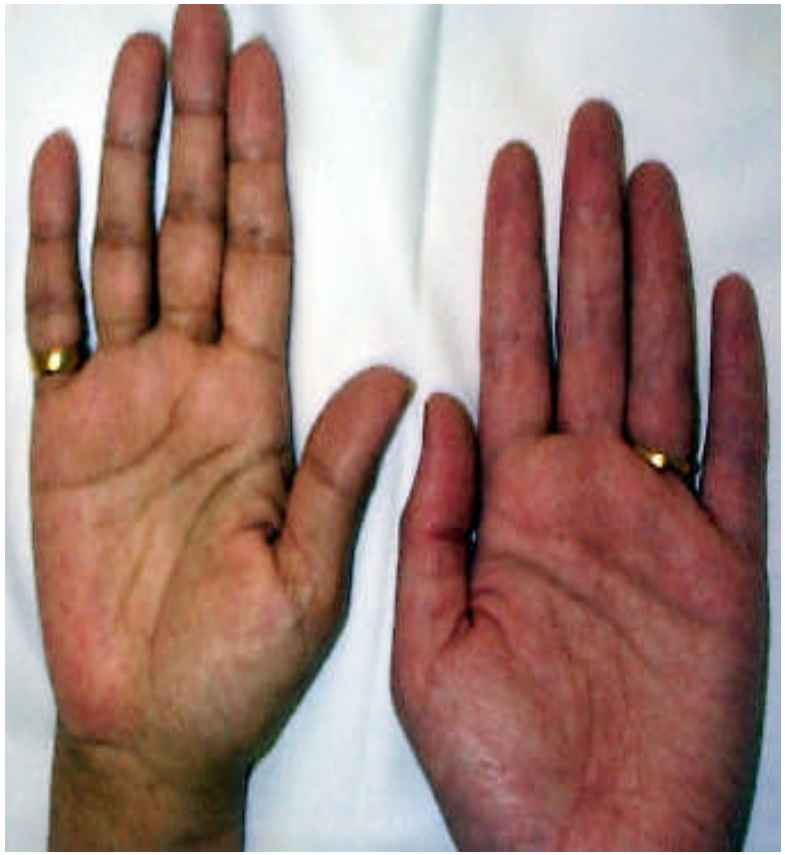
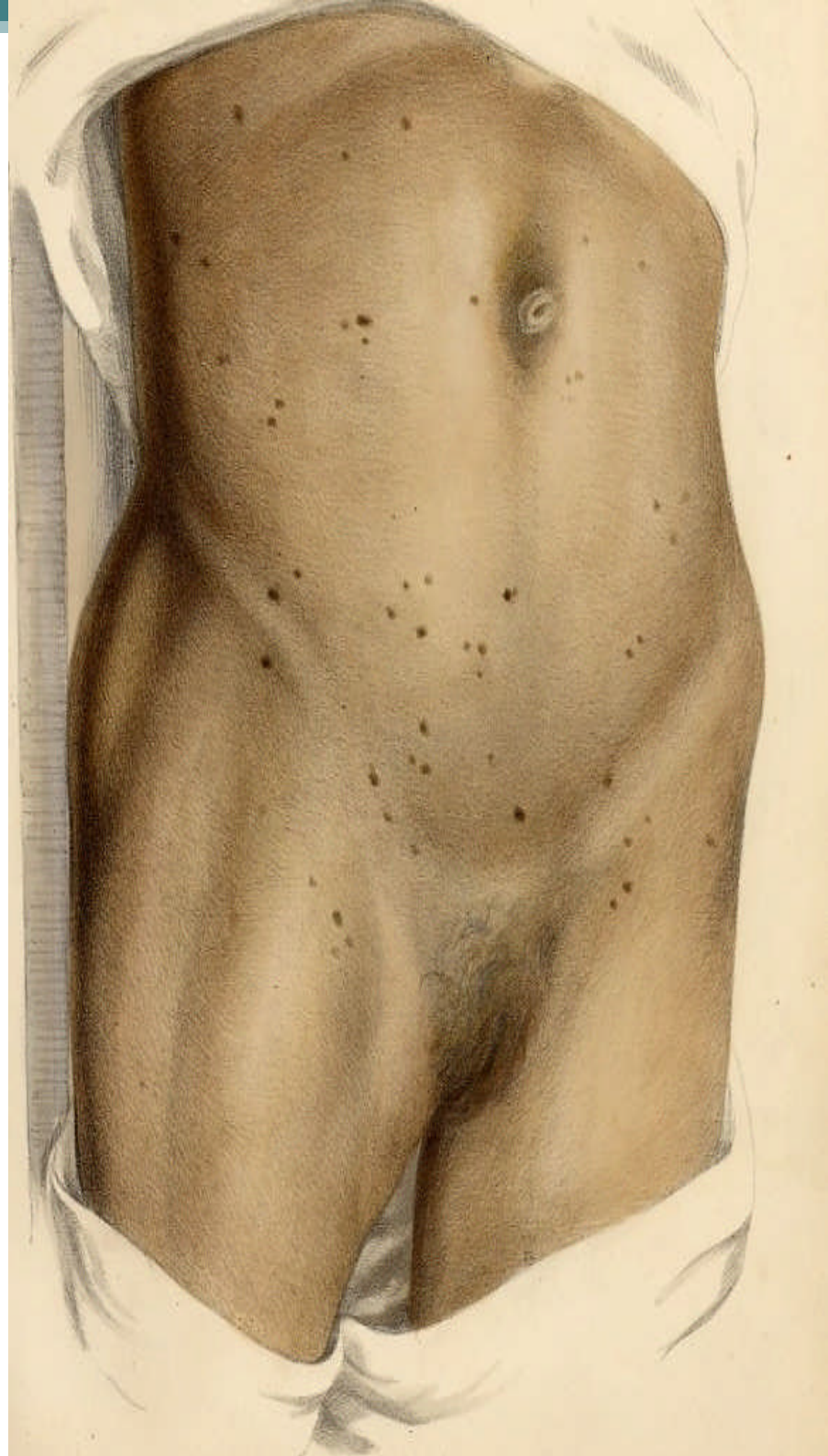
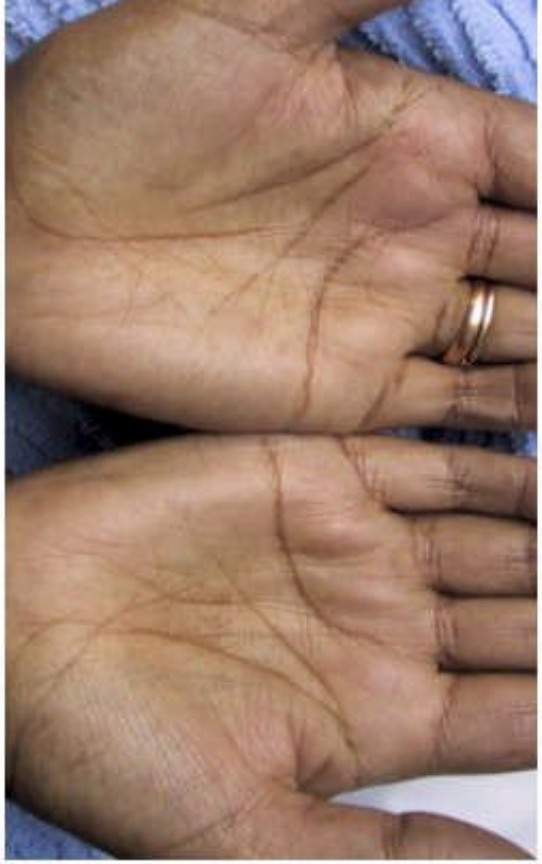


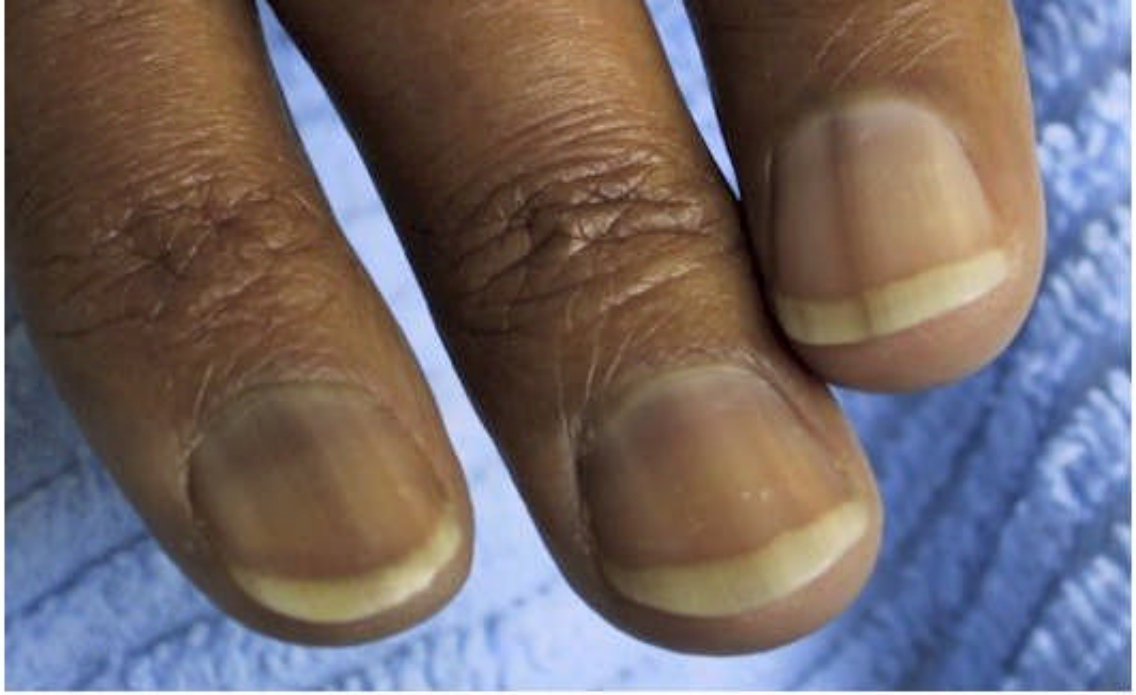
Addison's disease

Abdomen of [Elizabeth Lawrence], exhibiting general dinginess of the integumet, with several small circumscribed deposits of darker pigment.

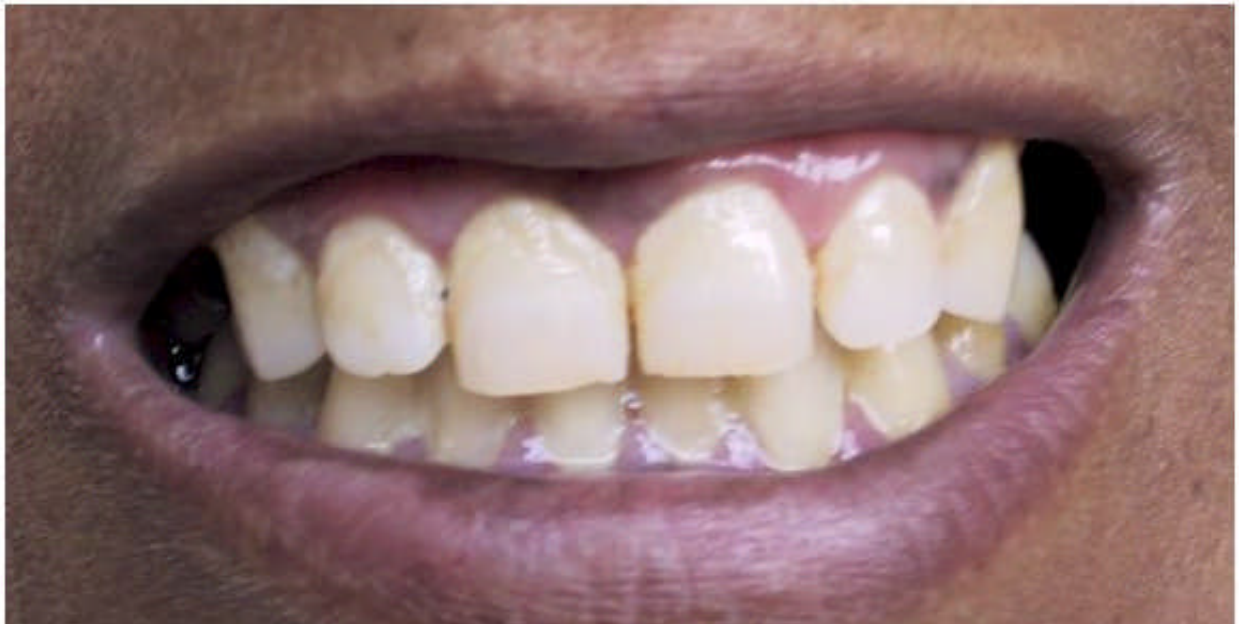






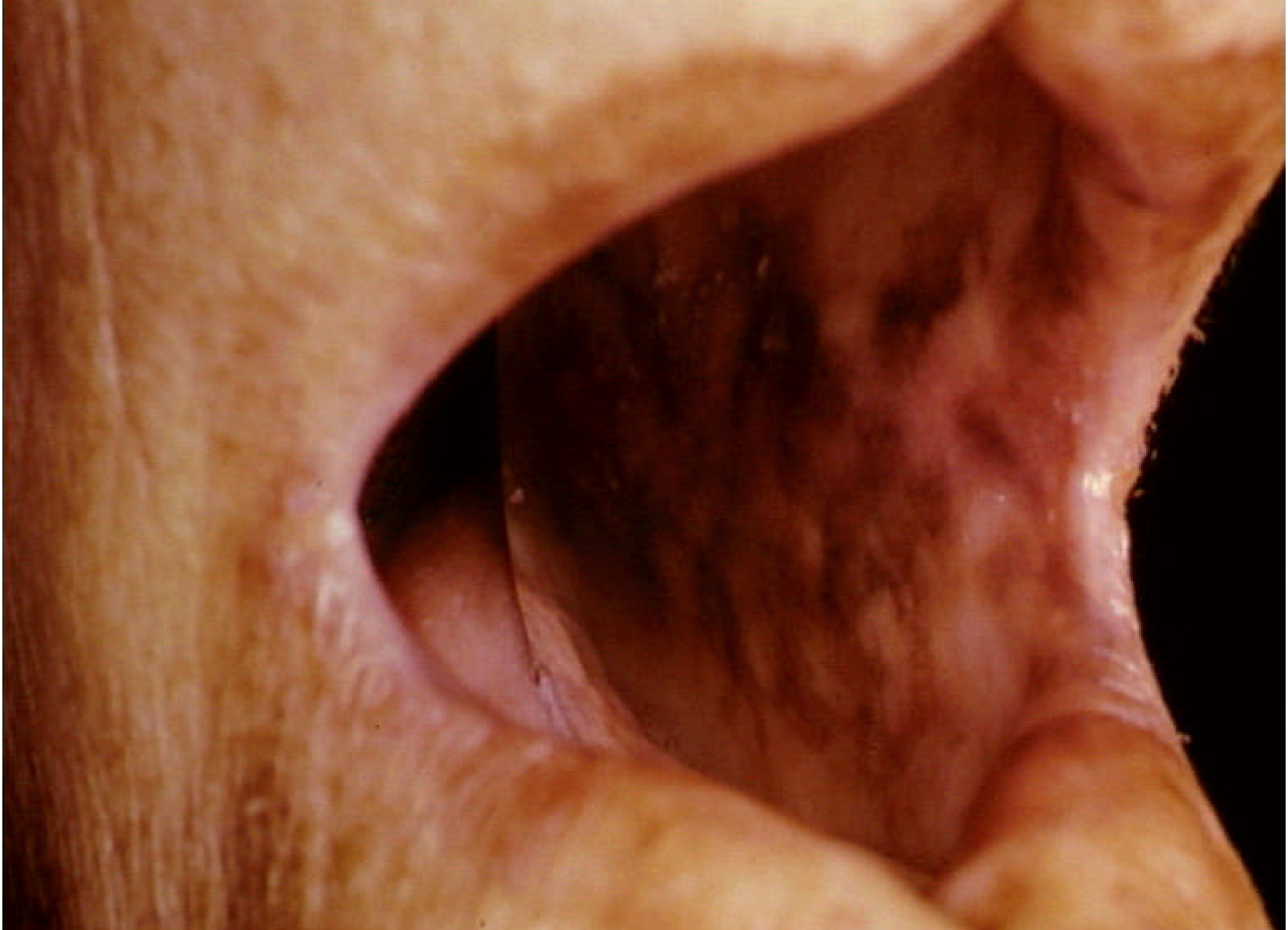


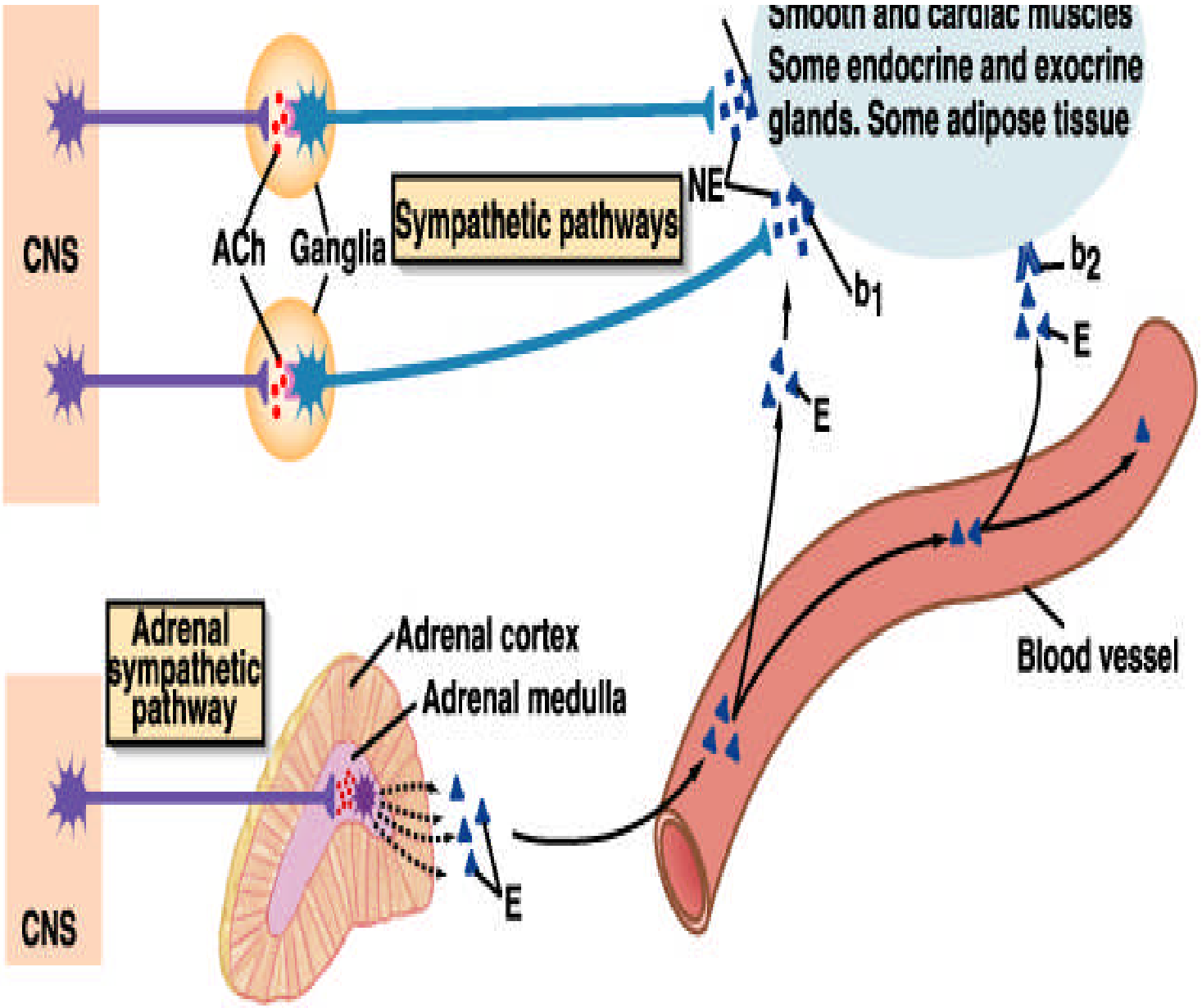
Addison's disease:



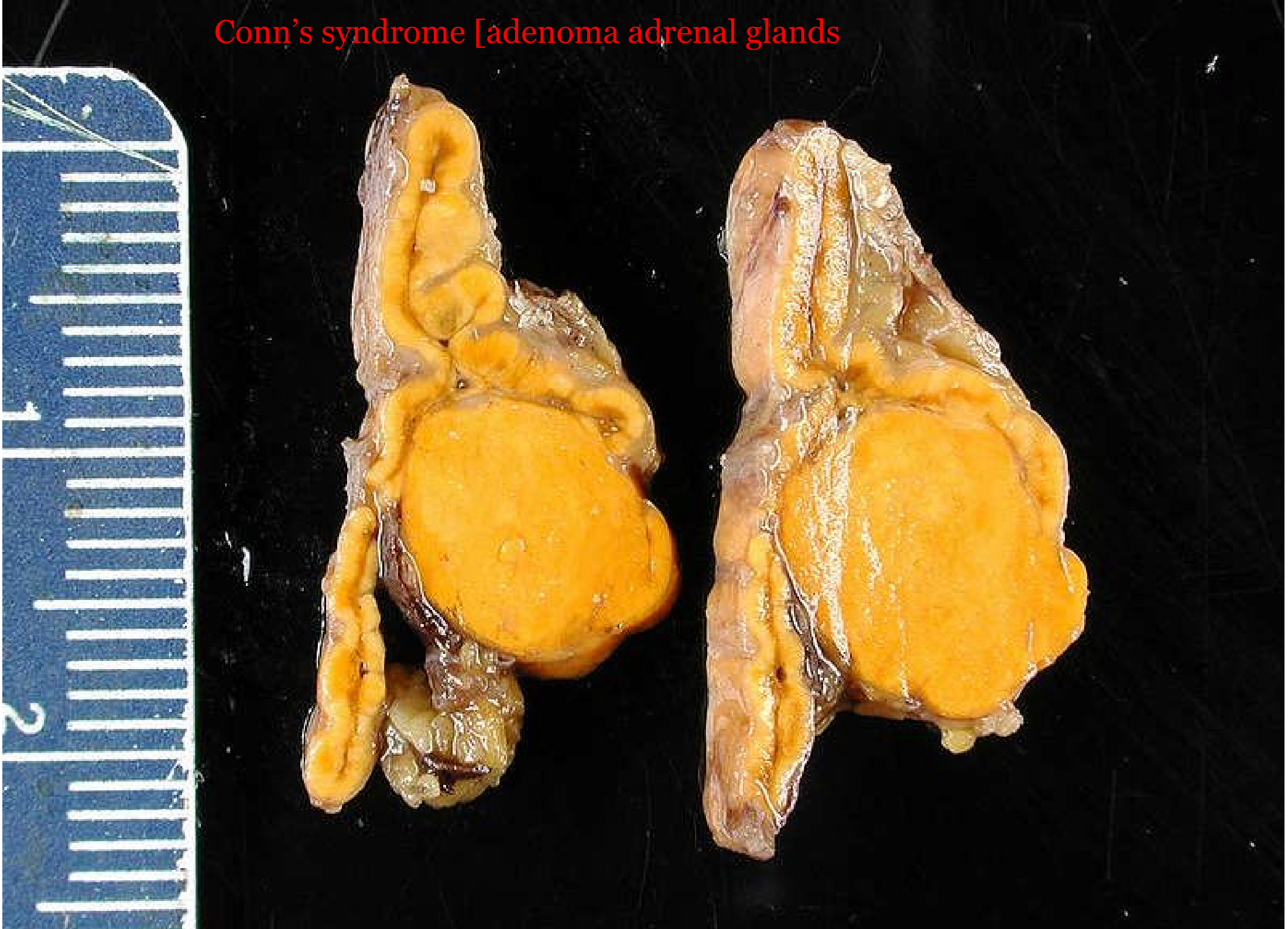
- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.

- She was treated many years ago for pulmonary TB. What are the other causes of this condition?

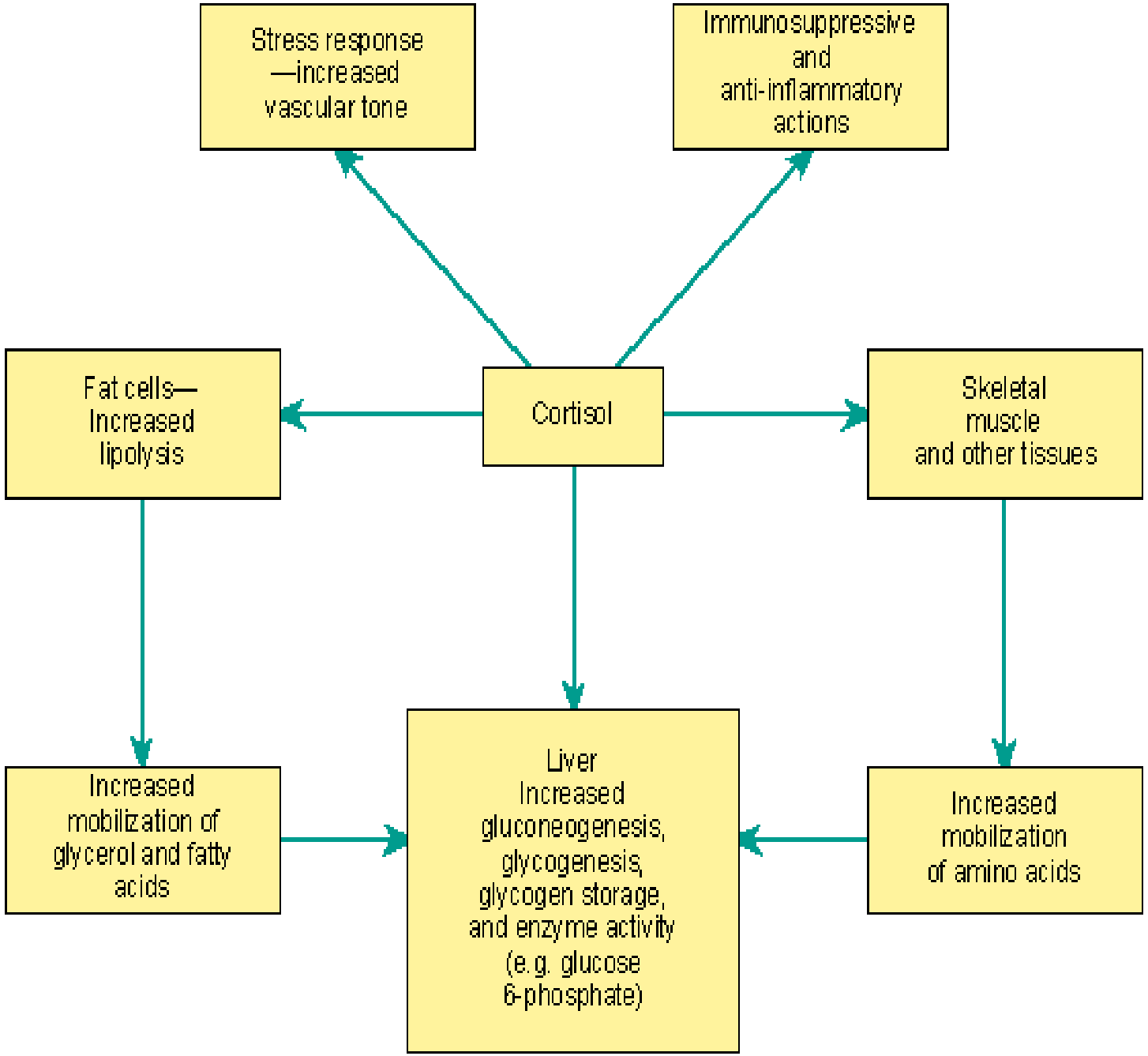



Smooth and cardiac muscles
Some endocrine and exocrine glands. Some adipose tissue
CNS
ACh
Ganglia
Sympathetic pathways
NE
b1
b2
E
E
Adrenal sympathetic pathway
Adrenal cortex
Adrenal medulla
Blood vessel
CNS
E

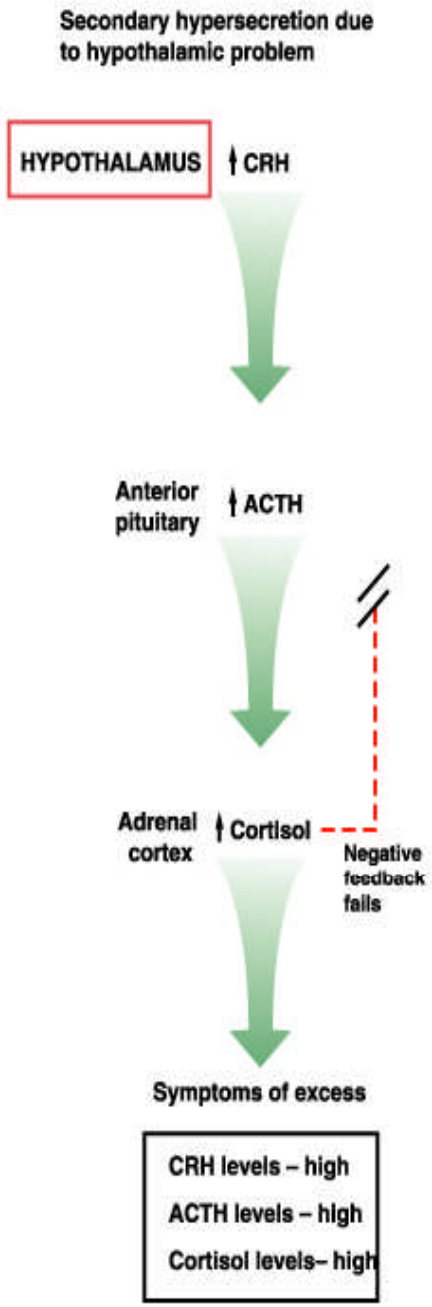
Conn’s syndrome [adenoma adrenal glands



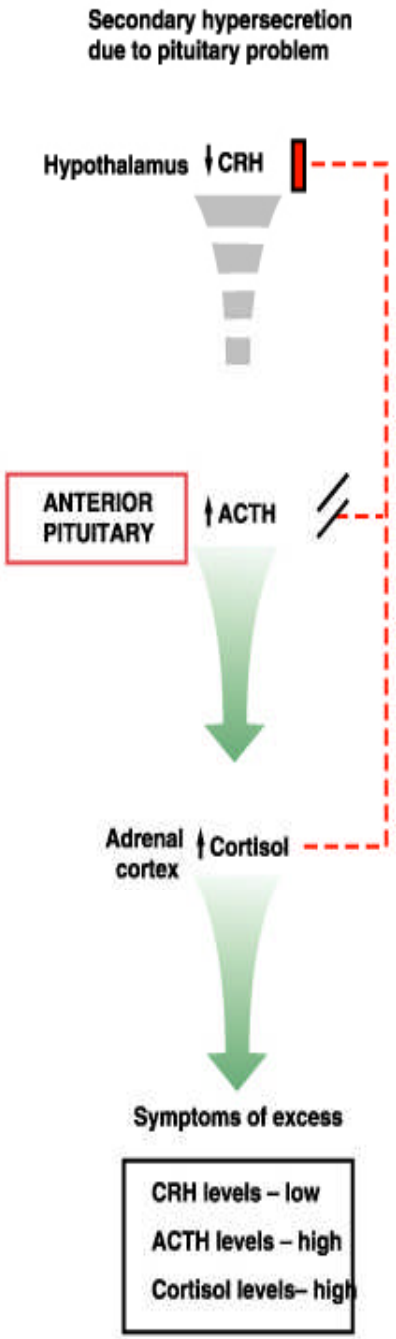
Biologic Actions-Glucocorticoids



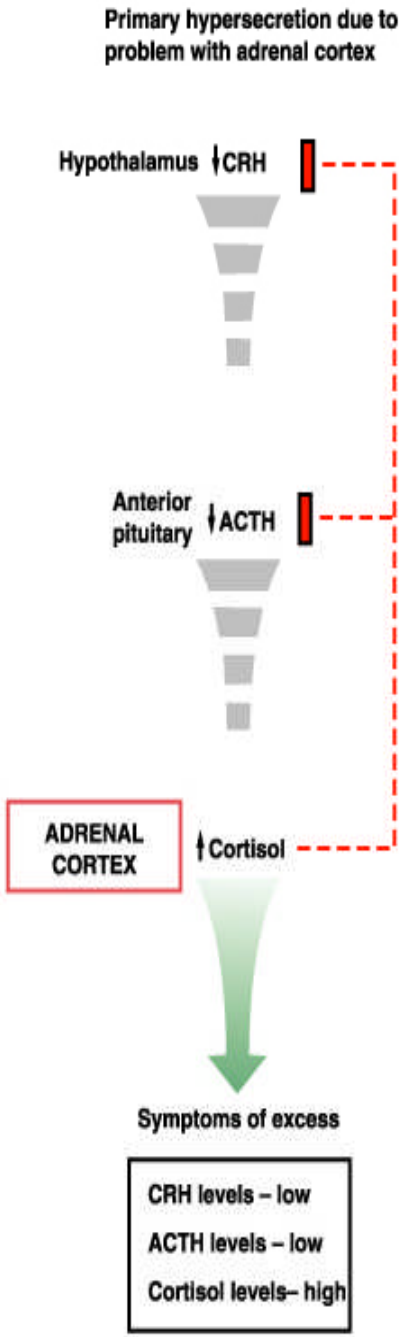
Pathophysiology



Pathophysiology



Pathophysiology

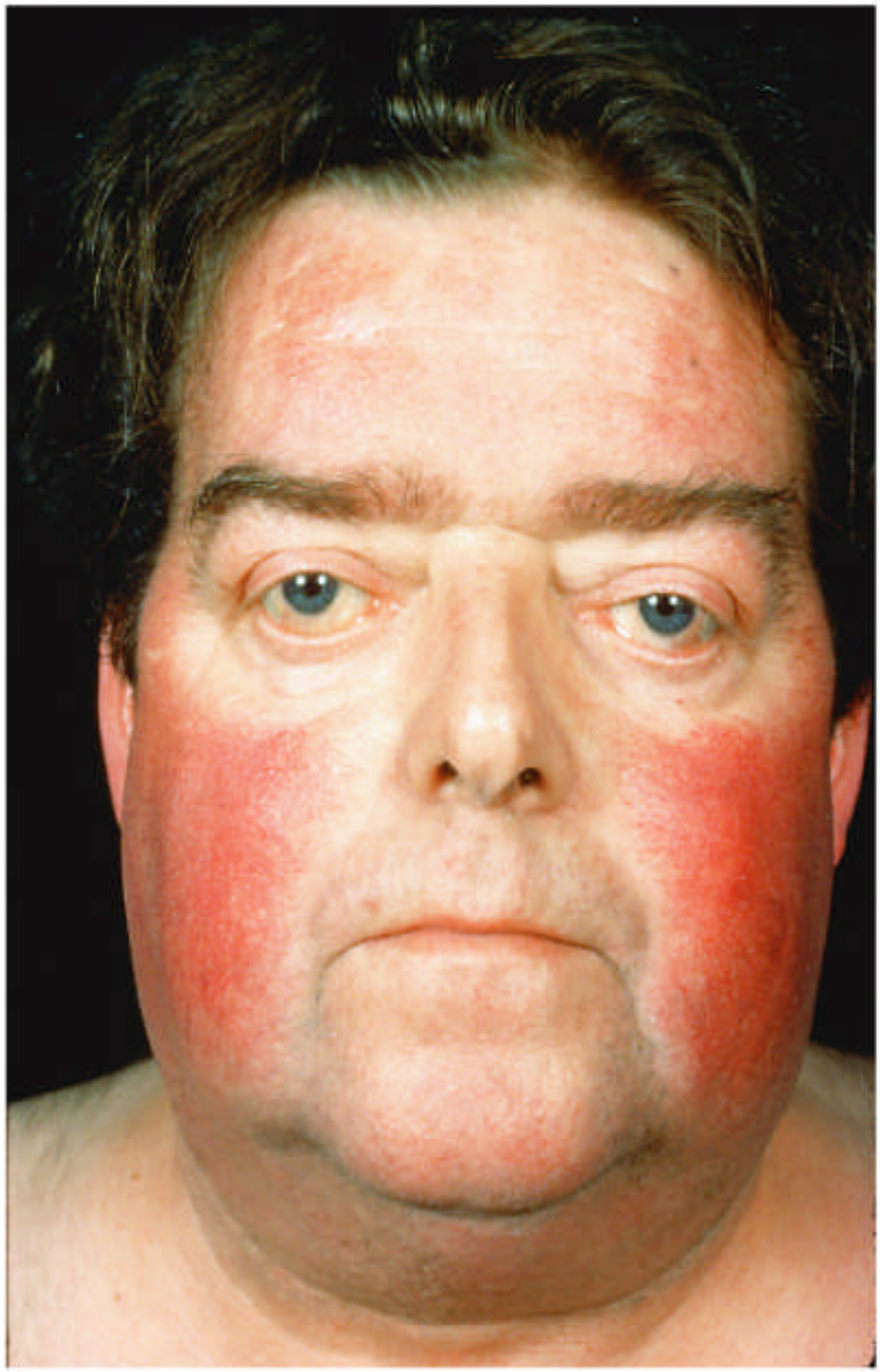


Pathophysiology

Major Functions of Cortisol and Their Clinical Expression

Effect	Clinical expression: Cortisol Deficiency	Clinical expression: Cortisol Excess
Carbohydrate metabolism		
Increased gluconesgenesis	Hypoglycemia	Hyperglycemia
Decreased glucose utilization		
Decreased sensitivity to insulin	Insulin sensitivity	Insulin resistance
Protein metabolism		
Decreased extrahepatic amino acid utilization	Hypoglycemia	Decreased protein sturcture of bone, skin, muscle
Increased gluconeogenesis		Poor wound healing
Fat metabolism		
Increased lipolysis, decreased lipogenesis	Weight loss	Hyperlipemia
Distribution of fat		Redistribution of body fat, truncal obesity
Circulatory		
Maintain ECF volume	Vasodilation	Hypertension
Maintain capillary integrity	hypotension	
Mineralocorticoid		
Sodium retention	Hypovolemia	Hypervolemia
	Hyponatremia	Hypernatremia
Potassium excretion	Hyperkalemia	Hypokalemia
Inflammatory and immune responses		
Stabilize lysosomes	Propensity	Decreased inflammatory response
Suppress synthesis of antibodies	toward autoimmune	Increased susceptibility to infection
Decrease capillary permeability	disease	Decreased fibrous tissue formation
Decrease phagocytosis		
Hematopoietic		
Stimulate red cell production	Anemia	Erythrocytosis
Lympholysis	Lymphocytosis	Lymphopenia
Inhibit neutrophil accumulation at inflammatory sites		Leukocytosis
Central nervous system	Anorexia	Euphoria
	Fatigue	Depression
Hypothlamic-pituitary feedback control of ACTH	Increased ACTH secretion	Decreased ACTH secretion
	Pigmentation	If secondary to stimulation by hypothalamic-pituitary axis,

Pathophysiology



Pathophysiology