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Adrenal insufficiency and Addison's disease

1. Adrenal insufficiency and Addison's disease

In 2024, NICE published guidance on adrenal insufficiency (including Addison's disease) ([NICE 2024, NG243](#)).

We suspect that, for most of us, a quick reminder of the physiology and common presentations in primary care may be helpful. We'll address that first, before going into the detail of the NICE guidance.

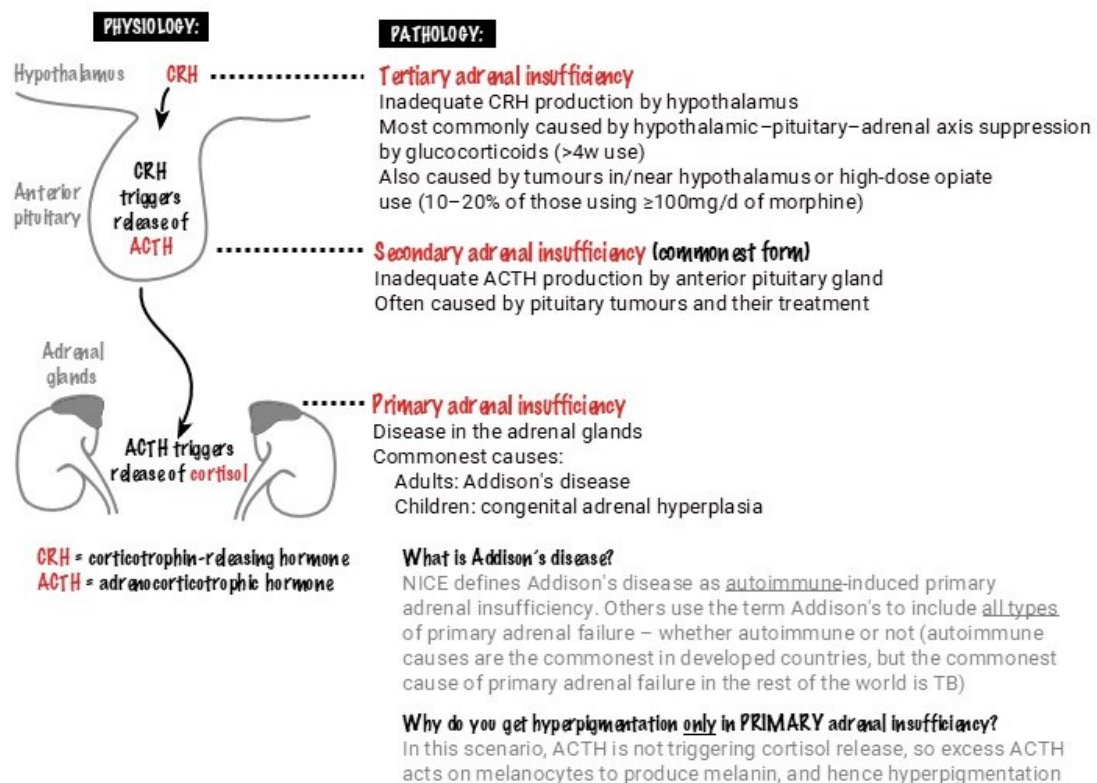
It is worth noting that we have traditionally been told that the physiological requirement for glucocorticoids was equivalent to 7.5mg/d of prednisolone. NICE tells us it is now thought the requirements are lower: 3 to 5mg/day of

prednisolone.

This article was updated in November 2024.

1.1. Physiology and pathology

Just a quick reminder of this before we start:



What do the adrenal glands produce?

The adrenal cortex produces:

- Glucocorticoids (cortisol): affects the body's response to stress/illness, blood pressure, glycaemic regulation.
- Mineralocorticoids (aldosterone): regulate salt and water levels.

- Sex hormones: oestrogen/testosterone.

The adrenal medulla produces catecholamines such as adrenaline (usually unaffected by the hypothalamic–pituitary axis).

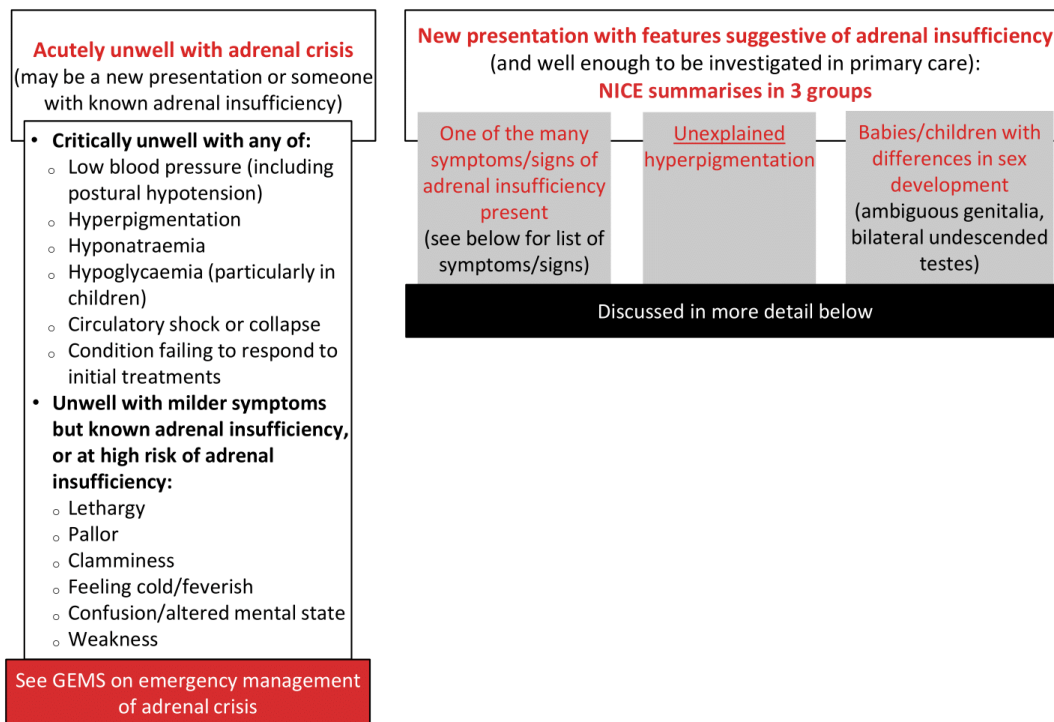
How common is adrenal insufficiency?

NICE tells us ([NICE press release](#) 28 August 2024):

- There are approximately 1200 hospital admissions/year for adrenal crisis (based on data from 2022–23).
- Around 6–8000 people in England have primary adrenal insufficiency.
- Around 8–16 000 people in England have secondary adrenal insufficiency.

1.2. Presentation

In primary care, adrenal insufficiency may present because someone is acutely unwell or because other features make us consider the diagnosis. NICE suggests how adrenal insufficiency may present:



Thinking about those presenting who are not acutely unwell:

NICE suggests that we suspect adrenal insufficiency in 3 key scenarios

THINK ABOUT THE POSSIBILITY of adrenal insufficiency in....

Babies/children with differences in sex development
(ambiguous genitalia, bilateral undescended testes)

(relatively rare presentation in primary care, we suspect)

CONSIDER adrenal insufficiency if....

Unexplained hyperpigmentation

Hyperpigmentation is *COMMON* in those with primary adrenal insufficiency and IS THE *CLEAREST INDICATION OF ADRENAL INSUFFICIENCY*, BUT it may not be seen in brown or black skin: ask whether the person has noticed changes in their skin colour, and assess buccal mucosa or any surgical scars.

Why is hyperpigmentation an indicator of primary adrenal failure? In this scenario, ACTH is not triggering cortisol release so excess ACTH acts on melanocytes to produce melanin – hence hyperpigmentation.

CONSIDER adrenal insufficiency if....

1 or more of the following

(features **must** be persistent and with no other explanation)

Listed from most to least clinically distinguishing

- Weight loss
- Salt craving
- Nausea/vomiting
- Lack of appetite/unable to eat a full meal
- Diarrhoea
- Dizziness/light-headedness on standing
- Hyponatraemia*
- Hyperkalaemia
- Lethargy (often profound)
- Early puberty
- Muscle weakness
- Hypoglycaemia (particularly in children)
- Faltering growth (particularly in children)
- Hypotensive crisis (particularly in children)
- ↓
- Prolonged neonatal jaundice

*One study showed that 84% of those with adrenal insufficiency had hyponatraemia – so always consider this as a cause when you see a low sodium (Lancet 2021;397:613).

Why do you get these symptoms? Many are caused because salt loss in the urine results in reduced blood volume, leading to orthostatic hypotension, salt craving, GI upset and electrolyte imbalances.

REMEMBER:

Some of these symptoms are common so NICE also reminds us that **adrenal insufficiency is much more common if:**

CURRENT/RECENT GLUCOCORTICOID USE

- Recently stopped glucocorticoids (by any route, not just oral) having been on them for >4w (>3w if <16y)
- On glucocorticoids at physiological doses, but recent episode of physiological stress

Physiological dose defined as:

- ≥16y: a total daily dose of:
 - Hydrocortisone 15–25mg/d
 - Prednisolone 3–5mg/d
 - Dexamethasone 0.5mg
- 0–15y: a total daily dose of:
 - Hydrocortisone 8mg/m²

OTHER DRUGS

- Opioids, checkpoint inhibitors, adrenal enzyme inhibitors or drugs that affect production/metabolism/action of cortisol (such as antifungals or antiretrovirals)

COMORBIDITY

- Primary hypothyroidism
- Type 1 diabetes
- Premature ovarian insufficiency
- Autoimmune polyendocrinopathy syndrome
- Hypothalamic or pituitary tumours
- Hypothalamo-pituitary disease, including infections or infiltrative disorders

RADIOTHERAPY affecting hypothalamic-pituitary axis

- Radiotherapy to cranium, pituitary or nasopharynx

We think this contextualisation is important!

We do not think that NICE is asking us to consider the possibility of/test for adrenal insufficiency in everyone presenting to us with, for example, nausea. But we do think that NICE is saying **DO** remember to think about it in someone presenting with nausea who has a risk factor, for example has recently stopped steroids or had radiotherapy to their head.

You may wish to remember this as: **CONSIDER adrenal insufficiency if...**

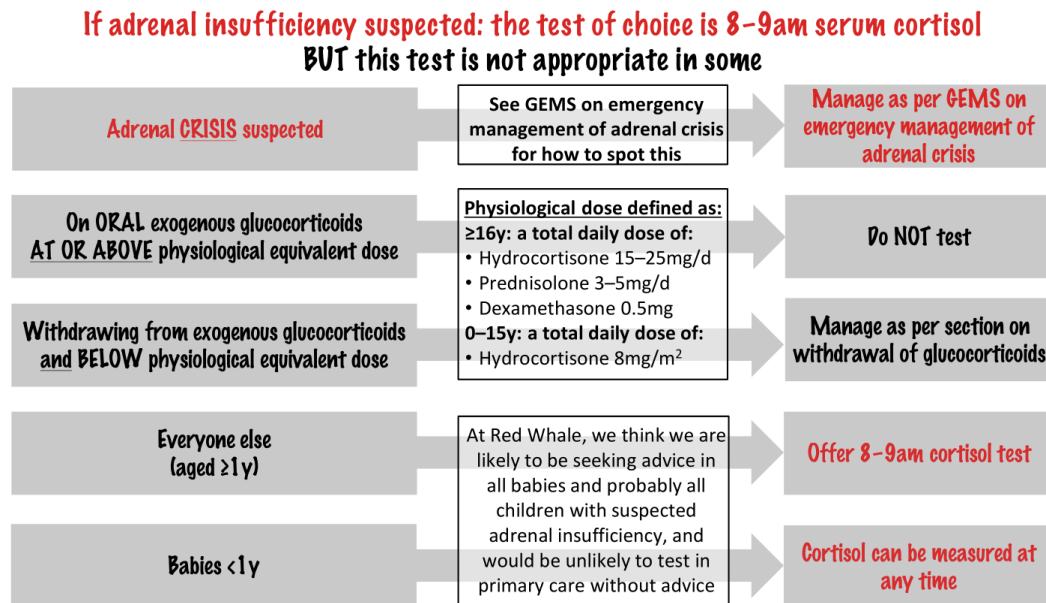
Relevant symptom from the list above
(that is persistent and with no other explanation)

especially if

Risk factor for
hypothalamic-pituitary-adrenal axis
dysfunction

1.3. Investigating suspected adrenal insufficiency

NICE advises:



8–9am serum cortisol: the practicalities

- **Shift workers on nights:** allow a few days for circadian rhythms to normalise or do a different test (e.g. short synacthen test).
- **If on ORAL oestrogen:** stop for 6w before testing (if for contraception, use alternative contraceptive method; if for HRT, transdermal oestrogen may be used). *Why? Cortisol levels are falsely elevated because oestrogen causes a rise in levels of cortisol-binding globulin.*
- Those on non-oral glucocorticoids (inhaled, intramuscular, topical) at physiological levels or above may have a low 8–9am serum cortisol.

- **After intramuscular/intra-articular glucocorticoid injection:** wait 4w before testing (includes hydrocortisone, triamcinolone, methylprednisolone (depo-medrone) (BNF)).

Interpreting the results of 8–9am serum cortisol

- Applies to those from age 1y upwards. Seek advice on interpreting cortisol results in those <1y.
- Applies only to modern immunoassays: if alternative assays used, follow local guidance.

Level	Likelihood of adrenal insufficiency	Action
<150nmol/L	May have adrenal insufficiency	• If acutely unwell: manage as per GEMS on adrenal crisis (start treatment and admit). Otherwise: • ADULTS (>16y): • Refer to endocrinology. • Consider starting treatment. • CHILDREN (1–15y): • URGENT referral to paediatrics/paediatric endocrinology.
150–300nmol/L	Uncertain	• Consider repeating serum cortisol. • If repeat test remains in this range, seek advice/refer to endocrinology/paediatric endocrinology.
>300nmol/L	Unlikely	• Consider alternative diagnosis.

1.4. Management of adrenal insufficiency

In brief, the management of adrenal insufficiency involves:

- Replacement of missing steroids (glucocorticoids for all, mineralocorticoids for some; see below).

- Patient education:
 - Understanding of sick day rules and adjusting doses of glucocorticoids in times of physiological/psychological stress to mimic normal adrenal physiology.
 - Recognising and managing adrenal crises.
- Monitoring for general wellbeing and for features of under- or over-replacement. In children, monitoring growth and progression through puberty is particularly important.

What needs replacing?

All types of adrenal insufficiency require GLUCOCORTICOIDS.

Some of those with PRIMARY adrenal insufficiency also require mineralocorticoids. *Why? In PRIMARY adrenal insufficiency, the problem lies in the adrenal gland itself. This means the glucocorticoids are not produced by the adrenal cortex, but, in addition, the mineralocorticoids (and androgens/oestrogens) may not be produced and may need replacement. Mineralocorticoids are NOT needed in secondary or tertiary adrenal insufficiency.*

At Red Whale, we think the decision on who needs which is one for the endocrinologists!

Which drug? What dose?

NICE gives doses for babies, children and those aged >16y. Here, we reproduce only the details for adults ($\geq 16y$). At Red Whale, we think that primary care will always be following advice from the specialist.

Do note that the doses may need to be increased in those on enzyme

inducers (e.g. antiretrovirals).

Congenital adrenal hyperplasia is a form of primary insufficiency, and dosing is similar to that in the table below, but NICE says higher doses may be needed based on specialist advice: follow advice from the specialist.

Treatment	PRIMARY adrenal insufficiency <i>(but seek advice for those with congenital adrenal hyperplasia because higher doses may be needed)</i>	SECONDARY and TERTIARY adrenal insufficiency
First-choice glucocorticoid	Hydrocortisone Total daily dose 15–25mg orally in <u>2–4</u> divided doses	Hydrocortisone Total daily dose 15–25mg orally in <u>2–3</u> divided doses
Alternative glucocorticoid (e.g. if multiple daily doses are not appropriate)	Prednisolone (only once stopped growing) Total daily dose 3–5mg orally or Modified-release hydrocortisone (if they have stopped growing) (off licence, NICE gives no doses)	
Mineralocorticoid <i>(only needed in <u>some</u> with <u>primary</u> adrenal insufficiency)</i>	Fludrocortisone Total daily dose 50–300mcg orally, or sometimes higher (although this is off licence) <i>Used if needed to normalise serum electrolytes, plasma renin, postural symptoms and salt craving – dose adjusted accordingly in response to these things.</i> If persistent hyponatraemia despite maximum fludrocortisone dose, consider adding sodium chloride supplements (specialist decision)	Not needed

Subcutaneous pumps, intramuscular or intravenous hydrocortisone should NOT be given for routine daily dosing.

1.5. Adrenal crisis: emergency management by healthcare professionals

Please follow the link for a PDF version of the GEMS for download/printing:

[Adrenal crisis: GEMS](#)

Emergency management of ADRENAL CRISIS

NICE 2024, NG243

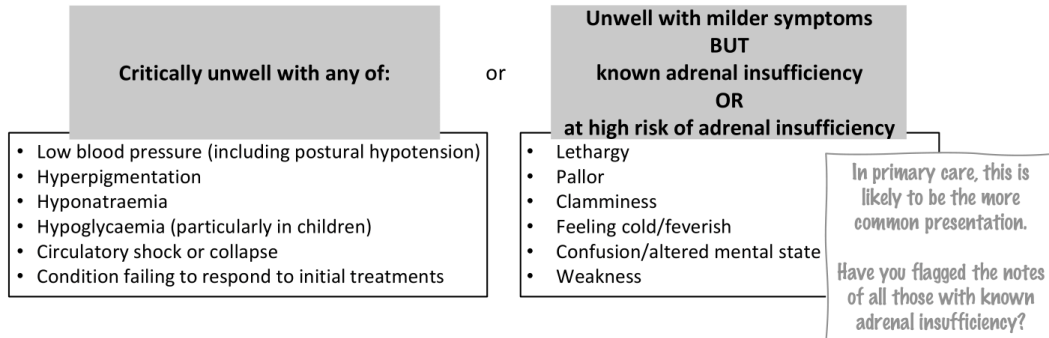


*** NICE guidance on emergency management applies to those $\geq 16y$ ***

For those $<16y$, NICE recommends using the British Society of Paediatric Endocrinology and Diabetes (BSPED) Consensus Guidelines on Adrenal Insufficiency (<https://www.bsped.org.uk/adrenal-insufficiency>). The central tenets of treatment (hydrocortisone, rapid transport to hospital and fluids) all apply, but doses depend on age/weight.

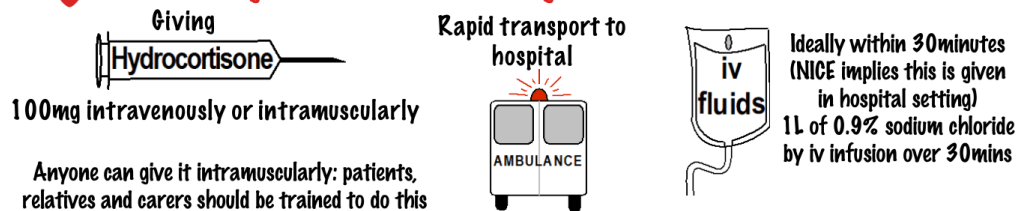
Recognising an adrenal crisis

Consider adrenal crisis as cause if:



Emergency management of adrenal crisis (in those $\geq 16y$)

The 3 essential ingredients in the management of adrenal crisis:



Once in hospital

- Ensure frequent monitoring of BP, heart rate, electrolytes, glucose.
- Hydrocortisone by iv infusion over 24h (or im/iv injections 4x daily) until haemodynamically stable and able to absorb oral glucocorticoids. Patient will be switched to oral drugs when possible (at higher than usual dose – often using doses specified in sick day rules) until cause resolved and person is clinically stable.
- Continue to give iv fluids (0.9% sodium chloride) until haemodynamically stable (rate determined by haemodynamic parameters and electrolyte state).
- Identify and treat underlying cause.
- Seek advice from endocrinologists throughout admission.

Prevention is better than treatment!

Patients need to be confident in using the sick day rules: this should reduce the need to use emergency kits.

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature. The information presented herein should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular, we suggest you carefully consider the specific facts, circumstances and medical history of any patient, and recommendations of the relevant regulatory authorities. We also suggest that you check drug doses, potential side-effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages. December 2024. For full references see the relevant Red Whale articles.

1.6. Adrenal crisis: prevention with sick day rules

In normal circumstances, at times of physiological or psychological stress, the adrenals pump out more cortisol. In adrenal insufficiency, the adrenals can't do this. This means that the patient has to recognise that that a physiological/psychological stress is occurring, and take additional glucocorticoid to prevent an adrenal crisis. This is called 'sick day rules'.

Emergency kits (containing injectable glucocorticoids) for prevention and management of an adrenal crisis are described in the next section.

It's a lot for a patient to take on board!

Sick day rules

NICE recommends that for those ≤ 16 y, we follow the sick day rules from [British Society of Paediatric Endocrinology and Diabetes \(BSPED\) Consensus Guidelines on Adrenal Insufficiency](#). We refer you there because the sites includes calculated doses based on patient weight and surface area.

NICE covers the sick day rules for those ≥ 16 y, and its recommendations are set out in the table below. We have included recommendations for inpatients, surgery and pregnancy, for completeness. The decisions relating to most of these groups of patients will not be taken in primary care.

Note that patients on modified-release hydrocortisone need a supply of immediate-release hydrocortisone to cover sick day situations such as those above.

Sick days rules for significant PHYSIOLOGICAL stress

NICE defines physiological stress as:

- Fever.
- Physical trauma requiring medical attention.
- Invasive procedure/surgery.
- Pregnancy/pregnancy loss/labour.

Illness (see below for procedures, surgery, admission to hospital)

Take additional doses until acute illness/physical trauma has resolved

- **If on hydrocortisone:** take at least 40mg oral hydrocortisone/d (in 2–4 divided doses).
- **If on prednisolone:** take at least 10mg oral prednisolone in 1–2 daily doses. (If already taking ≥ 10 mg prednisolone, additional sick day dosing is not needed, but daily dose can be split into 2 equal doses.)

These doses should not be continued long term (risk of over-replacement).

If vomits within 30mins of taking oral dose

- Take a further dose once the vomiting subsides, at double the original dose.
- If vomiting recurs within 30mins, give intramuscular hydrocortisone and attend A&E.

If unable to absorb oral glucocorticoids (e.g. prolonged diarrhoea and vomiting)

- Give 100mg hydrocortisone (im or iv) and admit.

Invasive procedures, surgery, admitted to hospital

Having invasive procedure OR being admitted for surgery	Give im or iv glucocorticoids, following Association of Anaesthetists guidelines (Woodcock et al, Anaesthesia 2020:75:654). What does this mean for those requiring bowel procedures and needing laxative/enema? The guideline suggests: admit. May need fluids and will need iv/im glucocorticoid cover, although it also says that some with tertiary adrenal insufficiency may not need this if not having a prolonged period of nil by mouth. We suggest that this is a decision for the person responsible for doing the procedure, not primary care! Our job is to clearly flag the adrenal insufficiency to them. What does this mean for those needing dental work? Not <u>specifically</u> addressed in the NICE guidance or the Association of Anaesthetists guideline (Woodcock et al, which refers only to general and regional anaesthesia, not local anaesthesia). We think this is a question for the dentists/endocrinologists, and will depend on the type of procedure being done. Addison's UK Clinical Advisory panel recommends that patients suggest the following to dentists for ADULTS (last reviewed December 2024): • Major dental surgery (including extraction under local anaesthesia): 100mg im hydrocortisone just before anaesthesia, and double-dose oral medication for 24h postoperatively. • Dental work (e.g. root canal work with local anaesthetic): double oral dose (up to 20mg hydrocortisone) 1h prior to surgery, and double-dose oral medication for 24h postoperatively. • Minor dental work (e.g. replace filling, scale and polish): take an extra dose 60 mins before procedure and an extra dose if hypoadrenal symptoms occur afterwards, then back to normal dose.
In hospital	Follow NICE guidance as it relates to those in hospital (oral/im/iv hydrocortisone, depending on how ill they are).

Sick day rules for significant **PSYCHOLOGICAL** stress

NICE defines this as sudden, intense psychological and emotional stress, e.g. bereavement, exams, significant life events such as getting married or divorced. Severe mental health crises are also covered in this section.

General points	• Try to reduce/manage stress by: • Using condition-specific support groups that offer peer support/other support groups. • Exploring with employer/education provider what reasonable adjustments can be made. • Exploring self-management (activities the patient can do to reduce their stress). • Considering using IAPT services.
Management of psychological stress	• Consider sick day rules for 1–2 days during psychological stress, namely: • If on hydrocortisone: take at least 40mg oral hydrocortisone/d (in 2–4 divided doses). • If on prednisolone: take at least 10mg oral prednisolone in 1–2 daily doses. (If already taking ≥ 10mg prednisolone, additional sick day dosing not needed, but dose can be split into 2 equal doses.)
Severe mental health crisis (e.g. psychosis)	• Oral hydrocortisone or oral prednisolone (see row above for doses; duration likely to depend on speed of recovery/resolution of crisis phase; seek advice so as to treat adequately but not for unnecessary duration). • Consider using 100mg im hydrocortisone if unable to take oral glucocorticoids.

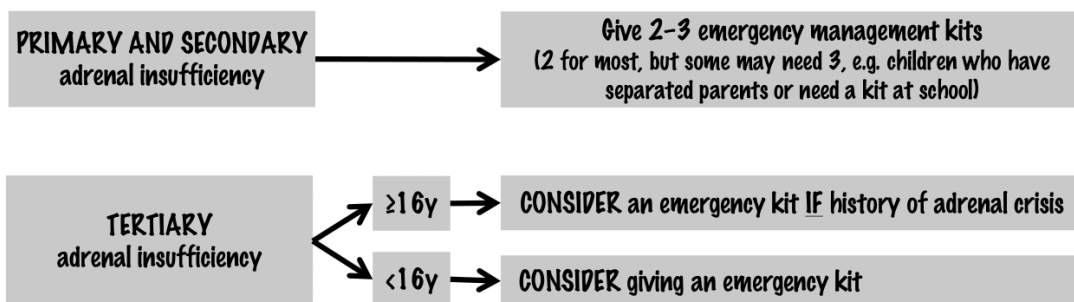
1.7. Adrenal crisis: emergency management kits

Emergency kits are for people to use when needed: patients, carers and families should know WHEN and HOW to use them.

Who should have a kit?

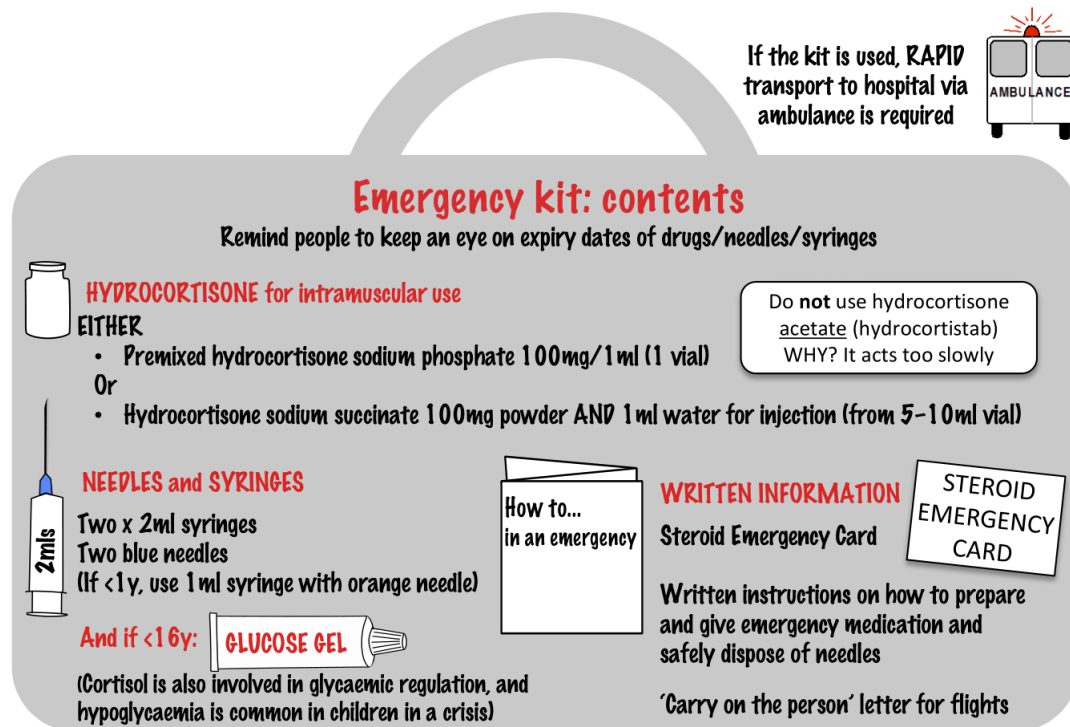
Clearly, this is a decision for the specialist, but NICE recommends:

Who should have an emergency kit?



Why are those with tertiary adrenal insufficiency less likely to need an emergency kit? They usually still have some function of the hypothalamic–pituitary–adrenal axis so are less likely to have an adrenal crisis.

Contents of kit



1.8. Helping patients with self-management

There's a lot for patients to take in!

- Understanding sick day rules/emergency kits is **CRITICAL!** They need to know **WHAT** to do and have the confidence to do it! Their relatives also need to be confident in recognising an adrenal crisis and using the emergency kit.
- The [Addison's Disease Self-help Group](#) has lots of useful information (there doesn't seem to be a support group for other forms of adrenal insufficiency).
- Remind patients to wear a medic alert bracelet.
- They get free prescriptions.
- NICE also says they should:
 - Be on the lookout for features of under- or over-replacement

(discussed later in the section on specialist reviews and monitoring).

- Be aware of how to dose themselves if travelling through time zones, fasting, or doing shift work or other activities that affect sleep patterns.
- Know not to stop their medication abruptly, except on medical advice.

1.9. Drug interactions

NICE doesn't discuss this, but many drugs can interfere with the hypothalamic–pituitary–adrenal axis.

WATCH OUT FOR and PAY ATTENTION TO(!) those automatic warnings that flash up each time you prescribe.

[The Society of Endocrinology \(exogenous steroids treatment in adults\)](#)

recommends taking special care with those on adrenal replacement/long-term glucocorticoid therapy and the following potent CYP3A4 inhibitors):

- **Potent protease inhibitors:** atazanavir, darunavir, fosamprenavir, ritonavir (+/- lopinavir), saquinavir, tipranavir.
- **Antifungals:** itraconazole, ketoconazole, voriconazole, posaconazole.
- **Long-term clarithromycin.**

Also remember that in those with undiagnosed thyrotoxicosis, or if thyroid replacement is started in someone with newly diagnosed hypothyroidism, this can also trigger an adrenal crisis in those with adrenal insufficiency ([NEJM 2019;381:852](#)).

1.10. Specialist reviews and monitoring

NICE recommends that those with adrenal insufficiency are followed-up by the relevant specialist team (we presume that, for most, this means endocrinology).

Frequency of appointments

- For adults, this should be based on need, with increased frequency of appointments as appropriate (e.g. for those who are more vulnerable or who have a change in clinical circumstances).
- For children and young people, this should be at least every 6 months (and annually face-to-face to measure height and weight in order to adjust dose of medication, and because abnormal growth rate is a sign of under- or over-replacement).

Monitoring

- Lying and standing BP.
- Bloods: electrolytes, HbA1c and, in adults, lipids.
 - (Cortisol day series levels should not routinely be used to check hydrocortisone dosing.)
- Bone density scan at least every 5 years in adults.

In addition, in children and young people:

- Height and weight.

- Progression through puberty.
- Signs and symptoms of low blood glucose.
- Bone age if still growing (left hand and wrist X-ray), bone density once they have stopped growing.

At specialist review, the following should be covered:

- Understanding of the condition and its management, including sick day rules.
- Adherence to medication.
- How frequently the patient needs to increase doses to cover sick days/using emergency injections.
- Frequency of adrenal crises, hospital admissions and infections.
- Psychological wellbeing and the ability to carry out everyday tasks.

Aim for physiological replacement doses, and monitor for signs and symptoms of glucocorticoid under- or over- replacement.

Signs and symptoms of glucocorticoid UNDER-replacement	Signs and symptoms of glucocorticoid OVER-replacement <i>(for those on a higher dose than standard replacement)</i>
• Weight loss. • Decreased appetite. • Early satiety. • Nausea. • Fatigue that is significantly affecting the person's ability to carry out activities of daily living. • Muscle weakness. • Worsening hyperpigmentation (in primary adrenal insufficiency).	• Weight gain. • Increased appetite. • Disturbed sleep. • Skin thinning. • New or worsening diabetes. • New or worsening hypertension. • Cushingoid appearance. • Acne. • Skin infections. • Thrush. • Frequent, low-impact or fragility fractures. • Height loss.
In children and young people, also consider: • Abnormal growth rate. • Timing of puberty. These are indicators of under- and over-replacement.	

For those with primary adrenal insufficiency, in addition to the above:

- Monitor for signs/symptoms of mineralocorticoid under- or over-replacement:
 - Under-replacement: light-headedness, salt-craving.
 - Over-replacement: swollen ankles, high BP.
- Consider measuring renin and adjusting fludrocortisone dose if needed.

1.11. Managing adrenal insufficiency in and around pregnancy

Women with adrenal insufficiency should be cared for by specialists from before conception to the postnatal period.

Primary care has a role in:

- Ensuring appropriate preconception counselling from secondary care.
- Specialist care during pregnancy/postnatal period.
- Continuing to follow appropriate sick day rules.
- If doses are increased during the pregnancy, reducing back to pre-pregnancy doses after delivery.

For those who want the detail, this is what the NICE guideline recommends:

Period	Action
Preconception	• Offer counselling by clinicians experienced in managing adrenal insufficiency in pregnancy. • Emphasise the safety of glucocorticoids, and the importance

	of continuing them (and mineralocorticoids if needed) in pregnancy.
Antenatally	General care in pregnancy • Ensure they know to inform the GP as soon as they are aware of pregnancy for referral to an MDT experienced in managing adrenal insufficiency in pregnancy. • Consider increasing glucocorticoid doses (and mineralocorticoid doses, if being used) in third trimester (depending on clinical symptoms, sodium level, postural BP). • Remind patient of the need to continue to follow sick day rules at times of significant physiological or psychological stress.
	Fever, infection or physical trauma needing medical attention, and short-term vomiting related to illness or early pregnancy • Take an additional 20mg of hydrocortisone immediately AND follow sick day rules for non-pregnant people: • If on hydrocortisone: take at least 40mg oral hydrocortisone/d (in 2–4 divided doses). • If on prednisolone: take at least 10mg oral prednisolone in 1–2 daily doses. (If already taking ≥ 10mg prednisolone, additional sick day dosing not needed, but dose can be split into 2 equal doses.)
	Pregnancy-related vomiting (morning sickness) • Advise to try to take glucocorticoid doses when not feeling nauseated. • Seek help if unwell.
	Hyperemesis gravidarum • Manage as an inpatient.

	• Immediately inject 100mg hydrocortisone im AND go to emergency department/early pregnancy unit. • Hospital will manage with antiemetics, fluids, iv/im hydrocortisone and specialist advice.
Intrapartum care	Follow the NICE guidelines on intrapartum care specific to this situation (NICE 2019, NG121). In brief: Vaginal delivery • Continue their regular oral steroids AND, when established in first stage of labour, give iv/im hydrocortisone (minimum dose 50mg every 6h until 6h after delivery). Caesarean section (planned or emergency) • Continue their regular oral steroids AND, when starting anaesthesia, give intravenous hydrocortisone (dose depends on whether they have already had steroids in labour). • Give a further dose of hydrocortisone 6h after the baby is born.
Postpartum care	• Use sick day rules for 48h, then resume usual doses. • If ongoing physiological stress, continue sick day dosing. • If doses were increased in the third trimester, slowly decrease back to usual pre-pregnancy doses.

1.12. End-of-life care in those with adrenal insufficiency

NICE recommends:

- Continue glucocorticoids, swapping to once-daily formulations and

appropriate routes of administration (subcutaneous, intramuscular if unable to take orally) unless a shared decision has been made to withdraw adrenal support.

1.13. Preventing adrenal insufficiency when withdrawing glucocorticoids

Inappropriately-rapid withdrawal of glucocorticoids can trigger adrenal insufficiency or an adrenal crisis.

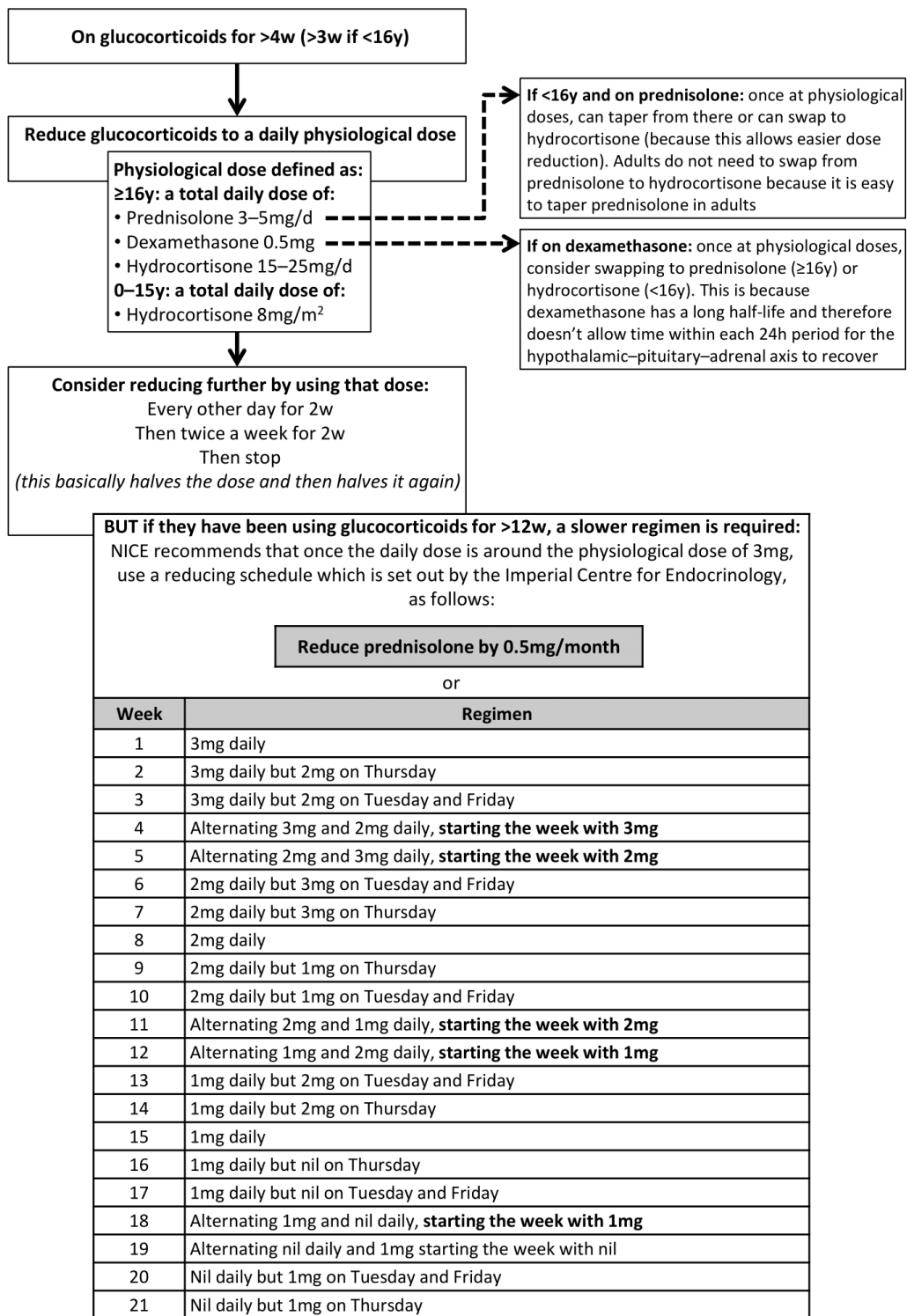
In those who have been on glucocorticoids for more than 4 weeks (3w if <16y), NICE recommends a tapering regimen to prevent adrenal insufficiency. The decision to taper should be made by the team which initiated therapy. In most cases, this will NOT be primary care; polymyalgia rheumatica may be an exception, although we are likely to follow EULAR 2015 guidance because that is written specifically for polymyalgia rheumatica (see our article on *Polymyalgia rheumatica*).

In brief, this involves:

- Reducing to physiological dose.
- Tapering from physiological dose until off therapy.

Warn people when tapering below physiological dose to:

- Expect temporary symptoms, including fatigue, reduction in appetite, low mood.
- Continue to follow sick day rules, including for surgery and invasive procedures.
- Look out for signs and symptoms of adrenal insufficiency.



Monitoring of those going below physiological doses

- Monitor for signs and symptoms of adrenal insufficiency.
- If these symptoms develop:

- Prescribe double the physiological dose of glucocorticoid daily until symptoms resolve.
- Then reduce to physiological dose for 1w.
- Then taper using the slower regimen outlined above (for those who have been on glucocorticoids for >12w).

Testing 8–9am cortisol in those going below physiological doses

NICE recommends:

- **In those ≥ 16 y:** only test if the person develops signs/symptoms of adrenal insufficiency despite following the slow-dose tapering regimen set out above (for those who have been on glucocorticoids for >12w).
- **In those <16y:** testing may be considered when reducing from physiological doses, even in the absence of symptoms/signs.

If an 8–9am cortisol is tested in those withdrawing from glucocorticoids:

Level	Action during glucocorticoid tapering
<150nmol/l	Restart glucocorticoids and refer to endocrinology.
150–300nmol/l	Consider repeating the test. If it remains at this level, seek advice from endocrinology.
>300nmol/l	Adrenal insufficiency is unlikely to be the cause of symptoms. Continue glucocorticoid withdrawal.



Adrenal insufficiency and Addison's disease

- Often difficult to spot because symptoms can be common and vague. Think about the 3 key presentations:
 - Babies and children with differences in sex development.
 - Unexplained hyperpigmentation.
 - One or more persisting symptom from NICE's list outlined above (but remember that adrenal insufficiency is much more likely in patients with these symptoms if they also have a risk factor (such as stopping steroids)).
- If adrenal crisis suspected: act immediately to replace steroids and admit.
- For the majority, an 8–9am cortisol is the test of choice.
- Management is by the specialists and involves:
 - Replacing glucocorticoids (and mineralocorticoids in some with primary adrenal insufficiency).
 - Ensuring patients understand the sick day rules, and know how and when to administer drugs from the emergency kit.
 - Regular specialist review to monitor BP, electrolytes, other relevant bloods and bone density for adults every 5y. In children, particular care is taken to monitor growth rate and progression through puberty.
- Iatrogenic adrenal insufficiency can be minimised by careful tapering of steroids. This can take many weeks!
- Prevention is by sick day rules and patients using emergency kits if they suspect they are having a crisis. It is a lot for patients to understand and cope with!
- All patients should be under specialist follow-up, although the frequency may vary depending on how confident they are with self-management.
- Extra care is required in pregnancy/postpartum period so refer for advice BEFORE conception.



Reflect on the challenge of diagnosis: when might you now consider adrenal insufficiency where before you might not have done?

Do you have a supply of hydrocortisone sodium phosphate/succinate in the practice emergency kit?

Search your practice population for patients with adrenal insufficiency. Are all their notes flagged so that clinicians are alerted to their diagnosis and know to check that sick day rules have been followed/for symptoms of adrenal insufficiency if they present with illness/are being referred for a procedure?

Organise reception training on the symptoms of an adrenal crisis and the importance of promptly alerting the duty doctor.



Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

For professionals:

- [The Society of Endocrinology – adrenal crisis](#)
- [The Association of Anaesthetists - guidelines for the management of glucocorticoids during the perioperative period for patients with adrenal insufficiency](#)
- [The British Society for Paediatric Endocrinology and Diabetes - adrenal insufficiency](#)

For patients:

- [Addison's Disease Self-help Group](#) (include sections on emergency kits and sick day rules; there doesn't appear to be a patient group for other forms of adrenal insufficiency)
- [Society for Endocrinology – exogenous steroids leaflet](#)

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