

ADRENAL INSUFFICIENCY - EMERGENCY MANAGEMENT PRACTICE GUIDELINE[®]

DOCUMENT SUMMARY/KEY POINTS

- Acute adrenal insufficiency can occur in patients with known adrenal (primary) disease, hypothalamo- pituitary (secondary) disorders or after adrenal suppression from glucocorticoid therapy. It also should also be considered as a new diagnosis in any unwell neonate or child.
- The management of acute adrenal crisis involves the immediate administration of intramuscular (IM) or intravenous (IV) hydrocortisone (**do not delay treatment, if IV access is difficult give an IM dose**), fluid resuscitation and treatment of hypoglycaemia and electrolytes disturbances (low sodium, high potassium) if present.
- Patients with known adrenal insufficiency require additional steroid during intercurrent illness, significant injury, surgery or anaesthesia.
- When in doubt, err on the side of giving stress cover.
- Trebling or quadrupling the usual dose of hydrocortisone may not be sufficient especially in patients with secondary or iatrogenic adrenal insufficiency as low maintenance doses, 5-10 mg/m²/day are commonly used in these patients.
- This document provides empiric guidelines for stress doses in emergency situations. However, after the emergency resuscitation phase it is preferable to refer to the patient's individualised stress letter, discuss with the endocrinologist on call.
- Where possible an ALERT should be placed in the patient's Medical Records.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 st May 2014	Review Period: 3 years
Team Leader:	Staff Specialist	Area/Dept: Endocrinology, CHW

CHANGE SUMMARY

- New SCHN guideline: Replaces local facility guidelines on adrenal insufficiency.

READ ACKNOWLEDGEMENT

- All clinical staff working in any SCHN Emergency Departments or Intensive Care areas or Endocrinology are to read and acknowledge they understand the contents of this document.

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1 What is adrenal insufficiency?

Adrenal insufficiency occurs when the adrenal gland is unable to produce sufficient glucocorticoid and/or mineralocorticoid hormones.

In health, the adrenal glands produce approximately 6-8mg/m²/day of cortisol. However, during illness there is a physiological rise in cortisol production, and substantially more is secreted. Therefore, in patients with adrenal insufficiency, glucocorticoid doses **must be** increased during times of illness.

2 Types of adrenal insufficiency

Primary: diseases of the adrenal gland

ACTH is high in the untreated state, for example in congenital adrenal hyperplasia, Addison's disease or adrenoleukodystrophy. These patients will likely have features of glucocorticoid and mineralocorticoid deficiency.

Secondary: diseases of the pituitary or hypothalamus

ACTH is deficient e.g. idiopathic hypopituitarism, craniopharyngioma/other sellar or suprasellar tumours. These patients will predominantly have features of glucocorticoid deficiency.

Iatrogenic: chronic corticosteroid use

This is a subgroup of secondary adrenal insufficiency and can occur following withdrawal from 2 weeks or more of corticosteroid use or as anti-inflammatory doses of corticosteroids are tapered, e.g. Crohn's disease, juvenile arthritis, systemic lupus erythematosus (SLE), asthma, and autoimmune based neurological disorders. These patients will predominantly have features of glucocorticoid deficiency.

3 Assessment of suspected or known Adrenal Insufficiency

Children with adrenal insufficiency may present to the Emergency Department as a new diagnosis or, in existing patients, during intercurrent illness or injury.

New presentations of adrenal insufficiency: Consider in any unwell neonate or child. An intercurrent illness or other stress (e.g. surgery) may precipitate an adrenal crisis.

Clinical features may include:

- weakness & lethargy
- weight loss
- depression, anorexia, vomiting
- pigmentation (only in primary adrenal insufficiency due to excess adrenocorticotrophic hormone [ACTH] production)
- hypotension (often with postural drop), collapse
- hypoglycaemia (fingerprick blood glucose level [BGL])

Biochemical features may include:

- Low sodium and high potassium (in the presence of aldosterone deficiency in primary adrenal insufficiency e.g. Congenital Adrenal Hyperplasia [CAH] or Addison's)
- Elevated serum urea and creatinine (from associated dehydration)
- Hypoglycaemia (from lack of glucocorticoid)
- Elevated plasma renin (as an index of volume depletion)
- Elevated plasma ACTH (in primary adrenal insufficiency)

4 Investigation of new onset adrenal insufficient patients

- Discuss with Senior Emergency doctor and Endocrine team.
- Try to get these investigations *before* giving hydrocortisone **if clinical condition permits**.
- Please refer to the table below as there are different sample requirement at the Westmead and Randwick laboratories.

Table 1: Investigations in new onset adrenal insufficient patients

	Westmead Campus	Randwick Campus
EUC	1mL lithium hep tube	1mL serum (or lithium hep tube)
Blood gas	Take specimen in blood gas syringe to one of the wards with blood gas analyser (on ice)	Take specimen in blood gas syringe to one of the wards with blood gas analyser (on ice)
BGL (immediate glucometer, or from blood gas & then formal glucose)	0.5mL in lithium heparin or fluoride oxalate (FLOX) tube (use FLOX tube if transport likely to be delayed)	0.5mL in lithium heparin or fluoride oxalate (FLOX) tube (use FLOX tube if transport likely to be delayed)
Cortisol & 17OH-Progesterone	2mL in serum or lithium hep tube	1mL in serum tube
Aldosterone	2mL in lithium hep tube, ON ICE, to be spun down ASAP	1mL in serum tube, NOT on ice
ACTH	2mL in purple top EDTA tube, ON ICE, to be spun down ASAP	1mL in purple top EDTA tube, ON ICE, to be spun down ASAP
Renin	2mL in purple top EDTA tube, NOT on ice	1mL in purple top EDTA tube, NOT on ice
Urine steroid profile*	10mL in yellow top container	30mL in yellow top container,

***Note:** if the patient is not a neonate and not acutely unwell a 24 hour collection should be performed (24hr urine bottle, preservative free, available from Pathology).

EDTA: ethylenediaminetetraacetic acid

EUC: electrolytes, urea and creatinine.

5 Investigation of known adrenal insufficient patients

- Electrolytes, urea and creatinine [EUC] and BGL (immediate bedside glucometer and then formal glucose)
- Consider venous or capillary acid-base if very unwell

6 Management of Acute Adrenal Crisis

1. **GIVE STRESS HYDROCORTISONE COVER IM or IV** (see [flowchart](#) for dose):

Give as a STAT dose, and then continue stress cover in 3-4 divided doses per day.

In a known adrenally insufficient patient do not delay administration to secure venous access.

NB: Fludrocortisone is not usually required acutely as high doses of hydrocortisone give sufficient mineralocorticoid cover.

2. **Fluids:**

If the patient is shocked give 10-20mL/kg 0.9% sodium chloride IV bolus and repeat as necessary. Ongoing maintenance plus deficit for dehydration given as 0.9% sodium chloride with 5% glucose.

3. **Check BGL hourly initially:**

If BGL is less than 3.5mmol/L give 2mL/kg of 10% glucose; check BGL in 30minutes and repeat if necessary.

4. **Check Sodium and Potassium:** The reference range for plasma Potassium for children over the age of one month is 3.5 to 5.5mmol/L.
(For children less than one week it is 4.5 to 6.5mmol/L, and for one week to one month it is 3.8 to 6mmol/L. This is due to both sampling artefact and neonatal physiology).

If potassium is greater than 5.5mmol/L place on a cardiac monitor, perform a 12 lead electrocardiogram [ECG] and treat as below (modified from the SCH and CHW guidelines on hyperkalaemia).

Potassium greater than 5.5mmol/L without ECG changes: cardiac monitor, discuss with senior doctor or endocrinologist to consider if medical management is required.

Potassium greater than 5.5mmol/L with ECG changes (peaked T waves, wide QRS) **or potassium greater than 6.5mmol/L *regardless* of ECG findings**, manage as above plus:

- Discuss with senior doctor to consider further management (including the following).
- Administration of IV Calcium Gluconate or IV Calcium Chloride as below.

NB: Calcium gluconate is better tolerated and causes less phlebitis than calcium chloride.

- **If using calcium gluconate injection:**
 - IV calcium 0.11- 0.13 mmol/kg (0.5mL/kg of calcium gluconate 0.22mmol/mL - max 3g calcium gluconate) slow IV over 5minutes
 - **If using calcium chloride injection:**
 - IV calcium 0.11-0.13 mmol/kg (0.2mL/kg of calcium chloride 10% - max 1g calcium chloride) slow IV over 5minutes
 - **Central administration is preferred. If central access is not available discuss with senior doctor. If peripheral access needs to be used, ensure that a large peripheral vein is used, the IV line is patent, and flush the line after delivery. Avoid Extravasation.**
 - Glucose 5 – 10mL/kg bolus push of 10% glucose solution. The insulin response to the glucose bolus is the most potent temporary treatment for hyperkalaemia.
 - Insulin, 0.1Units/kg IV (ultra-short acting or short acting insulin), may be necessary with the glucose. However, the patient will need to be monitored for hypoglycaemia so check BGL every 30 minutes for 4 hours.
 - Salbutamol, either via nebuliser or intravenously.
Note that there can be a small increase (approximately 0.1mmol/L) in potassium within the first 3 minutes of administration.
 - Salbutamol nebuliser:
 - 2.5 mg if patient weighs less than 25 kg
 - 5 mg if patient weighs greater than 25 kg
 - Salbutamol IV: 4-5 micrograms/kg over 15-20 minutes
 - Intravenous sodium bicarbonate, 8.4%.
Note: each mL of 8.4% sodium bicarbonate solution contains 84 mg of sodium bicarbonate which gives 23 mg (or 1mmol) of sodium and 61 mg (or 1mmol) of bicarbonate.
Administer 1mmol/kg sodium bicarbonate, 8.4%, slow push (only useful in reducing potassium level if patient has a metabolic acidosis).
As the 8.4% solution is hypertonic and may be painful through small veins, consider dilution to 4.2% in neonates and infants, in which case the dose is 2mL/kg of 4.2%.
 - Resonium 1g/kg orally (or rectally in neonates)
- 5. Look for underlying cause**, for example sepsis or non-compliance with medication.
- 6. Consider repeating the IV or IM steroid dose** if there is a poor response to initial resuscitation.

7 Patients with, or at Risk of Adrenal Insufficiency during intercurrent illness

Patients with known adrenal insufficiency must be given increased doses of replacement hydrocortisone at times of physical stress. Parents should be well educated about what they need to do, but may need assistance. Some patients will have a letter that states their stress dose of hydrocortisone.

- If moderately unwell and/or fever $>38^{\circ}\text{C}$, AND not vomiting, give stress dose of hydrocortisone orally (see [Table 2](#) and [Flowchart](#) below).
- If the child has vomiting or diarrhoea, oral absorption is unreliable, give hydrocortisone intramuscularly or intravenously (see [Table 2](#) and [Flowchart](#) below).
- Give additional glucose containing fluids e.g. fruit juice, cordial or IV glucose if vomiting persists, to avoid hypoglycaemia.
- Treatment should continue for at least 24 hours after the child has recovered from the illness/episode.

8 Patients with known Adrenal Insufficiency Peri and Post-Anaesthetic/Operation

- At induction give single dose IV stress hydrocortisone (see [Table 2](#)). Some patients will require stress hydrocortisone for the next 24 hours or longer (given 6-8 hourly), depending on whether there is ongoing post-operative pain or other physical stress.

GENERAL IMPORTANT POINTS:

- When in doubt, err on the side of giving stress cover
- Trebling or quadrupling the usual dose of hydrocortisone may not be sufficient especially in patients with secondary or iatrogenic adrenal insufficiency as low maintenance doses, $5\text{-}10\text{ mg/m}^2/\text{day}$ are commonly used in these patients.
- When stress doses of steroids are required for prolonged periods of time consider prophylactic use of proton pump inhibitor or histamine $[\text{H}_2]$ receptor antagonist (for prevention of peptic ulceration) and blood glucose monitoring to detect hyperglycaemia.
- Patients with iatrogenic adrenal insufficiency due to long term steroid use may already be receiving a steroid dose that is equivalent to a stress dose of hydrocortisone. Therefore they may not require an increase during stress if they are still tolerating and absorbing oral steroids. However, they may still need IM hydrocortisone in episodes of diarrhoea, vomiting or any situation where they cannot take oral steroids. Refer to [Table 3](#) (Relative Glucocorticoid Potency) to calculate hydrocortisone equivalents and the need for additional stress doses.
- In general, hydrocortisone is the steroid of choice for stress dosing. Methylprednisone, methylprednisolone (both IV preparations) and dexamethasone (IV or oral) have no mineralocorticoid activity and are unsuitable.

- Important to have a low threshold for obtaining senior paediatric review/endocrine consultation.
- Consider Intensive Care referral when children not responding to test dose steroids, for severe electrolyte or glucose abnormalities, haemodynamic instability and staff worried about the care of child.

Table 2: Empiric hydrocortisone stress doses to be used when individualised patient dose letter is not available or may be outdated

Stress Doses for Age and Weight		
Age and Weight (kg)	Dose of hydrocortisone for injection* (IM or IV) Stat dose (may be repeated if clinically indicated)	Dose of oral hydrocortisone*
Less than 6months (less than 7 kg)	25mg	8mg three times daily
6months to 2years (8-12 kg)	50mg	16mg three times daily
3-10 years (13-30 kg)	75mg-100mg	24mg three times daily
Greater than 10years (greater than 30kg)	100-200mg	40mg three times daily

*If available, please use the patient's individualised stress letter. The doses above are based on 60-100mg/m²/day of stress hydrocortisone (adapted from Maguire A, Craig M et al. Management of Emergency or 'Stress' Situations where Hypoglycaemia or Cortisol Deficiency Occur. Hormones and Me Booklet, Merck Serono 2011.

However, after the initial dose is given it is important to discuss ongoing dosing with the endocrinologist on call (as prescribing practices vary and the evidence guiding practice is empiric).

Table 3: Relative glucocorticoid potency

Natural/Synthetic Glucocorticoid	Relative glucocorticoid potency
Hydrocortisone	1
Prednisone	4
Methylprednisolone	5
Dexamethasone	30

Example: A 14 year old boy (150cm, 35kg, BSA= 1.2m²) with Crohn's Disease on 40mg prednisone orally daily, who develops a high fever is already receiving the equivalent of 160mg hydrocortisone per day (calculation 40 x 4=160). This is equivalent to 133mg/m²/day hydrocortisone, therefore no additional stress dosing required unless there is concern about oral absorption, vomiting or diarrhoea.

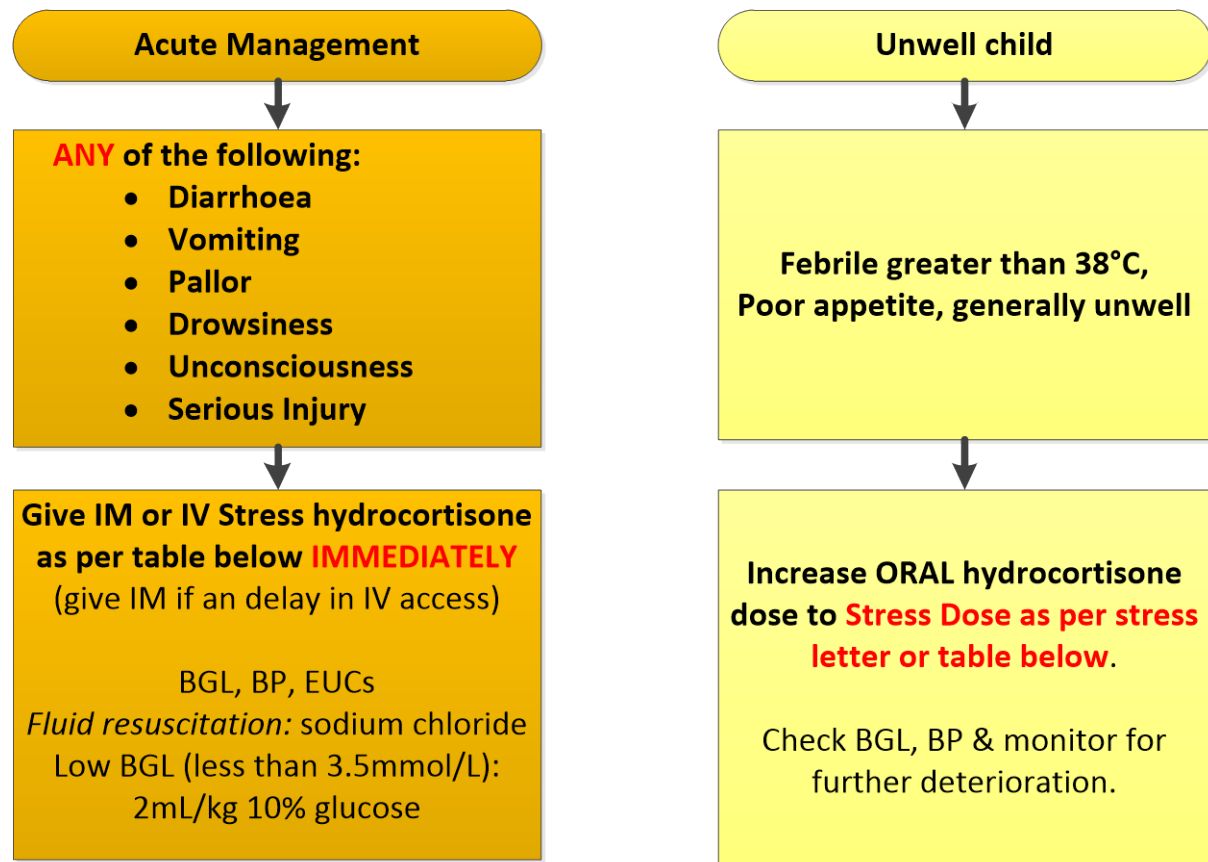
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Flowchart for the Management of Adrenal Insufficiency



Stress Doses for Age and Weight		
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Contact Endocrine Doctor on call

Most known endocrine patients will arrive with Solucortef Actovials (hydrocortisone for injection). These vials are safe for use.

Note: extra hydrocortisone will do no harm...**NOT giving hydrocortisone can cause serious problems.**