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Adrenal Gland

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PHYSIOLOGY

The adrenal glands (Fig. 64-1) lie at the superior pole of each kidney and are composed of two distinct regions: the cortex and the medulla. The adrenal cortex comprises three anatomic zones: the outer *zona glomerulosa*, which secretes the mineralocorticoid aldosterone; the intermediate *zona fasciculata*, which secretes cortisol; and the inner *zona reticularis*, which secretes adrenal androgens. The adrenal medulla, lying in the center of the adrenal gland, is functionally related to the sympathetic nervous system and secretes the catecholamines epinephrine and norepinephrine in response to stress.

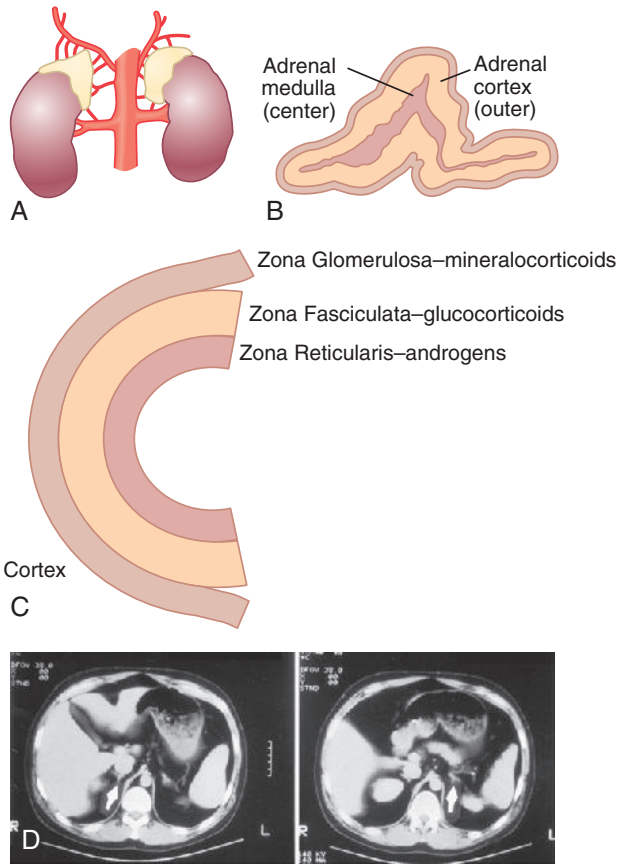

FIGURE 64-1 **A,** Anatomic location of the adrenal glands. **B,** Distribution of adrenal cortex and medulla. **C,** Zones of the adrenal cortex. **D,** Magnetic resonance images of the abdomen showing the position and relative size of the normal adrenal glands *(arrows)*. (**D,** From Nieman LK: Adrenal cortext. In Goldman L, Schafer AI, editors: Cecil-Goldman medicine, ed 24, Philadelphia, 2012, Saunders, Figure 234-1.)

The synthesis of all steroid hormones begins with cholesterol and is catalyzed by a series of regulated, enzyme-mediated reactions (Fig. 64-2). Glucocorticoids affect metabolism, cardiovascular function, behavior, and the inflammatory and immune responses (Table 64-1). Cortisol, the natural human glucocorticoid, is secreted by the adrenal glands in response to adrenocorticotropic hormone (ACTH), a 39-amino-acid neuropeptide that is regulated by corticotropin-releasing hormone (CRH) and vasopressin (AVP) produced in the hypothalamus (see Chapter 62). Glucocorticoids exert negative feedback on CRH and ACTH secretion. The brain hypothalamic-pituitary-adrenal (HPA) axis (Fig. 64-3) interacts with and influences the functions of the reproductive, growth, and thyroid axes at many levels, with major participation of glucocorticoids at all levels.

The renin-angiotensin-aldosterone system (Fig. 64-4) is the major regulator of aldosterone secretion. Renal juxtaglomerular cells secrete renin in response to a decrease in circulating volume or a reduction in renal perfusion pressure or both. Renin is the rate-limiting enzyme that cleaves the 60-kD angiotensinogen molecule, synthesized by the liver, to produce the bioinactive decapeptide angiotensin I. Angiotensin I is rapidly converted to the octapeptide angiotensin II by angiotensin-converting enzyme in the lungs and other tissues. Angiotensin II is a potent vasopressor; it stimulates aldosterone production but does not stimulate cortisol production. Angiotensin II is the predominant regulator of aldosterone secretion, but plasma potassium concentration, plasma volume, and ACTH level also influence aldosterone secretion. ACTH also mediates the circadian rhythm of aldosterone, and as a result, the plasma concentration of aldosterone is highest in the morning. Aldosterone binds to the type I mineralocorticoid receptor. In contrast, cortisol binds to both the type I mineralocorticoid receptor and type II glucocorticoid receptors. The intracellular enzyme 11β-hydroxysteroid dehydrogenase (11β-HSD) type II, which catabolizes cortisol to inactive cortisone, limits the functional binding to the former receptor. The availability of cortisol to bind to the glucocorticoid receptor is modulated by 11β-HSD type I, which interconverts cortisol and cortisone. Binding of aldosterone to the cytosol mineralocorticoid receptor leads to sodium (Na^+) absorption and potassium (K^+) and hydrogen (H^+) secretion by the renal tubules. The resultant increase in plasma Na^+ and decrease in plasma K^+ provide a feedback mechanism for suppressing renin and, subsequently, aldosterone secretion.

Adrenal androgen precursors include dehydroepiandrosterone (DHEA) and its sulfate and androstenedione. These are synthesized in the zona reticularis under the influence of ACTH and other adrenal androgen-stimulating factors. Although they