

2316 may also occur. Even after cure, long-term health may be affected by persistently impaired health-related quality of life and increased risk of cardiovascular disease and osteoporosis with vertebral fractures, depending on the duration and degree of exposure to significant cortisol excess.

Diagnosis The most important first step in the management of patients with suspected Cushing's syndrome is to establish the correct diagnosis. Most mistakes in clinical management, leading to unnecessary imaging or surgery, are made because the diagnostic protocol is not followed (Fig. 406-10). This protocol requires establishing the diagnosis of Cushing's beyond doubt prior to employing any tests used for the differential diagnosis of the condition. In principle, after excluding exogenous glucocorticoid use as the cause of clinical signs and symptoms, suspected cases should be tested if there are multiple and progressive features of Cushing's, particularly features with a potentially higher discriminatory value. Exclusion of Cushing's is also indicated in patients with incidentally discovered adrenal masses.

A diagnosis of Cushing's can be considered as established if the results of several tests are consistently suggestive of Cushing's. These tests may include increased 24-h urinary free cortisol excretion in three separate collections, failure to appropriately suppress morning cortisol after overnight exposure to dexamethasone, and evidence of loss of diurnal cortisol secretion with high levels at midnight, the time of the physiologically lowest secretion (Fig. 406-10). Factors potentially affecting the outcome of these diagnostic tests have to be excluded such as incomplete 24-h urine collection or rapid inactivation of dexamethasone due to concurrent intake of CYP3A4-inducing drugs (e.g., antiepileptics, rifampicin). Concurrent intake of oral contraceptives that raise CBG and thus total cortisol can cause failure to suppress after dexamethasone. If in doubt, testing should be repeated after 4–6 weeks off estrogens. Patients with pseudo-Cushing states, i.e., alcohol-related, and those with cyclic Cushing's may require further testing to safely confirm or exclude the diagnosis of Cushing's. In addition, the biochemical assays employed can affect the test results, with specificity representing a common problem with antibody-based

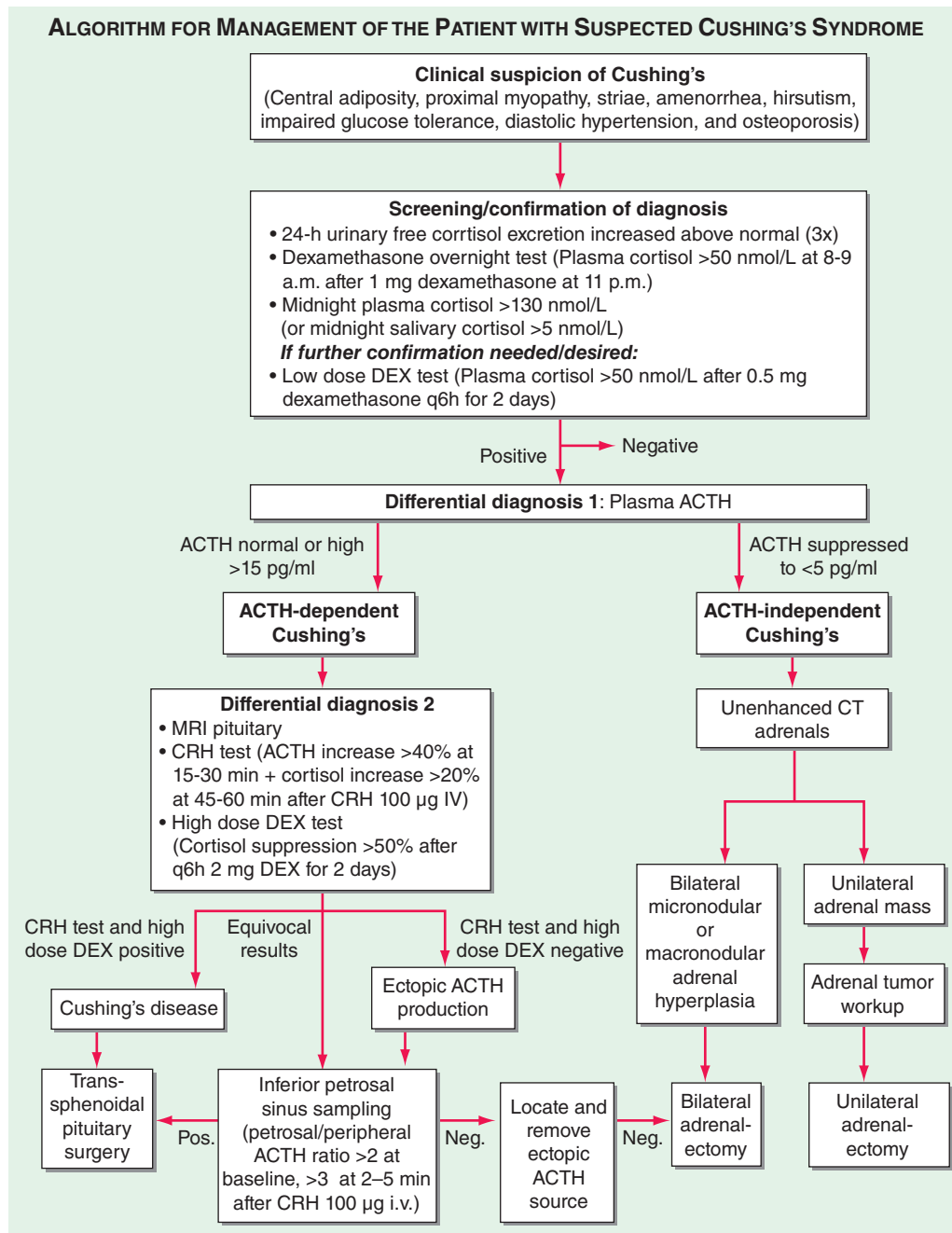


FIGURE 406-10 Management of the patient with suspected Cushing's syndrome. ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; CT, computed tomography; DEX, dexamethasone; MRI, magnetic resonance imaging.