LRI Children's Hospital

Adrenal Crisis

Staff relevant to:	Clinical staff working within the UHL Children's Hospital
Approval date:	September 2022
Revision due:	September 2025
Written by: Reviewed by:	Paediatric endocrine team Savitha Shenoy
Version:	3.1
Trust Ref:	C29/2017

Contents

Abbreviations: Adrenal insufficiency – AI
Hypothalamo-pituitary-adrenal axis – HPA axis
Blood Glucose - BG

Helpful Contact numbers:

- Endocrine Secretary : 01162587737
- Paediatric Endocrine Specialist Nurses* :01162585326 (Office)
  Specialist Nurses mobile numbers: 07921 545455
  07929 776711

*Both nurses work part-time so please do not leave urgent voice mail messages.

- On-call Paediatric Endocrine Consultant

Working hours – refer to Medirota for COW Endocrine Consultant and their contact mobile number or via swtichboard

- Out of hours - East Midlands Paediatric Endocrine Consultant on-call: via Switchboard
- For non-urgent message: team can be contacted via email paediatricendocrineteam@uhl-tr.nhs.uk

Emergency management of children suspected to be in Adrenal Crisis flow chart

- New presentation of suspected adrenal crisis
- Known adrenal insufficiency (AI) presenting in adrenal crisis
- Suspected adrenal crisis due to HPA axis suppression from steroid treatment

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Investigations: (ref: Section 3)

- Secure venous access and complete all the investigations

Refer to **section 3** for details

Obtaining key biochemical samples prior to hydrocortisone in new presentation is crucial to identify diagnosis, if possible to achieve without delaying treatment

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Management: (ref: Section 4.1- 4.2)

- Correct BG < 3mmol/L – 2ml/kg 10% glucose and recheck BG in 15 mins
- Correct shock - 10ml/kg of 0.9% sodium chloride as a bolus and repeat if necessary
- Correct electrolyte imbalance (severe hyponatraemia/hyperkalemia) – refer to **section 4.2**
- Consider Sepsis – IV antibiotics
- Emergency Hydrocortisone dose - see below

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Emergency Hydrocortisone dose:

Age	IV hydrocortisone Dose	Indications
Less than 1 year	**25mg**	**Give IM hydrocortisone if acutely unwell and unable to get IV access.**
1 to 5 years	**50mg**	
6 years & over	**100mg**	Omit the dose if parent/paramedic has administered the dose in preceding 4 hours

Contact the on-call Paediatric Endocrine Consultant as soon as possible (Out of hours via switchboard and ask for the on call East Midlands Paediatric Endocrine Consultant on call) to notify and for advice on on-going management

Ongoing management flowchart:

On-going management: (**ref: Sections 4.2 to 4.6)**

Admission to PICU/HDU if very unwell

1 hourly blood gas and 2-4 hourly U&E monitoring until stable

Maintenance IV fluid including dehydration correction if necessary - 0.9% sodium chloride / 5% glucose is usually an appropriate starting point

Correct electrolyte imbalance – severe hyponatraemia/hyperkalaemia –**Section 4.2**

Close monitoring of vital signs including BP

Ongoing Hydrocortisone treatment – as below – ref: **Section 4.3**

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On-going Hydrocortisone regime – first dose 4 hours after emergency dose	
Children (28 days & older)	**Hydrocortisone dose and frequency**
Severe illness	2mg/kg/dose (max 100mg) IV initially 6 hourly* *Consider giving 4 hourly or as Hydrocortisone IV infusion as alternative regime in very unwell children – **see table 4**
Stable and/or improving	1mg/kg/dose (max 50mg) IV 6 hourly
Stable and tolerating drinks / diet	Start oral sick day Hydrocortisone regime: 30mg/m^2/day in 4 equally divided doses (**Appx - 2**) + oral Fludrocortisone if indicated (**section 4.4)**
Neonates (<28 days corrected gestational age)	**Hydrocortisone dose and frequency**
Severe illness	4mg/kg/dose IV initially 6 hourly* * Consider giving 4 hourly or Hydrocortisone IV infusion as alternative regime in very unwell – **see table 4**
Stable and improving	2mg/kg/dose IV 6 hourly
Stable and tolerating oral feeds	Start oral sick day Hydrocortisone regime: 30mg/m^2/day in 4 equally divided doses (**Appx-2**) + oral Fludrocortisone if indicated (**section 4.4**)

Contact the on-call Paediatric Endocrine Consultant as soon as possible (Out of hours via switchboard and ask for the on call East Midlands Paediatric Endocrine Consultant on call) to notify and for advice on on-going management

1. Introduction and who this guideline applies to

This guideline is intended for the use of clinicians working within the UHL Children's Hospital and Children's ED caring for;

1) Children and young people who may present with adrenal crisis if they have pre-existing adrenal condition and at risk of adrenal crisis which are –

   Central/Secondary Adrenal Insufficiency (AI) (ACTH deficiency) due to Hypopituitarism (pituitary hormone deficiencies) which includes septo-optic dysplasia, pituitary surgery/irradiation and traumatic brain injury.

   Primary Adrenal Insufficiency (AI) such as: Congenital Adrenal Hyperplasia (CAH), Congenital Adrenal Hypoplasia, Addison's disease due to APECED syndrome, previous history of adrenalectomy and other rare conditions (for example Smith-Lemli-Opitz on hydrocortisone replacement)

2) New first clinical presentation where adrenal crisis is suspected as likely diagnosis

3) This guideline is also applicable for those children presenting in suspected adrenal crisis when they are at risk of/confirmed to have hypothalamo-pituitary-adrenal axis (HPA) suppression (tertiary adrenal insufficiency) from long-term steroid treatment such as:

   - Patients on long term continuous systemic steroids (e.g. prednisolone) for underlying chronic medical conditions. Daily physiological glucocorticoid requirements in children are around 8mg/m2/day as Hydrocortisone. Thus children taking any preparation of steroid equivalent preparation at doses higher than this on continuous basis for three weeks or longer should be considered to be at risk of HPA suppression and potential to have adrenal crisis. Refer to table 1 for steroid inflammatory equivalence dose.

   - Weaning regime of long-term steroid treatment. The BNF for children (BNFc) recommends that gradual withdrawal of systemic corticosteroids should be considered in those whose disease is unlikely to relapse and have received more than 40mg prednisolone (or equivalent) daily for >1 week or 2 mg/kg/day for 1 week or 1mg/kg/day for 1 month.

   - The BTS/SIGN 2019 Asthma guidelines state a dose of >800 micrograms Beclomethasone diproprionate daily or equivalent (Fluticasone > 400 microgram/day) puts a child at risk of clinical adrenal insufficiency

   - Abrupt cessation of long-term steroid treatment

*Some of the patients in this group may already have been confirmed to have HPA suppression and may have been provided a BSPED steroid card which covers their emergency steroid regime which parents should be familiar with

Table 1: Steroid inflammatory equivalence chart (equivalences relative to 5mg prednisolone)		
Steroid	**Route**	**Equivalent dose**
Hydrocortisone	Enteral/ Intravenous	20 mg
Prednisolone	Enteral	5 mg
Methylprednisolone	Intravenous	4mg
Dexamethasone	Enteral/ Intravenous	750 microgram
Deflazacort	Enteral	6 mg
Betamethasone	Enteral	750 microgram
Prednisolone enema	rectal	1 x 20mg enema ~ 9mg oral prednisolone
Triamcinolone	Intra-articular / intramuscular	See notes below *

*** Triamcinolone withdrawal**: In patients who have received more than physiological doses of Kenalog (more than one injection during a three-week period), withdrawal should not be abrupt. The dose should be reduced and the dosage interval increased until a dose of not more than 40 mg and a dosage interval of at least three weeks have been achieved. Clinical assessment of disease activity may be needed

2. Definition and clinical features of Adrenal Crisis:

Definition of adrenal crisis in children:

An acute deterioration in health that is associated with

- Acute haemodynamic disturbance (hypotension or sinus tachycardia relative to age-related normal levels)
- Or a marked abnormality in one or more electrolytes (hyponatraemia, hyperkalaemia)
- Or hypoglycaemia
- That is not attributed to another illness, the features of which show significant resolution following parental glucocorticoid administration

Clinical features:

These may be evident as deficiency of Cortisol, Aldosterone or both.

Infants	**Child/young person**	**Features of Aldosterone deficiency**
Hypoglycaemia Jaundice Neonatal hepatitis Poor feeding Weight faltering Hyperpigmentation Collapse/death	Nausea, vomiting Weight loss Hypotension/ Postural hypotension Hypoglycaemia Worsening fatigue Hyperpigmentation Collapse/death h/o recurrent infections	Muscle weakness, fatigue Weight loss Nausea & vomiting Salt craving Hypotension/dizziness Hyponatraemia Hyperkalaemia Metabolic acidosis

Key Points in the assessment of a child with suspected adrenal crisis:

- The diagnosis should be considered in a child presenting with some/all of the clinical signs: shock, hypotension and volume depletion, hyponatraemia, hyperkalaemia (latter not always present), hypoglycaemia and increased serum urea and creatinine.

- There may be a more insidious onset with recurrent infections, recurrent episodes of hypoglycaemia or hyponatraemia. Other mild symptoms include history of postural dizziness or poor feeding in younger patients. Hence, diagnosis of adrenal insufficiency rather than adrenal crisis must be considered even if not all of the signs and symptoms of adrenal crisis are present.

- An adrenal crisis is often triggered by intercurrent illness such as gastro-enteritis or infection, trauma, or non-compliance with steroid replacement therapy or abrupt cessation of on-going long term steroid treatment.

- Some conditions can mimic the presentation of AI e.g. sepsis, obstructive uropathy (in neonates) as pseudohypoaldosteronism; thus highlighting the importance of taking the correct samples prior to treatment with hydrocortisone.

3. Investigations

The investigations required depend on whether this is:

A: **New** presentation of adrenal crisis

B: Child **known to have AI (primary or secondary) presenting in crisis**

C: At risk of AI from HPA axis suppression

3A. NEW PRESENTATION OF SUSPECTED ADRENAL CRISIS;
Take all of the following samples prior to the administration of Hydrocortisone treatment :
Blood samples:

- U&E (**ORANGE** top), Glucose (**YELLOW** top), Blood Gas
- Cortisol (1.2 ml Serum No Gel - **WHITE** top) *
- 17(OH) Progesterone (1.2 ml Serum No Gel - **WHITE** top)*
- ACTH (1.2 mls filled EDTA – **2 x RED** top **on ice**) - send to the lab within 30 mins*
- Renin (1.2 mls filled EDTA – **RED** top) – send to the lab within 30 mins*
- Aldosterone (1.2 mls filled EDTA – **RED** top)- send to the lab within 30 mins*

1 x **ORANGE** TOP
1 x **YELLOW** top
2 x **WHITE** top
2 x **RED** top
2 x **RED** top on ICE
All bottles to be filled to full 1.2 mls

Urine*:

- A spot random urine sample (white - **UNIVERSAL POT**) of at least 5mls or more (even smaller volume can still be processed so send whatever volume can be obtained) should be collected for **Urine Steroid profile** prior to administration of Hydrocortisone and sample needs to be sent to the lab within 30 mins. **Consider urine catheter sample in neonates and infants to avoid delay in securing urine sample and to avoid delay in treatment.**
- Urine for U&E (white – **UNIVERSAL POT**) as a separate sample – can still be sent if sample collected soon after Hydrocortisone administered.

** Urine steroid profile sample takes priority over urine U&E if urine sample obtained prior to administering Hydrocortisone is small.

* Please alert the on-call lab staff both in hours (Ext: 16560) and out of hours (duty biochemist on 16561 or via switchboard) so the samples are received and processed appropriately. Please hand deliver the samples to the lab rather than rely on porter and it's important to get lab staff attention so samples are not left in the box. Do not send these samples via 'chute system'. The samples can be taken at any time including out of hours provided lab staff are alerted to receive the samples promptly.

Other samples: FBC, CRP, Blood and urinalysis, mc&s prior to giving antibiotics

Obtaining biochemical (blood and urine) investigations before hydrocortisone administration is a key management step to identify the underlying diagnosis. If investigations are taken after hydrocortisone is given, the hydrocortisone will interfere with the interpretation of the results of the investigations. Treatment with hydrocortisone should not be delayed.

Key point to consider:

Neonate with urosepsis or obstructive renal condition can present with severe hyponatraemia +/- hyperkalemia with h/o failure to thrive,vomiting,etc – Pseudohypoaldosteronism (PHA) is a possible aetiology rather than adrenal condition such as CAH. Urine sample taken prior to first dose of Hydrocortisone for urine steroid profile, urine U&E and urine for mc&s prior to administering antibiotics is crucial to make an early diagnosis. Urine sample taken after administration of Hydrocortisone and antibiotics is unhelpful in differentiating the conditions. Hence, please consider a catheter sample if there is delay in collecting the sample. Renal ultrasound is also helpful in differentiation as urinary tract abnormality can be associated with PHA.

3B. A child known to have adrenal insufficiency/at risk of adrenal insufficiency

FBC, Gas, Glucose, U&E
Blood and Urine Cultures if clinically indicated

3C. A child at risk of adrenal insufficiency from HPA suppression

FBC, Gas, Glucose, U&E, Cortisol, ACTH
Blood and urine cultures if clinically indicated

4. Management:

4.1 Assess A B C & Emergency Hydrocortisone management

- Ensure airway and breathing are adequate.
- Monitor the patient using a cardiac monitor.
- Correct shock with fluid - 10 mL/kg 0.9% Sodium Chloride bolus IV and repeat if necessary
- Treat hypoglycaemia (blood glucose below 3.0 mol/L) using 2 mL/kg 10 % glucose - recheck blood glucose after 15 minutes and repeat bolus if necessary.
- Correct electrolyte abnormality (hyponatraemia, hyperkalaemia) with emergency measures (**refer to section 4.2 – Fluid and electrolyte management**)
- Identify and treat potential precipitating causes such as sepsis
- Give emergency dose of hydrocortisone (Table 2) – **AFTER** diagnostic blood and urine tests are collected (see section 3A) if safe to delay. This dose can be omitted if parent or paramedic has administered the correct dose within 4 hours from the time of first assessment in hospital. It is safer to repeat the dose if there are any queries or concerns if accurate dose/technique has been followed.

Table 2: Emergency Management of Adrenal Crisis with Hydrocortisone

Intramuscular (IM) or Intravenous (IV) hydrocortisone dose		
Age	**IM or IV hydrocortisone Dose**	**Other points to consider**
Less than 1 year	**25mg**	Dose can be given IM if no IV access If parent/paramedic has already administered this emergency dose in the preceding 4 hours, avoid this dose and prescribe maintenance dose as in section 4.3.
1 to 5 years	**50mg**	
6 years and over	**100mg**	

* Fludrocortisone is not necessary at this stage as the emergency dose of Hydrocortisone provides mineralocorticoid cover.

4. 2 Fluid & electrolyte management:

- Fluid and electrolyte imbalance should be corrected appropriately including dehydration correction if necessary.

- 0.9% Sodium chloride / 5% glucose is usually a good starting point for initial fluid management if the clinical and biochemical picture suggest that the low sodium has arisen primarily because of salt wasting.

- In primary AI, insufficient mineralocorticoid will cause hyponatraemia due to renal losses but in secondary AI, cortisol deficiency can lead to a lack of free water clearance which can contribute to hyponatraemia. In this latter scenario, a degree of fluid restriction may be more appropriate.

- **Appendix 1** highlights differences between primary and secondary AI

Hyponatraemia management:

- Hyponatraemia is a particular risk, either already present at first presentation or at risk of evolving with start of treatment due to physiological processes.

- 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.

- Hence, 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

d) When duration of illness or being unwell is more than one day

Key considerations in severe hyponatraemia
a) Avoid increasing plasma Na concentration by >10 mmol/l/day (~0.5 mmol/l/hr) in these circumstances. 0.9% sodium chlorine 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 in adrenal crisis, careful monitoring of electrolytes is required – 1 hourly blood gas and serum U&E monitored 2-4 hourly until stable. This is particularly important when hydrocortisone treatment is started because in addition to its' mineralocorticoid action, hydrocortisone will also switch off arginine vasopressin secretion leading to a diuresis and potentially a rapid rise in plasma sodium concentration. d) 1 ml /kg of 3% sodium chlorine 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) Need admission to HDU/PICU for close monitoring 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 management:

a) 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)
b) 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).
c) If persistent hyperkalaemia - Insulin and Glucose – short-acting insulin (Actrapid or Novorapid): 0.1 units/kg in 5 to 10 ml/kg of 10% glucose IV over 30 minutes
d) If significant metabolic acidosis, consider Sodium bicarbonate 1 mmol/kg IV over 30 minutes
e) Consider cation exchange resins – calcium or sodium polystyrene sulfonate (resonium) – 125 to 250 mg/kg QDS orally or PR in neonates.
f) Need admission to PHDU/PICU. Potassium levels must be checked within 15 minutes post treatment and 1-2 hours after treatment.

4.3 On-going hydrocortisone treatment:

Hydrocortisone has to be continued after emergency dose of hydrocortisone is administered and is summarised in table 3. First dose of ongoing treatment has to be administered **4 hours** from administration of the emergency dose.

Table 3: Ongoing Hydrocortisone regime – start 4 hours after emergency dose	
Children (28 days and older)	**Hydrocortisone dose and frequency**
Severe illness	2mg/kg/dose (max 100mg) IV initially 6 hourly* *Consider giving 4 hourly or as Hydrocortisone IV infusion as alternative regime in very unwell children – see table 4*
Stable and/or improving	1mg/kg/dose (max 50mg) IV 6 hourly
Stable and tolerating drinks / diet	Start oral sick day Hydrocortisone regime: 30mg/m^2/day in 4 equally divided doses (Appendix-2) + oral Fludrocortisone if indicated (section 4.4)
Neonates (<28 days corrected gestational age)	**Hydrocortisone dose and frequency**
Severe illness	4mg/kg/dose IV initially 6 hourly* * Consider giving 4 hourly or Hydrocortisone IV infusion as alternative regime in very unwell – see table 4*
Stable and improving	2mg/kg/dose IV 6 hourly
Stable and tolerating oral feeds	Start oral sick day Hydrocortisone regime: 30mg/m^2/day in 4 equally divided doses (Appendix-2) + oral Fludrocortisone if indicated (section 4.4)

Some children who are extremely unwell and on PICU setting may be suitable to have IV Hydrocortisone infusion rather than IV bolus doses. The dose regime and preparation of infusion is summarised in table 4. Once child is stable and improving, the infusion can be swapped over to 6 hourly IV Hydrocortisone boluses as in table 3.

Table 4: Intravenous Infusion (IVI) hydrocortisone doses			
Weight	**Total dose in 24 hours**	**Infusion rate (50mg hydrocortisone in 50ml 0.9% sodium chloride*)**	**Additional considerations**
≤10kg	25 mg	1 ml/hr	* Could 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 PlasmaLyte solutions
10.1 to 20kg	50 mg	2 ml/hr	
20.1 to 40kg	100 mg	4 ml/hr	
40.1 to 70kg	150 mg	6 ml/hr	
Over 70kg	200 mg	8 ml/hr	
Stable and/or improving	Can stop infusion and start 6 hourly bolus as in table 3 Change to oral sick day steroids when stable and tolerating oral fluids / diet		

Oral sick day Hydrocortisone regime:

- When the child is stable/improving and tolerating oral fluids/diet, oral sick day Hydrocortisone regime can be started.
- A total daily hydrocortisone dose of around 30mg/m^2/day given as four evenly spaced doses 6 hourly is recommended.
- Parents of children who have known diagnosis of AI or those confirmed to have HPA suppression from long-term steroid may have their individual oral sick day steroid dose regime (along with a BSPED steroid card) and this dose regime can be prescribed.
- Newly diagnosed patients and those children where their sick day regime is unclear/unavailable, a total daily hydrocortisone dose of 30mg/m^2/day given as four evenly spaced doses given 6 hourly is recommended. A guide to the oral sick day steroid dose which provides the equivalent dose to 30mg/m^2/day is given in **Appendix 2.**
- The actual dose may vary depending on the strength and preparation of the available hydrocortisone medication. Hydrocortisone tablet is available as 10mg strength tablets. Alternative Hydrocortisone preparation is available as Alkindi capsule (**Appendix 3**) which comes in strengths of 0.5 mg/1mg/2mg strength and preferable to use in neonates and children under the age of 5 years where smaller doses are required.
- Hence, a pragmatic approach for convenience may be to divide the total daily sick day steroid dose according to the strength of the hydrocortisone preparation prescribed with dose rounded up to nearest suitable dose for ease of administration.

4.4 Fludrocortisone:

- **Fludrocortisone** is an oral mineralocorticoid that is necessary in primary AI but not for secondary AI. (Appendix 1)
- The dose for this does not need adjustment in the event of sick day episode or adrenal crisis and should be continued as usual.
- When the child is on IV Hydrocortisone, the mineralocorticoid effect of hydrocortisone at stress doses is often sufficient to cover the mineralocorticoid requirement and hence Fludrocortisone is not necessary.
- When the Hydrocortisone is changed to oral sick day dose, oral Fludrocortisone needs to be started.
- For those children who are already on Fludrocortisone, their normal dose of once daily Fludrocortisone can be prescribed to start at their normal time in

morning. The most recent clinic letter on DIT3 or CITO should provide the accurate up-to-date dose of Fludrocortisone and this can be confirmed with the parents of the child.

- For children with new presentation of primary AI, the initial dose of oral Fludrocortisone is 50 – 100 microgram once daily. Some children, particularly neonates, may need oral sodium chloride supplements in addition to Fludrocortisone. Hence, discussion with Paediatric Endocrine team is advisable.

4.5 Monitoring clinical progress:

- Admission to PICU/HDU is advisable if child is very unwell and has issues such as severe electrolyte imbalance that needs close monitoring or if child is receiving Hydrocortisone infusion.
- Close observation on the ward including blood pressure
- Strict fluid input and output monitoring
- Regular blood sugar, blood gas and U&E monitoring – every 4 hours to start and then depending on progress
- Fluid and electrolyte imbalance should be corrected appropriately
- Weigh child on admission and where possible compare this weight to previous recorded measures. Monitor weight daily.

4. 6 Other aspects of treatment:

- In cases of combined cortisol deficiency and diabetes insipidus, close monitoring of electrolytes and fluid balance is required and early discussion with paediatric endocrinology consultant on call is required for advice on Desmopressin therapy regime.
- In cases of combined cortisol deficiency and hypothyroidism (e.g. hypopituitarism) supplementation with hydrocortisone is recommended for 48 hours before starting levothyroxine as this may precipitate an adrenal crisis.

5. Education & Discharge planning:

For all the newly diagnosed AI patients:

The endocrine team responsible for on-going care should be informed as soon as possible so they can review the child and organise planning for discharge. Education should be initiated as soon as possible to ensure that the child or young person and their family are confident in managing AI on discharge home. A checklist for

education, information sharing and discharge planning for all newly diagnosed adrenal insufficiency children is provided in **Appendix 4**.

For children with known AI presenting with adrenal crisis:

- Notify the named Consultant under whose care the child is of the admission and discharge (if not already done at admission) by phone (normal working hours) or by email if out of hours.
- Children who are well and tolerating normal food/fluids can be discharged home even if they are on sick day Hydrocortisone regime.
- Sick day regime can be changed to their 'normal daily dose' when the child has been apyrexial for at least 24 hours with no diarrhoea/vomiting. The sick day regime does not need to be continued for the duration of length of course of antibiotics if child is on oral antibiotics.
- Advise the parents to continue normal dose of Fludrocortisone (if child on Fludrocortisone).
- If the parents have used their emergency Hydrocortisone injection prior to admission, please provide a prescription for Hydrocortisone injection 100 mg/ml vial for use in emergency (doses as in Table 2) and needle supply. Ensure parents feel confident to administer the injection. If parents are unsure or request retraining on injection technique, this can be arranged via paediatric endocrine specialist nurses and copy of instruction (**Appendix 8**) can be provided.
- Education to ensure that the child or young person and their family are confident in managing AI on discharge home.
- The Endocrine team is responsible to ensure that every child is provided with BSPED steroid card (**Appendix 5**) (which provides normal maintenance dose, sick day dose, contact details for the endocrine team,etc) completed for parents to carry. A new card has to be completed following any change in their treatment plan. At discharge, their current BSPED steroid card has to be reviewed and updated/renewed as necessary.
- A copy of the 'Patient Information: Sick days: When to give additional steroids' **(Appendix 6)** can be provided if they do not have a copy provided already in clinic.

6. Education and Training

No new training is required to implement this guideline.

7. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
• Compliance with hydrocortisone doses (IM/IV or oral) • Time to discharge • Discussion with endocrine consultant prior to discharge	Clinical notes review	Endocrine team	Every 5 years	Audit meetings

8. Supporting References

1. Emergency and peri-operative management of adrenal insufficiency in children and young people: BSPED consensus guidelines. Developed by the Paediatric Adrenal Insufficiency Group On Behalf of the British Society of Paediatric Endocrinology & Diabetes (BSPED). For further information scan QR code below or visit BSPED |BSPED Adrenal Insufficiency Consensus Guidelines (https://www.bsped.org.uk/adrenal-insufficiency)

2. Simpson H, Tomlinson J, Wass J, Dean J, Arlt W. Guidance for the prevention and emergency management of adult patients with adrenal insufficiency. Clin Med (Lond). 2020 Jul;20(4):371-378. doi: 10.7861/clinmed.2019-0324. PMID: 32675141; PMCID: PMC7385786.

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5. Rubens M, Kanaris C. Fifteen-minute consultation: Emergency management of children presenting with hyperkalaemia. Arch Dis Child Educ Pract Ed. 2021 Aug 3:edpract-2021-322080. doi: 10.1136/archdischild-2021-322080. Epub ahead of print. PMID: 34344762.

6. Key Words

Adrenal Insufficiency, Hypothalamo-pituitary-adrenal axis, Endocrine, Hydrocortisone, Hyponatraemia, Hyperkalaemia, Fludrocortisone

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead Dr Savitha Shenoy (Consultant Paediatric Endocrinology)	**Executive Lead** Chief Medical Officer
Details of Changes made during review: • The guidelines was rewritten completely based on the most up-to-date published guidelines and publications (ref: BSPED guideline son topic) • Flowchart was updated to reflect change in management pathway • IV Hydrocrtisone infusion as an alternate regime was added • Dosage of IV bolus and oral sick day Hydrocortisone doses was amended • Guide to oral sick day doses as a table has been included as appendix to aid in prescribing doses based on body surface area • Checklist for discharge planning for all new patients has been implemented • Number of helpful appendices have been added and link to helpful websites has been included • Contact numbers and emails for the team has been updated V 3.1 Added hyperlink and QR code to BSPED Clarified where the links direct users to in appendix 4 BSPED adrenal insufficiency card – updated Updated appendix 8: hydrocortisone injection emergency kit instruction page to include paediatric advice	

Appendix 1: Management of fluid and electrolyte abnormalities in primary and secondary AI

Definition:	Primary AI (elevated ACTH levels)	Secondary AI (suppressed ACTH)
Glucocorticoid treatment	Usually Hydrocortisone	Usually Hydrocortisone (or Prednisolone)
Mineralocorticoid treatment	Fludrocortisone	Not required
Differences in fluid and electrolyte abnormalities and treatment between primary and secondary AI		
	Acute illness (primary AI)	**Acute illness (secondary AI)**
Possible abnormality of sodium and potassium	May have hyponatraemia and hyperkalaemia. Dehydration is due to mineralocorticoid deficiency causing salt and water loss.	ACTH and hence cortisol deficiency is associated with an inability to excrete a water load. Hyponatraemia, if present may be due to excess water. Potassium is usually normal. Thus patients may not be significantly fluid deplete.
Other possible electrolyte abnormalities	Hypoglycaemia Hypercalcaemia Metabolic acidosis	Hypoglycaemia
Treatment	Correct hypoglycaemia Glucocorticoids in stress doses have some mineralocorticoid action. Sick day oral hydrocortisone or intravenous hydrocortisone along with IV 0.9% NaCl will usually result in resolution of biochemical abnormality. In some cases, specific treatment for hyperkalaemia is required	Correct hypoglycaemia The volume and type of IV fluid may need to be adapted to the individual circumstance. This may include checking that adequate glucocorticoids have been provided

Appendix 2: Pre-calculated oral hydrocortisone sick day stress doses

A pragmatic approach for convenience may be to divide the total daily sick day steroid dose according to the strength of the hydrocortisone preparation prescribed (for example if the child or young person uses hydrocortisone 10mg tablets and the sick day dose is 6 mg four times a day, then it may be more practical to give 10 mg followed by 5 mg for the other three doses).

Weight (kg)	BNFc surface area	Total daily sick day steroid dose (mg) equivalent to 30/m^2/day	**Sick day hydrocortisone: dose**	**Frequency**
1	0.1	3	**0.8**	4 x a day
2	0.16	5	**1.2**	4 x a day
3	0.21	6	**1.5**	4 x a day
4	0.26	8	**2**	4 x a day
5	0.3	9	**2.5**	4 x a day
6	0.34	10	**2.5**	4 x a day
7	0.38	11	**3**	4 x a day
8	0.42	13	**3**	4 x a day
9	0.46	14	**3.5**	4 x a day
10	0.49	15	**4**	4 x a day
15	0.65	20	**5**	4 x a day
20	0.79	24	**6**	4 x a day
25	0.92	28	**7.5**	4 x a day
30	1.1	33	**7.5**	4 x a day
35	1.2	36	**10**	4 x a day
40	1.3	39	**10**	4 x a day
45	1.4	42	**10**	4 x a day
50	1.5	45	**10**	4 x a day
55	1.6	48	**12.5**	4 x a day
60	1.7	51	**12.5**	4 x a day
65	1.8	54	**12.5**	4 x a day
70	1.9	57	**15**	4 x a day
75	1.9	57	**15**	4 x a day
80	2.1	63	**15**	4 x a day

Appendix 3: Alkindi preparation of Hydrocortisone - Page 1of 2

What is Alkindi®?

Diurnal

Alkindi contains a medicine called hydrocortisone. Hydrocortisone belongs to a group of medicines known as corticosteroids. Hydrocortisone is a synthetic version of the hormone cortisol. Cortisol is made naturally by the adrenal glands in the body. Alkindi is used when the body is not making enough cortisol, because part of the adrenal gland is not working (adrenal insufficiency, often caused by an inherited condition called congenital adrenal hyperplasia).

REMEMBER:

Never add granules to liquid

Discard empty capsules

Reporting of side effects

If your child gets any side effects, talk to your doctor or pharmacist, this includes side effects not listed in the Alkindi package insert. You can also report side effects directly to United Kingdom Yellow Card Scheme. Website: **www.mhra.gov.uk/yellowcard** or search for MHRA Yellow Card in the Google Play or Apple App store. By reporting side effects, you can help provide more information on the safety of this medicine.

Important

Alkindi packaging contains a patient information leaflet about taking Alkindi. Please read the leaflet carefully, if you have any questions please ask your doctor or pharmacist.

Notes

Scan to view the dosing guide video

Diurnal Europe BV, Van Heuven Goedhartlaan 935 A, 1181LD Amstelveen, The Netherlands.

Tel. +31 (0)20 6615 072
Email: info@diurnal.co.uk

Date of preparation June 2022

Inf EU-GB-0177

Alkindi preparation – Page 2 of 2

Dosing Guide

Information for use only with patients who have been prescribed Alkindi® (hydrocortisone granules in capsules for opening)

How to open the Alkindi capsule and give the granules

1. Hold capsule so that the text is at the top and tap the capsule to make sure the granules are at the bottom

2. Gently squeeze the bottom of the capsule

3. Twist off the top of the capsule

4. Pour all granules out of capsule

Either pour all the granules directly onto the child's tongue

OR pour all the granules directly onto a spoon and place them in the mouth

OR for children who are able to take soft food, sprinkle the granules onto a spoonful of cold or room temperature soft food (such as yoghurt or fruit puree) and give immediately

Whichever method is used, tap the capsule to ensure all the granules are removed.

If you give the granules directly into the mouth, give a drink (e.g. water, milk, breast-milk or formula-milk) immediately after administration to help ensure all granules are swallowed.

If you give the granules sprinkled onto a spoonful of soft food, administer immediately (within 5 minutes) and do not store for future use.

DO NOT add the granules to liquid before administration as this can result in less than the full dose being given, and might also dissolve the taste masking of the granules allowing the bitter taste of hydrocortisone to become apparent.

Alkindi granules come in a capsule that must be opened before use, discard the empty capsule after use out of reach of children. Do NOT swallow the capsule — small children may choke.

Appendix 4: Education, Information Sharing and Discharge planning

Every child with AI requires a comprehensive package of information and education along with a management plan for urgent care. Education should be initiated as soon as possible to ensure that the child/young person and their family are confident in managing AI on discharge home. The clinical team responsible for on-going care should ensure these are actioned at the earliest.

Information, Education and Training required prior to initial discharge / at time of diagnosis	
Written information about adrenal insufficiency (BSPED, ESPE, SPEG etc.)	
Recommend use of BSPED steroid card which covers the below: **(Appendix 5)**	
• Current steroid treatment plan and doses (and mineralocorticoid if relevant)	
• Sick day oral steroid dose	
• Emergency hydrocortisone injection dose	
• Contact numbers for the endocrine team	
Emergency hydrocortisone injection kits (for home, nursery/school and any other regular residence (grandparents, parents not co-habiting) and injection leaflet (**Appendix 8)**	
Training to administer hydrocortisone injection (in person, virtual, YouTube) https://www.pituitary.org.uk/news/2020/08/hydrocortisone-injection-video(Solu-cortef; hydrocortisone sodium succinate - powder for dilution) https://www.youtube.com/watch?v=R5_BScN6HwE (Glass vial: hydrocortisone sodium phosphate	
Provide parents information on when to give additional steroids – **Appendix 6**	
Provide information on attending the Paediatric A&E facility for emergency	
Provide information for appropriate support group if applicable. livingwithCAH.com, addisonsdisease.org.uk, pituitary.org.uk	
Emergency contact numbers for local paediatric team and regional paediatric endocrinology team if applicable.	
Registered with the ambulance service (Red alert category) **Appendix 7**	
Medical alert added to notes / electronic hospital systems (Nervecentre) to flag that child has adrenal insufficiency	
Arrange an outpatient followup appointment to be reviewed promptly soon after discharge and review information at subsequent clinic visits	
Advice to wear a medicalert bracelet / necklace	
Letter to the GP to be sent promptly with diagnosis and medications that need to be provided as repeat prescription	
Recommended actions for family	
Download MyCortisol app	
Inform nursery / school	
Ensure adequate supplies of hydrocortisone for sick days and travel	
Medic alert bracelets / necklace / mobile phone medical ID	
Contact appropriate patient support group	
Regularly check that hydrocortisone injections are in date	
Subsequent visits (frequency dependent upon patient's needs)	
Review child/young person and family understanding of condition and sick day rules	
Update sick day doses based on up to date measurements.	
Ensure appropriate supply of medication/equipment	
Ambulance/Trak Alert/Medicalert jewellery in place	
School/Nursery/ other carers training up to date	
Review how any sick days were managed. Check if emergency hydrocortisone was required	

Appendix 5: BSPED adrenal insufficiency card

[bsped-ai-card-nov-2022-v1-4.pdf]

Sick days: When to give additional steroids			
Situation	**Change to usual steroid dose**	**Length of change**	**When to get help?**
Minor Illness			
Mild cold / runny nose with no fever. Minor playground bumps and bruises	No change		
Moderate or severe illness			
Fever, flu, infection, childhood illnesses (usually not well enough to go to school)	Sick day doses required	For as long as the illness lasts	Contact GP or medical team if not improving after 24-48 hours
Vomiting or diarrhoea	Sick day doses required		
	If sick day dose tolerated (kept down for at least 30 minutes with no frequent diarrhoea or vomiting), then continue oral sick day dosing		
	If sick day dose not tolerated, give IM hydrocortisone injection		If an IM injection of hydrocortisone is required, then dial 999 and inform them that the patient is having an adrenal crisis
Drowsy and unresponsive	**Give IM hydrocortisone injection**		
Major trauma or severe shock (e.g., suspected fracture, road traffic accident, head injury with loss of consciousness).	**Give IM hydrocortisone injection**		
Other (discuss with medical team)			
Routine or travel vaccinations	Consider 1 or 2 doses of sick day steroids. Continue if symptomatic		
Long haul flight	Give usual morning dose at 6 to 8 hourly intervals		
Child or centre specific recommendations			
Surgical and dental procedures			
Minor surgery (e.g., dental extraction under local anaesthetic)	Sick day dose prior to procedure Return to usual dose immediately afterwards	Continue sick day doses for up to 24 hours if in pain or unwell	Inform medical staff including dentist and anaesthetist that you/your child have adrenal insufficiency and take steroids
Major surgery (e.g., operation requiring general anaesthetic)	Sick day steroids (oral or IV) on day of procedure even when fasting. Intravenous hydrocortisone given on induction as per local hospital protocol	As per local policy or contact treatment centre for advice	

4

British Society for Paediatric Endocrinology and Diabetes: Adrenal Insufficiency Card

PAEDIATRIC STEROID CARE PLAN FOR SICK DAYS AND EMERGENCIES

IMPORTANT MEDICAL INFORMATION FOR PARENTS/CARERS & HEALTHCARE STAFF

This patient has adrenal insufficiency and is steroid dependent. Steroids should never be missed. Any stress situation, such as illness or surgery will require additional treatment

Name	**Address**
DOB	
NHS / CHI Number	
GP Contact Details	**Next of Kin Contact Details**
Paediatric Lead Consultant & Hospital	**Paediatric Endocrine Team Contact Details**
Diagnosis	**Date of issue**

Print double sided and 'flip pages short edge'. *BSPED AI Card.v1.4 Nov 2022* 1

Steroid Treatment Regimen		
Medication (and preparation) *e.g., Hydrocortisone (10mg tablet)*	**Time** *e.g., 6am*	**Dose** *e.g., 5mg (half a tablet)*

Oral sick day steroid treatment regimen in the event of an illness (See back page for more information on when this is required)		
Medication (and preparation)	**Time**	**Dose**
If patient takes fludrocortisone, no change in dose is necessary		

Emergency Steroid Injection		
If they show no sign of improvement, have persistent vomiting or diarrhoea, become drowsy or unresponsive, or has had a major accident or injury give intramuscular (IM) injection of hydrocortisone immediately		
Age less than 1-year: 25mg	**Age 1 to 5 years: 50mg**	**Age 6 years and over: 100mg**
Dial 999 stating they are having an ADRENAL CRISIS; they should be taken to the nearest A&E without delay		

Important information for medical emergency teams

If this patient is unwell and brought to hospital, the following management should be instituted promptly:

1. **Administer Emergency IM/IV hydrocortisone**
   Age less than 1-year 25mg
   Age 1 to 5 years 50mg
   Age 6 years and over 100mg
   (Check if this has been given by parent, caregiver, or ambulance crew)
2. Check **blood glucose**. Give 2ml/kg 10% dextrose IV if glucoses <3mmol/L
3. If **circulation** is compromised, give 10 ml/kg 0.9% saline bolus
4. Obtain U&E & **start IV fluids** 0.9% Saline/5% dextrose at a maintenance rate
5. **Ongoing hydrocortisone doses**:
   - Continue with IV hydrocortisone 2mg/kg (max 100mg) every 4-6 hours (or hydrocortisone infusion if very unwell).
   - Once stable, the IV bolus dose of hydrocortisone is 1mg/kg (max 50mg) every 6 hours.
   - For neonates (< 28 days) the IV bolus dose of hydrocortisone is 4mg/kg every 4-6 hours. Once stable the IV bolus dose is 2mg/kg every 6 hours.
   - Please refer to BSPED guidance for full details.
6. Once tolerating oral fluids, swap to oral sick day dosing until back to normal self (usually 2-3 days of sick day dosing).

Important: Please observe until patient is tolerating oral steroids at sick day dosing. Contact your acute paediatric or paediatric endocrine team if admission is required.

If the patient needs a **general anaesthetic or surgery,** please contact the paediatric endocrine team for a perioperative plan.
The recommended doses for hydrocortisone can also be found on the BSPED website below.

For further information scan the **QR code** or visit **website** to see BSPED guidance:
https://www.bsped.org.uk/adrenal-insufficiency

Appendix 6: Patient Information: Sick days: When to give additional steroids

Situation	Change to usual hydrocortisone dose	Length of change	When to get help?
Minor Illness			
Mild cold / runny nose with no fever. Minor playground bumps and bruises	No change		
Moderate or severe illness			
Fever, flu, infection, childhood illnesses (usually not well not enough to go to school)	Sick day doses required	For as long as the illness lasts	Contact GP or medical team if not improving after 24-48 hours
Vomiting or diarrhoea	Sick day doses required		
	If sick day dose tolerated (kept down for at least 30 minutes with no diarrhoea or continuous vomiting), then continue oral sick day dosing		
	If sick day dose not tolerated, give IM hydrocortisone injection		If an IM injection of hydrocortisone is required then dial 999 and inform them that the patient is having an adrenal crisis
Drowsy and unresponsive	Give IM hydrocortisone injection		
Major trauma or severe shock (e.g. suspected fracture, road traffic accident, head injury with loss of consciousness)	Give IM hydrocortisone injection		
Other (discuss with medical team)			
Routine or travel vaccinations	Consider 1 or 2 doses of sick day steroids. Continue if necessary		
COVID-19 vaccine	Sick day doses required	Sick day steroids for 48 hours	
Long haul flight over 12 hours	Give usual morning dose at 6 to 8 hourly intervals		
Child or centre specific recommendations			
Surgical and dental procedures			
Minor surgery (e.g. dental extraction under local anaesthetic)	Sick day dose prior to procedure	Return to usual dose immediately afterwards Continue for 24 hrs if in pain/unwell	Inform medical staff including dentist and anaesthetist that you/your child have adrenal insufficiency and take steroids
Major surgery (e.g. operation requiring general anaesthetic)	Sick day steroids (oral or IV) on day of procedure even when fasting. Intravenous hydrocortisone will be given on induction as per local hospital protocol	As per local policy or contact treatment centre for advice	

Appendix 7: Ambulance alert letter

NHS
University Hospitals of Leicester
NHS Trust

Caring at its best

University Hospitals of Leicester
Leicester Royal Infirmary
Paediatric Endocrinology
Infirmary Square
Leicester
LE1 5WW

Administrative Enquiries
Secretary: 0116 2587737
Appointments: 0300 303 1563

Web: www.leicesterhospitals.nhs.uk

East Midlands Ambulance Service NHS Trust
1 Horizon Place
Mellors Way
Nottingham Business Park
Nottingham
Nottinghamshire NG8 6PY

Email: cadadmin@nhs.net

Date:

Re: Patient's name:…….

Patient's date fo birth: ……..

NHS Number: ……..

Patients' address: ……

Hospital Name ……..

Hosptial Consultant name:

Consutlant secretary contact :…….

GP name/address: …….

I would be very grateful for your support in enabling your crew to administer emergency Hydrocortisone to the above patient if required. This patient has the condition (Congenital Adrenal Hyperplasia/Primary Adrenal Insufficiency/ACTH deficiency) needing daily steroid treatment and in times of illness is in danger of going into an adrenal/addisonian crisis.

If he/she has a vomiting illness, during which he/she is unable to keep oral Hydrocortisone down, or has any episode of serious injury or sudden unexplained collapse he/she should **have _____mg of** IV/IM Hydrocortisone administered as emergency treatment.

Although this patient may have an emergency injection kit at home there may not always be someone available who is in a position to be able to administer the injection. I understand that your Paramedics also carry Hydrocortisone emergency kits now and are authorised to inject patients with this disorder under the 2006 JRCAL guidelines.

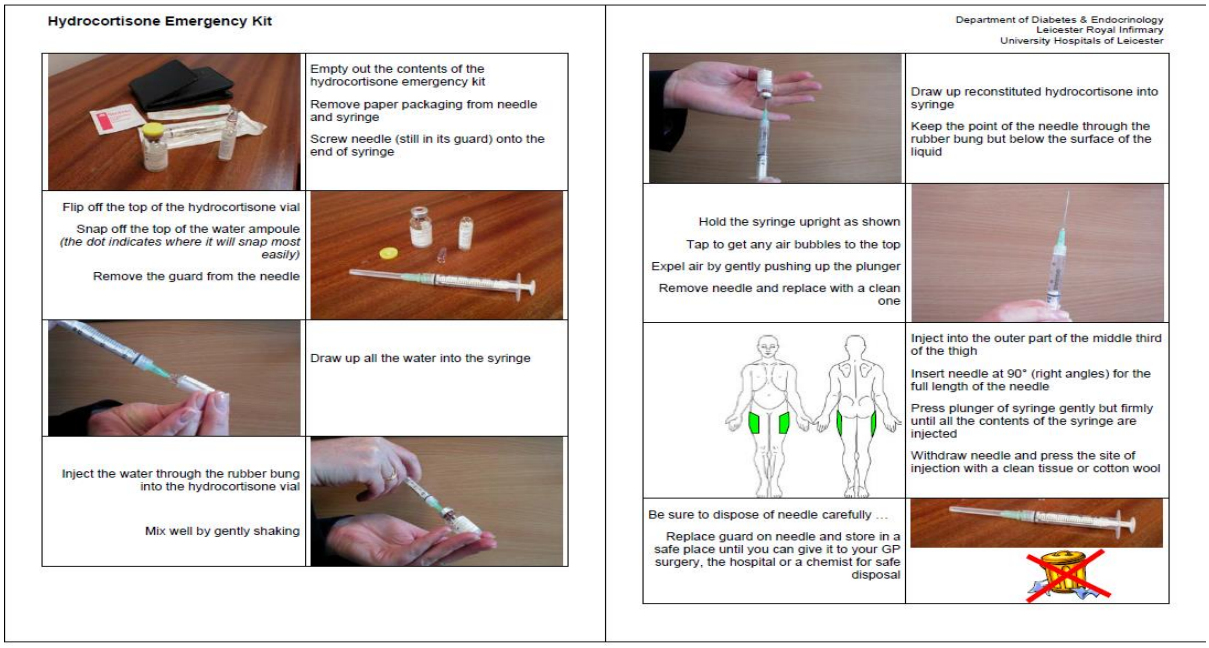
If called out for this patient, it is important for him/her to have emergency hydrocortisone administered by your crew and his/her blood glucose checked and treated if low. He/she should then be transferred to the nearest hospital.

I very much appreciate your co-operation in supporting this patient and if you are in any doubt about his/her management, please contact either the GP or Consultant mentioned above.

Thank you

Paediatric endocrine team, Leicester Royal Infirmary

Appendix 8: Hydrocortisone injection emergency kit instructions



Hydrocortisone Emergency Kit

Empty out the contents of the hydrocortisone emergency kit

Remove paper packaging from needle and syringe

Screw needle (still in its guard) onto the end of syringe

Flip off the top of the hydrocortisone vial

Snap off the top of the water ampoule *(the dot indicates where it will snap most easily)*

Remove the guard from the needle

Draw up all the water into the syringe

Inject the water through the rubber bung into the hydrocortisone vial

Mix well by gently shaking

Department of Diabetes & Endocrinology
Leicester Royal Infirmary
University Hospitals of Leicester

Draw up reconstituted hydrocortisone into syringe

Keep the point of the needle through the rubber bung but below the surface of the liquid

Hold the syringe upright as shown

Tap to get any air bubbles to the top

Expel air by gently pushing up the plunger

Remove needle and replace with a clean one

Inject into the outer part of the middle third of the thigh

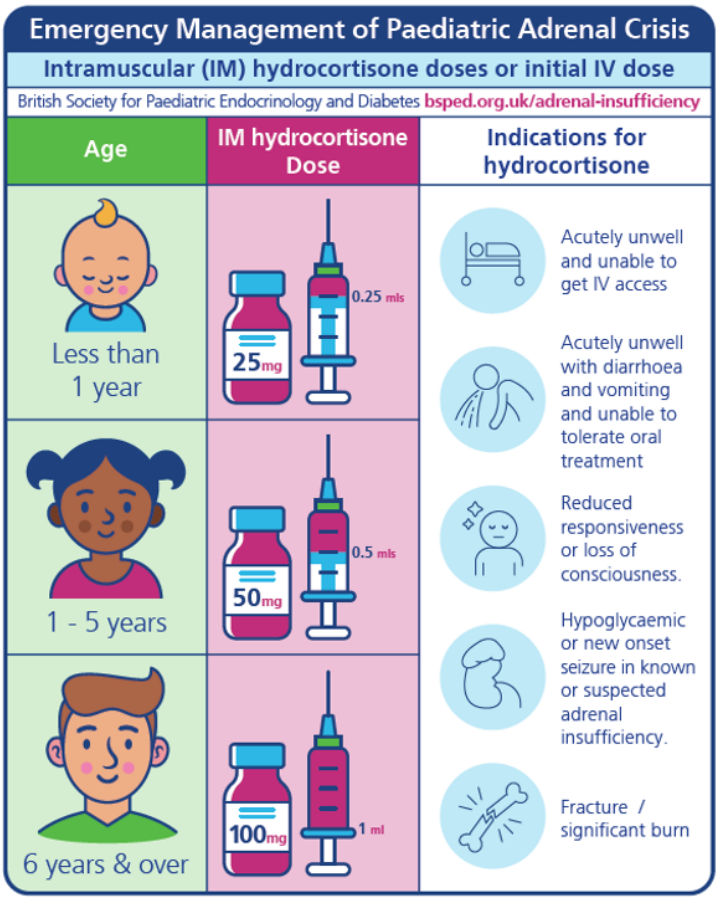
Insert needle at 90° (right angles) for the full length of the needle

Press plunger of syringe gently but firmly until all the contents of the syringe are injected

Withdraw needle and press the site of injection with a clean tissue or cotton wool

Be sure to dispose of needle carefully …

Replace guard on needle and store in a safe place until you can give it to your GP surgery, the hospital or a chemist for safe disposal



Appendix 9: My cortisol app

App for your mobile phone

- **My Cortisol** – There is a free app available for Android and Apple devices to help with emergency care of children with cortisol deficiency.