PAEDIATRIC ENDOCRINE EMERGENCY PROTOCOLS

M ANAGEMENT OF CHILDREN AND YOUNG PEOPLE PRESENTING WITH AN ADRENAL CRISIS

(New presentation or with pre-existing adrenal insufficiency)

SETTING	Emergency Departments, Children's Assessment Units, Paediatric Inpatient Wards
FOR STAFF	General Paediatricians, Emergency Medicine Clinicians, Paediatric Endocrinology Teams.
PATIENTS	Children and young people presenting with a suspected adrenal crisis **Please see separate guidance for children with Duchenne's Muscular Dystrophy presenting with a suspected adrenal crisis.**

These guidelines have been produced to guide clinical decision making for the medical and nursing staff. **They do not replace the clinical judgement of a senior clinician**. Each case should be fully assessed individually with respect to the particular needs and circumstances of that patient.

Key Points:

- Adrenal crisis most commonly presents in children with known adrenal insufficiency who develop an intercurrent illness or injury.
- Consider a new presentation of adrenal insufficiency in a child presenting with unexplained severe dehydration and shock.
- Please note children who are on steroid treatment or who have been on steroid treatment are at risk of adrenal crisis.
- The key elements of treatment for an adrenal crisis include fluid resuscitation, steroid replacement and management of glucose and electrolytes.

An adrenal crisis is a life-threatening emergency and needs to be managed promptly.

All children and young people presenting with an adrenal crisis should be discussed with the paediatric endocrinologist on call.

Contents

If the child is undergoing a major or minor surgical procedure or receiving a general anaesthetic, please see separate guidance:
Surgical Management of Children and Young People with Adrenal Insufficiency

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Paediatric Endocrine Clinical Guidelines (sharepoint.com)

Definition

Adrenal crisis: Adrenal ("Addisonian") crisis occurs when the adrenal glands cannot produce sufficient cortisol in response to an increased need. The major clinical features of adrenal crisis are hypotension and volume depletion. Combined glucocorticoid and mineralocorticoid deficiency results in urinary sodium loss, hyponatremia, hyperkalaemia, increased serum urea, and, especially in children, hypoglycaemia.

Causes of Adrenal Insufficiency

Primary adrenal insufficiency: These are disorders of the adrenal gland e.g. autoimmune adrenal insufficiency (Addison's disease) or congenital adrenal hyperplasia. These conditions typically lead to an elevated ACTH at presentation.

Secondary adrenal insufficiency: These conditions lead to disruption of the hypothalamic-pituitary axis and deficiency of CRH and/or ACTH e.g. congenital hypopituitarism, brain tumour, acquired (traumatic brain injury, meningitis, steroid-induced adrenal suppression). At presentation there is an inappropriately normal or low ACTH.

Key Points for the assessment of a child with suspected adrenal crisis

History and Examination

History can give added weight to diagnosing adrenal insufficiency:

- History of chronic fatigue, weakness, abdominal pain, anorexia, weight loss, vomiting, diarrhoea, salt craving, skin pigmentation, dizziness, confusion
- History of recurrent infections
- In babies - poor feeding, poor weight gain
- History of known adrenal insufficiency or exogenous glucocorticoid use.
- Other autoimmune conditions in the index case or family, may be a clue to the presence of Addison's Disease.
- Undiagnosed ACTH deficiency - history may include headache, visual changes, seizures, focal neurological signs.

Examination findings may include:

- Hypotension, dehydration and shock
- Hypoglycaemia
- Jaundice in babies
- Presence of fever and other signs of intercurrent illness
- CNS signs (in Adrenoleukodystrophy)
- Volume depletion i.e. prolonged CRT, increased heart rate, low blood pressure
- Seizures *due to hyponatraemia*
- Neonatal hepatitis in babies.
- Hyperpigmentation- look in skin creases, gums and nail bed. Areas not exposed to sunlight.

Remember:

- Some conditions can mimic the presentation of adrenal insufficiency e.g. sepsis, obstructive uropathy (in neonates), pseudohypoaldosteronism, thus highlighting the importance of taking the correct samples **prior** to treatment with hydrocortisone. **However, treatment should never be delayed in very sick children.**

Initial treatment of an Adrenal Crisis:
New presentation and Children with known Adrenal Insufficiency

- All patients with known adrenal insufficiency who present as unwell should be considered to have an incipient adrenal crisis, and follow this protocol.
- Beware if child appears well on admission clinical improvement may be due to IM hydrocortisone administered by parents/paramedics- this improvement may be transient.
- All children requiring IM or IV hydrocortisone must be observed for a minimum of 6 hours.

1. ABC as per APLS guidelines

2. Obtain IV access. (***Bloods should be obtained prior to administration of hydrocortisone. However, if there are difficulties in obtaining venous access please give hydrocortisone intra-muscularly.***

Investigations:

All Children ***(do not delay treatment if samples difficult to obtain and do NOT wait for results before giving hydrocortisone):***

- Blood glucose (both Point of Care and Laboratory glucose)
- Urea and Electrolytes
- Blood gas: Acidosis indicates mineralocorticoid deficiency
- Blood and Urine Cultures, FBC, CRP

Additional Investigations required if first presentation ***(do not delay treatment if samples difficult to obtain and do NOT wait for results before giving hydrocortisone)***

- Cortisol
- ACTH (EDTA to go on ice to lab within 30 mins)
- 17 hydroxyprogesterone
- Plasma renin
- Aldosterone
- Adrenal antibodies
- Urine: urinary steroid profile and urinary sodium (consider urgent catheter specimen in neonate)

3. Steroid Replacement

Give IV bolus of hydrocortisone promptly (doses shown below). **DO NOT WAIT FOR BLOOD RESULTS TO COME BACK**. If IV access is not immediately available, give IM hydrocortisone while establishing intravenous access.

Child's Age	Dose IM/IV
Less than 1 year	25mg
1-5years	50mg
6 years and over	100mg

Note parents who have children with known adrenal insufficiency have been trained to give intramuscular hydrocortisone in an emergency. If this has already been given, the next dose of hydrocortisone can be given in 4-6 hours after this administration. If there is any doubt if it has been given, repeat the dose.

4. Hypoglycaemia

- If blood glucose <3.0mmol/L, give 2ml/kg of 10% glucose bolus. Recheck glucose after 15 minutes and give further IV glucose bolus until blood glucose > 4mmol/L.

- Continue to monitor blood glucose frequently, ensure adequate glucose in maintenance fluids to ensure normoglycemia.

5. Intravenous Fluids

Patients will almost always have a significant volume depletion.

- If signs of shock, or moderate to severe dehydration give 10ml/kg 0.9% sodium chloride bolus repeat as required.
- Check electrolytes immediately at presentation to inform fluid usage. Patient may have hyponatraemia and hyperkalaemia as well as other electrolyte abnormalities.
- Severe hyponatraemia can present as seizures/loss of consciousness and correction will need to be managed carefully. In some cases, specific treatment for hyperkalaemia is required- ***(see section 'Ongoing Management- Fluids and Electrolytes*** **for guidance on management of hyponatraemia and hyperkalaemia page 6)**
- Consider repeating the IM/IV hydrocortisone if poor response to initial steroid and fluid replacement.
- Initially start maintenance fluids – Plasma-Lyte® 148 & Glucose 5%; 100ml/kg for 1st 10kg, 50ml/kg/day for 2nd 10kg, 20mls/kg/day >20kg. (Note some patients may require Plasmalyte 148 with 10% Glucose to maintain normoglycemia).
- In patients with hypopituitarism who are on desmopressin for diabetes insipidus please do not prescribe their regular desmopressin without discussing with the paediatric endocrinologist on call.

6. If signs of sepsis, start antibiotics

Identify and treat the illness or injury that may have precipitated the adrenal crisis.

7. Monitoring

- Monitor vital signs (including blood pressure), blood gas and blood glucose hourly for 2 hours, then 2-4 hours once acidosis corrected.
- Urea & electrolytes 2 hourly initially

Interval can be extended once clinically improving, glucose stable and electrolytes normalising.

- Maintain strict fluid balance
- Regular senior review

Ongoing Management

1. **Discuss patient daily** or more frequently with paediatric endocrine consultant on call.

2. **Continue hydrocortisone**:

Children (>28 days)	Hydrocortisone dose and frequency
Severe illness	**2mg/kg (max 100mg)** IV bolus initially then bolus dose 6 hourly. (Can consider 4 hourly or as infusion in severely unwell children)
Stable and improving	**1mg/kg (max 50mg) IV 6 hourly**
Stable and tolerating drinks/diet	Oral sick day steroids: **30mg/m^2/day in 4 equally divided doses**. Restart fludrocortisone if indicated.

Neonates (<28 days)	Hydrocortisone dose and frequency
Severe illness	**4mg/kg IV initially 6 hourly** (Can consider 4 hourly or as infusion in severely unwell children)
Stable and improving	**2mg/kg IV 6 hourly** (Can consider 4 hourly or as infusion in severely unwell children)
Stable and tolerating drinks/diet	Oral sick day steroids: **30mg/m^2/day in 4 equally divided doses**. Restart fludrocortisone if indicated.

Hydrocortisone infusion

*Hydrocortisone can be given by continuous infusion in severely unwell children **(after initial dose has been given)** on the advice of the paediatric endocrinologist.*

Weight	Total dose of hydrocortisone in 24 hours	Infusion rate (50mg hydrocortisone in 50mL 0.9% sodium chloride)	Additional considerations
Less than 10kg	25mg	1 mL/hr	Consider more concentrated infusion in those needing fluid restriction (e.g. 100mg hydrocortisone in 50mLs 0.9% sodium chloride). The hydrocortisone infusion can be run alongside 0.9% sodium chloride, 5% glucose and Plasma-Lyte® solutions.
10.1 to 20kg	50mg	2 mL/hr	
20.1 to 40kg	100mg	4 mL/hr	
40.1kg to 70kg	150mg	6 mL/hr	
Over 70kg	200mg	8 mL/hr	

3. Fluids and Electrolytes

Features warranting slow or particularly careful rehydration in hyponatraemia.

Rapid correction of acute and chronic hyponatraemia can be associated with a significant risk of cerebral oedema and / or osmotic demyelination syndrome. There is a substantial risk of seizures with plasma Na <110 mmol/L and an elevated risk of the osmotic demyelination syndrome if plasma Na concentration <105 mmol/L.

A careful approach to rehydration is therefore needed in children with:

a. Severe hyponatraemia; plasma sodium < 120 mmol/l.
b. Reduced consciousness, seizures or other signs compatible with cerebral oedema.
c. Diabetes insipidus - (In patients with hypopituitarism who are on desmopressin please do not prescribe their regular desmopressin without discussing with the paediatric endocrinologist on call.

Key considerations in severe hyponatraemia

a. Avoid increasing plasma Na concentration by >10 mmol/L/day (~0.5 mmol/L/hr) in these circumstances. Sodium chloride 0.9% with stress doses of glucocorticoid can increase sodium concentrations more rapidly than this. Therefore, the IV fluid may need to be changed to one containing less sodium.
b. A slow, measured, increase in serum sodium can be achieved by linking sodium input (fluid) to output (urine) (i.e. giving a little more sodium than that present in the urine).
c. In patients with adrenal crisis careful monitoring of electrolytes is required. This is particularly important when hydrocortisone treatment is started because in addition to its mineralocorticoid action, hydrocortisone will also switch off ADH secretion leading to a diuresis and potentially a rapid rise in plasma sodium concentration.
d. 1mL/kg of 2.7% sodium chloride will increase the plasma Na concentration by about 1 mmol/L. This can be considered especially in the context of abnormal neurology or on-going severe symptomatic hyponatraemia. This bolus may need to be repeated. Close supervision and regular clinical assessment and monitoring of electrolytes is required.
e. Consider admission to PHDU/PICU
f. The rate of correction of hyponatraemia may be dependent on the underlying aetiology. The sodium should not rise >10mmol/L in 24 hours.

Hyperkalaemia treatment

a. Rehydration with sodium chloride and the administration of hydrocortisone are key measures that will reduce potassium in the context of adrenal crisis.
b. If plasma potassium is > 7.0 nmol/L or there are ECG changes – IV 10% calcium gluconate: 0.5 mL/kg (0.11 mmol/kg) slow IV administration over 10 minutes with ECG monitoring to stabilise myocardium. Maximum single dose 4.5 mmol (20 mL)
c. Nebulised salbutamol is a quick and readily available treatment that drives potassium into cells – 0 - 5 years: 2.5 mg; ≥5 years: 5 mg (three doses back-to-back).
d. If persistent hyperkalaemia - Insulin and glucose:
short-acting insulin (Actrapid): 0.1 units/kg in 5 to 10 mL/kg of 10% glucose IV over 30 minutes
e. If significant metabolic acidosis, consider sodium bicarbonate 1 mmol/kg IV over 30 minutes
f. Consider cation exchange resins – calcium or sodium polystyrene sulfonate (resonium) – 125 to 250 mg/kg QDS orally or PR in neonates.
g. Consider admission to PHDU/PICU. Potassium levels must be checked within 15 minutes post treatment and 1-2 hours after treatment.

Preparing for Discharge

- DO NOT discharge without informing the Paediatric Endocrinologist On-Call
- Arrange open access to local hospital for times of illness, ensure open access documentation signposts users to **this protocol** if they should present unwell.
- Ensure that the child has appropriate follow up in place with the endocrine team
- Ensure GP is informed of diagnosis, glucocorticoid treatments including sick day rules so that the family can get further supplies on repeat prescription.
- Prescribe injectable intramuscular hydrocortisone for home emergency use: Please prescribe **PAEDIATRIC EMERGENCY HYDROCORTISONE INTRAMUSCULAR INJECTION KIT** with the following doses. Paediatric endocrine nurses will TEACH PARENTS how to administer this:

Child's Age	Dose
Under 1 year	25mg
1-5years	50mg
Over 6 years	100mg

Paediatric endocrine nurses will arrange the following for patients newly diagnosed with adrenal insufficiency who are **under the care of an endocrinologist.**

- To give patient/parent a completed steroid replacement therapy card.
- Inform Welsh Ambulance Service for flagging of patient so that they are prioritised appropriately in an emergency.
- Teach the families about sick day rules - families should know how to increase the dose of hydrocortisone during illness.
- Provide family with written information about adrenal insufficiency
- Provide guidelines for the child's management at school/nursery.
- Teach parents to administer IM hydrocortisone in an emergency.
- Give family emergency contact numbers
- Add emergency alert to notes/ Welsh Clinical Portal.
- Advise about wearing medical alert bands
- **Patients and parents should be well trained in adrenal crisis recognition and management.**

- **Implementation**
  This guideline will be disseminated to the network centre lead at each DGH and they will inform their department that the guideline is available.

References

1. **Miller BS, Spencer SP, Geffner ME, Gourgari E, Lahoti A, Kamboj MK, Stanley TL, Uli NK, Wicklow BA, Sarafoglou K**. Emergency management of adrenal insufficiency in children: advocating for treatment options in outpatient and field settings. J Investig Med. 2020 Jan;68(1):16-25. doi: 10.1136/jim-2019-000999. Epub 2019 Feb 28. PMID: 30819831; PMCID: PMC6996103.
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3. **Park J, Didi M, Blair J.** The diagnosis and treatment of adrenal insufficiency during childhood and adolescence. *Arch Dis Child 2016; 101:860-865*
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5. **Wieteska, Susan** (2016) Advanced Paediatric Life Support: A Practical Approach to Emergencies
6. BNF for Children (2022) British National Formulary for Children 2022. London: British Medical Association and the Royal Pharmaceutical Society for Great Britain.
7. BSPED Adrenal Insufficiency Consensus Guidelines 2022