What is Cushing’s Syndrome?

- Cushing’s Syndrome is a condition where the body has too much cortisol. It can be caused by taking replacement cortisol in excess of what your body can use, or from your body producing too much cortisol.
- Adrenal, pituitary, or ectopic tumors can cause the body to produce too much cortisol. When a pituitary tumor causes overproduction of adrenocorticotropic hormone, ACTH, it’s called Cushing’s Disease. ACTH signals the adrenal glands to produce cortisol.
- Surgery to correct Cushing’s Syndrome can cause adrenal insufficiency.
- The three most common tests used to diagnose Cushing’s syndrome are the 24-hour urinary free cortisol test, measurement of midnight plasma cortisol or late-night salivary cortisol, and the low-dose dexamethasone suppression test.

What is Adrenal Insufficiency?

- Adrenal insufficiency, (AI) happens when the adrenal glands don’t produce enough cortisol. There are over 60 different causes of AI, including autoimmune, head injury, and steroid treatment for another condition.
- AI is life-threatening because cortisol is essential to maintain many basic body functions, such as blood pressure and heart rate. Most adrenal insufficient patients are dependent on cortisol replacement for life.
- The non-specific symptoms of AI, such as nausea, fatigue, and pain are often mistaken for other conditions.
Testing for Adrenal Insufficiency

- Initial testing for adrenal insufficiency can be simple and labs ordered by any physician.
- The morning cortisol and the baseline ACTH sampled and interpreted together, should indicate the direction for further testing and/or referral to a specialist.
- The ACTH stimulation test is often ordered first. It is important to request that the baseline ACTH is sampled BEFORE the injection.
- If the problem originates in the pituitary or hypothalamus, it can go undetected by the ACTH stim test alone, leading to misdiagnosis.

Tests used to evaluate the HPA axis

- The morning serum cortisol checks baseline adrenal cortisol production. It should be drawn between 8 and 9am.
- The baseline ACTH test evaluates pituitary corticotropin, (ACTH) production. It should be drawn simultaneously with the morning cortisol sample.
- The ACTH stimulation test evaluates stimulated adrenal cortisol response. This test is used to confirm or exclude PAI if the baseline cortisol result is indeterminate. Lack of appropriate response may indicate adrenal atrophy in chronic SAI patients. Adequate response to the ACTH stimulation test does not eliminate the possibility of secondary or tertiary AI.
- The Overnight Metyrapone and the Insulin Tolerance Test (ITT), are used to measure stimulated pituitary ACTH production if SAI or TAI is suspected. Choice of which test to use is based on patient profile. Current recommendations favor the Overnight Metyrapone. It is more accurate, less expensive, and easier to administer than the ITT.

Pre-testing considerations

The following hormones or drugs may interfere with accurate test results.

- Glucocorticoids or corticosteroids in any form, including topical, inhaled, injected, and oral tablets/capsules.
- Birth control or other estrogens, including soybean food products and menopause formulas.
- Drugs that inhibit cortisol biosynthesis, such as etomidate, ketoconazole, fluconazole, metyrapone, and suramin.
- Drugs that accelerate the metabolism of cortisol and most synthetic glucocorticoids by inducing hepatic mixed-function oxygenase enzymes, such as phenytoin, barbiturates, mitotane, and rifampin.
- High dose progestins or chronic administration of opiates.

Recommended times for discontinuing steroids before testing are 12 hours for Hydrocortisone, 24 hours for Prednisone.

Dexamethasone is commonly prescribed for patients suspected of adrenal insufficiency who require testing to confirm the diagnosis. It is not read by radioimmunoassay, the most common type of lab test for cortisol. This is an accurate way to assess HPA axis function provided that testing is done within the first two weeks of treatment. After this time period Dexamethasone will begin to suppress HPA axis function.

For more information on testing after HPA axis suppression has occurred, please see our "Glucocorticoid tapering and adrenal suppression testing guide" in the research library at www.adrenalinsufficiency.org.