

Guideline for the Management of Adrenal Insufficiency in Adults

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Adrenal crisis is a life-threatening emergency that can occur in patients with adrenal insufficiency.

Patients with adrenal crisis frequently present with non-specific symptoms, therefore, there should be a high degree of suspicion in individuals with adrenal insufficiency who present acutely.

If adrenal crisis is suspected clinically, treatment should be given **WITHOUT DELAY**. It is safer to treat and reassess later if there is any doubt whether an adrenal crisis may be occurring.

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This guideline is for use by the following staff groups: Doctors, Advanced Nurse Practitioners, Nurses, Physician Associates & Pharmacists.

Lead Clinician(s)			
Dr Ramalingam Bhaskar	Consultant, Diabetes & Endocrinology		
Dr Mohammad Abdus Salam	Locum Consultant, Diabetes & Endocrinology		
Dr Divya Garg	Locum Consultant Physician in Diabetes & Endocrinology		
Swapna George	Endocrine Specialist Nurse		
Approved by the Specialty Medicine Divisional Management Board on:	7 th March 2022		
Approved by Medicines Safety Committee on:	9 th March 2022		
Review Date: This is the most current document and is to be used until a revised version is available	9 th March 2025		

Date	Amendment	Approved by:
24/09/2021	New document approved	Specialist Medicine
		DMB/ MSC

Key amendments to this guideline

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This guideline will focus on following aspects as promoted by NHS England national patent safety alert (NatPSA)

- Steroid Emergency card
- Emergency management of adrenal crisis
- Management of adult patients with adrenal insufficiency during surgery & procedures
- Long term management with patient education
- Sick day rules

Introduction

Adrenal insufficiency is an often-unrecognised endocrine disorder, which can lead to adrenal crisis and death if not identified and treated.

The commonest causes of primary adrenal insufficiency include Addison's disease, congenital adrenal hyperplasia, bilateral adrenalectomy and adrenal haemorrhage.

Causes of secondary adrenal insufficiency are pituitary disease, pituitary tumours and their treatment (surgery and radiotherapy), and, also termed tertiary adrenal insufficiency, hypothalamic–pituitary–adrenal axis (HPA) suppression from exogenous steroids or, more rarely, from treatment of primary brain or nasopharyngeal tumours with radiotherapy when the hypothalamus and/or pituitary is included in the treatment field.

Omission of steroids in patients with adrenal insufficiency, particularly during physiological stress such as an intercurrent illness or surgery, can also lead to an adrenal crisis.

An incidence of adrenal crisis in primary adrenal insufficiency of 8.3 crises in 100 patient years and 3.6–5.2 per 100 patient years in secondary adrenal insufficiency has been reported.

Patients with adrenal crisis frequently present with non-specific symptoms, therefore, there should be a high degree of suspicion in individuals with adrenal insufficiency who present acutely. If adrenal crisis is suspected clinically, treatment should be given WITHOUT DELAY. It is safer to treat and reassess later if there is any doubt whether an adrenal crisis may be occurring. There are no adverse consequences of initiating life-saving hydrocortisone treatment.

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Clinical Features

Most commonly, patients with adrenal crisis feel 'generally unwell' with severe fatigue/lethargy, dizziness, nausea, vomiting, diarrhoea, abdominal pain and/or hypotension. Drowsiness and coma are late features.

Biochemically, patients may have hyponatraemia, hyperkalaemia (in primary adrenal failure only, in secondary or central hypoadrenalism potassium will be normal), hypoglycaemia and/or Acute Kidney Injury secondary to dehydration.

In patients with type 1 diabetes, adrenal insufficiency may present with recurrent hypoglycaemia.

Precipitating factors:

The commonest causes of crisis in known adrenal insufficiency are gastrointestinal illness (23%), other infections (25%), peri-surgery (10%) and physiological stress/pain (9%).

Investigations:

- Basic tests (all patients): FBC, U&Es, Capillary blood glucose, venous blood gas.
- Investigation of the precipitating cause (i.e., cultures for infection)

If adrenal crisis is suspected in patients not already known to have adrenal insufficiency:

- Take paired sample of cortisol and ACTH before starting hydrocortisone (<u>if this will not</u> <u>delay the hydrocortisone treatment</u>). The sample needs to be sent to the lab immediately as ACTH is a time sensitive test.
- Formal confirmation of diagnosis can be safely carried out after clinical recovery.

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Patients who are issued with steroid alert card need steroid cover during intercurrent illness, surgery & invasive procedures

Type of procedure	Pre-operative and operative needs	Post-operative needs
Surgery under anaesthesia (general or regional) Including major bowel surgery, procedures needing ITU, endoscopy, Caesarean delivery	100 mg hydrocortisone IV before anaesthesia then 200mg hydrocortisone infusion in 48ml 0.9% Sodium Chloride over 24 hours IV peri-operatively or 50 mg hydrocortisone IV 6 hourly	Continue hydrocortisone infusion while nil by mouth Double oral dose for 48-72 hours. Return to normal dose until symptomatically well
Bowel procedures requiring laxatives/enema	Consider intravenous fluids and injected glucocorticoid (hydrocortisone 50 mg IM or IV 6 hourly) during preparation, especially for fludrocortisone or vasopressin-dependent patients Hydrocortisone 100 mg intravenously or intramuscularly at the start of procedure	Oral double dose of steroids for 24 hours
Labour and vaginal birth	 100 mg hydrocortisone IV/IM at onset of birth then 50 mg IV 6 hourly until 6 hours after delivery or 200mg hydrocortisone infusion in 48ml 0.9% Sodium Chloride over 24 hours IV and then until 6 hours after delivery 	Double oral dose for 48 Hours, may have to be extended if postpartum period is complicated If well, then return to normal dose.
Body surface and intermediate surgery	Hydrocortisone 100 mg, intravenously at induction, followed by immediate initiation of a continuous infusion of hydrocortisone 200 mg/24 hours. Alternatively, hydrocortisone 50 mg IM 6- hourly or Dexamethasone 6–8 mg intravenously, if used, will suffice for 24 hours.	Double oral dose for 48 hours. If well, then return to normal dose.

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Patient (and their family) education for long term management

- Sick Day Rules as mentioned below
- Teach how to inject emergency hydrocortisone injection
- Provide with emergency steroid Kit
- Replace emergency steroid kit before discharge if used before or during acute admission
- Encourage wearing medical alert bracelets or pendants.
- Issue emergency steroid card.
- Issue steroid safety leaflet.
- Self-help group website(https://www.addisons.org.uk/)
- Remind never to miss the steroid dose

Sick Day Rule 1

Moderate intercurrent illness: Fever, infection requiring antibiotics, surgical procedure under local anaesthesia- **Double usual daily glucocorticoid dose**

Sick Day Rule 2

Severe intercurrent illness, persistent vomiting or diarrhoea (e.g. GI viral illnesses), during preparation for colonoscopy or in case of acute trauma or surgery- **Hydrocortisone 100 mg intramuscularly or intravenously at onset**, followed by initiation of a continuous infusion of hydrocortisone 200 mg over 24 hours Or hydrocortisone 50mg every 6 hours* IM or IV

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Steroid Emergency Card (Adult)	45
(Adult)	
IMPORTANT MEDICAL INFORMATION FOR HEALTHCARE S THIS PATIENT IS PHYSICALLY DEPENDENT ON DAILY STEROID T as a critical medicine. It must be given/taken as prescribed and omitted or discontinued. Missed doses, illness or surgery can adrenal crisis requiring emergency treatment.	THERAPY d never
Patients not on daily steroid therapy or with a history of stero may also require emergency treatment.	oid usage
Name	
Date of Birth NHS Number	
Why steroid prescribed	
Emergency Contact	
When calling 999 or 111, emphasise this is a likely adrenal	
insufficiency/Addison's/Addisonian crisis or emergency ANI symptoms (vomiting, diarrhoea, dehydration, injury/shock)	

Emergency treatment of adrenal crisis

- Immediate 100mg Hydrocortisone i.v. or i.m. injection.
 Followed by 24 hr continuous i.v. infusion of 200mg Hydrocortisone in Glucose 5% OR 50mg Hydrocortisone i.v. or i.m. qds (100mg if severely obese).
- 2) Rapid rehydration with Sodium Chloride 0.9%.
- 3) Liaise with endocrinology team.



Scan here for further information or search https://www.endocrinology.org/adrenal-crisis

- All clinicians prescribing steroids (e.g. in clinics or authorising repeat prescriptions) should ensure that their patients have been issued a Steroid Emergency Card, where necessary.
- For inpatients, the ward clinical team can contact the hospital pharmacy to replace the card, lost by patients or which are damaged.

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Worcestershire Acute Hospitals



Emergency Hydrocortisone Injection Kit

- 1 x Injectable hydrocortisone sodium succinate (powder that requires mixing Solu-Cortef®)
- 1x 10ml sterile water for injection ampoule (advise patient to aseptically add 2 ml of sterile water for injections to the contents of one vial of Solu-Cortef® 100 mg, shake and withdraw for use)
- 1 x Syringe that can hold 2ml of liquid
- Please note that the kit may also contain a prefilled ampoule of 100mg hydrocortisone sodium phosphate (Efcortesol®) instead of Solu-Cortef®.
- Provide patient with instruction leaflet downloadable from: <u>https://www.addisonsdisease.org.uk/the-emergency-injection-for-the-treatment-of-adrenal-crisis</u> the site also include links to watch administration videos for patients.
- 1 x NHS steroid emergency card
- Emergency Kit contains 2 injection hydrocortisone 100mg, 2 water for injection 10mls, 2 syringes 2mls, 4 intramuscular needles 23G, 2 skin wipes, one red steroid emergency card, one sick day rules booklet
- Please ensure that the patient has full emergency kit provided at the time of discharge. Please replace any content, if used during an acute admission.

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Worcester Acute Hospital Trust Red steroid card and sick day rule booklet order information:

- 1. Steroid emergency card Xerox order number for Worcester Acute Trust: WR5 735
- 2. Patient information booklet sick day rule for Adrenal insufficiency: WAHT- PI 0705
- 3. Patient information booklet how to do injection hydrocortisone: WAHT PI 0703

4. To add on PAS/ Bluespier alert: Click to display warning and enter 242226. Risk of Adrenal Crisis, then submit.

The following patients need to be given a **Steroid Emergency Card**:

- 3 or more short courses of high-dose oral glucocorticoids within the last 12 months, and for 12 months after stopping (see Table 1)
- 3 or more intra-articular/intramuscular glucocorticoid injections within the last 12 months, and for 12 months after stopping
- Repeated courses of dexamethasone as an antiemetic in oncology regimens, and for 12 months after stopping (the Steroid Emergency Card should be given on first cycle of dexamethasone when future cycles are anticipated).
- Prolonged courses of dexamethasone (>10 days) for the treatment of severe Covid-19
- Inhaled steroids >1000 microgram/day beclomethasone or >500 microgram/day fluticasone (or equivalent dose of another glucocorticoid), and for 12 months after stopping
- Patients taking inhaled corticosteroids at doses described in Table 4 and any other form of glucocorticoid treatment (including potent/very potent topical glucocorticoids, intra-articular injection, regular nasal glucocorticoids).
- Topical high-dose (>/= 200g/ week) potent or very potent glucocorticoids used across a large area of skin for 4 weeks or more, or factors increasing absorption assessed on a case-by-case basis, and for 12 months after stopping.
- Potent or very potent topical glucocorticoids applied to the rectal or genital areas and used at high dose (more than 30g per month) for more than 4 weeks, and for 12 months after stopping
- Patients prescribed any form of ongoing glucocorticoid treatment (except small amounts of a mild or moderate topical glucocorticoid which should be assessed on a case-by-case basis) in conjunction with medicines known to be potent CYP3A4 inhibitors

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The following patients need to be given a **Steroid Emergency Card** and **'Sick Day Rules' advice** as they are at risk of adrenal crisis:

- Patients taking oral prednisolone 5mg or above (or equivalent dose of other oral glucocorticoids) for more than 4 weeks, and for 12 months after stopping oral steroids (see Table 2 below)
- Patients receiving intra-articular or intramuscular glucocorticoid injections who also use glucocorticoids by another route (e.g. inhaled steroids, nasal steroids etc.)
- Patients with respiratory disease such as COPD and asthma on high dose inhaled steroids receiving repeated courses of oral steroids (3 or more courses over the past 6 months).
- Concomitant use of CYP3A4 enzyme inhibitors (see list below) and glucocorticoids (any route of administration except small amounts of topical mild or moderate potency glucocorticoid which should be assessed on a case by case basis)

Table 1: Short-term oral glucocorticoids (one week course or longer and has been on long-term course within the last year or has regular need for repeated courses)

Medicine	Dose (equivalence as per BNF)	
Betamethasone	6mg per day or more	
Budesonide	12mg per day or more(*)	
Deflazacort	48mg per day or more	
Dexamethasone	6mg per day or more	
Hydrocortisone	160mg per day or more	
Methylprednisolone	32mg per day or more	
Prednisone	40mg per day or more	
Prednisolone	40mg per day or more	
Triamcinolone	4mg per day or more	

(*) based on best estimate

Table 2: Long-term oral glucocorticoids (i.e., 4 weeks or longer)

Medicine	Dose (equivalence as per BNF)
Betamethasone	750 microgram per day or more
Budesonide	1.5mg per day or more(*)
Deflazacort	6mg per day or more
Dexamethasone	750 microgram per day or more
Hydrocortisone	20mg per day or more
Methylprednisolone	4mg per day or more
Prednisone	5mg per day or more
Prednisolone	5mg per day or more
Triamcinolone	4mg per day or more

(*) based on best estimate

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Table 3: Inhaled or nasal glucocorticoid doses

Medicine	Dose (*)
Beclometasone (as non-proprietary,	800-1000 microgram per day
Clenil, Easihaler, or Soprobec)	
Beclometasone (as Qvar, Kelhale or	400-500 microgram per day (check if using
Fostair)	combination inhaler and MART regimen)
Budesonide	800-1000 microgram per day
	(check if using combination inhaler and
	MART regimen)
Ciclesonide	320-480 microgram per day
Fluticasone propionate	400-500 microgram per day
Fluticasone furoate (as Trelegy and	100-200 microgram per day
Relvar)	
Mometasone	400 microgram per day

*Dose equivalence as per **Inhaled corticosteroid doses for NICE's asthma guideline** (2018)

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CYP3A4 enzyme inhibitors increasing cortisol concentration and risk of HPA axis suppression

Patients prescribed any form of ongoing glucocorticoid treatment, at any dose, in conjunction with any of the medications below which are potent CYP3A4 inhibitors, should be issued with a Steroid Emergency Card

Potent Protease inhibitors:

Atazanavir Darunavir Fosamprenavir Ritonavir (+/- lopinavir) Saquinavir Tipranavir

Non-nucleoside reverse transcriptase inhibitors: Efavirenz

Antifungals:

Itraconazole Ketoconazole Voriconazole Posaconazole

Antibiotics:

Clarithromycin—long term courses only

Others:

Cobicistat

*Some of the antiretroviral therapy drugs are used as single tablet regimes; hence clinicians need to search carefully for the constituent compounds if they are not familiar with this pharmacological field.

Such cases should be flagged early to endocrinology and infectious disease team with specialist pharmacy input.

Please check for any HIV drug interactions on the following link: <u>https://www.hiv-druginteractions.org/checker</u>

Legal liability guideline statement

- Guidelines or Procedures issued and approved by the Trust are considered to represent best practice.
- Staff may only exceptionally depart from any relevant Trust guidelines or Procedures and always only providing that such departure is confined to the specific needs of individual circumstances.
- In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional, it is fully appropriate and justifiable such decision to be fully recorded in the patient's notes.

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References

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Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Dr May Thin Khine (ST3)
Dr Divya Garg (Consultant)
Dr Ramalingam Bhaskar (Consultant)
Alison Hall (Lead Nurse- Diabetes)
Dr Mohammad Abdus Salam (Consultant)
Dr Andrew Bates (Consultant)
Dr Irfan Babar (Consultant)
Dr Munir Babar (Consultant)
Dr Andreea Ganea-Arnold(Consultant)
Swapna George (Endocrine Specialist Nurse)
Helen Payton (Specialist Pharmacist)
Lindsay Stewart (Specialist Pharmacist)

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Specialty Medicine Divisional Management Board
Medicines Safety Committee

Supporting Document 1 - Equality Impact Assessment Tool

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page.

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Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council	Herefordshire CCG
Worcestershire Acute Hospitals NHS Trust	~	Worcestershire County Council	Worcestershire CCGs
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust	Other (please state)

Name of Lead for Activity	Dr Ramalingam Bhaskar

Details of			
individuals	Name	Job title	e-mail contact
completing this assessment	Dr Ramalingam Bhaskar	Consultant	RAMALINGAM.BHASKAR@NHS.NET
	Dr Mohammad Salam	Consultant	Mohammad.salam@nhs.net
Date assessment completed	01/10/2021		

Section 2

Activity being assessed (e.g., policy/procedure, document, service redesign, policy, strategy etc.)		Title: Guideline for the Management of Adrenal Insufficiency in Adults			
What is the aim, purpose and/or intended outcomes of this Activity?	Suspect, diagnose and manage, and also prevent adrenal crisis				
Who will be affected by the development & implementation of this activity?	Image: Service User Image: Staff Image: Service User Image: Staf				
Is this:	 Review of an existing activity New activity Planning to withdraw or reduce a service, activity or presence? 				

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What information and evidence have you reviewed to help inform this assessment? (Please name sources, e.g., demographic information for patients / services / staff groups affected, complaints etc.	Journal of endocrinology & metabolism Addison's disease self-group Society for Endocrinology guidelines, NICE guidelines
Summary of engagement or consultation undertaken (e.g., who and how have you engaged with, or why do you believe this is not required)	Colleagues in endocrinology department, junior doctors in medicine
Summary of relevant findings	Adrenal crisis is serious problems, but can be prevented and also if happened can be diagnosed and treated

Section 3 Please consider the potential impact of this activity (during development & implementation) on each of the equality groups The potential impact for backwise for each Equality Group and explain your rationale. outlined below. Please tick one or more impact box below for each Equality Group and explain your rationale. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g., staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential <u>positive</u> impact	Potential <u>neutral</u> impact	Potential <u>negative</u> impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age	~			Persons will be treated as per guidelines irrespective of age,
Disability	~			Persons will be treated as per guidelines irrespective of any disability
Gender Reassignment		✓		Treatment will be given irrespective of sex reassignment
Marriage & Civil Partnerships	~			Treatment will be given irrespective of marriage status
Pregnancy & Maternity	~			Treatment will be given as per guidelines
Race including Traveling Communities	✓			Treatment will be given irrespective of communities' identity
Religion & Belief	√			Treatment will be given irrespective any religion
Sex	 ✓ 			Treatment will be given irrespective of gender
Sexual Orientation		✓		Treatment will be given irrespective sexual orientation
Other Vulnerable and Disadvantaged Groups (e.g., carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)	×			Treatment will be given irrespective of whether they belong to any group

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Equality Group	Potential <u>positive</u> impact	Potential <u>neutral</u> impact	Potential <u>negative</u> impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)	~			The guidelines will help to deliver care without any health inequalities

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
	None			
How will you monitor these actions?	N/A			
When will you review this EIA? (e.g., in a service redesign, this EIA should be revisited regularly throughout the design & implementation)	N/A			

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carers etc., and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person	Dr Ramalingam Bhaskar
completing EIA	

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Date signed	01/10/2021
Comments:	None
Signature of person the Leader	
Person for this activity	
Date signed	
Comments:	
Comments:	



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Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue?	No
3.	Does the implementation of this document require additional manpower?	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff?	NO
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval.

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