Diagnosis of Cushing's Syndrome

Who to test, initial screening, result interpretation, and testing in special populations.

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Diagnosis of Cushing's Syndrome Guideline
Nieman et al. · JCEM 2008;93:1526-1540

GRADE · 1 · Strong · 2 · Suggest For · 2- · Suggest Against · Ungraded / Best Practice

1 Who to Test

1 Obtain a **thorough drug history** to exclude exogenous glucocorticoid exposure before any biochemical testing.

1 Test for Cushing's syndrome in: **unusual features for age** (e.g., osteoporosis, hypertension in the young); **multiple/progressive** features; children with **falling height percentile + rising weight**; or an **adrenal incidentaloma** compatible with adenoma.

1 **Against** widespread testing in any other patient group.

2 Initial Testing

1 Choose **one** initial test based on suitability: **24h urine free cortisol** (≥2 measurements), **late-night salivary cortisol** (2 measurements), **1 mg overnight DST**, or a **longer low-dose DST** (2 mg/d × 48h).

1 **Against** random serum cortisol or plasma ACTH, urinary 17-ketosteroids, insulin tolerance test, loperamide test, or cause-directed tests (pituitary/adrenal imaging, 8 mg DST) for initial screening.

3 Interpreting Results

1 **Normal result + high pretest probability** (incidentaloma, suspected cyclic disease): refer to endocrinology for further evaluation. **Any abnormal result:** refer to endocrinology to confirm/exclude.

2 **Normal result + low pretest probability:** re-evaluate in 6 months only if signs/symptoms progress.

1 **Subsequent testing:** repeat with another recommended test; dexamethasone-CRH test or midnight serum cortisol in specific situations. **Against** the desmopressin test outside research settings.

2 **Concordant abnormal** results → evaluate for cause; **concordant normal** → stop evaluation. **Discordant results** or suspected cyclic disease with high pretest probability → further evaluation and follow-up.

4 Special Populations

POPULATION	PREFERRED APPROACH
Pregnancy	Use UFC; **against** dexamethasone testing for initial evaluation
Epilepsy (enzyme-inducing AEDs)	**Against** dexamethasone testing (accelerated clearance) — use nonsuppressed cortisol in blood, saliva, or urine instead
Severe renal failure	1 mg overnight DST preferred over UFC for initial testing
Suspected cyclic Cushing's	UFC or midnight salivary cortisol preferred over DSTs
Adrenal incidentaloma (mild CS suspected)	1 mg DST or late-night cortisol preferred over UFC

Nieman LK, Biller BM, Findling JW, et al. The Diagnosis of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2008;93(5):1526-1540.