A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.
ADRENAL SUPPRESSION SECONDARY TO EXOGENOUS GLUCOCORTICOID:

GUIDANCE FOR CHILDREN ON LONG TERM STEROID THERAPY

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This document provides guidance on management and monitoring of children on long term steroids who are at risk of secondary adrenal suppression.
There is limited evidence in the area of monitoring/management during the discontinuation of long term steroid therapy. This guidance is developed to ensure safe practice, as there have been reported fatalities secondary to adrenal suppression.

Background to condition:
Oral glucocorticoids (steroids) are widely used for their anti-inflammatory and immunosuppressive properties in many conditions eg duchenne muscular dystrophy, juvenile idiopathic arthritis/chronic childhood rheumatic conditions, inflammatory bowel disease, atopic conditions, nephrotic syndrome, childhood cancers, solid organ transplant etc.

Physiological cortisol production is equivalent to approximately 10 mg/m²/day Hydrocortisone.

Steroid equivalence for glucocorticoid activity
1 mg Prednisolone = 4 mg hydrocortisone
1 mg Triamcinolone = 4 mg hydrocortisone
1 mg Methylprednisolone = 5 mg hydrocortisone
1 mg Deflazacort = 6 mg hydrocortisone
1 mg Dexamethasone = 25 mg hydrocortisone

Who is at risk?
1- All pharmacological doses of oral steroid used clinically for treatment in current paediatric clinical practice are greater than physiological dose. Therefore, children treated with higher than physiological dose of steroid (> 2.5 mg/m²/day Prednisolone or > 10 mg/ m²/day hydrocortisone or equivalent) for greater than 4 weeks maybe at risk of secondary adrenal suppression.
2- Continuous treatment for > 6 months will increase the risk. Children treated for > 12 months are at very high risk.
3- Concurrent treatment with other forms of steroid eg intra-articular, inhaled, topical, nasal, eye drops will increase the risk. (Refer to separate guidance for monitoring of children on inhaled steroid)
4- Repeated use of intra-articular, inhaled, topical, nasal, eye drop steroids may also lead to adrenal insufficiency.

The absence of cushingoid appearance does not mean that the patient is not at risk of adrenal suppression. However, if a child has cushingoid appearance, he/she should be assumed to have adrenal suppression. The absence of clinical symptoms of adrenal insufficiency does not mean that the patient is not at risk of adrenal suppression.
All children commencing long term steroid or treated for > 6 months

Steroid card/sick day plan (IM hydrocortisone education ideally)

If planning to discontinue long term steroid therapy

Wean treatment dose of steroid down to
Prednisolone equivalent of 2.5 mg/m²/day over 4-6

Convert to oral hydrocortisone 10 mg/m²/day in three divided doses
Need to double dose of oral hydrocortisone (48 hours) during acute illness
Inform endocrine team (page 18301) or link endocrine consultant for specialty

Synacthen test after at least 8 weeks of oral hydrocortisone
- Omit hydrocortisone the night before and morning of synacthen test
- Recomence hydrocortisone until results of synacthen test available
- Inform endocrine team if peak cortisol to synacthen ≤ 450 nmol/L
  and review in endocrine clinic

FLOW CHART SUMMARY OF MANAGEMENT AND MONITORING OF CHILDREN ON LONG TERM ORAL STEROID THERAPY
(A) Management of children maintained on prolonged (> 6 months) oral steroid (> 2.5 mg/m²/day Prednisolone or > 10 mg/m²/day hydrocortisone equivalent)

An investigation of adrenal axis in this group of children whilst they remain on steroid is not necessary as these children have definite secondary adrenal insufficiency. The treatment dose of steroid of is greater than double the physiological dose.

However, all children on oral steroid and who are likely to remain on treatment for > 6 months should be

1- Issued with steroid card/medical bracelet.
2- Counsellled not to discontinue steroid abruptly.
3- Provided with sick day plan during intercurrent illnesses, especially when unable to tolerate steroids due to vomiting.
   Ideally, families should be provided with education to be able to inject IM hydrocortisone in such instances or have immediate access to IM hydrocortisone as per the recommendations of the British Society for Paediatric Endocrinology & Diabetes (BSPED) and the Scottish Paediatric Endocrine Group (SPEG).
4- Provided with IV hydrocortisone cover during acute inpatient admission, surgery, and general anaesthetic.

(a) Stress doses of oral steroid (ie double of oral dose of steroid for 2 days) during mild acute illness are not needed for children on ≥ 2.5 mg/m²/day Prednisolone or ≥ 10 mg/m²/day hydrocortisone equivalent.

(b) For children managed with on/off steroid therapy (eg 10 days on/off etc), an oral sick day plan may be needed during the period the child is not on steroid treatment. This could be in the form of 48 hours of usual steroid therapy or in the form of oral hydrocortisone 20 mg/m²/day TDS.

(c) Stress doses of oral steroid (ie double of oral dose of steroid for 2 days) during mild acute illness are needed for children on ≤ 2.5 mg/m²/day Prednisolone or ≤ 10 mg/m²/day hydrocortisone equivalent.

Dose of Regular Steroid | Sick day/stress dose
------------------------|---------------------
≥ 5 mg/m²/day Prednisolone Or ≥ 10 mg/m²/day hydrocortisone equivalent* | No additional increase in dose
≤ 2.5 mg/m²/day Prednisolone or ≤ 10 mg/m²/day hydrocortisone equivalent* | Double dose of steroids for 48 hours

* see equivalent doses on page 1

(B) Management of children discontinuing prolonged (> 6 months) oral steroid

Normal endogenous cortisol secretion resumes in 6-8 weeks in most cases although normal secretion may not resume for 6-12 months especially in those following prolonged periods of oral steroid treatment (> 12 months) and/or those who have had concurrent treatment with other forms of steroid (eg topical, inhaled or intra-articular etc).

42% of children who discontinued long term oral steroid therapy have an abnormal response to synacthen test despite a weaning regime. No clinical or biochemical factors could predict those with abnormal response (Wildi-Runge S et al J Pediatr 2013).
All children should be
1- Issued with steroid card/medical bracelet.
2- Counsedled not to discontinue steroid abruptly.
3- Provided with sick day plan during intercurrent illnesses, especially when unable to tolerate steroids
due to vomiting.
   Ideally, families should be provided with education to be able to inject IM hydrocortisone in such
   instances or have immediate access to IM hydrocortisone as per the recommendations of the British
   Society for Paediatric Endocrinology & Diabetes (BSPED) and the Scottish Paediatric Endocrine
   Group(SPEG).
4- Provided with IV hydrocortisone cover during acute inpatient admission, surgery, and general
   anaesthetic.

**B1. Discontinuing steroid (Duration of treatment > 6 months)**

These children are at a higher risk of secondary adrenal suppression and therefore a longer
recommended period of weaning may be necessary.

Wean steroid dose down to a physiological dose equivalent (ie 2.5 mg/m$^2$/day Prednisolone or
equivalent) in the duration that symptoms of the underlying condition permits (or at least 4-6 weeks),
then change to hydrocortisone (10 mg/m$^2$/day Hydrocortisone) as it has a shorter half-life and aids in
the recovery of adrenal function. Inform endocrinology team. Once the child has been on
physiological dose of oral hydrocortisone for at least 8 weeks, perform synacthen test.

Omit evening and morning dose of hydrocortisone to perform synacthen test. Recommence oral
hydrocortisone after synacthen test until results of synacthen test available.

Consider discussing weaning plan with endocrinology earlier for children who have been treated with
steroid for > 12 months or younger children (< 5 years).

**B2. Discontinuing steroid (Duration of treatment ≤ 6 months or intermittent treatment eg multiple
short courses)**

Some of these patients may be at risk of adrenal suppression.

For safe practice, we recommend the consideration of synacthen test in the children in this group
when off steroids for at least 2 weeks or just before next steroid treatment if there are symptoms of
suggestive of adrenal insufficiency or other clinical concerns*.

* Symptoms of adrenal insufficiency include
  Significantly tired/lethargy
  Weight gain/weight loss
  Multiple and increased frequency of intercurrent illnesses (Taking longer to recover)

**INTERPRETATION OF SYNACTHEN TEST**

1- Peak synacthen > 450nmol/L
   Normal
   - No need for further investigations unless clinical concerns.

2- Peak synacthen 300-450nmol/L
   Mild to moderate adrenal suppression
- Inform endocrinology and refer to endocrine clinic.
- **Sick Day Plan**
- Stress dose oral hydrocortisone (double oral dose for 2 days) for mild acute illness.
- IM hydrocortisone for vomiting illness.
- Repeat synacthen test in 6 months if remain off steroids.

3- **Peak synacthen < 300 nmol/L**
   - Significant adrenal suppression
   - Inform endocrinology and refer to endocrine clinic.
   - **Replacement and Sick Day Plan**
   - Recomence oral hydrocortisone at physiological dose 10 mg/m²/day.
   - Stress dose oral hydrocortisone (double oral dose for 2 days) for mild acute illness.
   - IM hydrocortisone for vomiting illness.
   - Repeat synacthen test in 6-12 months if remain off steroids.

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**Emergency management of adrenal crisis**

**INTRAMUSCULAR HYDROCORTISONE REGIME FOR VOMITING ILLNESS (FOLLOW SICK DAY PLAN, PARENTS SHOULD BE AWARE)**

<table>
<thead>
<tr>
<th>Age</th>
<th>IM Hydrocortisone Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6months</td>
<td>12.5mg</td>
</tr>
<tr>
<td>6 months-5years</td>
<td>25mg</td>
</tr>
<tr>
<td>5-10years</td>
<td>50mg</td>
</tr>
<tr>
<td>&gt;10years</td>
<td>100mg</td>
</tr>
</tbody>
</table>

(C) **Hospital management of children with secondary adrenal suppression during severe illness**

Management of children with secondary adrenal suppression due to steroid treatment during acute illness requiring admission is the same as any child with primary adrenal insufficiency.

If severely unwell,
- Check blood sugar and urea & electrolytes including full blood count
- If capillary glucose <3mmol/l give 2-4 ml/kg of 10% dextrose
- Fluid bolus may also be required (10-20ml/kg 0.9% saline) if indicated.
- Give hydrocortisone bolus and start infusion (table below).
- Give bolus IV hydrocortisone if unwell even if IM hydrocortisone has been given at home.
- Start IV maintenance fluids + deficit (with dextrose containing fluids)
- Consider double dose hydrocortisone therapy once able to tolerate oral medications

Child may already be on double hydrocortisone therapy and possibly received intramuscular dose of hydrocortisone at home.

*Beware clinical improvement may be due to IM hydrocortisone.*

If the child has received a hydrocortisone bolus, either at home or in hospital, we would advise at least overnight admission.

<table>
<thead>
<tr>
<th>Age</th>
<th>Hydrocortisone Bolus [if no IM dose given]</th>
<th>Hydrocortisone infusion [50mg hydrocortisone in 50mls 0.9% saline]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>Dose</td>
<td>Infusion Rate</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------</td>
<td>---------------</td>
</tr>
<tr>
<td>&lt;6months</td>
<td>12.5mg</td>
<td>1ml/hr</td>
</tr>
<tr>
<td>6 months-5years</td>
<td>25mg</td>
<td>1ml/hr</td>
</tr>
<tr>
<td>5-10 years</td>
<td>50mg</td>
<td>2ml/hr</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>100mg</td>
<td>3ml/hr</td>
</tr>
</tbody>
</table>

**Management of children with secondary adrenal suppression during surgery**

- For minor surgery/procedure (< 1 hour), bolus IV hydrocortisone should be given at induction (See table above).
- When the child is able to eat and drink, give usual steroid dose or stress dose oral steroid for the next 24-48 hours (hydrocortisone 20 mg/m²/day or equivalent) if usually on hydrocortisone or equivalent of 10 mg/m²/day.
- Beware of children undergoing tonsillectomy, as may not tolerate intake and may need hydrocortisone infusion.
- For major surgery especially major bowel surgery where the child has to be NBM after surgery, bolus hydrocortisone should be given at induction and a hydrocortisone infusion commenced.
- When the child is able to eat and drink, give usual steroid dose or stress dose oral steroid for the next 48 hours (hydrocortisone 20 mg/m²/day or equivalent).