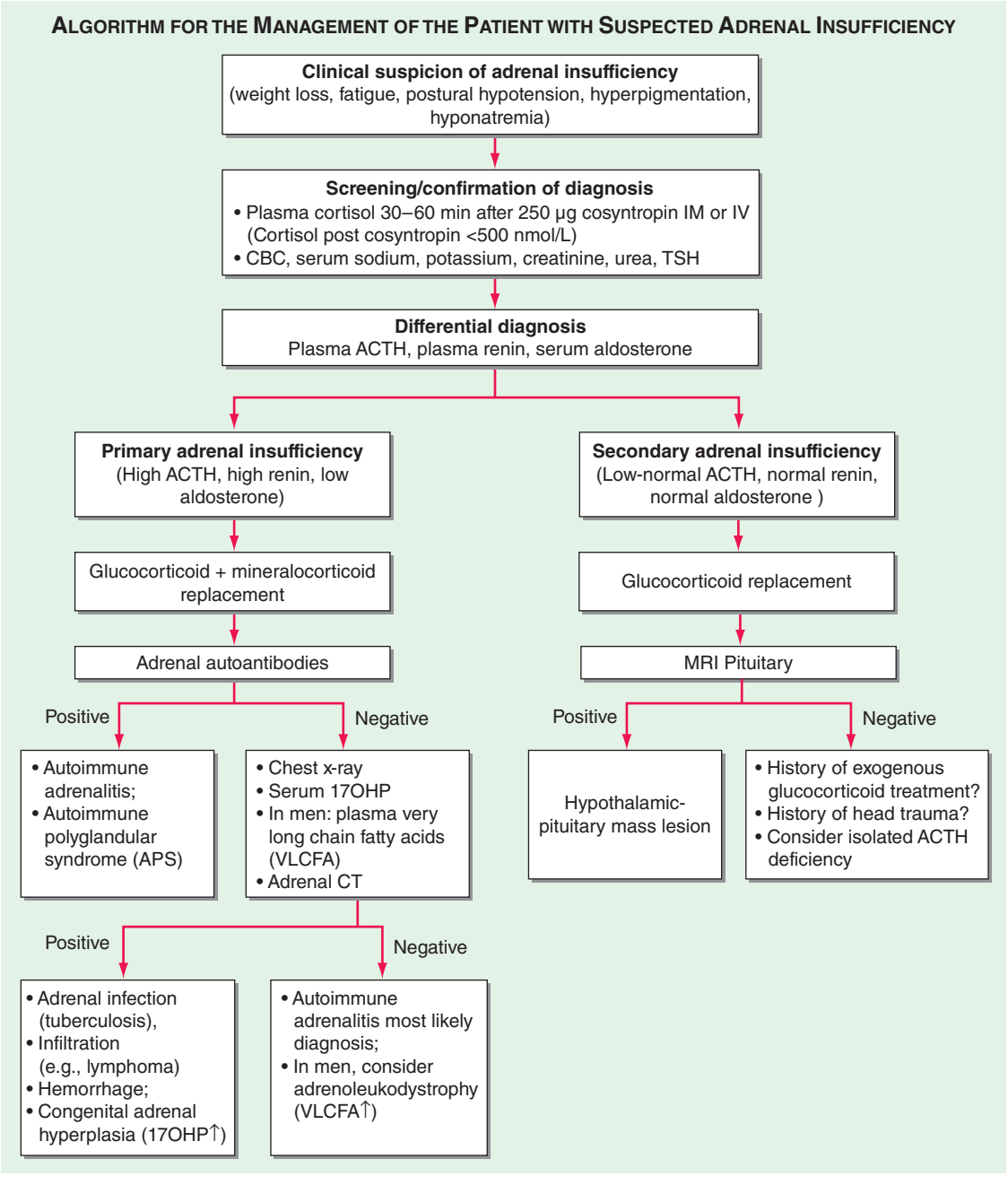

FIGURE 406-16 **Management of the patient with suspected adrenal insufficiency.** ACTH, adrenocorticotropic hormone; CBC, complete blood count; MRI, magnetic resonance imaging; PRA, plasma renin activity; TSH, thyroid-stimulating hormone.

Plasma renin cannot serve as a monitoring tool during pregnancy, because renin rises physiologically during gestation.

Adrenal androgen replacement is an option in patients with lack of energy, despite optimized glucocorticoid and mineralocorticoid replacement. It may also be indicated in women with features of androgen deficiency, including loss of libido. Adrenal androgen replacement can be achieved by once-daily administration of 25–50 mg DHEA. Treatment is monitored by measurement of DHEAS, androstenedione, testosterone, and sex hormone–binding globulin (SHBG) 24 h after the last DHEA dose.

CONGENITAL ADRENAL HYPERPLASIA

(See also Chap. 410) Congenital adrenal hyperplasia (CAH) is caused by mutations in genes encoding steroidogenic enzymes involved in glucocorticoid synthesis (*CYP21A2, CYP17A1, HSD3B2, CYP11B1*) or in the cofactor enzyme P450 oxidoreductase that serves as an electron donor to CYP21A2 and CYP17A1 (Fig. 406-1). Invariably, patients affected by CAH exhibit glucocorticoid deficiency. Depending on the exact step of enzymatic block, they may also have excess production of mineralocorticoids or deficient production of sex steroids (Table 406-10). The diagnosis of CAH is readily established by measurement of the steroids accumulating before the distinct enzymatic block, either in serum or in urine, preferably by the use of mass spectrometry–based assays (Table 406-10).

Mutations in *CYP21A2* are the most prevalent cause of CAH, responsible for 90–95% of cases. 21-Hydroxylase deficiency disrupts glucocorticoid and mineralocorticoid synthesis (Fig. 406-1), resulting in diminished negative feedback via the HPA axis. This leads to increased pituitary ACTH release, which drives increased synthesis of adrenal androgen precursors and subsequent androgen excess. The degree of impairment of glucocorticoid and mineralocorticoid secretion depends on the severity of mutations. Major loss-of-function mutations result in combined glucocorticoid and mineralocorticoid deficiency (classic CAH, neonatal presentation), whereas less severe mutations affect glucocorticoid synthesis only (simple virilizing CAH, neonatal or early childhood presentation). The mildest mutations result in the least severe clinical phenotype, nonclassic CAH, usually