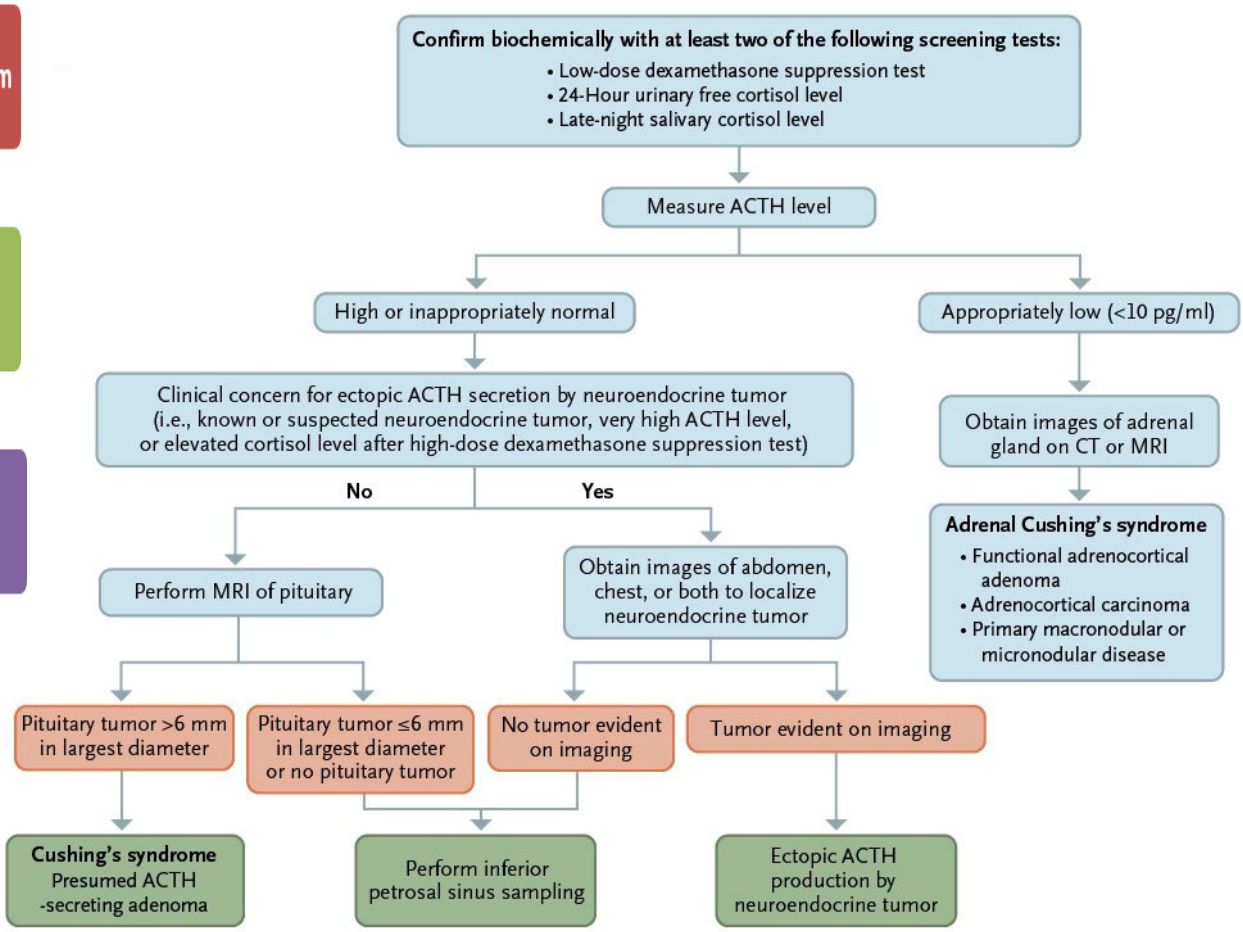
Cushing's Syndrome

1) Confirm Hypercortisolism

2) Assess if ACTH-Dependent

3) Localize Lesion



Treatment of Ectopic Cushing's Syndrome

Medication	Mechanisms	Comments*
Metyrapone	Inhibits 11β-hydroxylase, an enzyme responsible for the final step in cortisol synthesis	May cause abdominal discomfort and nausea
Ketoconazole	Is best known as an antifungal agent but can be used off-label to inhibit cortisol synthesis	• Has a black-box warning for hepatotoxicity • Is contraindicated in patients with aminotransferase levels more than three times as high as the upper limit of the normal range
Levoketoconazole	Is a stereoisomer of ketoconazole that inhibits cortisol synthesis	• Is associated with hepatotoxicity and prolongation of the corrected QT interval • Unlike ketoconazole, does not have a black-box warning
Etomidate	• Is best known as a general anesthetic but can be used off-label for severe hypercortisolemia (inhibits 11β-hydroxylase) • Is administered as a continuous intravenous infusion • Has a rapid onset of action	• Is associated with the risk of sedation • Requires intravenous administration • Requires close monitoring in the intensive care unit
Mitotane	• Is typically used as chemotherapy for adrenocortical cancer • Can suppress adrenocortical hormone production	• Has a black-box warning for adrenal crisis • Has toxic effects that can include hepatotoxicity, nausea, diarrhea, hyperlipidemia, ataxia, and bone marrow suppression • May induce cytochrome P-450 3A4 (CYP3A4) activity, leading to interaction with other medications
Mifepristone	Is a progesterone and glucocorticoid-receptor antagonist	• Is associated with hypokalemia and hypertension • Is associated with endometrial thickening
Osilodrostat	Inhibits 11β-hydroxylase, the enzyme responsible for the final step in cortisol synthesis	Also inhibits aldosterone synthase