

Brochure for Primary Care Physicians, to increase awareness of Cushing's syndrome (CS)

AIM

Produce a brochure to **increase awareness of CS** for Primary care physicians.

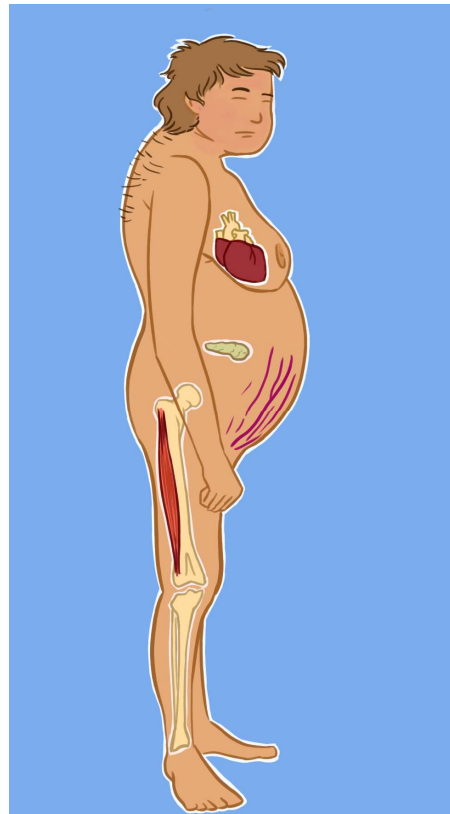
Increase the suspicion on possible CS, to reach an **earlier diagnosis** and **reduce the long-term morbidity and mortality** associated with this condition.

Could this patient have Cushing's syndrome?

Consider CS especially if **clinical symptoms progress over time**.

Photos illustrating these changes in appearance **can be useful** to the physician.

- **Female**
- **Purple striae** (stretch marks) and/or **easy bruising**
- **Central obesity** or **rapid weight gain**
- **High blood pressure**
- **Diabetes mellitus (DM)**
- **Muscle atrophy**
- **Excessive body hair** and **menstrual irregularity**



Is Cushing's syndrome so rare?



Yes, it has a **low incidence of 2-3 patients/million inhabitants/year**.

But it is **often associated with** common abnormalities:

- **Poorly controlled diabetes mellitus** (1-3% of DM are CS)
- **Obesity**
- **Poorly controlled hypertension** (0.5-1% of HT have CS)
- **Osteoporosis** (11% of older patients with osteoporosis and vertebral fractures had CS)
- **Depression**

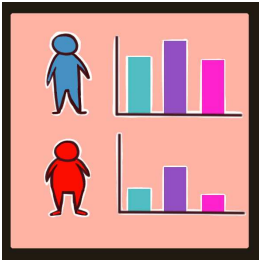
Since screening tests are not completely specific, false positive results (i.e., abnormal test results in healthy subjects) may appear.

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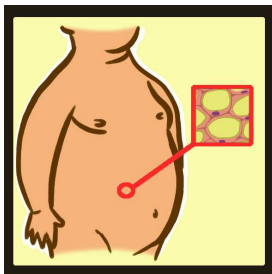
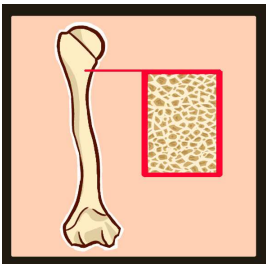
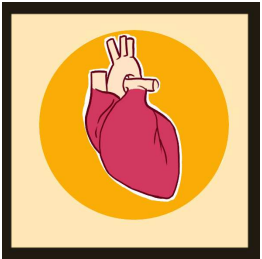
Could it be missed?

Yes!

What consequences will a delayed diagnosis have?



- **Decreased Quality of life**
- **Increased cardiovascular risk** (including heart attack, pulmonary embolism, stroke and deep vein thrombosis)
- **Decreased bone mass** (leading to fractures)
- **Increased body fat mass** (leading to obesity, especially abdominal)
- **Increased mortality** (4-5 times higher Standard Mortality Ratio compared to normal population)



There should be a “*High degree of suspicion*” if:

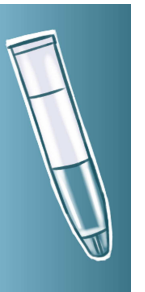
After excluding exogenous glucocorticoid use (including injections, transdermal, rectal, nose or eye drops), the patient presents:

- **Multiple, progressive features of CS** (easy bruising, facial plethora, proximal muscle weakness, striae (especially if reddish purple and > 1cm wide))
- **Adrenal incidentaloma** (accidentally discovered adrenal tumor)
- **Unexplained osteoporosis or hypertension** unusual for age

How can CS be confirmed?

Choose a screening test with high diagnostic accuracy, which is simple:

- 24-hour urinary excretion of free cortisol**, at least twice (it will be above the normal range)
- Late night salivary cortisol** (can be collected at home in a specially designed tube which contains a small column of material to be chewed for 1-2 minutes - Salivette_R - and is stable for several days, so can be sent by post to the receiving laboratory).



- 1 mg overnight Dexamethasone suppression test** (given at 23:00-24:00 and obtain a blood sample for cortisol at 8:00-9:00: should be < 2 mcg/L=55 nmol/L)

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If any result is abnormal, or they are **discordant** or **in doubt**:
Send the patient to an endocrinologist

NO TEST IS PERFECT, or has an optimal specificity, so **false positive results may occur!**

- Specificity: Ability to rule out a disease in a healthy individual
- Sensitivity: capacity to detect the disease in an affected individual

The more sensitive a test, less negative results in an affected individual (false negative results). The more specific a test, less positive results in healthy individuals (false positive results).

		General population	
		Sick population	Healthy population
TEST'S RESULTS	No disease	False -	OK
	Disease	OK	False +

Can CS be easily ruled out?

If results are normal and concordant: **No further evaluation is necessary and CS can be ruled out**

CS may be cyclical but is **usually progressive**; if in doubt, testing should be repeated at 6 months.

Special populations/considerations which may complicate a diagnosis of CS

Certain conditions are associated with **high cortisol** and some clinical features of CS, but are **not CS** include:

Depression and other psychiatric conditions

Poorly controlled diabetes mellitus

Adrenal incidentaloma

Alcohol dependence

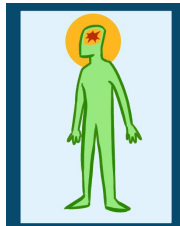
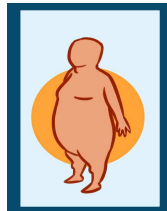
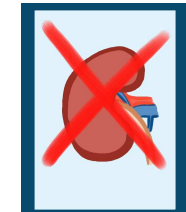
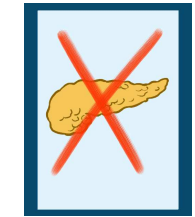
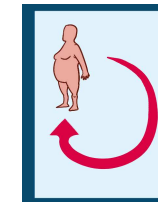
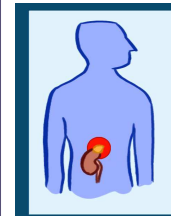
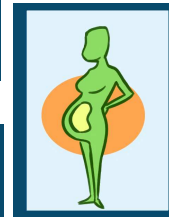
Extreme obesity

Pregnancy

Epilepsy

Renal failure

Cyclical CS



Suspect CS in children if:

- Decreasing height percentile with increasing weight
- Simple obesity is not associated with slowing of statural growth rate

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