

## Acute Adrenal Insufficiency (Adrenal Crisis) - Full Clinical Guideline

Reference No.: CG-DIABEND/2024/005 v2.0

### 1. Introduction

#### Adrenal insufficiency

Adrenal insufficiency is caused by the failure of the adrenal gland to produce adequate cortisol. It may be a primary (Addison's disease due to disorders of the adrenal gland) or secondary (affecting the hypothalamus or pituitary). A common cause of adrenal insufficiency is the prolonged exogenous use of glucocorticoids (see below)

#### Adrenal crisis

Acute adrenal insufficiency or "Adrenal Crisis" is a potentially life-threatening emergency caused by a lack of cortisol. Adrenal crises may occur as the first presentation of adrenal insufficiency, or occur in patients with known adrenal insufficiency for whom cortisol replacement has been inadequate e.g. due to omitted doses of steroids or due to acute illness/stressors. The most common causes are mainly infection and fever (45%), but a number of other significant causes including surgery and pregnancy are also associated with Adrenal crises. Patients with additional comorbidities are especially prone to crisis

An internal audit at Royal Derby Hospital showed a lack of consistency in the management of adult patients admitted to hospital with adrenal insufficiency. A recent search of the National Reporting and Learning System (NRLS) identified 4 deaths, 4 patients admitted to critical care and around 320 other issues with steroid replacement therapy for patients with adrenal insufficiency or emergency treatment of adrenal crisis. This guideline covers the presentation, investigation and management of acute adrenal insufficiency as well as how to manage known adrenal insufficiency patients admitted for elective or emergency surgery & procedures.

## 2. Causes of Adrenal Insufficiency

Primary adrenal insufficiency	Secondary adrenal insufficiency	Iatrogenic (Tertiary Adrenal Insufficiency)
Autoimmune: Addison's disease Adrenal haemorrhage Adrenal metastases or lymphoma Infection Infiltration Bilateral adrenalectomy Congenital adrenal hyperplasia Drugs ACTH insensitivity Metabolic disease	Secondary to pituitary/hypothalamic disease or surgery. Symptoms of pituitary disease may be evident on examination (see below).	Adrenal insufficiency can result from administration of exogenous glucocorticoids (oral, topical, inhaled, intranasal or parenteral) with doses equivalent to 5 mg or more of prednisolone per day for longer than four weeks.

**Commented [Office1]:**  
Regarding your questions:

1. No need to go into details. Most important thing is to outline the 3 main categories Primary, secondary and prolonged steroid us.
2. Again, I don't think we need to go into too much details. Main things to mention are:
  - a- Adrenal insufficiency can be secondary to pituitary disease
  - b- Look out for symptoms and signs of pituitary disease when patients present
  - c- If due to pituitary failure, do not replace Thyroxine before managing acute adrenal insufficiency
  - d- Refer to endocrine to advise about need for pituitary investigations (MRI, pituitary hormone tests etc..)
3. A few notes added to the document.

## 3. Symptoms and signs of Acute Adrenal insufficiency

Diagnosis of adrenal insufficiency is often delayed or missed because symptoms are non-specific.

- Volume depletion
- Hypotension/significant postural drop
- Hyponatremia
- Hyperkalemia
- Fever, extreme lethargy, weight loss
- Abdominal pain, nausea, vomiting
- Hyperpigmentation (primary disease only)
- Hypoglycemia
- Symptoms of other pituitary axis deficiencies (secondary AI):
  - Symptoms and signs will vary depending on hormones affected but may include clinical features of hypothyroidism, gonadotrophin deficiency +/- diabetes insipidus (if posterior pituitary affected).
- Patients may present with adrenal insufficiency in isolation or may have a background of other autoimmune diseases.

**Commented [HA2]:** Worth mentioning.

## 4. Investigations

Investigations for suspected adrenal crises in patients **NOT** known to have AI

**\*\*If the patient is acutely unwell with clinical features of adrenal crisis, treatment should take priority and diagnostic tests can be performed at a later stage\*\***

**Commented [HA3]:** ? 9 AM cortisol

Send a pre-treatment random cortisol & ACTH (separate purple top container sent urgently to lab FAO of duty biochemist within 15-30 minutes (**on ice for samples taken at Burton site**) in patients with suspected adrenal crises. However, do not delay treatment to take a sample!

A low random cortisol can be useful for establishing a diagnosis for patients admitted with adrenal crises. A 9 AM cortisol lower than 100nmol/L is very suggestive of a diagnosis of

adrenal insufficiency whereas a concentration of more than 500nmol/L almost excludes the diagnosis.

**\*\*\*If clinical suspicion of adrenal insufficiency is high treatment should be commenced even if random cortisol is normal.\*\*\***

#### Short Synacthen Test

For patient in whom adrenal insufficiency is suspected but who is not acutely unwell/in crisis, the corticotrophin or short synacthen test is the gold standard diagnostic test.

#### **Short Synacthen Test**

*Procedure: – Full Guidelines Available on Koha*

- Take a baseline cortisol & ACTH
- Inject 250 micrograms synacthen (IM or IV)
- Take a repeat cortisol at 30 minutes
- Normal result: A 30 minute cortisol of >420 nmol/L

#### Other Investigations

U&E: Low Sodium, High Potassium, high Urea

Random Glucose: Low

VBG: Low pH/Acidosis; Low sodium and high potassium

FBC

LFT

CRP

## **5. Management**

**DO NOT** wait for the results if adrenal crises is suspected. In all patients send bloods for FBC, UE, LFT, Random cortisol, ACTH, venous blood gas and capillary blood glucose level.

- **Close monitoring is required during management.**
- **Hydrocortisone 100mg IV or IM STAT**  
Follow this with 50-100 mg hydrocortisone IM/IV every 6 hours or 200mg/24 hour infusion. IV/IM is readily available from Pharmacy and is the first option in emergency treatment.
- **Rapid IV Rehydration**  
500ml - 1L crystalloid (e.g. normal saline) in first hour, followed by further fluids as required.
- **Contact endocrinology for**
  - Urgent review
  - Advice on dose tapering
  - Further diagnostic tests (if new diagnosis) – this may include MRI pituitary and pituitary hormone profile if secondary adrenal failure is suspected. . The Endocrine team will also advise about tapering glucocorticoids and need for Fludrocortisone (Primary Adrenal Failure ONLY)
- **Regular monitoring of electrolytes and strict input output chart.**

- **Identify the trigger for the adrenal crises if possible and treat accordingly.**
- **Pituitary Failure:** In cases of adrenal insufficiency due to pituitary failure, DO NOT replace levothyroxine prior to managing the adrenal crisis.
- Once the patient is stabilised from the point of view of adrenal insufficiency, refer to endocrine for consideration of further investigations e.g. MRI pituitary and pituitary hormone profile

## **6. Management prior to discharge**

It has been found that a major factor in the precipitation of adrenal crises is a lack of adequate education of the patient and their caregiver in terms of what actions to take in the event of an imminent AC.

### **Educate patient/caregiver on:**

- Need for lifelong corticosteroid replacement
- Risks of inadequate corticosteroid replacement
- How to adjust for illness/periods of increased stress (**Sick Day Rules, see below**)
- How to recognise adrenal crisis and treat it with intramuscular hydrocortisone
- Need to inform managing team of diagnosis if undergoing medical/dental/surgical procedures
- **Carry a Steroid Emergency Card at all times (see point 7 below)**
- Wear a MedicAlert Identification
- Read the Emergency crisis leaflets

### **Sick Day Rules**

#### **1. During illness with fever**

During an illness with fever or an illness that requires bed rest and/or antibiotics, patients should double or triple their daily oral glucocorticoid dose.

#### **2. During illness with prolonged vomiting or diarrhoea**

Patients should double or triple their glucocorticoids if they are able to keep down the medications. However, patients should be taught to treat themselves with intramuscular hydrocortisone during periods of illness with prolonged vomiting or diarrhoea. If emergency intramuscular hydrocortisone is required, the patient should immediately seek urgent medical attention and may need to attend A&E out of hours.

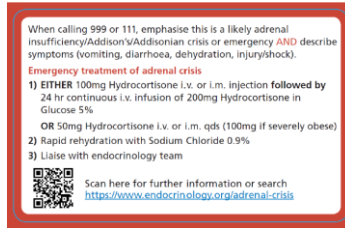
It is essential to avoid over-replacement by resuming the lower standard dose as soon as possible after the crisis has passed.

## **7. Steroid Emergency Card to support early recognition and treatment of adrenal crisis in adults**

A National Patient Safety Alert was released in August 2020 for all organisations that initiate steroid prescriptions to ensure prescribers issue a Steroid Emergency Card to all eligible patients.

**\*\*Please make sure your patient has been issued with a Steroid Emergency Card before they are discharged from the hospital\*\***

Steroid Emergency cards should be stocked in all major acute clinical areas.



## **8. Management of patients with Adrenal insufficiency undergoing surgery or invasive procedures**

<b>Type of Procedure</b>	<b>Pre-operative/Operative</b>	<b>Post-Operative</b>
Lengthy/Major Surgery with Long Recovery Time	100mg hydrocortisone IM/IV just before anaesthesia. Followed by: 100mg IM or IV 6 hourly 200mg/24 hours IV infusion	100mg IM or IV 6 hourly or 200mg/24 hours IV infusion until able to eat & drink normally If well, double oral dose for 48+ hours Then return to normal dose
Major Surgery with Rapid Recovery Time	100mg hydrocortisone IM/IV just before anaesthesia. Followed by: 100mg IM or IV 6 hourly 200mg/24 hours IV infusion	100mg IM or IV 6 hourly or 200mg/24 hours IV infusion until able to eat & drink normally If well, double oral dose for 24-48 hours Then return to normal dose
Labour/Vaginal Birth	100mg hydrocortisone IM/IV at start of active labour Followed by: 100mg IM or IV 6 hourly 200mg/24 hours IV infusion until delivery	Double oral dose for 24-48 hours after delivery then return to normal dose
Minor Surgery	100mg hydrocortisone IM/IV just before anaesthesia	Double oral dose for 24 hours then return to normal dose
Minor Procedure	Extra oral dose 60 minutes before procedure	Extra oral dose 60 minutes after procedure then return to normal dose
Bowel procedures requiring laxatives/enema.	All patients must be discussed with endocrinology consultant in advance. Most patients do not require admission however, some higher risk patients may do (especially for fludrocortisone or desmopressin dependent patients). All patients advised to take double dose oral steroids as soon as bowel prep is started AND Hydrocortisone 100 mg intravenously/intramuscularly at the start of procedure.	Double oral dose for 24 hours then return to normal dose
Other Invasive Procedure	100mg hydrocortisone IM/IV just before commencing	Double oral dose for 24 hours then return to normal dose
Major Dental Surgery	100mg hydrocortisone IM/IV just before anaesthesia	Double oral dose for 24 hours then return to normal dose
Dental Surgery	Double oral dose 1 hour before procedure	Double oral dose for 24 hours then return to normal dose
Minor Dental Procedure	Extra oral dose 60 minutes	Extra dose if hypoadrenal

before procedure

symptoms occur, then return  
to normal dose

**Additional Notes:**

- For any nil-by-mouth regimen, please arrange an intravenous saline infusion to prevent dehydration and maintain mineralocorticoid stability, e.g. 1000ml every 8 hours if >50kg.
- Monitor electrolytes and blood pressure post-operatively for all procedures requiring injected steroid cover. If the patient becomes hypotensive, drowsy or peripherally shut down, administer 100mg hydrocortisone IV or IM immediately & contact the on call endocrine team.
- Please ensure back-up supplies of oral and injectable hydrocortisone are available for resuscitation before commencing surgery. Even at full steroid cover, post-operative resuscitation may occasionally be required.

**Useful contacts:**

On call Endocrine Consultant/SpR: **07879 115507**  
(09:00 – 17:00)

Endocrine Specialist Nurse: **07557 480441**  
(09:00 – 17:00)

**Selected References:**

- (1) Society for Endocrinology Endocrine Emergency Guidance: Emergency management of acute adrenal insufficiency (adrenal crises) in adult patients.
- (2) Surgical Guidelines for Addison's disease and other forms of Adrenal Insufficiency. Addison's Clinical Advisory Panel
- (3) Diagnosis and Treatment of Primary Adrenal insufficiency: An Endocrine Society Clinical Practice Guideline
- (4) Exogenous steroids, adrenal insufficiency and adrenal crisis-who is at risk and how should they be managed safely. David Erskine- Specialist Pharmacy Services (SPS) Helen Simpson on behalf of Society for Endocrinology Steroid Emergency Card working group
- (5) Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency. Guidelines from the Association of Anaesthetists, the Royal College of Physicians and the Society for Endocrinology UK

**Documentation controls**

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	2	2024	Dr Hisham Ali	Review
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