Through its effects on the renal mineralocorticoid receptor, aldosterone promotes sodium reabsorption, which secondarily increases the reabsorption of water, expanding the extracellular fluid volume and elevating cardiac output.

The long-term effects of hyperaldosteronism-induced hypertension are cardiovascular compromise (e.g., left ventricular hypertrophy and reduced diastolic volumes) and an increase in the prevalence of adverse events such as stroke and myocardial infarction. *Hypokalemia* was considered a mandatory feature of primary hyperaldosteronism, but increasing numbers of normokalemic patients are now diagnosed. Hypokalemia results from renal potassium wasting and, when present, can cause a variety of neuromuscular manifestations, including weakness, paresthesias, visual disturbances, and occasionally frank tetany.

The diagnosis of primary hyperaldosteronism is confirmed by elevated ratios of plasma aldosterone concentration to plasma renin activity; if this screening test is positive, a confirmatory *aldosterone suppression test* must be performed, because many unrelated causes can alter the plasma aldosterone and renin ratios.

In primary hyperaldosteronism, the therapy varies according to cause. Adenomas are amenable to surgical excision. In contrast, surgical intervention is not very beneficial in patients with primary hyperaldosteronism due to bilateral hyperplasia, which often occurs in children and young adults. These patients are best managed medically with an aldosterone antagonist such as spironolactone. The treatment of secondary hyperaldosteronism rests on correcting the underlying cause stimulating the renin-angiotensin system.

Adrenogenital Syndromes

Disorders of sexual differentiation, such as *virilization* or *feminization*, can be caused by primary gonadal disorders (Chapter 22) and several primary adrenal disorders. The adrenal cortex secretes two compounds—dehydroepiandrosterone and androstenedione—that can be converted to testosterone in peripheral tissues. Unlike gonadal androgens, ACTH regulates adrenal androgen formation (Fig. 24-46); thus, excess secretion can occur either as a "pure" syndrome or as a component of Cushing disease. The adrenal causes of androgen excess include *adrenocortical neoplasms* and a group of disorders that have been designated *congenital adrenal hyperplasia (CAH)*.

Adrenocortical neoplasms associated with virilization are more likely to be *androgen-secreting adrenal carcinomas* than adenomas. Such tumors are often also associated with hypercortisolism ("mixed syndrome"). They are

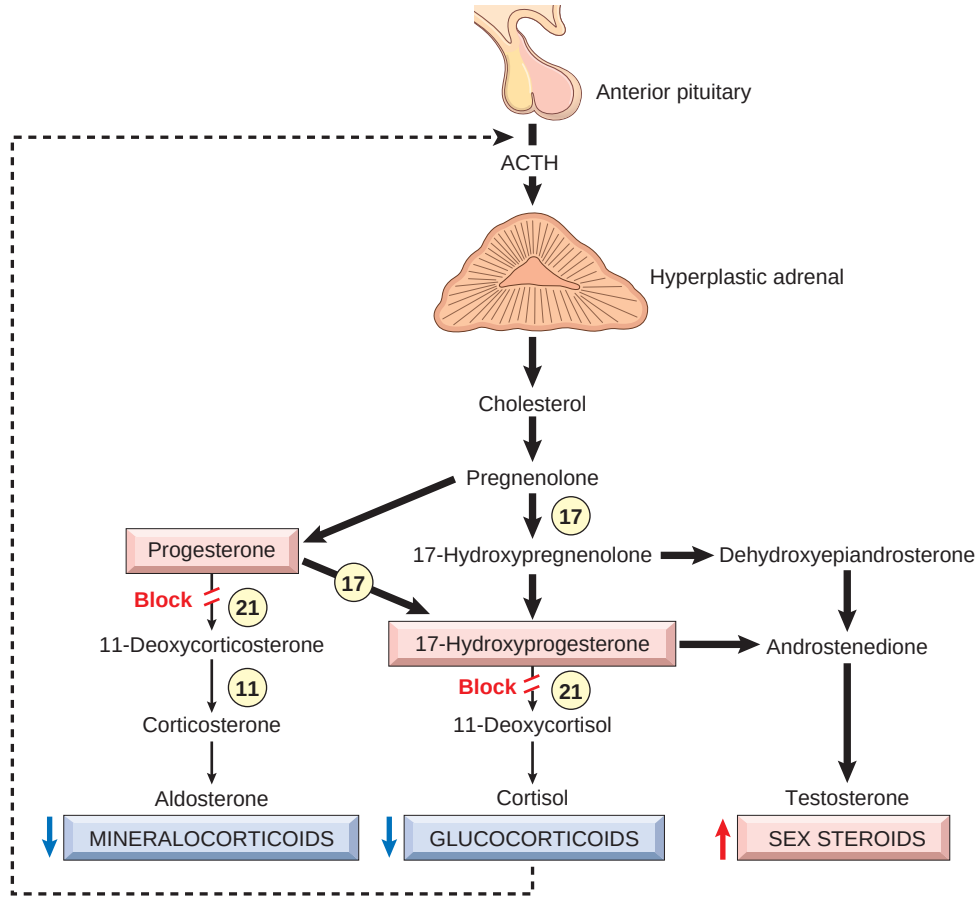

Figure 24-46 Consequences of C-21 hydroxylase deficiency. 21-Hydroxylase deficiency impairs the synthesis of both cortisol and aldosterone at different steps (shown as "Block" in the biosynthesis pathway). The resultant decrease in feedback inhibition *(dashed line)* causes increased secretion of ACTH, resulting ultimately in adrenal hyperplasia and increased synthesis of testosterone. The sites of action of 11-, 17-, and 21-hydroxylase are shown by the numbers in circles.