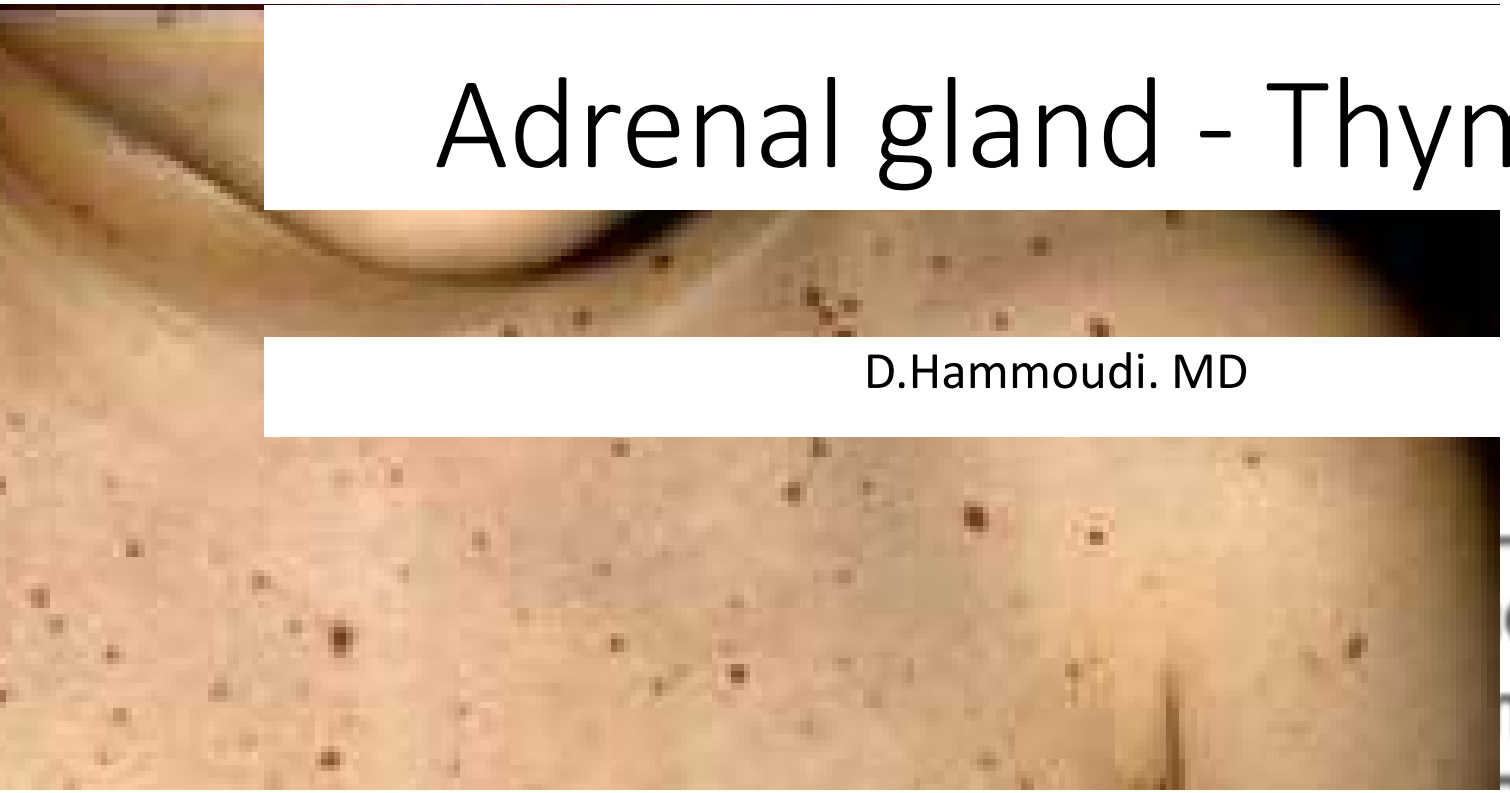
rome confirmed

ma ACTH

Adrenal gland - Thymus

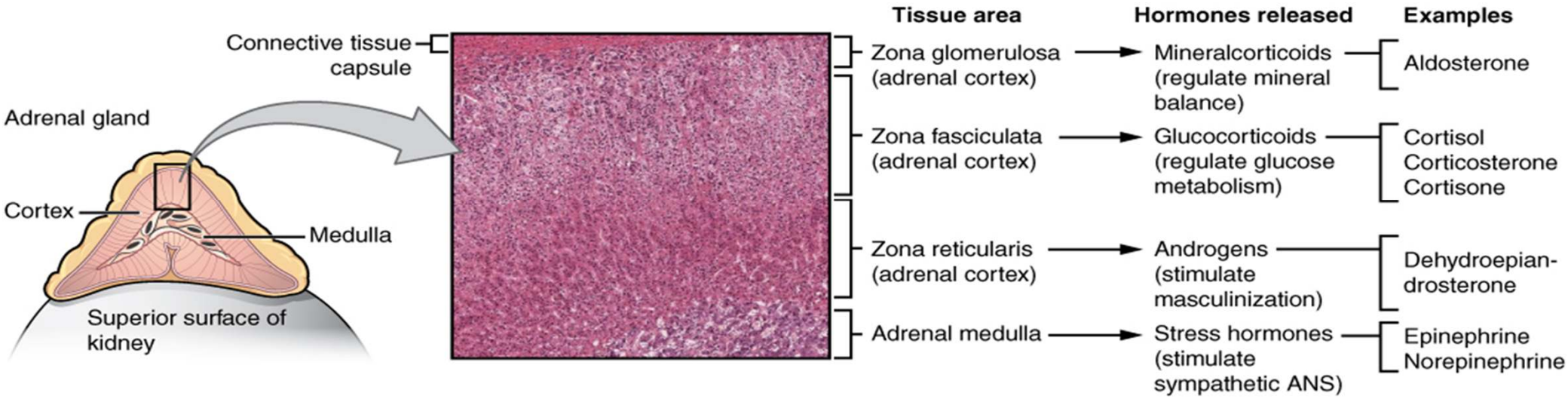


D.Hammoudi. MD

o

na

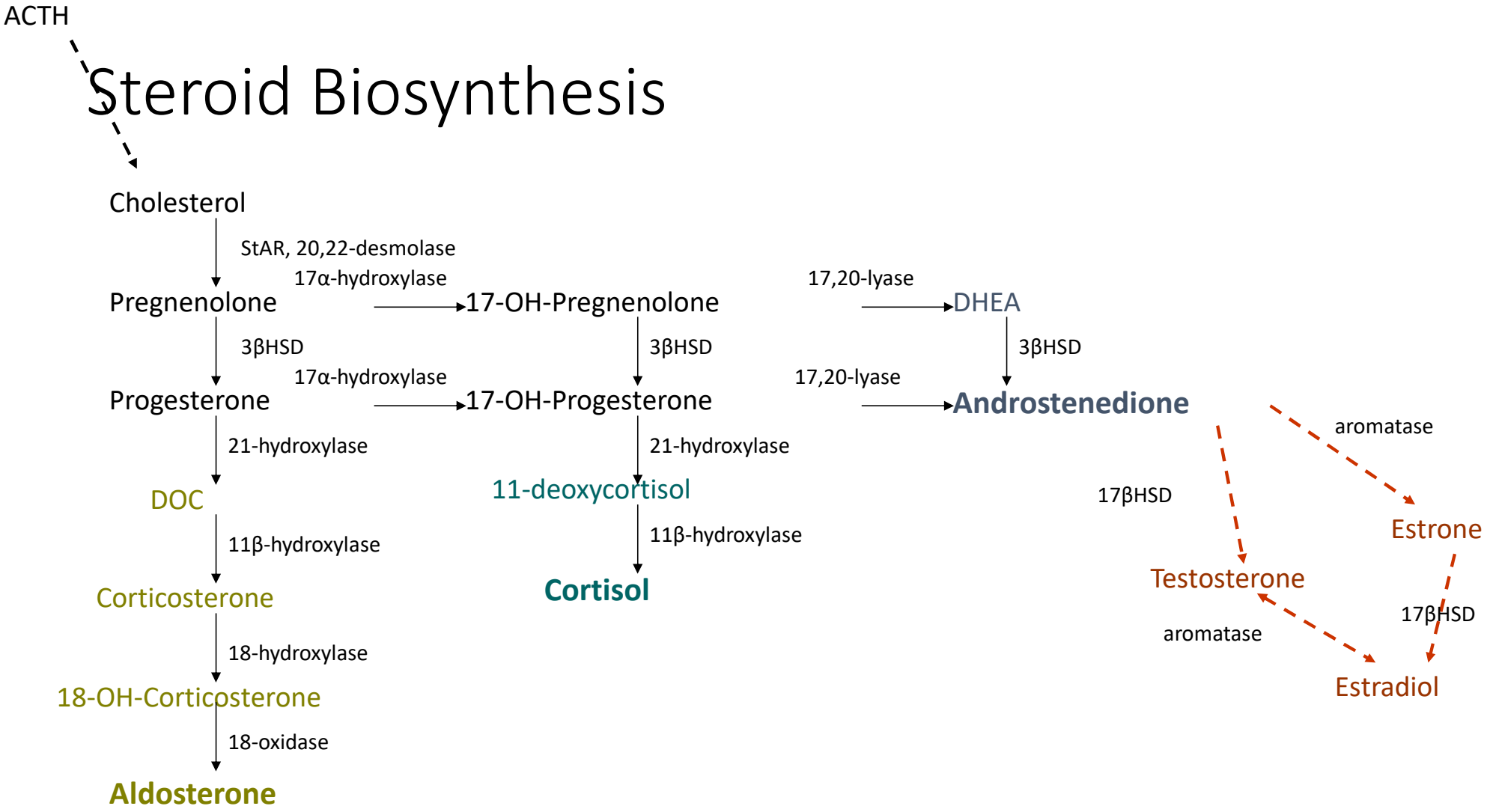
Adrenal glands



Glucocorticoids are chiefly produced in the zona fasciculata of the adrenal cortex
Cortisol (or hydrocortisone) is the most important human glucocorticoid.

Glucocorticoids are corticosteroids that bind to the glucocorticoid receptor

Steroid Biosynthesis



- **GLUCOCORTICOIDS**

(regulate metabolism & are critical in stress response)

– **CORTISOL responsible for control and &metabolism of:**

a. CHO (carbohydrates)

– **increase glucose formed**

– **increase glucose released**

CORTISOL

FATS-control of fat metabolism

- **stimulates fatty acid mobilization from adipose tissue**

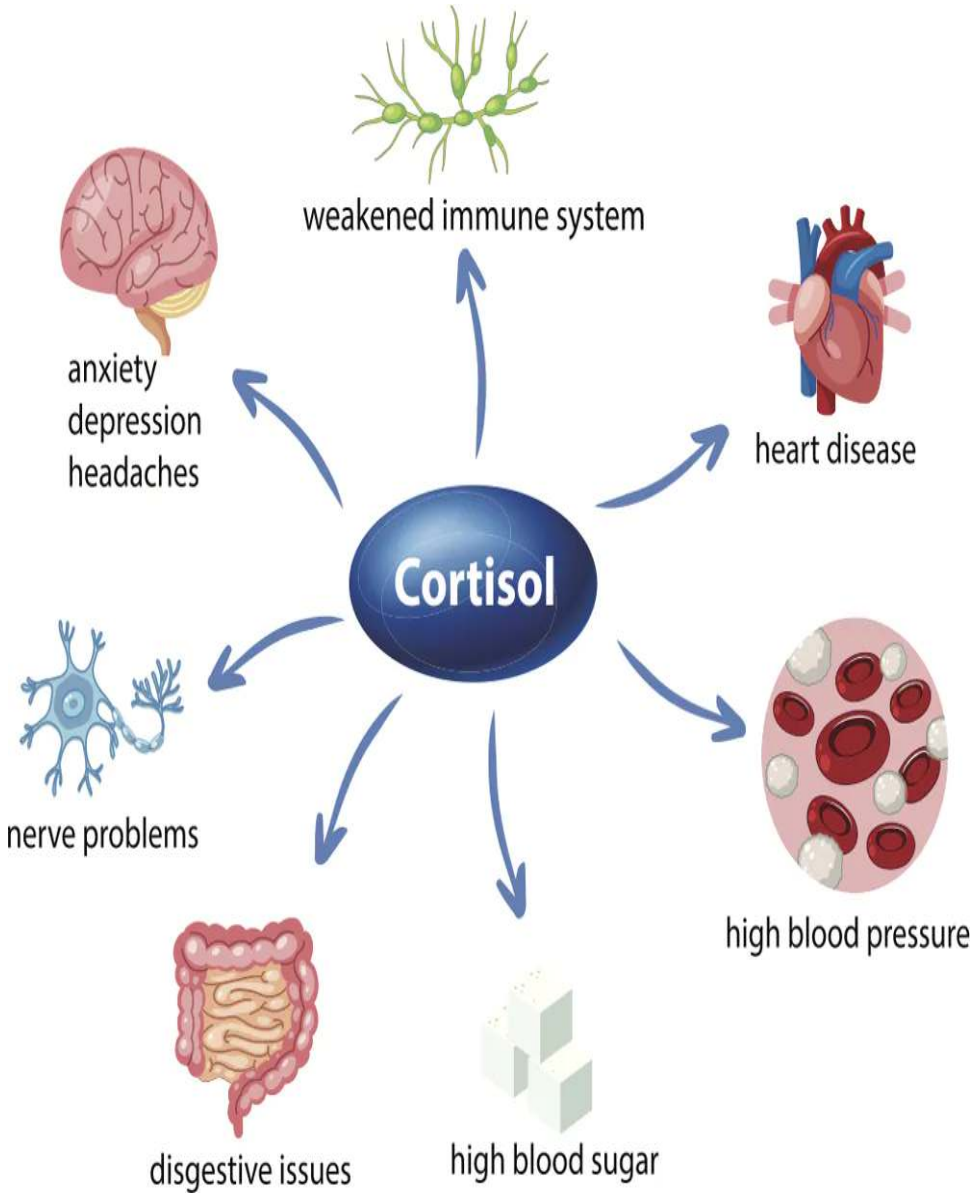
PROTEINS-control of protein metabolism

– **stimulates protein synthesis in liver**

– **protein breakdown in tissues**

– **decrease inflammatory and allergic response**

– **decrease immune system therefore prone to infection**



Glucocorticoid effects may be broadly classified into two major categories:
1/immunological
2/metabolic.

In addition, glucocorticoids play important roles in

1. **fetal development and body fluid homeostasis.**
2. **Immune**
3. **Metabolic**
4. **Developmental**
5. **Arousal and cognition**
6. **Body fluid homeostasis**

Cortisol and Immune

- up-regulate the expression of anti-inflammatory proteins.
- down-regulate the expression of proinflammatory proteins.

- Glucocorticoids are also shown to play a role in the development and homeostasis of T lymphocytes.
  - with either **increased or decreased sensitivity of T cell lineage to glucocorticoids.**

Metabolic

Involved in glucose metabolism.

In the fasted state, cortisol stimulates several processes that collectively serve to increase and maintain normal concentrations of glucose in blood.

Metabolic effects:

•Stimulation of gluconeogenesis, in particular, in the liver: This pathway results in the synthesis of glucose from non-hexose substrates, such as amino acids and glycerol from triglyceride breakdown.

•Mobilization of amino acids from extrahepatic tissues: These serve as substrates for gluconeogenesis.

•Inhibition of glucose uptake in muscle and adipose tissue: A mechanism to conserve glucose

•Stimulation of fat breakdown in adipose tissue: The fatty acids released by lipolysis are used for production of energy in tissues like muscle, and the released glycerol provide another substrate for gluconeogenesis.

•Increase in sodium retention and potassium excretion leads to hypernatremia and hypokalemia

•Increase in hemoglobin concentration, likely due to hindrance of the ingestion of red blood cell by macrophage or other phagocyte.

•Increased urinary uric acid

•Increased urinary calcium and hypocalcemia

•Alkalosis

•Leukocytosis

Excessive glucocorticoid levels resulting from administration as a drug or hyperadrenocorticism have effects on many systems.
Some examples include inhibition of bone formation, suppression of calcium absorption (both of which can lead to osteoporosis), delayed wound healing, muscle weakness, and increased risk of infection.
These observations suggest a multitude of less-dramatic physiologic roles for glucocorticoids.

Developmental

- Glucocorticoids have multiple effects on fetal development.
- An important example is their role in **promoting maturation of the lung and production of the surfactant necessary for extrauterine lung function.**

- In addition, glucocorticoids are necessary for **normal brain development, by initiating terminal maturation**, **remodeling axons and dendrites, and affecting cell survivaland may also play a role in hippocampal development**.

- Glucocorticoids **stimulate the maturation of the Na^+/K^+/ATPase, nutrient transporters, and digestion enzymes, promoting the development of a functioning gastro-intestinal system.**

- Glucocorticoids also support the development of the **neonate's renal system by increasing glomerular filtra**tion.

Body fluid homeostasis

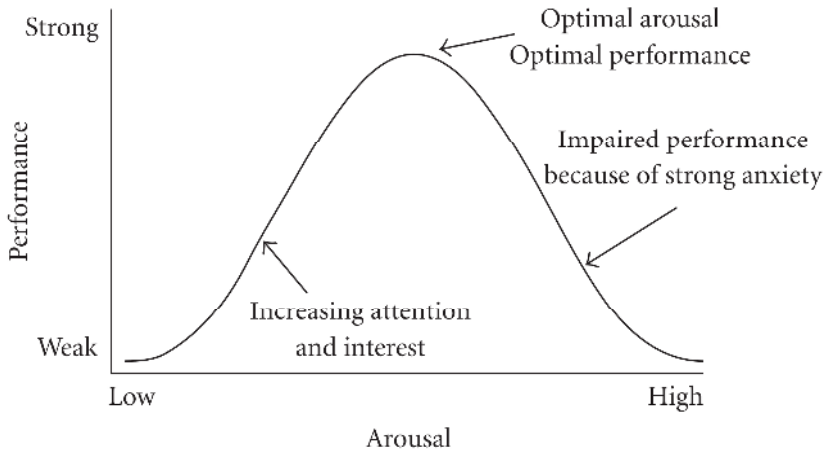
- Glucocorticoids could act centrally, as well as peripherally, to assist in the normalization of extracellular fluid volume by regulating body's action to atrial natriuretic peptide (ANP).

- Centrally, glucocorticoids could inhibit dehydration induced water intake
- Peripherally , glucocorticoids could induce a potent diuresis.

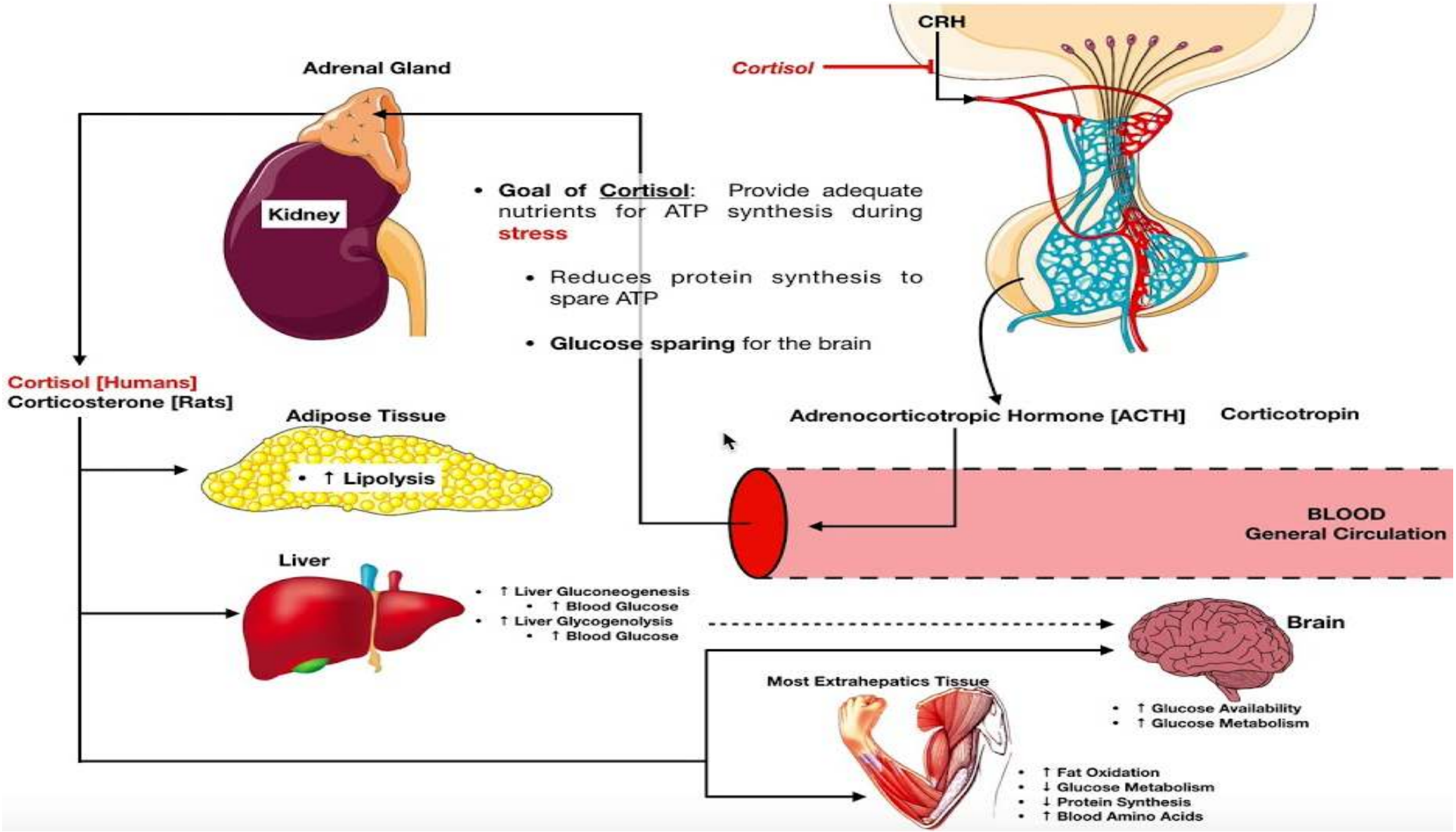
Arousal and cognition

- A graphical representation of the Yerkes-Dodson curve
- Glucocorticoids act on the hippocampus, amygdala, and frontal lobes. Along with adrenaline, these enhance the formation of flashbulb memories of events associated with strong emotions, both positive and negative.
- Glucocorticoids have also been shown to have a significant impact on vigilance (attention deficit disorder) and cognition (memory).

Figure 1: The Yerkes-Dodson Human Performance and Stress Curve



The **Yerkes-Dodson law**," performance increases with physiological or mental arousal (stress) but only up to a point. When the level of stress becomes too high, performance decreases. There's more: The shape of the **curve** varies based on the complexity and familiarity of the task

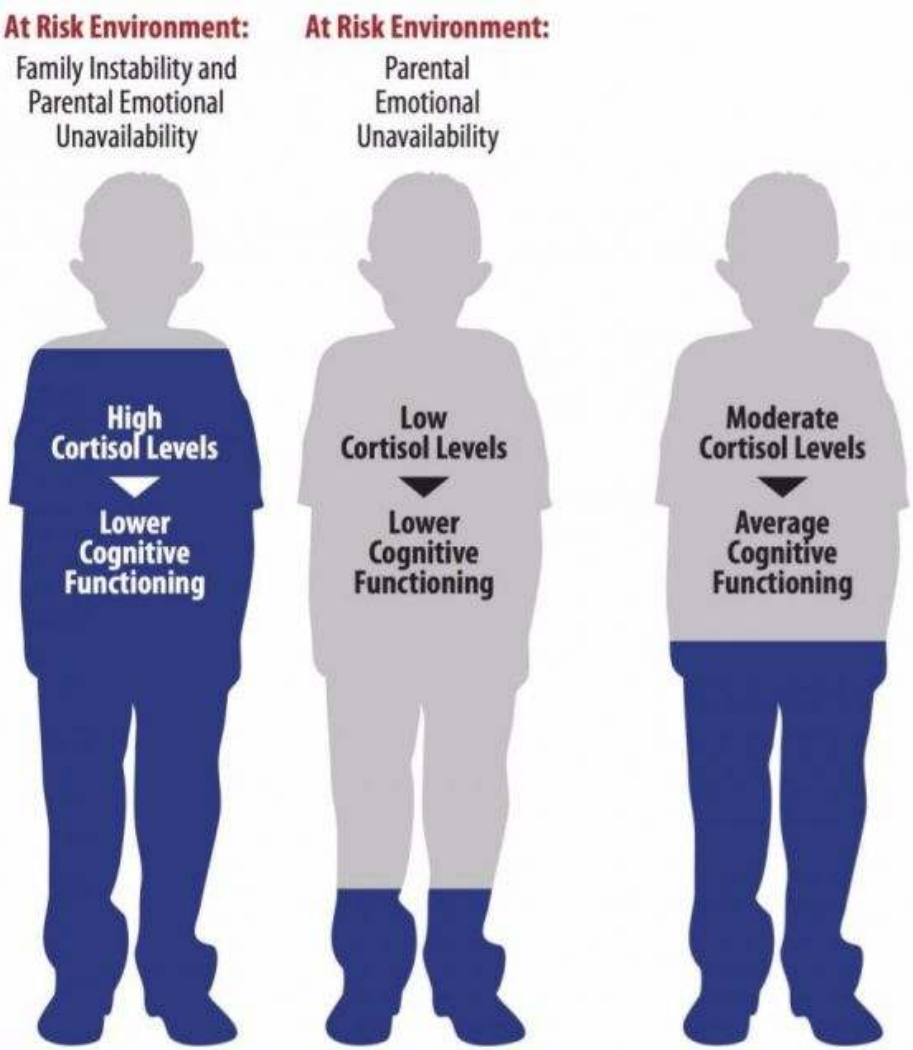

CRH
Cortisol
Adrenal Gland
Kidney
• Goal of Cortisol: Provide adequate nutrients for ATP synthesis during stress
• Reduces protein synthesis to spare ATP
• Glucose sparing for the brain
Cortisol [Humans]
Corticosterone [Rats]
Adrenocorticotropic Hormone [ACTH]
Corticotropin
Adipose Tissue
• ↑ Lipolysis
BLOOD
General Circulation
Liver
• ↑ Liver Gluconeogenesis
• ↑ Blood Glucose
• ↑ Liver Glycogenolysis
• ↑ Blood Glucose
Brain
• ↑ Glucose Availability
• ↑ Glucose Metabolism
Most Extrahepatics Tissue
• ↑ Fat Oxidation
• ↓ Glucose Metabolism
• ↓ Protein Synthesis
• ↑ Blood Amino Acids

ACTH

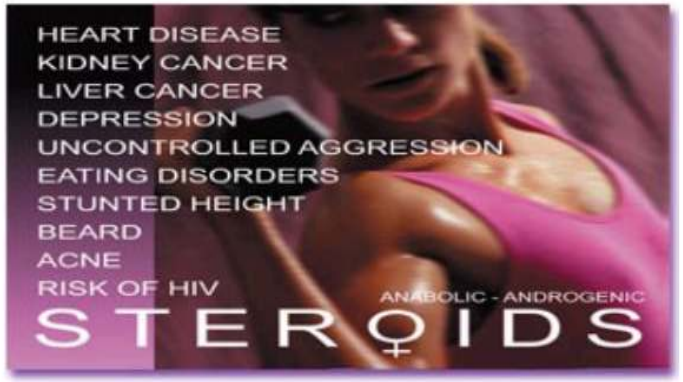
cortisol

↓ – **levels cause stimulation of ACTH**

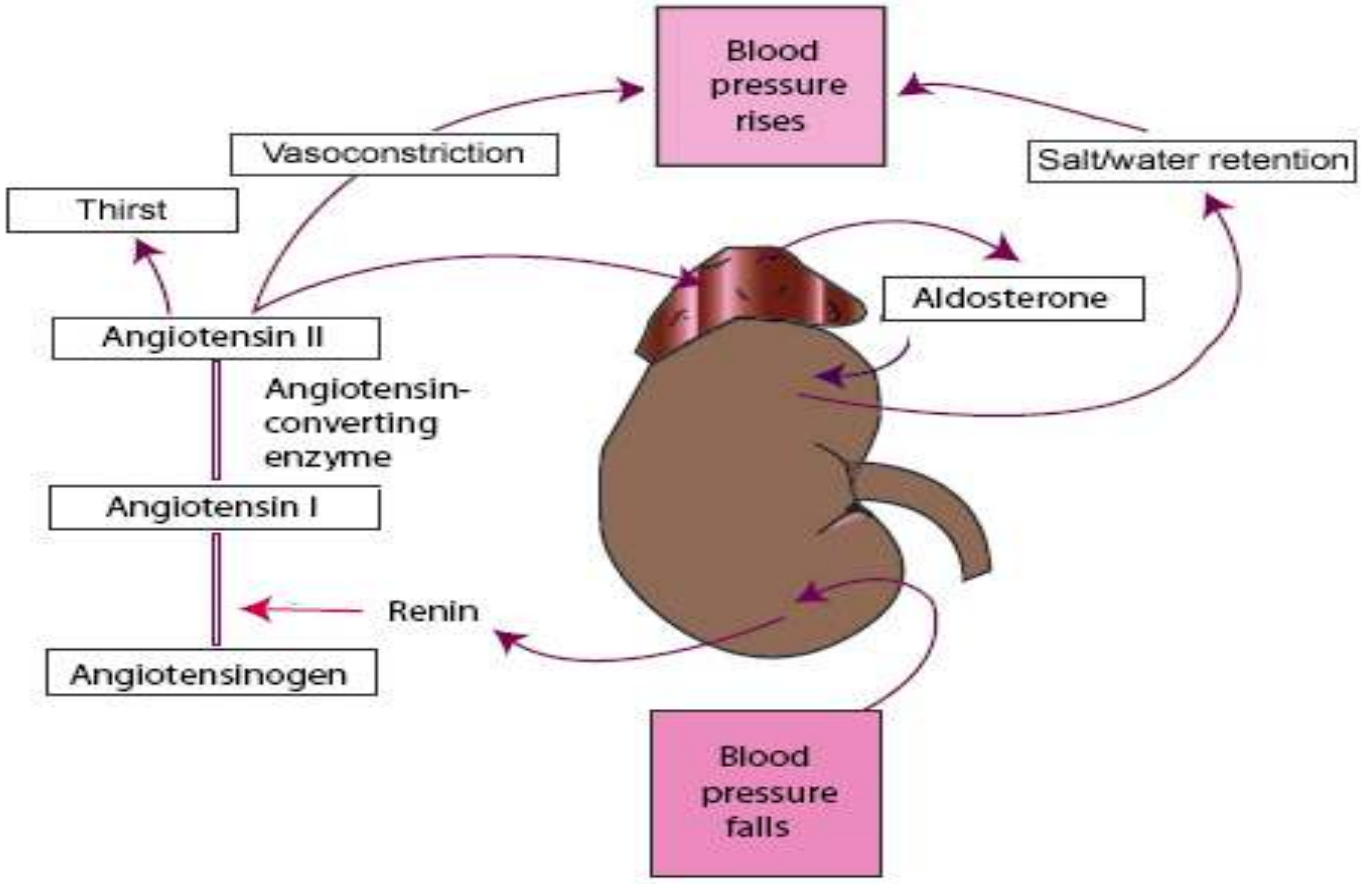
↑ – **levels cause dec. release of ACTH**



Too many steroids



Adrenal physiology :Renin-angiotensin system

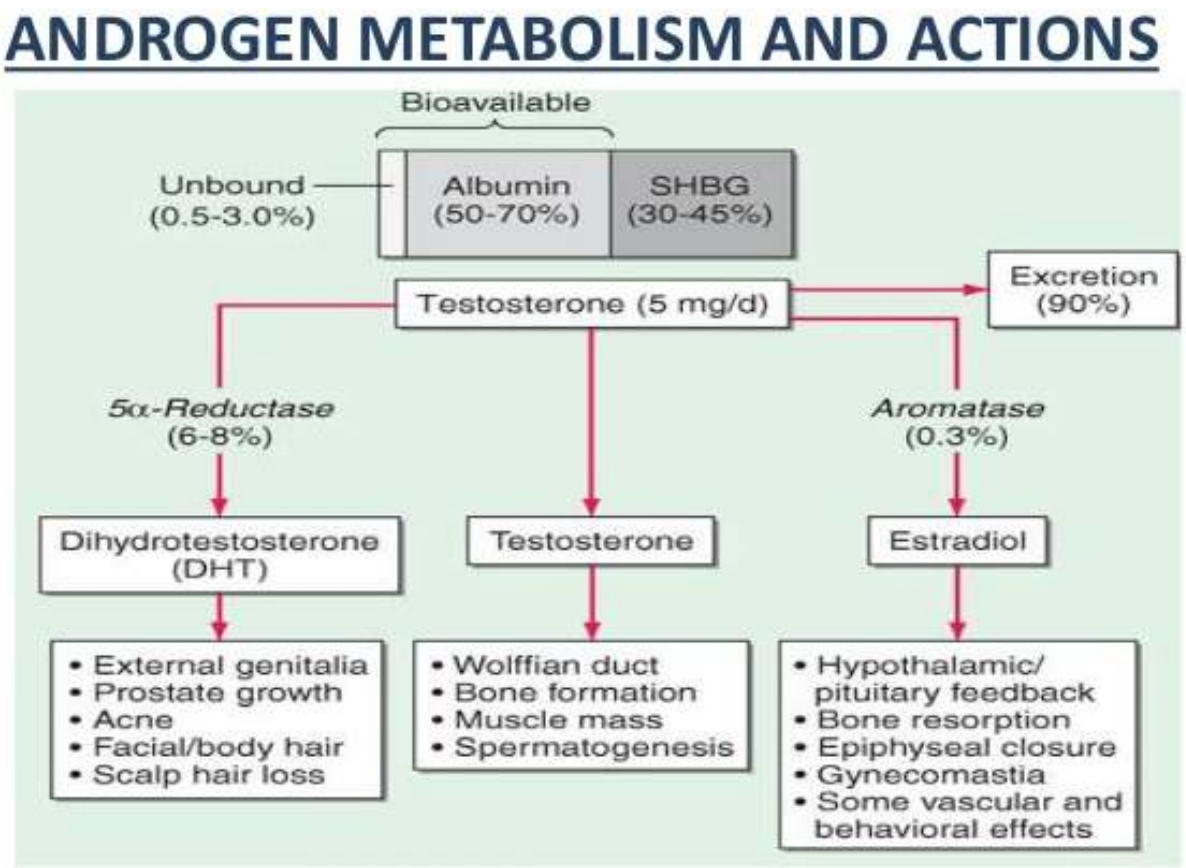


<u>Mineralocorticoids</u> (F & E balance)
– Aldosterone (renin from kidneys controls adrenal
cortex production of aldosterone)

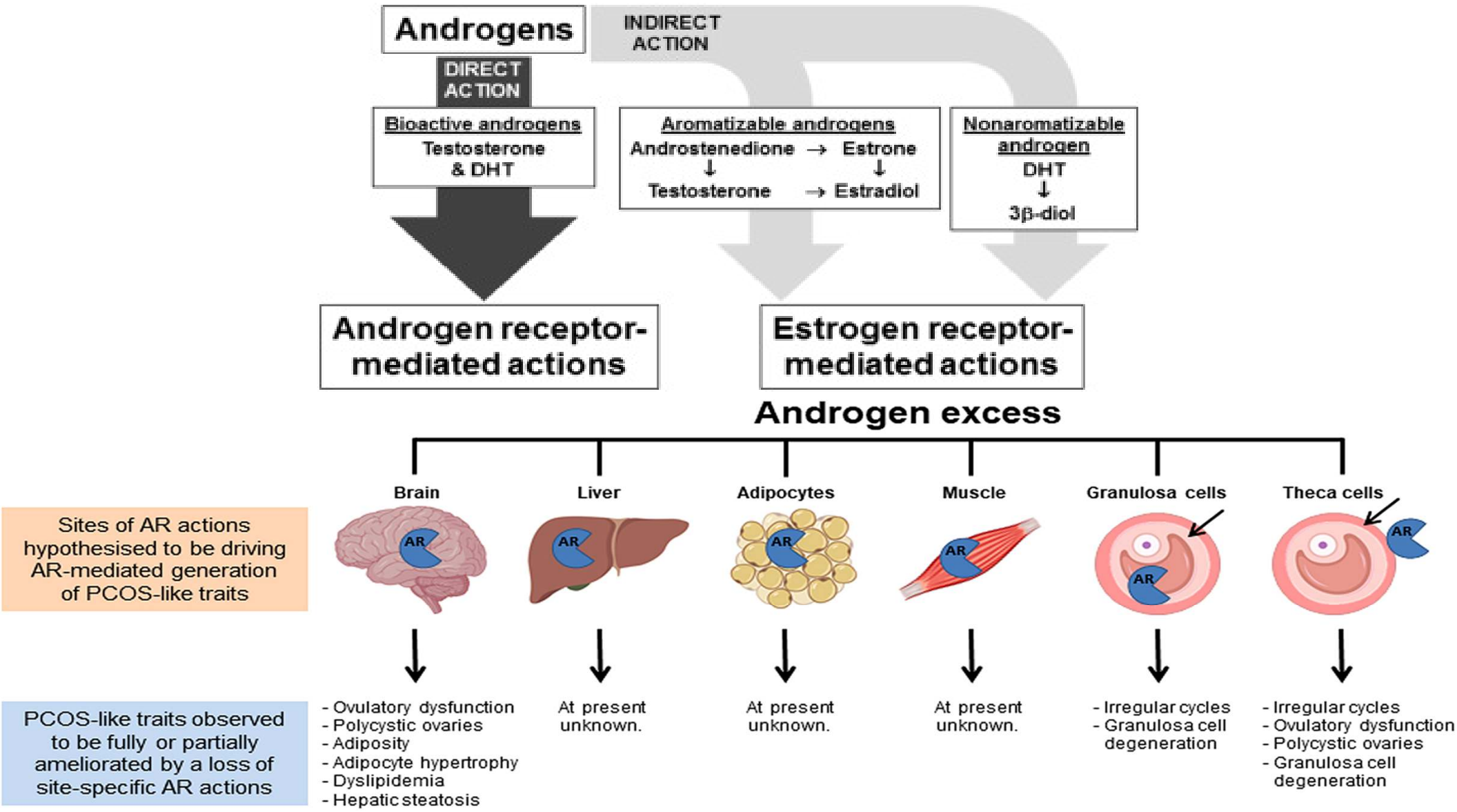
- Na retention
- Water retention
- K excretion

ANDROGENS = SEX HORMONES

- **– hormones which male characteristics**
- **• release of testosterone INCREASED**
- **Clear more in women than men**

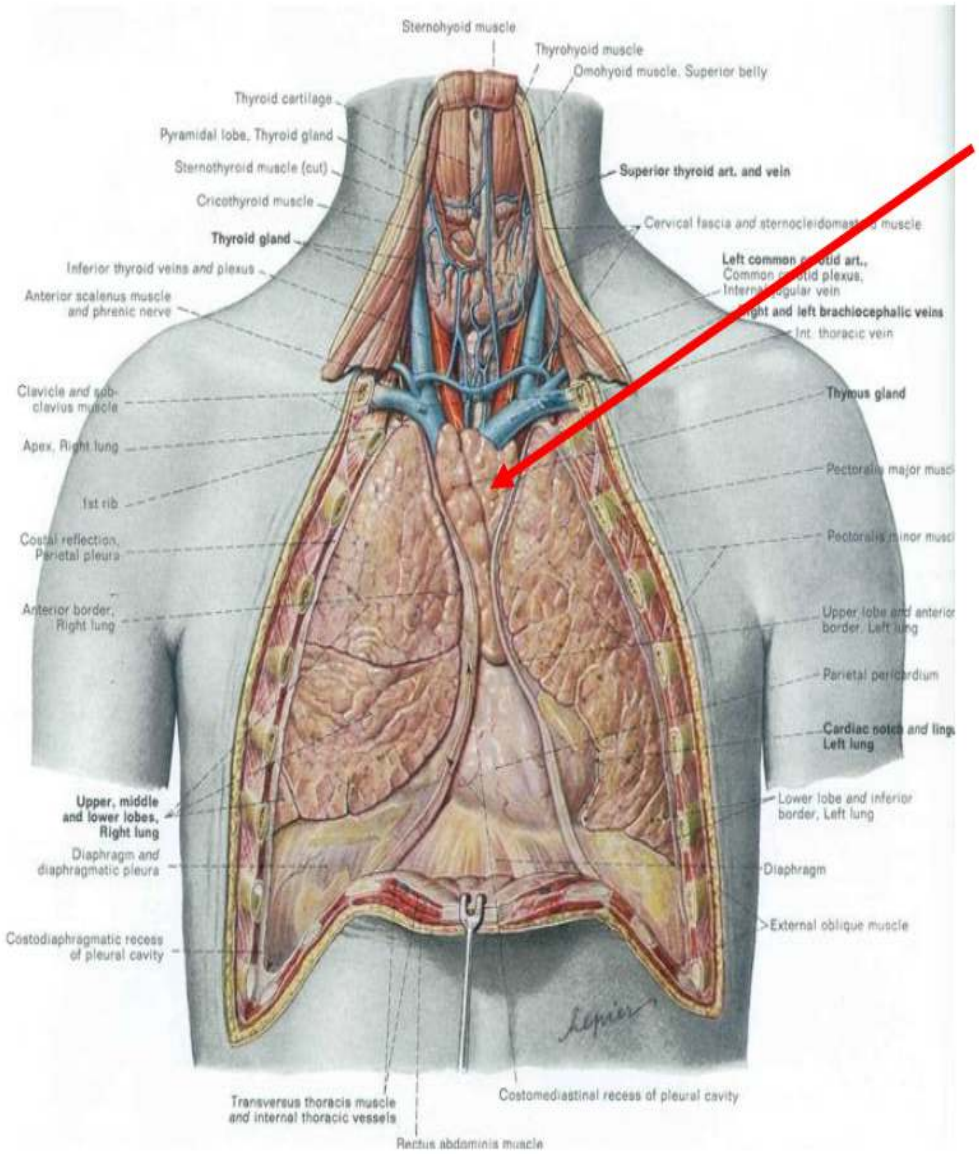


Details will be discussed in male reproduction

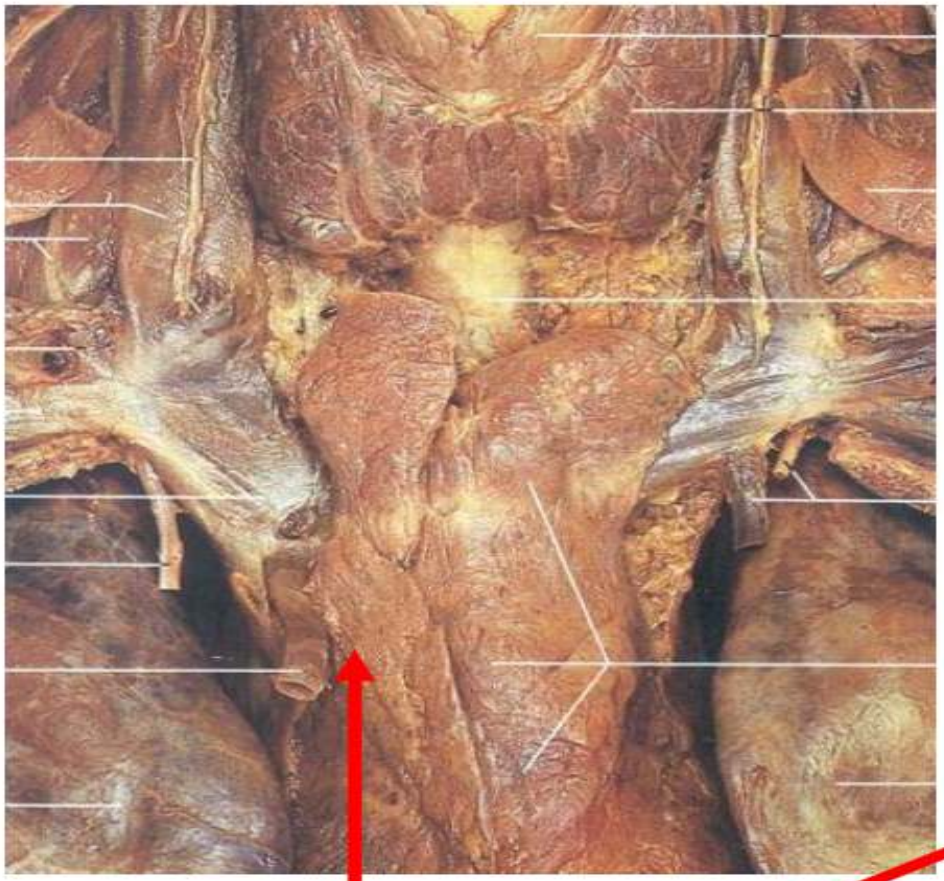

Androgens
INDIRECT ACTION
DIRECT ACTION
Bioactive androgens
Testosterone & DHT
Aromatizable androgens
Androstenedione → Estrone
↓ ↓
Testosterone → Estradiol
Nonaromatizable androgen
DHT
↓
3β-diol
Androgen receptor-mediated actions
Estrogen receptor-mediated actions
Androgen excess
Brain
Liver
Adipocytes
Muscle
Granulosa cells
Theca cells
AR
Sites of AR actions hypothesised to be driving AR-mediated generation of PCOS-like traits
PCOS-like traits observed to be fully or partially ameliorated by a loss of site-specific AR actions
- Ovulatory dysfunction
- Polycystic ovaries
- Adiposity
- Adipocyte hypertrophy
- Dyslipidemia
- Hepatic steatosis
At present unknown.
At present unknown.
At present unknown.
- Irregular cycles
- Granulosa cell degeneration
- Irregular cycles
- Ovulatory dysfunction
- Polycystic ovaries
- Granulosa cell degeneration

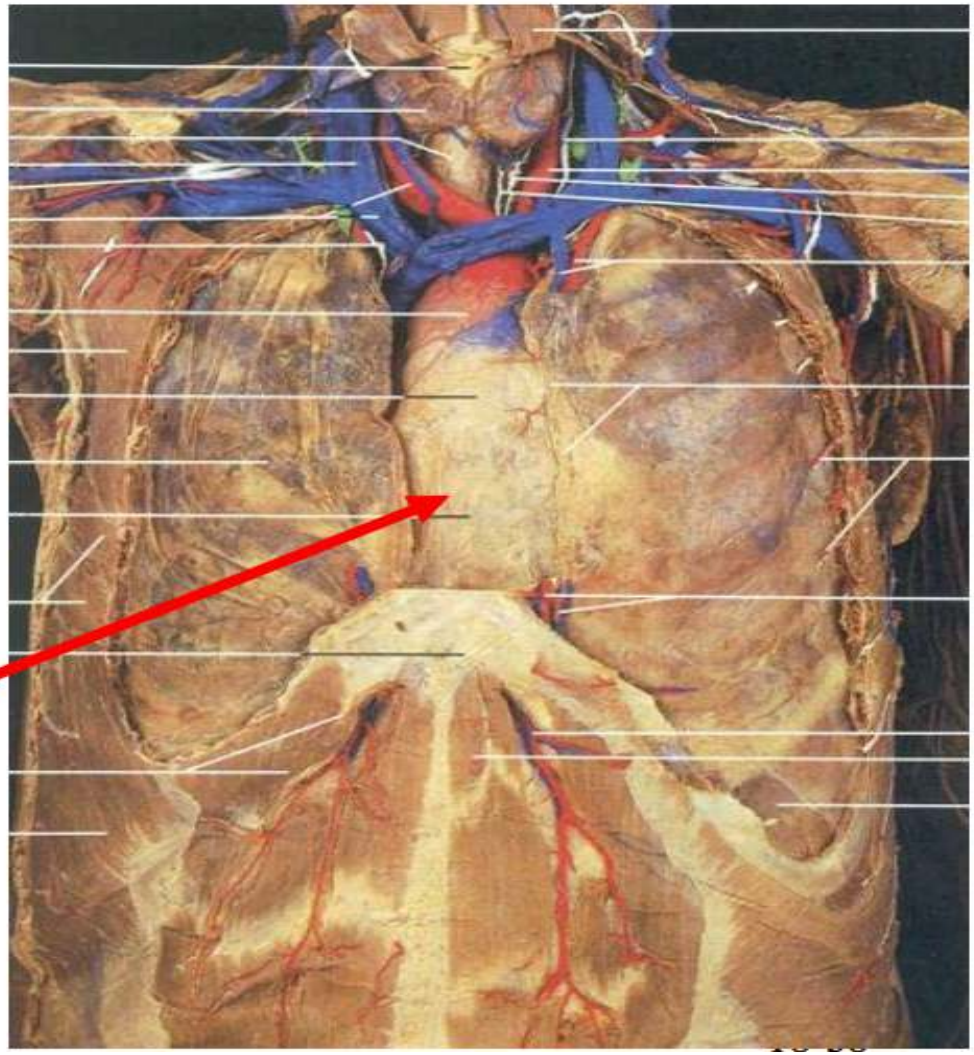
THYMUS GLAND

- Located in the upper thorax region.
- • Large in infants and children, it decreases in size throughout adult hood.
- • By old age, it is composed mostly of fibrous connective tissue and fat.
- • Thymus produces a hormone called **thymosin.**
- • During childhood, it acts as an incubator for the maturation of a special group of whiteblood cells(T lymphocytes or T cells)**.**
- • T cells are play a great role in immune response.



Adult THYMUS





Adult
THYMUS

- Many body organs not normally considered endocrine organs contain isolated cell clusters that secrete hormones.

- Examples include
  - the heart (atrial natriuretic peptide);
  - gastrointestinal tract organs (gastrin, secretin, and others);
  - the placenta (hormones of pregnancy—estrogen, progesterone, and others);
  - the kidneys (erythropoietin and renin);
  - the thymus; skin (cholecalciferol);
  - adipose tissue (leptin and resistin).
  - Bones