NOTES
ADRENAL HORMONES

SYNTHESIS OF ADRENOCORTICAL HORMONES

osms.it/adrenocortical-hormone-synthesis

- *Synthesized from cholesterol:* carbon skeleton, 21-carbon molecules; circulation supplies cholesterol which enters adrenal gland cells via endocytosis
  - Some synthesized *de novo* → both forms stored in cytoplasmic vesicles
- Cytochrome p450 using O_2, adrenodoxin reductase, adrenodoxin transfers H^+ from NADPH producing energy using reduction reactions
- Different enzymes found in different layers according to which hormones synthesized
- Cholesterol desmolase found in all layers
  - Rate-limiting step; stimulated by adrenocorticotropic hormone (ACTH); converts cholesterol to pregnolone
- Corticosteroid is common name for steroid hormones made in cortex: include mineralocorticoids, glucocorticoids

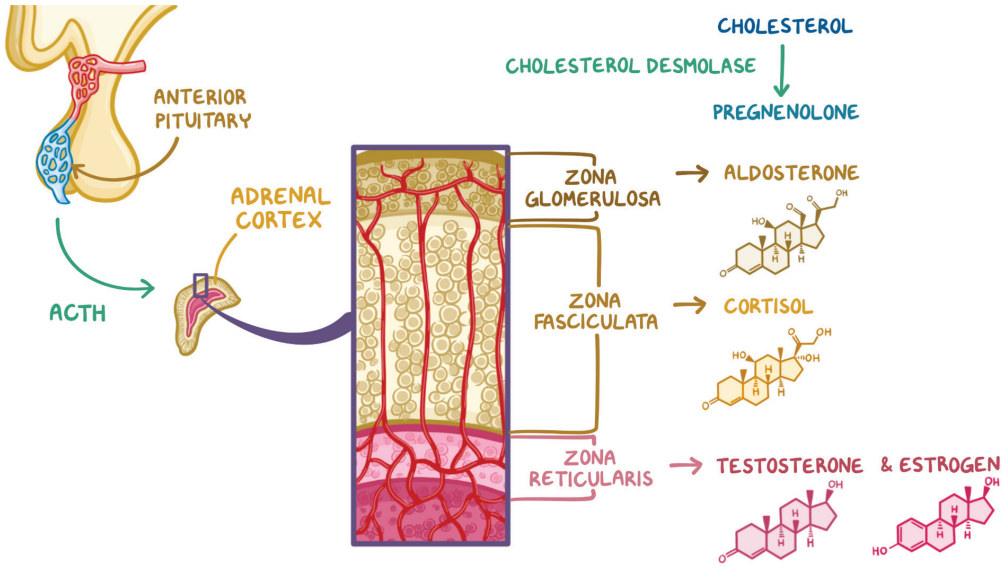

Figure 33.1 Three zones of adrenal cortex secrete steroid hormones under control of ACTH, which is released by anterior pituitary. Adrenal cortex cells first convert cholesterol to prognenolone using enzyme cholesterol desmolase. Prognenolone is then converted into aldosterone in zona glomerulosa, cortisol in zona fasciculata, and testosterone and estrogen in zona reticularis.

Mineralocorticoids

- Synthesized in zona glomerulosa
- *Example:* aldosterone
- Aldosterone synthase required and found only in zona glomerulosa, converts cortisone → aldosterone

Glucocorticoids

- Synthesized in zona fasciculata
- *Examples:* cortisol, corticosterone
- 17α-hydroxylase (if deficient corticosterone can be formed) → 3β-hydroxysteroid dehydrogenase → 21β- and 11β-hydroxylase

Androgens

- Synthesized in zona reticularis
- *Examples:* dehydroepiandrosterone (DHEA), androstenedione
- 17,20-lyase responsible for conversion of glucocorticoids into androgens
- DHEA, androstenedione have a weak androgenic effect
  - *Male:* converted to testosterone in testes
  - *Female:* main source of androgens
- Low quantity of testosterone, 17β-estradiol

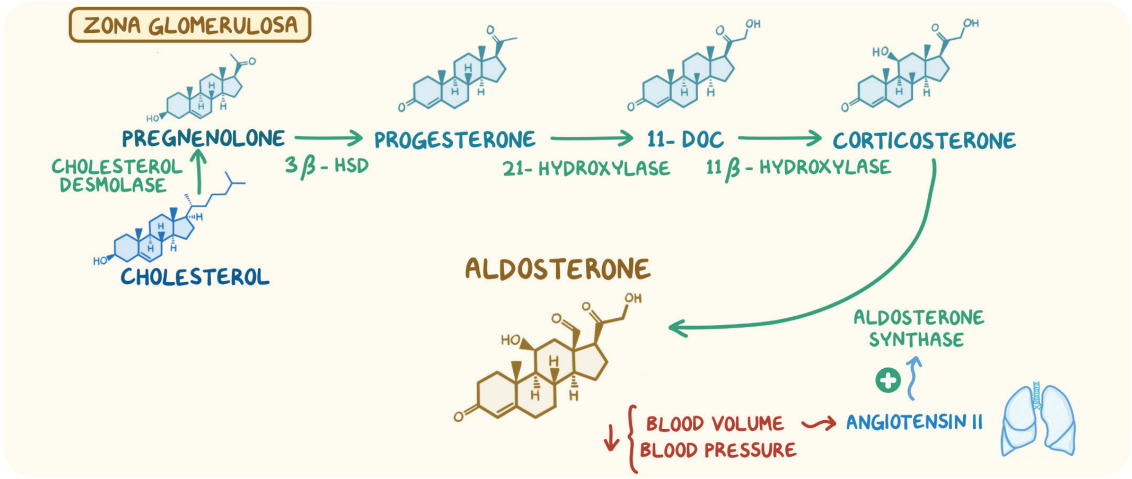

Figure 33.2 Aldosterone synthesis in zona glomerulosa. Aldosterone synthase is stimulated by hormone angiotensin II, which is produced in lungs in response to low blood pressure, volume.

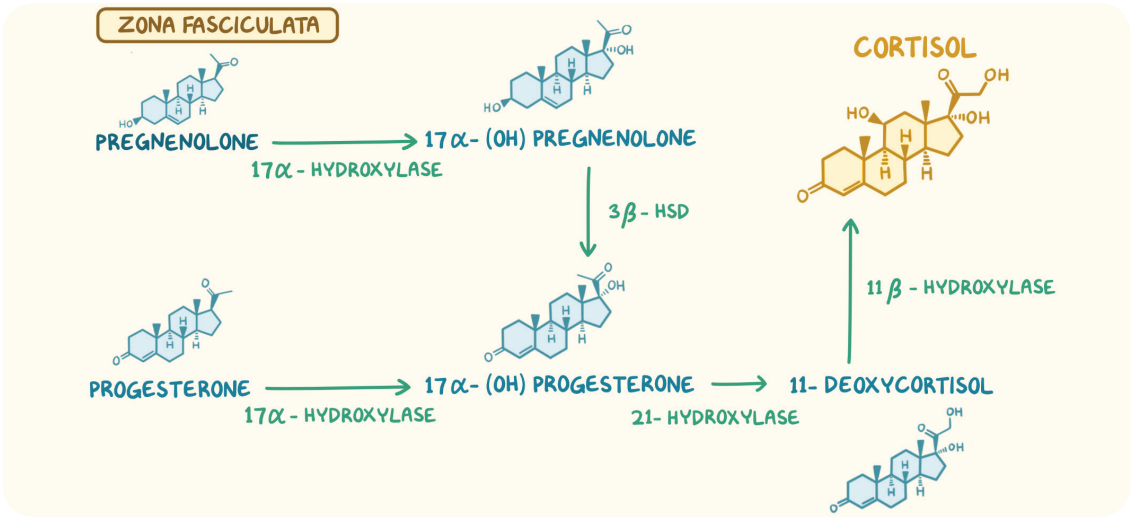

Figure 33.3 Cortisol synthesis in zona fasciculata.

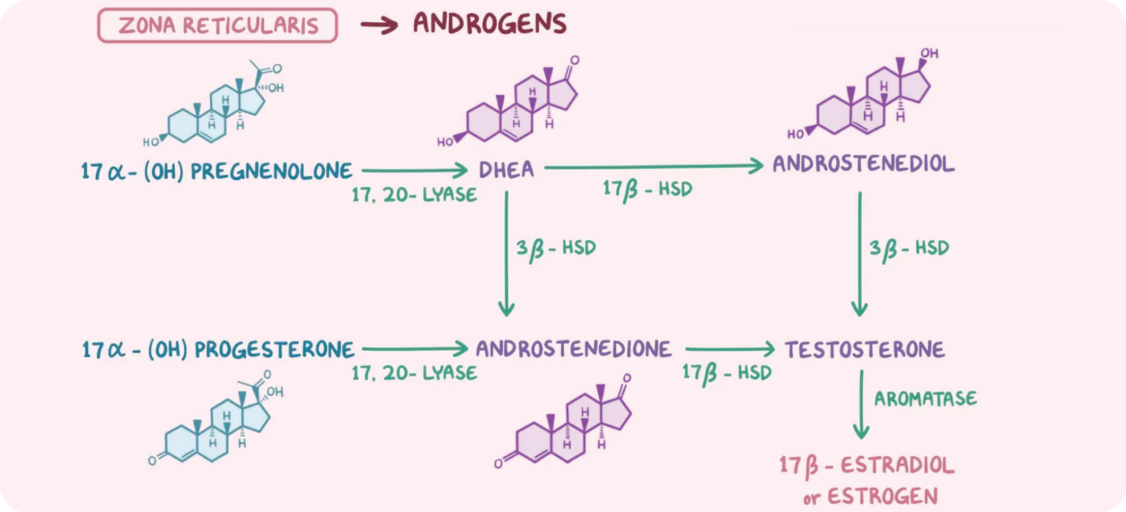

Figure 33.4 Androgen synthesis in zona reticularis.

CORTISOL

osms.it/cortisol

- Steroid glucocorticoid hormone secreted by adrenal cortex; has metabolic, anti-inflammatory, immunosuppressive, vascular effects
- Normal pulsatile secretion, approximately 10 surges in diurnal (daily) pattern
  - Concentration highest in morning, lowest in evening
  - *Diurnal pattern:* maintained by hypothalamic suprachiasmatic nucleus; acts as central pacemaker for hypothalamic-pituitary-adrenal (HPA) axis; adrenals maintain diurnal pattern of sensitivity to ACTH

Secretion regulation

- Stress (infection, trauma, initiation of "fight or flight" response, psychological stressors), ↑ sympathetic activity, physical activity, ↓ blood glucose → hypothalamus stimulated to release corticotropin-releasing hormone (CRH) → anterior pituitary releases adrenocorticotropic hormone (ACTH) → adrenal medulla secretes glucocorticoids (primarily cortisol) → target tissues
- Negative feedback of cortisol to hypothalamic-pituitary axis → ↓ cortisol

Major effects

- *Metabolic:* ↑ blood glucose (considered diabetogenic hormone) by ↑ hepatic glycogenolysis, ↑ lipolysis, ↑ protein catabolism, ↓ cellular insulin sensitivity, ↑ appetite
- *Immune:* ↓ intensity of immune, inflammatory responses by ↓ production of arachidonic acid metabolites (e.g. prostaglandin, thromboxane, leukotrienes), ↓ production of interleukins, interferon, tumor necrosis factor; ↓ T cell proliferation; ↓ neutrophil phagocytosis
- *Vascular:* involved in normal vascular blood pressure maintenance; supports vascular smooth muscle responsiveness to catecholamine vasoconstrictive effects
- *Other:* ↓ connective tissue fibroblast proliferation, ↓ bone formation, ↑ renal blood flow, ↑ erythropoietin release, alters sleep patterns

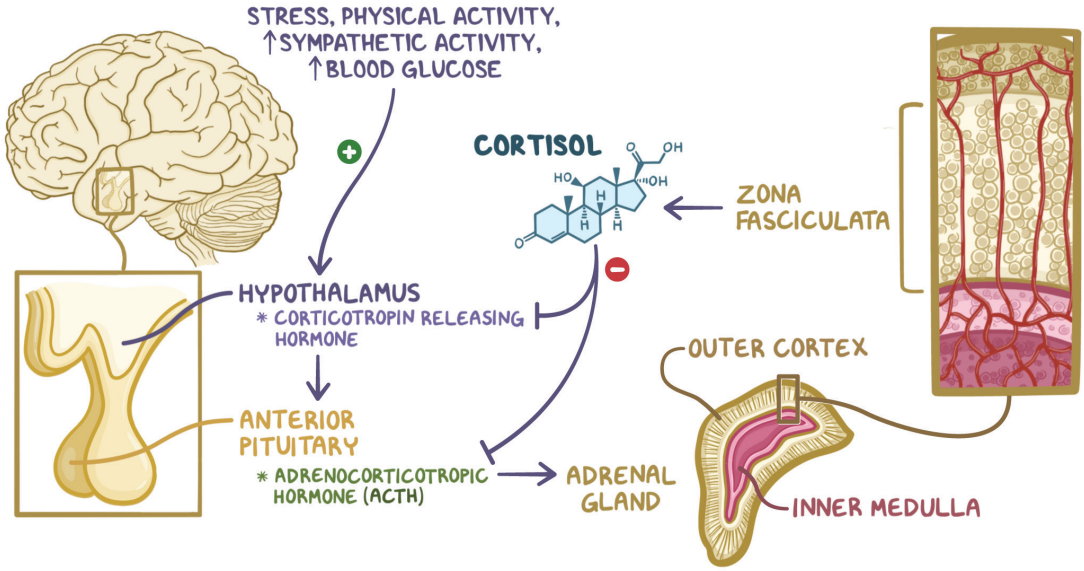

Figure 33.5 Cortisol secretion regulation.