

Cushing's Syndrome

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June, 2010

Major **A**spects of **G**rowth **I**n **C**hildren

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Cushing's Syndrome



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Introduction

Cushing's syndrome (CS) is a hormonal disorder caused by high levels of the hormone cortisol. The most common cause of CS is excess steroid medications. Otherwise, CS is caused by growths (tumors) in the body.

What are the Signs and Symptoms?

- Change in fat distribution, with more fat in the upper body, such as a rounded face, increased fat around the neck, a large abdomen, and thinning arms and legs.
- The skin becomes fragile and thin, with easy bruising and poor healing. Purplish pink stretch marks called striae may appear.
- Women may have excessive hair growth.
- The bones are weakened due to osteoporosis, resulting in risk of fracture.
- Changes in mood, including fatigue, irritability, anxiety and depression.
- Hypertension and diabetes
- Changes in the menstrual cycle in women. Men may describe diminished sexual libido and performance.

How is Cushing's Syndrome Diagnosed?

Demonstration of an elevated cortisol (called hypercortisolism)

- *24-Hour Urinary Free Cortisol Level:* An elevated urinary cortisol level from a 24-hour collection suggests CS. Usually, this test needs to be repeated several times.
- *1 mg overnight dexamethasone suppression test:* In this test, the patient takes 1 mg of dexamethasone orally at midnight, and a fasting cortisol is drawn at 8AM the next day. An elevated morning cortisol is suggestive of CS.

- *Salivary cortisol:* In this test performed at home, saliva is placed in a tube at midnight, and then sent for cortisol measurement.
- *LowDose Dexamethasone suppression Test:* In this test, dexamethasone tablets are taken by mouth every 6 hours for 2 days, and urine collections for cortisol are performed. This test may be accompanied by a CRH test, where CRH is administered through an IV at the end of the 2 days of dexamethasone, and blood cortisol is then measured. Elevated urinary or blood cortisol tests suggest CS.

What is the Cause of the Cushing's Syndrome?

Once CS is detected, the next step is to find the cause. Normally, the pituitary gland produces ACTH, which circulates in the blood and stimulates the adrenal glands to produce cortisol. Therefore, CS can arise from too much ACTH, or by production of cortisol by the adrenal gland. A blood ACTH test helps determine the cause:

- ACTH dependent: the blood ACTH is normal or high. This includes a pituitary tumor producing ACTH (referred to as **Cushing's disease** and is the most common cause), and ectopic ACTH production (the ACTH is produced elsewhere, such as by a carcinoid tumor or lung cancer).
- ACTH independent: the blood ACTH is very low. Cushing's syndrome consists of an adrenal growth, either benign or malignant, producing cortisol.

Next steps:

- If the patient has **ACTH independent CS**, then a CT scan of the adrenal glands should be performed to look for an adrenal mass.
- If the patient has **ACTH dependent CS**, the next step is a brain MRI scan to look for a pituitary tumor. If no pituitary tumor is seen, then the patient will undergo a catheterization procedure called petrosal sinus sampling, an outpatient procedure where catheters are introduced through a vein in the upper thigh/groin region, with local anesthesia and mild sedation.

The catheters are threaded through the blood vessels (petrosal sinus) which surround the pituitary gland. Levels of ACTH from the petrosal sinuses are measured and compared with ACTH levels in a forearm vein. ACTH levels higher in the petrosal sinuses than in the forearm vein indicate the presence of a pituitary adenoma; similar levels suggest ectopic ACTH syndrome.

How to Treat CS?

The treatment depends on the cause of the CS.

- For Cushing's disease, due to a pituitary tumor, the treatment is transsphenoidal surgery, through the nose or upper lip. The success rate of this procedure is over 80% when performed by a surgeon with extensive experience. If surgery fails, or only produces a temporary cure, surgery can be repeated, often with good results.
- If the evaluation suggests the presence of ectopic CS, then the treatment is directed to the source. For example, if a carcinoid tumor in the lung is detected, then there are several options for therapy, including surgery.
- If an adrenal growth is the cause, then surgery of the abnormal adrenal gland is necessary.
- If patients are not cured by this surgery, then further therapy, including use of medications that lower cortisol secretion from the adrenal gland, surgical removal of the adrenal glands, or radiation to the pituitary gland can be considered.

What Happens After Surgical Cure?

After curative surgery, cortisol levels will be very low, called adrenal insufficiency. Patients are given a synthetic form of cortisol (such as hydrocortisone or prednisone) at that time. Most patients can stop this replacement therapy in less than a year.