**Cushing’s Syndrome**
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Oral Pathology 2018
Section: Thursday AM

 **Overview**
Cushing's syndrome, also called endogenous pathologic hypercortisolism, is a syndrome developed from the chronic exposure to excess glucocorticoids, either from exogenous pharmacological doses of corticosteroids or from an endogenous source of prolonged, excessive amounts of cortisol.

**Etiology**
Cushing's syndrome is caused by a chronic exposure to excess cortisol. Endogenous Cushing's syndrome is divided between adrenocorticotropic hormone (ACTH)-dependent (about 80%) and ACTH-independent (about 20%) causes. Of ACTH-dependent cases, 80% are caused by a [pituitary adenoma](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/pituitary-adenoma) called Cushing’s disease and the rest are by ectopic ACTH secretion, mainly as a consequence of [neuroendocrine tumors](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/neuroendocrine-tumor).

**Clinical Presentation**
According to the *European Journal of Endocrinology*, the clinical presentation of Cushing's syndrome varies depending on the extent and duration of the cortisol excess. When hypercortisolism is severe the signs and symptoms include proximal muscle weakness, wasting of the extremities with increased fat in the abdomen, torso and face, and wide purple striae. Patients are also often referred to subspecialists for complaints that are gynecologic (oligomenorrhea, hirsutism, infertility), dermatologic (red facial skin, poor wound healing, striae, acne), orthopedic/rheumatologic (fractures, low bone mineral density), metabolic (hypertension, diabetes, dyslipidemia), infectious (community acquired and infections seen with immunosuppression), cardiovascular (stroke, myocardial infarction, pulmonary embolism), neurologic (decreased strength, headaches, decreased memory and cognition), psychiatric (depression, anxiety, mood change), and nonspecific (fatigue, backache, and weight gain).

**Demographic**
According to the Endocrine Society Guidelines, Cushing's syndrome is considered in patients with unusual features for their age, such as osteoporosis and livid striae in young men. It is also considered in patients with multiple progressive features, in children with decreasing height percentile and increasing weight, and in patients with [adrenal adenoma](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/adrenal-adenoma) found on a computed tomography scan. Endogenous Cushing's syndrome is more common in women than men. The incidence of Cushing's syndrome is quoted as 1/250,000, with no specific geographical variation.

**Biopsy / Histology / Radiographs**
As stated in the *International Journal of Endocrinology*, three tests are commonly used to establish the diagnosis: low-dose dexamethasone suppression test (1 mg overnight dexamethasone, 1 mg, is given at 11:00 hours and serum cortisol measured at 09:00 hours the next day and 48-hour test dexamethasone, 0.5 mg, is given at 09:00 hours, 15:00 hours, 21:00 hours and 03:00 hours, and serum cortisol measured at 09:00 hours at the start and end of the test), late-night salivary or midnight serum cortisol, and a 24-hour urinary free cortisol.

Depending on the results of these lab tests it will determine the imaging that is required. Typically a CT or MRI of adrenal glands or pituitary glands. If the patient has adrenal Cushing's syndrome, then an abdominal CAT scan or MRI will be ordered. If a pituitary adenoma is suspected, then a CAT scan or MRI of the brain will be ordered.Also, if an ectopic ACTH-producing tumor is suspected, then a CAT scan or MRI of the chest, abdomen, and pelvis will be ordered to locate it. Lastly, if ACTH is elevated but no microadenoma can be identified, and no ectopic source can be found, then inferior petrosal sinus sampling is required. Bilateral [adrenal hyperplasia](https://radiopaedia.org/articles/adrenal-hyperplasia) is one of the most common findings on abdominal CT.

Biopsy is not necessarily performed for detection of this syndrome. Histologically, a neoplastic proliferation of functioning adrenal cortical cells producing cortisol is seen. In comparison to an uninvolved adrenal cortex, cells are large with distinct cytoplasm. Vacuolated, clear-appearing cytoplasm that is lipid rich is seen in cells with distinct borders and nuclei that are relatively uniform. There are no radiologic features unique to this syndrome.

**Differential Diagnosis**
This may be commonly mistaken for adrenal cortical carcinoma and corticomedullary adenoma. Acute intercurrent illness causes hypercortisolemia and false-positive results for the diagnosis of Cushing's syndrome. Oral estrogens increase cortisol-binding [globulin](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/globulin) and lead to falsely elevated serum cortisol concentration, these should be stopped for 6 weeks before investigation. In most centers, during the investigation of ACTH-dependent Cushing’s syndrome the probability that a patient has pituitary disease is usually between 85% and 90%. Statistically, the endocrinologist has a far better chance of getting the correct diagnosis with almost no investigation whatsoever, once the presence of detectable plasma ACTH has been established.

**Treatment**
May include: Trans-sphenoidal surgery which is a selective microadenomectomy done by an experienced surgeon. Long-lasting remission without other [pituitary](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/pituitary) hormonal deficiency is achieved in 50–60% of cases. A medical therapy can also be given to lower cortisol in preparation for surgery or after an unsuccessful surgery. It’s usually used as an adjunctive treatment with other modalities such as pituitary radiotherapy. *Metyrapone*, increasing every 72 hours up to 500–1000 mg three or four times daily, and *ketoconazole*, increasing at 4–5-day intervals, up to 200–400 mg three times daily, are often used to inhibit cortisol synthesis, aiming for a mean serum cortisol of 150–300 mmol/liter, or correction of abnormal elevated urinary free cortisol excretion.

**Prognosis**
[Cushing's syndrome](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/cushings-syndrome) that is inefficiently treated has a 5-fold [standardized mortality rate](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/standardized-mortality-ratio). It can return to normal with timely control of hypercortisolemia, although some [cardiovascular risk](https://www-sciencedirect-com.citytech.ezproxy.cuny.edu/topics/medicine-and-dentistry/cardiovascular-disease) may remain. Depression often persists for years after its cured.

**Professional Relevance**
As a dental hygienist it’s important to provide the best treatment to patients, this includes being well informed about each patient’s medical history and any concerns or modifications that may be necessary due to any medical condition. With Cushing’s syndrome may come hypertension, heart failure, osteoporosis, diabetes mellitus, impaired healing, mental depression and/or psychosis. Through interviewing the dental hygienist must make sure the patient has taken their medication if they are on medical therapy for Cushing’s syndrome and any medication in relation to other conditions that may accompany this syndrome. For example, if patients have hypertension the dental hygienist must be careful to avoid the patient undergoing orthostatic hypotension, if the patient also has diabetes the dental hygienist must know if the patient has had a meal and taken their medication prior to the appointment.

**Citations**
1) Nieman, Lynnette K. “Cushing’s Syndrome: Update on Signs, Symptoms and Biochemical Screening.” *European Journal of Endocrinology*, vol. 173, no. 4, Oct. 2015, pp. M33–M38., doi:10.1530/eje-15-0464.

2) Daniel, Eleni, and John Newell-Price. “Cushing’s Syndrome.” *Medicine*, vol. 45, no. 8, Aug. 2017, pp. 475–479., doi:10.1016/j.mpmed.2017.05.007.

3) Lacroix, André, et al. “Cushing Syndrome.” *The Lancet*, vol. 386, no. 9996, 4 Sept. 2015, pp. 913–927., doi:10.1016/s0140-6736(14)61375-1.

4) Ernest Yorke, Yacoba Atiase, Josephine Akpalu, and Osei Sarfo-Kantanka, “Screening for Cushing Syndrome at the Primary Care Level: What Every General Practitioner Must Know,” *International Journal of Endocrinology*, vol. 2017, Article ID 1547358, 27 July 2017.pp:1-6., doi:10.1155/2017/1547358.