

Adrenal suppression secondary to exogenous glucocorticoids

See also: **Clinical guidelines for Adrenal Crisis and Acute Adrenal insufficiency**

Background to condition:

Glucocorticoids (also known as corticosteroids) are used widely for their anti-inflammatory and immunosuppressive properties in many different conditions e.g. Inflammatory Bowel Disease, induction treatment of Acute Lymphoblastic Leukaemia, Nephrotic Syndrome, Juvenile Rheumatoid Arthritis.

Patients for whom reduction and /or cessation of corticosteroid is planned, may be at risk of adrenal insufficiency if the duration of corticosteroid use was prolonged beyond 4 weeks, with increasing risk for longer exposure, such as 6-12+months.

In general, doses may be reduced quite rapidly to physiologic levels (10mg/m²/day), then weaned slowly over weeks to several months depending on individual situation.

If the patient has a Cushingoid appearance this should be assumed to reflect high or prolonged corticosteroid exposure with increased risk for adrenal suppression. However, the absence of cushingoid appearance does not mean that the patient is not at risk of adrenal suppression.

How to assess:

(Refer to the Adrenal Crisis and Acute Adrenal insufficiency CPG for assessment and management of adrenal crisis)

Hydrocortisone stress dose for significant illness/emergency is 50-100 mg/m²/day

Hydrocortisone stress dose for mild to moderate illness is 20-30 mg/m²/day

Hydrocortisone maintenance daily requirement is 10 mg/m²/day

As a general guide:

Hydrocortisone IM/IV Stat Dose

< 3 years: 25mg

3-12 years: 50mg

>12 years: 100mg

Refer to the Adrenal Crisis and Acute Adrenal Insufficiency CPG for ongoing dosing

Normal daily glucocorticoid requirement in adults, children and infants is hydrocortisone 5-10mg/m²/day. Any glucocorticoid dose of more than 10mg/m²/day of hydrocortisone equivalence for more than 4 weeks is supra-physiological and can lead to adrenal suppression.

The steroid equivalence table for glucocorticoid activity can be found here: <http://ww2.rch.org.au/pharmacopoeia/pages/hydrocortisone.html>

In brief the anti-inflammatory equivalents are:

1 mg prednisolone	= 4 mg hydrocortisone
1 mg methylprednisolone	= 5 mg hydrocortisone
1 mg dexamethasone	= 25 mg hydrocortisone

For example:

A 5 years old boy has been taking prednisolone 4 mg for 3 months.

- He weighs 30 kg and is 120 cm tall
- Prednisolone 4 mg is equivalent to hydrocortisone 16 mg
- His physiological maintenance hydrocortisone requirement is 10mg,
- His current dose is more than maintenance but less than his stress dose requirement of 50 mg.
- Hence, his current prednisolone dose may be adequate on a day-to-day basis but not for acute stress e.g. surgery, fractures.

Who is at risk?

Not at risk:

- Supra-physiological glucocorticoid use for less than 4 weeks.

At risk:

- Supra-physiological oral glucocorticoid use for greater than 4 weeks
- Inhaled glucocorticoid use of greater than Fluticasone 400 micrograms per day (or equivalent) for more than 3 months (1)
- Patients who are clinically Cushingoid

Management of cessation / weaning steroid dose:

- Not at risk:

Can cease abruptly if underlying condition allows, but usually require gradual taper of doses depending on underlying condition and treatment indication.

- At risk:

Normal secretion in most cases resume in 6 to 8 weeks however normal secretion may not resume for 6-12 months, especially in those with prolonged (6-12 months) use of supraphysiological glucocorticoids.

From an adrenal suppression viewpoint, it is safe to cut the steroid dose to an equivalent of 10mg/m²/d of hydrocortisone without need for a slow wean to this point; slower wean may however be necessary for treatment of the underlying condition.

Wean to physiological maintenance (hydrocortisone equivalences of 10mg/m²/day) as indicated for treatment of underlying condition *then* reduce hydrocortisone (or equivalent) by 2 mg one-two weekly over 6 to 12 weeks depending on patient condition and duration of glucocorticoid use; the faster rate of wean may be used in well patients with shorter (e.g. 3-6 months) duration of glucocorticoid use. If the patient is on more potent glucocorticoids such as prednisolone and dexamethasone, changing to hydrocortisone at this stage is recommended as it has a shorter half-life and may aid recovery of adrenal function.

If supraphysiological glucocorticoid use is longer than 12 months and/or patient is unwell, consider longer wean e.g. over 3-6 months.

Symptoms of extreme lethargy, depressed mood or exhaustion should alert the treating clinician to check for relapse of the underlying condition for which the glucocorticoids was used, or to consider return to a slightly higher glucocorticoid dose, with a slower weaning programme.

Check early morning serum cortisol 24-48 hours after stopping hydrocortisone (3-5 days if prednisolone).

- Morning serum cortisol level of <110 nmol/L indicates adrenal insufficiency (2).
- Morning serum cortisol level of >250 nmol/L indicates normal adrenal function (3).

Interpretation of Morning serum cortisol levels:

Serum early morning level (nmol/L)	Interpretation	Action
>250	Likely normal function	Cease precautions; however adrenal insufficiency precautions should still be followed in the following 6-12 months if clinical suspicion.
110-250	Borderline function	Seek endocrinology advise for management to consider stimulation testing.
<110 or symptomatic	Insufficient adrenal function	Restart maintenance glucocorticoids for prolonged wean +/- seek endocrinology for advise

All patients at risk of adrenal suppression need a sick day plan when their glucocorticoid doses are weaned to Hydrocortisone equivalent of 10 mg/m2/day or less.

Once the patient is identified to be at risk of adrenal insufficiency, he or she will require a management plan for intercurrent illnesses that can be generated using the proforma in the appendix below. This will include instructions for:

- Triple maintenance dose during fever or intercurrent illnesses, typically:
 - Triple for 3 days
 - Double for 2 days
 - Maintenance for 2 days

Then resume weaning; this needs to recommence from maintenance dose again

- Stress cover for general anaesthesia, surgery, fractures, severe illness
- Medi-alert bracelet
- Provision of home IM hydrocortisone injection education is generally not required for most patients, however may be appropriate for select patients for example:
 - Immunosuppressed patients.
 - Patients from remote areas.
 - Patients requiring prolonged wean e.g. more than 12 months.

These precautions can then stop once corticosteroids ceased and normal early morning cortisol levels documented.

Full recovery of adrenal function may not happen for 6 to 12 months even with normal cortisol levels on testing. Adrenal crisis guidelines should still be followed if there is clinical suspicion, especially during acute severe illnesses.

Information Specific to RCH – The inpatient Endocrinology team can be consulted for any queries.

References:

1. Schwartz RH, Neacsu O, Ascher DP, Alpan O. Moderate dose inhaled corticosteroid-induced symptomatic adrenal suppression: case report and review of the literature. *Clin Pediatr (Phila)* 2012;51:1184–1190.
2. Maguire AM, Biesheuvel CJ, Ambler GR, Moore B, McLean M, Cowell CT. Evaluation of adrenal function using the human corticotrophin-releasing hormone test, low dose Synacthen test and 9am cortisol level in children and adolescents with central adrenal insufficiency. *Clinical Endocrinology*. 2008;68:683–691
3. Tsai SL, Seiler KJ, Jacobson J. Morning Cortisol Levels Affected by Sex and Pubertal Status in Children and Young Adults *J Clin Res Pediatr Endocrinol*. 2013; 5(2): 85–89.

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Appendix 1. Adrenal crisis action plan.

MEASURES TO PREVENT ADRENAL CRISIS

*Guidelines for adjusting steroid medication for **PATIENT***

Please follow steps 1-4

Step 1:

For 3 days give [glucocorticoid]: [dose]

Step 2:

For 2 days give [glucocorticoid]: [dose]

Step 3:

For 2 days give [glucocorticoid]: [dose]

Step 4:

Return to current [glucocorticoid]

weaning dose- if unsure please contact Endocrinology

I can become very ill if I experience:

- Fever
- Vomiting
- Diarrhoea
- Broken bones etc...

However, the usual bumps and scratches associated with being a kid are ok!

It is essential that I:

- have my regular medication

If I become unwell I may go into **ADRENAL CRISIS**.

Signs of **ADRENAL CRISIS** can include:

- Being excessively tired, sleepy, lethargic, dizzy, confused or I may appear pale & sweaty and have signs of dehydration, such as dry lips.
- **UNWELL**
Generally unwell with fatigue, lethargy begin **STEP 1** and continue to monitor, if [patient] continues to become more unwell, take child to doctor, or call ambulance
- **VOMITING**
One or Two vomits – **begin STEP 1** of oral medication and follow up with fluids. Please continue to observe and follow up with fluids and sugars.
More vomiting/sleepy – take child to doctor, or call ambulance.

- **DIARRHOEA**
3 or more loose bowel actions with fatigue, lethargy and signs of illness.
Take child to doctor, or call ambulance
- **FEVER: 38.5 degrees Celsius or above**
Begin **STEP 1** and take to doctor for assessment.
- **BROKEN BONE OR CUT REQUIRING STITCHES**
Call ambulance, or take to doctor.

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