

Initial testing for Cushing's syndrome

The three tests that are useful in the initial evaluation of suspected Cushing's syndrome are late night salivary cortisol (twice), 24-hour urine free cortisol (UFC) (twice), and the overnight dexamethasone suppression test (ONDST). Late night salivary cortisol is a good first choice and convenient for the patient. Measurement of morning or random serum cortisol is unable to exclude the diagnosis and should not be used.

If Cushing's syndrome is suspected (patients with possible secondary hypertension, osteoporosis, or classic features such as fat redistribution, proximal myopathy, easy bruising, facial plethora or red/purple striae), measurement of morning or random serum cortisol is unable to exclude the diagnosis. In Cushing's syndrome, daytime serum concentrations of cortisol are often "normal" (i.e. within the reference interval), but the expected night-time drop in concentration is lost. The main utility of morning serum cortisol measurement is in ruling out adrenal insufficiency.

The three tests that are useful in the initial evaluation of suspected Cushing's syndrome are late night salivary cortisol, 24-hour urine free cortisol (UFC), and the overnight dexamethasone suppression test (ONDST). If suspicion is high, two different tests should be performed. If it is low, two negative LNSC results, two negative UFC results, or one negative ONDST result is generally sufficient to rule out the diagnosis.

Late night salivary cortisol is an excellent first choice and is convenient for the patient. As requesting doctor, simply provide the patient with two forms requesting "late night salivary cortisol." The collection centre provides the collection devices (Salivette®) to the patient, along with written instructions. At 11 pm, the patient removes a small swab from the device, holds it in their mouth for two minutes then places it back into the device.

If done on two consecutive evenings, the patient can return both collection devices to the collection centre during business hours, provided that they are kept in a refrigerator at home in the interim.

If 24-hour urine free cortisol is chosen as the initial test, the collection canisters and instructions are provided by the collection centre. As this test measures the total free cortisol excreted in urine across a 24-hour period, it is less susceptible to altered sleep-wake cycles than LNSC. Therefore, it may be a better choice for shift-workers.

The overnight dexamethasone suppression test also only requires the name of the test to be written on the form. Western Diagnostic Pathology will provide 1 mg oral dexamethasone to the patient, with instructions to take it at 11 pm and return to the collection centre the following morning at 8 am for the blood test. This test is preferable for excluding autonomous cortisol secretion in patients with adrenal incidentalomas. However, false-positive results can be caused by oestrogens (including the combined oral contraceptive pill); medications that accelerate the metabolism of dexamethasone, such as some anticonvulsants; and mis-timing of the dexamethasone dose in relation to the blood test.

Referral to an endocrinologist for further investigation is usually indicated for patients with abnormal results of the above tests.

Our chemical pathologists are available by telephone to provide further advice on testing and result interpretation:

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Further reading

Nieman LK, Biller BMK, Findling JW et al. The diagnosis of Cushing's syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2008; 93: 1526-40 (Available from:

<https://academic.oup.com/jcem/article/93/5/1526/2598096>)