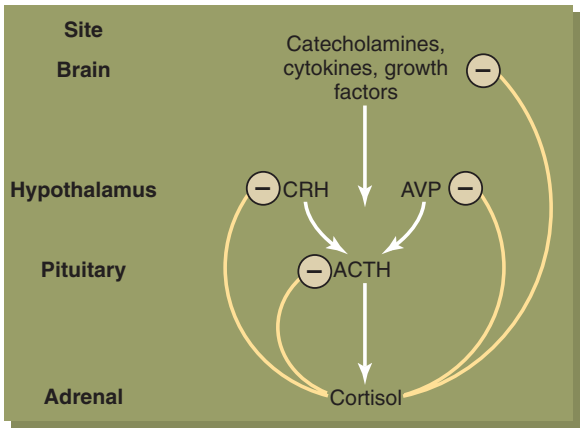

FIGURE 64-3 Brain hypothalamic-pituitary-adrenal axis. Minus signs indicate negative feedback. ACTH, Adrenocorticotropic hormone; AVP, arginine vasopressin; CRH, corticotropin-releasing hormone.

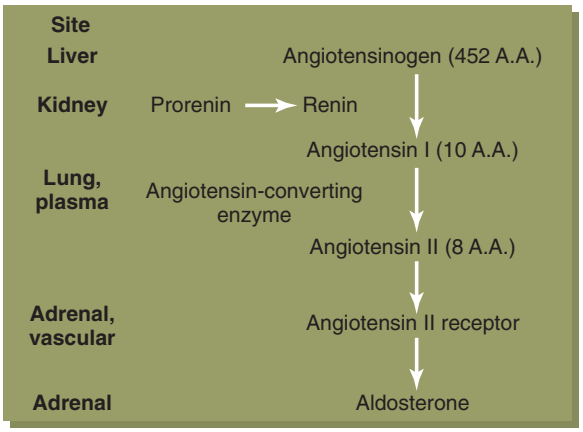

FIGURE 64-4 Renin-angiotensin-aldosterone axis. A.A., Amino acids.

TABLE 64-1 ACTIONS OF GLUCOCORTICOIDS

METABOLIC HOMEOSTASIS
Regulate blood glucose level (permissive effects on gluconeogenesis)
Increase glycogen synthesis
Raise insulin levels (permissive effects on lipolytic hormones)
Increase catabolism, decrease anabolism (except fat), inhibit growth hormone axis
Inhibit reproductive axis
Stimulate mineralocorticoid receptor by cortisol
CONNECTIVE TISSUES
Cause loss of collagen and connective tissue
CALCIUM HOMEOSTASIS
Stimulate osteoclasts, inhibit osteoblasts
Reduce intestinal calcium absorption, stimulate parathyroid hormone release, increase urinary calcium excretion, decrease reabsorption of phosphate
CARDIOVASCULAR FUNCTION
Increase cardiac output
Increase vascular tone (permissive effects on pressor hormones)
Increase sodium retention
BEHAVIOR AND COGNITIVE FUNCTION
Daytime fatigue
Nocturnal hyperarousal
Decreased short-term memory
Decreased cognition
EUPHORIA OR DEPRESSION
IMMUNE SYSTEM
Increase intravascular leukocyte concentration
Decrease migration of inflammatory cells to sites of injury
Suppress immune system (thymolysis; suppression of cytokines, prostanoids, kinins, serotonin, histamine, collagenase, and plasminogen activator)

(initially most significant on the extensor surfaces, palmar creases, and buccal mucosa) often occur secondary to the increased production of ACTH and other related peptides by the pituitary gland (E-Fig. 64-1). Laboratory abnormalities may include hyponatremia, hyperkalemia, mild metabolic acidosis, azotemia, hypercalcemia, anemia, lymphocytosis, and eosinophilia. Hypoglycemia may also occur, especially in children.

Acute adrenal insufficiency is a medical emergency, and treatment should not be delayed pending laboratory results. In a critically ill patient with hypovolemia, a plasma sample for cortisol, ACTH, aldosterone, and renin should be obtained, and then treatment with hydrocortisone (100 mg IV bolus) and parenteral saline administration should be initiated. Sepsis-induced adrenal insufficiency is recognized by a basal cortisol level lower than 10 µg/dL or a change in cortisol of less than 9 µg/dL after administration of 0.25 mg ACTH (1-24) (cosyntropin). In severe illness, albumin and cortisol-binding globulin (CBG) are low, resulting in a low level of total cortisol but not free cortisol; therefore, a low total cortisol level may not be diagnostic of adrenal insufficiency in this setting.

In a patient with chronic symptoms suggestive of adrenal insufficiency, a basal morning plasma cortisol measurement or a 1-hour cosyntropin test, or both, should be performed. In the latter test, 0.25 mg of cosyntropin is given intravenously or intramuscularly, and plasma cortisol is measured after 0, 30, and 60 minutes. A normal response is a plasma cortisol concentration higher than 20 µg/dL at any time during the test. A patient with a basal morning plasma cortisol concentration lower than 5 µg/dL and a stimulated cortisol concentration lower than 18 µg/dL probably has adrenal insufficiency and should receive treatment. A basal plasma morning cortisol concentration between 10 and 18 µg/dL in association with a stimulated cortisol concentration lower than 18 µg/dL probably indicates impaired adrenal reserve and a requirement for receiving cortisol replacement under stress conditions (see later discussion).

Once the diagnosis of adrenal insufficiency is made, the distinction between primary and secondary adrenal insufficiency needs to be established. Secondary adrenal insufficiency results from inadequate stimulation of the adrenal cortex by ACTH (see Chapter 62). Hyperpigmentation does not occur. In addition, because mineralocorticoid levels are normal in secondary adrenal insufficiency, symptoms of salt craving, as well as the laboratory abnormalities of hyperkalemia and metabolic acidosis, are not present, although hyponatremia may be observed. Hypothyroidism, hypogonadism, and growth hormone deficiency may also be present. To distinguish primary from secondary adrenal insufficiency, a basal morning plasma ACTH value should be obtained, along with a standing (upright for at least 2 hours) serum aldosterone level and a measurement of plasma renin activity (PRA). A plasma ACTH value greater than 20 pg/mL (normal, 5 to 30 pg/mL) is consistent with primary adrenal insufficiency, whereas a value lower than 20 pg/mL probably represents