Clinical Guideline

MANAGEMENT OF PATIENTS TAKING STEROID MEDICATION (GLUCOCORTICOIDS) DURING ILLNESS, SURGERY, PREGNANCY AND LABOUR OR OTHER INTER-CURRENT STRESS

SETTING	Trust wide (adults only)
FOR STAFF	**All Medical Staff and Non-Medical Prescribers**
FOR PATIENTS	This guidance is relevant to:

Group A: Adult endocrine patients with proven glucocorticoid (cortisol) insufficiency due to either **adrenal or pituitary/hypothalamic pathology** and who are taking daily replacement glucocorticoid medication

Group B: adult non-endocrine patients who are **taking supra-physiological glucocorticoid therapy** for inflammatory conditions (e.g. chronic obstructive airways disease, rheumatoid arthritis or inflammatory bowel disease) or haematological/oncological diseases at doses/durations that may suppress their own hypothalamic-pituitary-adrenal (HPA) axis.

Background

Group A patients

Adrenal insufficiency may occur as a primary (direct damage to the adrenal cortex) or secondary (damage to the upstream hypothalamic or pituitary pathways resulting in insufficient ACTH to stimulate the adrenal glands) endocrine condition. Primary adrenal insufficiency (often termed Addison's disease) occurs when the adrenal cortex is destroyed by autoimmune disease, infection, septicaemia, haemorrhage, metastases or following adrenal surgery. Primary adrenal insufficiency is associated with both glucocorticoid (cortisol) and mineralocorticoid (aldosterone) deficiency and these patients will be taking daily replacement therapy with a glucocorticoid (hydrocortisone, prednisolone or dexamethasone) and a mineralocorticoid (fludrocortisone). Secondary adrenal insufficiency is associated with just glucocorticoid (cortisol) deficiency and these patients will be taking daily replacement therapy with a glucocorticoid (hydrocortisone, prednisolone or dexamethasone) medication.

The most common **glucocorticoid replacement regimen** for endocrine patients with adrenal insufficiency is with hydrocortisone at doses of 10mg on waking, 5mg at midday and 5mg at around 5pm. The alternative regimen is with prednisolone 3-4mg on waking. These regimens offer the best

chance of mimicking the natural circadian rhythm and restoring the best quality of life. However, many different individualised regimens (e.g. shift workers, patients taking medication that affects steroid metabolism) are used and as a guide the *approximate* steroid equivalent doses are shown below:

Hydrocortisone 10mg = Prednisolone 2mg = Dexamethasone 0.2mg = Methylprednisolone 2mg

Modified-release hydrocortisone (e.g. Plenadren®)

Slow-release glucocorticoid preparations are increasingly becoming available (e.g. Plenadren®). Compared with three times daily immediate-release hydrocortisone, once daily modified-release hydrocortisone is taken in the morning on waking. A high cortisol concentration peak in the morning and gradual decline during the afternoon with modified-release hydrocortisone partially reflects the physiological profile. A common maintenance dose is 20mg to 30mg daily, although some patients may require a higher or lower dose.

Rescue therapy should be administered using immediate-release hydrocortisone using 'sick day rules' (see below). In the context of acute illness/procedure requiring hospitalisation, switch to hydrocortisone at doses of 10mg on waking, 5mg at midday and 5mg at around 5pm and adjust as needed for acute illness/procedure.

Group B patients

Patients with no known endocrine disease may also be vulnerable to adrenal insufficiency as a consequence of being prescribed steroid (glucocorticoid) medication for an inflammatory condition such as chronic obstructive airways disease, rheumatoid arthritis or inflammatory bowel disease. 7 per 1000 population are prescribed long-term oral glucocorticoid therapy.

The HPA axis becomes suppressed in response to glucocorticoid therapy for any duration of time when the dose of steroid per day used is

- Prednisolone 5mg or more across all routes of administration (oral, topical, inhaled, intranasal, intra-articular)
- Dexamethasone 0.5 mg/day or more across all routes of administration (oral, topical, inhaled, intranasal, intra-articular)
- Hydrocortisone 15 mg/day or more
- **Any oral doses received for more than 3 weeks**
- Patients who have recently completed a long course (>3 weeks) of oral steroids should also be considered at risk of HPA axis suppression.

Less commonly, chronic steroid use via inhaled, topical or other non-oral routes can suppress the HPA axis, especially when larger regular daily doses are used:

- Fluticasone >500 mcg/day
- Beclomethasone >1000 mcg/day
- Budesonide >1000mcg/day
- Nasal steroids > 1000mcg/day

For more details on group B patients, see Clinical Guideline "When To Issue A Steroid Emergency Card" or ask your ward pharmacist.

Patients taking drugs known to inhibit cortisol clearance or increase endogenous steroid metabolism (eg antifungals, anticonvulsants, rifampicin, topiramate and antiretroviral drugs) alongside exogenous steroids are at risk of adrenal insufficiency if their steroids are stopped.
All cases will need to be considered on an individual patient basis. In the context of inter-current illness, stress or surgery etc. when it is inappropriate to assess the HPA axis – simply assume insufficiency in this group of patients and manage accordingly.

Cortisol plays a critical role in the body's response to stress. It increases vascular tone thereby sustaining blood pressure, it mobilises energy to vital organs and it activates the immune system. In a deficient state, patients are at risk of adrenal crisis where they will become hypotensive, weak and lethargic. This may progress to confusion, coma and may even be fatal if untreated. In people with an intact HPA axis, cortisol levels rise rapidly and greatly when a stressor is encountered. In the patient groups described above – this natural response cannot occur due to HPA axis deficiency or suppression. **It is critical, therefore, that glucocorticoid medication is increased promptly in these patients (no increase in fludrocortisone is required as the additional glucocorticoid will address any mineralocorticoid deficiency).** Any increase should be proportionate to the stressor (see below).

A steroid emergency card has been introduced as a reminder to healthcare professionals, when patients are admitted as an emergency/ when undergoing elective surgery or a procedure/ in adrenal crisis to ensure steroid treatment is given appropriately and promptly. All patients with primary and secondary adrenal insufficiency under the care of the BRI endocrine department have been supplied with this card along with written personalised advice on how to manage their steroid replacement during acute illness (see next page).

Community 'Sick Day Rules' Advice for Any Serious Illness: to be shared with the patient, patient's family and GP

(Please note that the endocrine department has personalised written patient information for Group A patients under our care)

Group A patients	Group B patients
1. Double the normal dose of hydrocortisone for a fever of > 37.5 C or for infection requiring antibiotic 2. In patient on prednisolone, increase the dose of prednisolone to 10mg once a day 3. Contact GP if illness worsens or it lasts for more than 3 days. 4. Always seek medical help if temperature >40^{0}C (104^{0}F). In severe illness, call 999 ambulance. 5. For mild nausea/ vomiting/diarrhoea take 20mg hydrocortisone orally (or 5mg prednisolone or 0.75mg dexamethasone) immediately afterwards and sip rehydration/electrolyte fluids (e.g. Dioralyte) 6. If severe vomiting/diarrhoea, use the emergency injection (100mg hydrocortisone intramuscularly*) immediately and **seek urgent medical help.**	1. At risk of adrenal suppression. 2. Steroid medication should never be abruptly stopped. 3. Increased vulnerability in the context of acute illness - low threshold for seeking medical help.

In the context of severe shock (e.g. a road traffic accident or bereavement) or a long haul flight (>12 hours), an increase in steroid medication is often appropriate. Steroid medication typically does not require increasing for viral colds without fever or general stress such as exams etc.

***Steroid Emergency Pack**

All patients should have 100mg Hydrocortisone for injection with needle and syringe [Hydrocortisone sodium phosphate (ready mixed liquid) or Solu-Cortef (powder plus 2ml vial of water plus needles and syringes)] available at home for use in an emergency. This should be administered promptly by any patient or carer or health care professional that is called out to visit the patient at home. All endocrine patients receive appropriate advice and training on how to self-administer this injection from the endocrine nurse specialists. **If a patient is unwell enough to require an injection of hydrocortisone in the community, then they should also promptly attend their local hospital as an emergency for assessment.**

Endocrine patients under the care of the UHBW are routinely offered for their diagnosis of adrenal insufficiency and steroid dependence to be logged with the South West Ambulance Service to facilitate safe pre-hospital care.

Emergency Treatment of Adrenal Crisis

An adrenal crisis is a medical emergency. 8 out of 100 patients with adrenal insufficiency will experience an adrenal crisis per year and one in 200 patients will **die** from such a crisis.

- 100 mg hydrocortisone by iv injection, followed by 50 mg 6 hourly im/iv or 200 mg hydrocortisone via continuous iv infusion in glucose 5% over 24 hours.
- Rapid rehydration with sodium chloride 0.9%:
  - Resuscitation with 500 ml fluid bolus of sodium chloride 0.9% over 15 minutes and then replacement of any electrolyte deficits
  - Rehydration (3–4 litres of sodium chloride 0.9% solution in 24 h); careful monitoring of electrolytes and fluid balance
  - Allow free oral fluid intake unless contraindicated
- Cardiac monitoring (if necessary, transfer to the intensive care unit for monitoring)
- Refer to endocrinology for further advice on diagnosis, starting regular oral steroids or tapering steroids back to usual dose, and education regarding 'sick day rules' prior to discharge

Hospital Admission with Inter-current Illness

All patients who fit into groups A or B above will require an **increase** in their normal glucocorticoid medication when they are admitted to hospital with an inter-current illness; their steroid medication should **never be stopped or omitted** and should be switched to parenteral if the oral route is not viable (e.g. nil by mouth, vomiting, diarrhoea etc).

Group A patients	Group B patients
Double normal oral medication as per sick day rules	Double usual oral medication unless patients already on large baseline doses (e.g. patients receiving high dose prednisolone or dexamethasone as part of their chemotherapy regimen)
If illness is severe (e.g. MI, pancreatitis, significant trauma, severe sepsis), consider parenteral (im/iv) hydrocortisone at doses of 50 mg 6 hourly (or 200 mg of hydrocortisone over 24 hours as continuous iv infusion in glucose 5%).	
With recovery, the hydrocortisone should be gradually weaned back to the normal maintenance dose.	With recovery, return to usual treatment doses.

Endocrine patients with a diagnosis of adrenal insufficiency and steroid dependence will typically have a specific alert recorded on the Trust electronic patient record to help highlight their risk to all healthcare professionals involved in their care.

Surgery / Interventional Procedures

Any surgery requiring a general anaesthetic will require parenteral steroid cover for patients in both Groups A and B.

<table>
<tr><th></th><th>Group A patients</th><th>Group B patients</th></tr>
<tr><td rowspan="3">Major Surgery with Prolonged Recovery Time (e.g. abdominal/ cardiac surgery)</td><td colspan="2">Pre-procedure
100mg hydrocortisone im/iv immediately prior to procedure</td></tr>
<tr><td colspan="2">Post-procedure
50mg hydrocortisone im/iv 6 hourly (or 200 mg hydrocortisone via continuous iv infusion in glucose 5% over 24 hours).
Wean hydrocortisone by ~30% per day back to normal maintenance dosage.
Switch to oral hydrocortisone once a reliable route is available (oral, NG) during the weaning process.</td></tr>
<tr><td>Switch to standard replacement Hydrocortisone (10mg on waking, 5mg at 12pm and 5mg at 5pm) or prednisolone (4mg od, on waking)</td><td>Promptly return to usual treatment doses</td></tr>
<tr><td rowspan="3">Major Surgery with Rapid Recovery Time (e.g. joint replacement, caesarean section)</td><td colspan="2">Pre-procedure
100mg hydrocortisone im/iv immediately prior to procedure</td></tr>
<tr><td colspan="2">Post-procedure
50mg hydrocortisone im/iv every 6 hours.
Wean hydrocortisone by ~50% after 24 hours (25mg every 6 hours) to normal maintenance steroid dosages over the next 1-2 days.</td></tr>
<tr><td>Switch to standard replacement Hydrocortisone (10mg on waking, 5mg at 12pm and 5mg at 5pm) or prednisolone (4mg od, on waking)</td><td>Promptly return to usual treatment doses</td></tr>
<tr><td rowspan="2">Minor Surgery / Procedure (e.g. angiogram, hernia repair, cataract surgery)</td><td colspan="2">Pre-procedure
100mg hydrocortisone im/iv immediately prior to procedure</td></tr>
<tr><td>Post procedure
Double normal oral dose for 24 hours.
In patient on prednisolone, increase the dose of prednisolone to 10mg once a day</td><td>Post procedure
Double normal oral dose for 24 hours. If patient on prednisolone, increase the dose to 10mg once a day. Smaller proportional increase may be clinically more appropriate</td></tr>
<tr><td>Intestinal Procedures Requiring Bowel Prep (e.g. colonoscopy)</td><td>Admit (under the medical team organising the endoscopy) the day before the procedure ANY of the following patient criteria are met:
Hospital admission with adrenal crisis in preceding 2 years
Concomitant diagnosis of diabetes insipidus (DI) treated with DDAVP
Learning difficulties or other significant vulnerability</td><td>Out-patient management of bowel prep is reasonable but patient should be carefully advised by team organising endoscopy to follow the guidance below and to present promptly to ED if they become unwell.
Advise patient to increase their normal glucocorticoid medication on the day prior to procedure. If on hydrocortisone, increase to 20mg QDS orally and if on prednisolone then increase to 10mg BD.</td></tr>
</table>

	Treat above patient group with po / iv hydrocortisone 20mg QDS on day prior to procedure plus appropriate 0.9% saline/electrolytes iv **If patient becomes unwell, then treat as adrenal crisis (medical emergency)** and refer urgently to endocrine team as in-patient **If patient has DI then admission on a weekday and pre-arranged shared care with endocrinology is crucial for safe management.** **If none of the above patient criteria are met then out-patient management of bowel prep is reasonable but patient should be carefully advised by team organising the endoscopy to follow the guidance below and to present promptly to ED if unwell.** Advise patient to increase their normal glucocorticoid medication on the day prior to procedure. If on hydrocortisone, increase to 20mg QDS orally and if on prednisolone then increase to 10mg BD. On the day of the procedure, the patient should continue this increased steroid dosage with minimal clear water even when NBM (ensure surgeon/anaesthetist approves)	If normal prednisolone dosage is higher than 10mg BD then continue normal dosage but split to BD dosing to ensure safer absorption context of bowel prep. On the day of the procedure, the patient should continue this increased steroid dosage with minimal clear water even when NBM (ensure surgeon/anaesthetist approves)
	Procedure 100mg hydrocortisone im/iv immediately prior to procedure	
	Post procedure Double normal oral dose for 24 hours. If patient on prednisolone, increase the dose to 10mg once a day	**Post procedure** Double normal oral dose for 24 hours. If patient on prednisolone, increase the dose to 10mg once a day. Smaller proportional increase may be clinically more appropriate
Very Minor Procedures (e.g. dental extraction)	**Pre-procedure** Double normal oral dose for 24 hours. In patient on prednisolone, increase the dose of prednisolone to 10mg once a day for 24 hours	**Pre-procedure** Double normal oral dose for 24 hours. If patient on prednisolone, increase the dose to 10mg once a day. Smaller proportional increase may be clinically more appropriate

Pregnancy and Labour

Group A patients

All patients with endocrine (primary or secondary adrenal insufficiency) disease should be referred and managed through the Trust's joint endocrine antenatal service based at St Michael's Hospital.

Pregnancy is associated with a gradual, but significant physiological increase in corticosteroid binding globulin and total serum cortisol. Free cortisol levels rise during the third trimester, typically resulting in an increased requirement for hydrocortisone of between 2.5 and 10 mg daily. There is no routine approach, and this should be individualised by the endocrine team based on symptoms and baseline dosage. No biochemical monitoring of steroid replacement is required.

The fludrocortisone dose (adrenal patients only) may also need to be increased during late pregnancy. Clinical evaluation of salt cravings, blood pressure and serum electrolytes is the best means for dosage monitoring and adjustment.

Post-partum, the patient may need to modify their normal glucocorticoid regimen based on their sleep pattern to ensure adequate energy levels. Typically, the approach would be to alter the frequency of doses rather than to alter the total dosage for any prolonged period.

<table>
<tr><th></th><th>Group A patients</th><th>Group B patients</th></tr>
<tr><td rowspan="2">Labour and vaginal delivery</td><td colspan="2">Hydrocortisone 100 mg im/iv at onset of labour followed by 50 mg every 6 h im/iv (alternatively, hydrocortisone 100 mg iv followed by immediate initiation of a continuous infusion of 200 mg hydrocortisone over 24 hours in glucose 5%).
After delivery, resume enteral double hydrocortisone doses for 48h.</td></tr>
<tr><td>Promptly return to standard replacement Hydrocortisone (10mg on waking, 5mg at 12pm and 5mg at 5pm) or Prednisolone (4mg od on waking).</td><td>Promptly return to usual treatment doses.</td></tr>
<tr><td>Caesarean section</td><td colspan="2">See surgery under anaesthesia</td></tr>
</table>

For patients with a diagnosis of primary adrenal failure (Addison's disease) then additional information is available from the Addison's Disease Self Help Group (www.addisons.org.uk) and for patients with pituitary disease advice is available from The Pituitary Foundation (http://www.pituitary.org.uk).

All patients should be advised to wear some form of medical alert identification (i.e. bracelet, necklace etc) at all times. Many mobile phones also have medic alert Apps.

Queries

Adult Endocrine Nurse Specialists: 0117 342 6223 or adultendocrinenurse@uhbw.nhs.uk

Adult Endocrine Advice Bleep: 6216 (9am-5pm weekdays)

User Groups Consulted

Anaesthetics, Care of the Elderly, ED dept, Endocrinology, Endoscopy/Gastroenterology, Haematology, Surgery, Non-medical prescribers, Obstetrics, Oncology, Pharmacy, Respiratory Medicine, Rheumatology and Surgery