

# CUSHING'S SYNDROME & HPA AXIS SUPPRESSION

- Decrease glucocorticoid dose to physiologic dose “5-72.5 mg prednisolone / 15-20 mg hydrocortisone” <sup>[1] [2]</sup>
- Switch to a.m. prednisolone or consider alternate day therapy <sup>[1] [2]</sup>

## Measure morning cortisol level: <sup>[1]</sup>

- <3 ug/dL : Patient adrenally insufficient. Continue glucocorticoid. Retest in 4-6 weeks
  - 3-20 ug/dL : Need further testing. -Insulin tolerance test -CRH stim - Cortrosyn stim -Metyrapone test “check below for procedure”
  - >20 ug/dL : Recovered HPA axis. Can withdraw glucocorticoid therapy.
- During this phase of withdrawal patients are not at risk for adrenal insufficiency, nor do most experience symptoms of withdrawal syndrome. Therefore, the greatest concern at this time will be exacerbation of underlying disease.

## When to Screen? <sup>[3]</sup>

- Patient has received systemic corticosteroids for: > 2 consecutive weeks or >3 cumulative weeks in the last 6 months
- Patient has persistent symptoms of AS: – Weakness/fatigue, malaise, nausea, vomiting, diarrhea, abdominal pain, headache (usually in the morning), poor weight gain and/or growth in children, myalgia, arthralgia, psychiatric symptoms, hypotension\*, hypoglycemia\*



## How to Screen? <sup>[3]</sup>

- Measure early morning cortisol<sup>‡</sup> – GC dose tapered to physiologic dose prior to test – No oral GCs the evening and morning prior to the test<sup>†</sup> – Must be completed by 8:00 am or earlier – Fasting not required
- If morning cortisol is normal but patient has symptoms of AS, perform low-dose ACTH stimulation test<sup>‡</sup> to confirm diagnosis: – 1 µg of cosyntropin; cortisol levels taken at 0, 15–20 and 30 minutes<sup>\*\*</sup> – Peak cortisol < 500 nmol/L = AS (peak >500 nmol/L is normal)

## When to be Concerned? <sup>[3]</sup>

- Early morning cortisol < 85 nmol/L = diagnosis of AS
- Early morning cortisol < laboratory normal = possible AS; consider endocrinology referral for confirmation of diagnosis



## → Lab tests guide

### Insulin tolerance test:

→ patients fast for 8 hours. Then, lispro insulin 0.1 U/kg of body weight is administered rapidly as an intravenous bolus. Serial blood samples are subsequently obtained to measure GH, cortisol, and glucose concentrations at 0, 15, 30, 60, 75, 90, and 120 minutes. With each sample, the blood glucose level is simultaneously determined by using a bedside glucometer to document an appropriate reduction and to ensure safety. Performance of the test is considered adequate when the blood glucose level decreases below 50% of its baseline value.

### CRH-stim

→ Patient should fast for at least four hours prior to the test. human CRH at 1.0 µg/kg body weight is injected intravenously as a bolus over 30 seconds. Blood samples should be collected at 15 minutes and one minute before CRH administration and at 15, 30, 45, 60, 90, and 120 minutes after for measurements of cortisol and ACTH.

### Metyrapone test:

→ At 11 PM, the patient should take metyrapone (30 mg/kg, maximum 3 g) orally, with a snack to prevent gastric irritation. On the following morning, at 8 AM, blood should be drawn for cortisol and 11-deoxycortisol

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[1]- Hopkins, Rachel L., and Matthew C. Leinung. 2005. "Exogenous Cushing's Syndrome And Glucocorticoid Withdrawal". *Endocrinology And Metabolism Clinics Of North America* 34 (2): 371-384. doi:10.1016/j.ecl.2005.01.013.

[2]- Ahmet, Alexandra, Anne Rowan-Legg, and Larry Pancer. 2021. "Adrenal Suppression From Exogenous Glucocorticoids: Recognizing Risk Factors And Preventing Morbidity". *Paediatrics & Child Health* 26 (4): 242-247. doi:10.1093/pch/pxab015.

[3]- Iliopoulou, Amalia, Afroze Abbas, and Robert Murray. 2013. "How To Manage Withdrawal Of Glucocorticoid Therapy". *Prescriber* 24 (10): 23-29. doi:10.1002/psb.1060.

